Time for the end of GM/GE herbicide tolerant crops?

A report by GeneWatch UK

Time for the end of GM/GE herbicide tolerant crops?

A report by GeneWatch UK

August 2022

GeneWatch UK
53, Milton Road, Cambridge, CB4 1XA, UK
Phone: +44 (0)330 0010507
Email: mail@genewatch.org Website: www.genewatch.org
Registered in England and Wales Company Number 03556885

Table of Contents

Executive Summary

In countries growing genetically modified (GM) crops, the adoption of GM crops which are tolerant to weedkillers is reaching saturation. These herbicide-tolerant (HT) GM crops have been genetically engineered so they can be blanket-sprayed with the associated herbicides, with the aim of killing weeds whilst the crop still grows. They were first grown commercially in 1996, when they were introduced by the US company Monsanto (now owned by Bayer). Monsanto's glyphosate-based weedkiller has the brand-name RoundUp, hence the first GM generation of herbicide-tolerant crops are tolerant to glyphosate and are known as 'RoundUp Ready' (RR) crops.

Herbicide-tolerant GM crops, which include an herbicide-tolerant trait alone or in combination with other traits, account for around 88% of the land area planted with GM crops worldwide (ISAAA, 2019a). Because cotton grown in India and China accounts for most non-HT GM crops, HT crops account for virtually all the GM crops grown for use in food or feed. This reality is in sharp contrast to GM industry PR which acts as a distraction by emphasising potential new traits, including GM crops that tolerate flooding or drought, which were first promised more than 40 years ago but have not been delivered. Since 1996, most herbicide-tolerant GM crops have been RR crops which are genetically engineered to be tolerant to glyphosate, but this has recently been changing with increasing areas planted with new HT crops which are tolerant to additional herbicides, such as dicamba and 2,-4,D. These crops are mainly grown in North and South America, with the USA, Brazil and Argentina growing the largest quantities.

The aim of this report is to look at the economic, environmental and social impacts of growing RR crops and newer HT crops. This report reviews more than 25 years of experience with this technology.

We conclude that the cultivation of GM HT crops may be regarded as a temporary aberration, rather than the revolution originally proclaimed by the proponents of these crops. The growing failure of RoundUp Ready crops, due to the spread of glyphosate resistant (GR) weeds, provides an opportunity to phase out the use of RR crops and adopt new methods and technologies. The priority should be to reduce and replace the use of herbicides: not to replace RR crops with other herbicide-tolerant crops, whether or not these are GM crops or produced by different methods. It is particularly important that RR crops are not pushed into new countries which have so far avoided stepping onto the "transgenic treadmill", in which farmers are locked in to paying for ever more expensive seeds and herbicides. In seeking to expand markets for RR crops into new countries, the industry is dumping a failed technology on them.

Blanket spraying of RR crops with weedkiller leads to resistant weeds

RR crops are designed to make farming practices easier in that they allow farmers to apply the weedkiller glyphosate during the cropping season without risking harm to their crops, which are genetically engineered to be tolerant to it. This has led to an unprecedented increase in the use of glyphosate (Powles & Preston, 2006; Duke & Powles, 2008; Grube et al 2011; Vivian et al. 2013; Benbrook, 2016; Myers et al., 2016).

Initial benefits for farmers adopting RR crops have vanished with the emergence of glyphosate resistant (GR) weeds, sometimes known as 'superweeds' (Vila-Aiub et al. 2007, 2008; Cerdeira et al. 2011; Benbrook, 2012a; Allison, 2015; Zhou et al., 2015;

Duke et al., 2018). Such weeds have evolved because RR crops allow farmers to blanket spray their crops with the weedkiller glyphosate instead of using a mix of approaches to tackling weeds, including crop rotation. Since GR weeds are no longer affected by spraying with glyphosate, they require the use of additional weedkillers or pulling up by hand (Caulcutt, 2009; Zhou et al., 2015). With 55 evolved GR weed species already known worldwide (Heap, 2021), and new GR weed species evolving at an increasing rate, RR technology is becoming obsolete. GR weeds are common in all RR crop producing countries and these are also the countries with the greatest area infested with GR weeds (Heap, 2021; Heap and Duke, 2018; Alcántara de la Cruz et al., 2020; Yanniccari et al., 2021; Pannell et al., 2017). RR crop cultivation is leading to increased herbicide application, thus adding costs for farmers, and increasing risks to the environment and human health. On the two most important GM crops in the US, corn and soybean, the total applied toxicity of pesticides (not just glyphosate) has increased along with increasing GM adoption, notably since 2008 as GR weeds became a greater problem (Schulz et al., 2021).

In response to the problem of glyphosate resistant weeds, the industry has developed new GM herbicide tolerant crops which are resistant to additional weedkillers, such as 2,4-D and dicamba, as well as glyphosate. Such crops exacerbate concerns about adverse environmental impacts, pesticide residues in the food chain, and the future evolution of weeds which will become resistant to multiple herbicides (Mortensen et al. 2012, Roseboro, 2012).

Patents and monopolies add further costs and prevent seed saving

Just four large firms (Bayer, Corteva, ChemChina-Syngenta, and BASF) control around 70% of the global pesticides market and 60% of the global seed market (Clapp, 2021). Patents on GM seeds give companies monopoly control and allow them to prevent seed saving. This, along with market concentration in the industry, has led to significant increases in seed prices, with high premiums for GM seeds and restrictions on the non-GM varieties available on the market in some countries (Mascarenhas & Busch, 2006; Howard, 2009; Zilberman et al. 2010; Benbrook, 2012a; Filomeno, 2013; Benbrook, 2018; Brunharo et al., 2022). Farmers buying RR seeds are locked into a “transgenic treadmill” in which they are forced to pay for hikes in seed prices and for increasing amounts of herbicides and labour to tackle weed resistance (Binimelis et al., 2009; Mortensen et al., 2012).

RoundUp Ready crops do not have higher yields

Most farmers growing RR crops have adopted RR crop technology in the hopes of increasing their yields (Fernandez-Cornejo et al., 2014). However, there are no RR crops available today that increase the yield potential of a hybrid variety: any benefit to yields arises only if these crops improve weed control (Gurian-Sherman, 2009; Nolan & Santos, 2012; Bruns, 2014). A global meta-analysis of studies by Areal et al. (2013) reports no significant differences in yields between RR and conventional crops. Yield data from North America and Western Europe shows that Western Europe, where to date no herbicide tolerant resistant crops are grown, had a greater yield increase between 1961 and 2010 than North America for oil seed rape and maize (which are predominantly RR crops in North America) and that overall yields were similar or higher in Europe than in the USA (Hilbeck et al. 2013; Heinemann et al., 2014a, 2014b). There is also some evidence that supressed plant defence and enhanced disease susceptibility caused by glyphosate may have a negative impact on RR plants, through adverse effects on beneficial soil micro-organisms and plant nutrient uptake (Sanogo et al., 2000; King et al., 2001; Eker et al., 2006; Bellaloui et al. 2008; Bott et al., 2008; Johal and Huber, 2009; Zobiole et al., 2010a&b, 2011, 2012; Freitas-Silva et al., 2021).

Demand for non-GM seeds and ingredients is increasing

Farmers worldwide also need to consider the demand for non-GM ingredients, which is forecast to grow significantly (Mordor Intelligence, n.d.; Grand View Research, 2019; Fortune Business Insights, 2022).

Demand for animal feed that is segregated as non-GM has grown, particularly in Europe (Tillie & Rodríguez-Cerezo, 2015), where price premiums for non-GM crops reflect the preference of European consumers for non-GM products (Gaitán-Cremaschi et al., 2015; Fortune Business Insights, 2022). By 2021, around 60-70% of all milk egg, poultry and meat production in Germany was certified according to the GM-free VLOG standard (Southey, 2021). Brazil has increased its import share faster in countries with a strong non-GM preference versus other countries. This is explained statistically by Brazil's level of non-GM soybean production rather than by changes in prices. Garrett et al. (2013) find that the Netherlands, Italy, Spain, and Belgium increased imports from Brazil and simultaneously decreased imports from the United States, even as Brazil's currency increased in value in the late 2000s, which should have made Brazilian soybean producers less competitive than their North American counterparts on a pure cost basis. The South American non-GMO food market continues to grow, with Brazil expected to have the biggest market (Fortune Business Insights, 2022). Among US farmers, interest in growing non-GM varieties reportedly started increasing around 2014, with seed companies reporting strong demand for non-GM seed sales and some even reporting they had sold out of non-GM seeds due to the rapidly increasing demand (Bunge, 2015; Roseboro, 2015b; Doering, 2015; Kuphal, 2017). Retail sales of products verified by the Non-GMO Project, based in North America, rose dramatically from $248.8 million in 2010 to $8.5 billion in 2014 and 13.5 billion in 2015, with sales now over $26 billion (Non-GMO Project, 2014; 2015; 2022). However, the non-GM corn and soybean supply in the U.S. remains relatively small (Twellman, 2021).

Growing GM crops risks expensive contamination incidents

Cultivation of RR crops risks GM contamination of non-GM food and feed supplies (Price & Cotter, 2014). Contamination risks arise due to cross-pollination of non-GM crops and co-mingling of seeds or grains during harvest, transportation, storage, processing and distribution (Sohn et al., 2021). These risks cannot be eliminated through technical measures (Binimelis, 2008; Paull, 2018; Lu et al., 2019) and this causes legal and economic uncertainties for farmers, because contaminated crops have lower value (due to consumers' preference for non-GM crops) and may be rejected completely by some markets (e.g. organic markets, or any market where the GM crop has not been authorised by regulators).

Attempts to allow GM and non-GM crops to be grown together in a given country or region (known as "co-existence") creates tensions among neighbouring farmers because of the risk of GM contamination. Every actor and level of a supply chain will be economically affected under a coexistence scenario and costs of coexistence of GM and non-GM agricultural production systems are influenced by multiple factors (Gabriel & Menrad, 2015). At the producer level they include costs for cleaning of machinery and equipment, buffer zones of uncultivated land around the edge of non-GM fields, monitoring costs such as testing of seeds or crops and building additional farm storage facilities. For processors, costs to prevent contamination include: costs for testing of the incoming commodity as well as the produced outgoing goods, greater transportation distances to the next GM or non-GM plant respectively, building of additional storage facilities, complete second production line in an existing plant, cleaning or flushing of repositories, investment in additional personnel and equipment and in training programs for workers (Gabriel & Menrad, 2015). According to this study, the total additional costs of coexistence and implemented product segregation systems can amount up to 14% of the total product turnover at the gates of rapeseed oil mills or companies processing maize starch, respectively. In Switzerland, where GM crops are not grown, estimated coexistence measures if they were introduced could amount to up to 5-20% of the total costs for conventional production (Albisser Vögeli et al., 2011). The costs to prevent GM contamination are likely to be especially high for organic producers, since global organic farming standards do not allow GMOs in either seed or food (IFOAM, 2002).

Thus, allowing GM cultivation increases the cost of food supplies, because of the added costs of segregation. In countries where GM crops are grown, non-GM farmers, including organic farmers, bear risks and costs associated with protecting their crops from GM contamination and certifying their supply chain as GM-free for consumers.

When coexistence measures fail, contamination incidents can lead to the destruction of crops or entire fields (Furst, 1999; Smyth et al., 2002) and the rejection of shipments, product recalls and loss of markets (Ryan & Smyth, 2012; Smyth et al., 2002; Schaefer & Carter, 2015; USDA NASS, 2015; Reuters, 2016c), with multi-million dollar economic impacts.

GM contamination can also have environmental implications and risk the loss of local varieties of seed. Glyphosate tolerance, and other GM traits, can spread from GM maize to maize landraces, as has happened in Brazil (Fernandes et al., 2022). Maize is mainly produced by smallholders in Mexico, using landraces that are very well adapted to the local growth conditions. Contamination of these landraces, could threaten preservation of this very important maize genetic diversity (Snow, 2009). GM transgenes are already present in at least some maize landraces in Mexico (Piñeyro-Nelson et al., 2009; Quist & Chapela, 2001; Snow, 2009). Wild populations of the most widely cultivated cotton species in the world, *Gossypium hirsutum*, have also been contaminated by GM varieties, the majority of which are geographically located over 300 km away from all wild cotton populations (Wegier et al., 2011). In Spain, GM contamination of organic maize led to the loss of farmers' maize varieties adapted to the local climate (Cipriano et al., 2006). Such events could limit the future availability of high-value germplasm in breeding programs (Burgeff et al., 2014).

Impact of RR crops on farmers' choice, land rights and indebtedness

Patents on GM crops lead to restricted access to breeding material for farmers and breeders and thus hinder innovation in plant breeding and impede farmers' freedom of choice. In countries adopting GM crops the maize seed market is more concentrated with fewer available maize cultivars for farmers than in non-adopting countries, where it has become more difficult to find non-GM seeds (Roseboro, 2008; Hilbeck et al., 2013; Burgeff et al., 2014). In the USA, rising input costs, volatile production values, and rising land rents have left farmers with unprecedented levels of farm debt, low on-farm incomes, and high reliance on federal programs (Burchfield et al., 2022). Subsidies are largely directed at commodity production, including soy and corn, which are typically GM crops, and for which per acre costs tripled between 1990 and 2020.

Impacts of RR crop cultivation on smallholders in South America and elsewhere include land conflicts and the intensification of agro-industrial practices, including greater use of herbicides, increased farm sizes, land use changes and deforestation, seed price hikes, and the expansion of monocultures and indebtedness (Lapegna, 2013; Garrett and Rausch, 2016; Goldfarb and van der Haar, 2016; Leguizamón, 2016; McKay and Colque, 2016; Elgert, 2016; MASIPAG, 2013; Phélinas and Choumert, 2017; Schmidt et al., 2022; Dreoni et al., 2022).

RR crops have negative environmental impacts

The widespread adoption of RR crops in North and South America has contributed significantly to an increased environmental presence of glyphosate-based herbicides and their primary break-down product, AMPA, in rain, streams, rivers, lakes, ponds, wetlands, soil water, ground water, plants, soil, dust and sediment (Battaglin et al. 2005, 2014; Struger et al. 2008; Chang et al., 2011; Bohm et al., 2014; Majewski et al., 2014; Bento et al., 2016; Mamy et al., 2016; Bonansea et al., 2017; Alonso et al., 2018; Fernandes et al., 2019; Zheng et al. 2018; Clasen et al. 2019; Iturburu et al., 2019; Lupi et al., 2019; Lutri et al., 2020; Maggi et al., 2020; Medalie et al., 2019; Montiel-León et al., 2019; da Silva et al., 2021; Barbosa Lima et al., 2021; Botten et al., 2021; Brovini et al. 2021a,b; Cristofaro et al., 2021; Ramirez Haberkon et al., 2021; Carretta et al., 2022).

Negative environmental impacts due to growing herbicide-tolerant GM crops, including RR crops, include:

- impacts on farmland diversity of weeds, insects and birds through loss of important habitats due to blanket spraying of these crops with herbicide (Burke, 2003; Burke, 2005; Firbank et al., 2003; Gibbons et al., 2006; Cederlund, 2017; Pereira et al., 2018a, 2020);
- chronic toxicological effects of glyphosate and its metabolites on annelids (earthworms), arthropods (crustaceans and insects), molluscs, echinoderms, fish, reptiles, amphibians, birds, mammals, and non-target plants (Santadino et al., 2014; Zaller et al. 2014; Gaupp-Berghausen et al. 2015; Domínguez et al., 2016; Kissane & Shephard, 2017; Gill et al., 2018; Odetti et al., 2020; Ruuskanen et al., 2020a,b,c; Singh et al., 2020; Barbosa Lima et al. 2021);
- negative effects on pollinators, such as bees, including damage to habitat and ecosystems; toxicity; and effects on their behaviours, growth and development, metabolic processes, and immune defence (Fuchs et al., 2021; Strandberg et al., 2021; Battisti et al., 2021; Tan et al., 2022);
- toxic and chronic sub-lethal effects of glyphosate-based weedkillers on aquatic species including tadpoles, frogs, snails, crayfish, molluscs, crabs, fish, fresh-water fleas and corals (Relyea, 2005a,b and c; Pérez et al., 2012; Cuhra el al., 2013, 2014, 2015; Avigliano et al. 2014a,b; Gonçalves et al., 2019; Hendlin et al., 2020; Herek et al., 2021; Matozzo et al. 2020; Mohapatra et al., 2021; Moutinho et al., 2020; Riaño et al. 2020; Slaby et al., 2020; Suppa et al., 2020; Babalola et al., 2021; Le Du-Carrée et al., 2021, 2022; Ramsdorf et al., 2021; Rodríguez et al., 2021; Sánchez et al., 2021; Santos-Silva et al., 2021; Tresnakova et al., 2021; de Maria et al., 2021, 2022; Jia et al. 2022; Liu et al., 2022b; Pompermaier et al., 2022; Zhou et al., 2022); and
- adverse impacts of glyphosate-based herbicides on soil biota: such as effects on soil microbial communities (Jaworski, 1972; Schulz et al., 1985; Moorman et al., 1992; Dick and Quinn, 1995; Kremer and Means 2009; Nye et al., 2014; Newman et al., 2016); and impacts on overall ecosystem functioning, including interactions of crops with fungi and soil-borne pathogens (Johal &

Rahe 1984; Sanogo et al., 2000, 2001; Larson et al., 2006; Krzysko-Lupicka and Sudol, 2008; Johal and Huber, 2009; Kremer and Means, 2009; Zobiole et al., 2011; Lu et al., 2018; Martinez et al., 2018; Yang et al., 2020; Hertel et al. 2021, Van Bruggen et al, 2021; Vázquez et al., 2021; Chávez-Ortiz et al., 2022).

One important example of the effects of habitat loss is a major contribution to the dramatic decline in populations of the Monarch butterfly in the USA. Although other factors (such as climate change and deforestation) play a role, this decline is associated with the loss of the milkweed habitat where the butterflies lay their eggs, caused by blanket spraying the weedkiller glyphosate on RR crops (Hartzler, 2010; Zalucki & Lammers 2010; Brower et al., 2012; Pleasants & Oberhauser, 2012; Fallon, 2014; Flockhart et al., 2014; Vidal & Rendón-Salinas, 2014; Stenoien et al., 2016; Pleasants, 2017; Pleasants et al., 2016, 2017; Thogmartin et al., 2017; Belsky & Joshi, 2018; Malcolm, 2018; Taylor et al., 2020).

Glyphosate-contaminated runoff also likely contributes to harmful incidences of algal bloom in lakes (Dabney & Patiño, 2018; Berman et al., 2020).

In glyphosate-based herbicide formulations, glyphosate is the active ingredient that is supposed to kill the target weeds. Those formulations also contain various adjuvants, the so-called inert ingredients, including surfactants such as polyethoxylated tallow amine (POEA) which is found in Roundup. However, ecotoxicological assessment of pesticides usually focuses on the effects of the active ingredient, such as glyphosate, rather than on commercial formulations like Roundup (Cox & Surgan, 2006; Pereira et al., 2009; Mesnage & Antoniou, 2018; Sprinkle & Payne-Sturges, 2021; Martins-Gomes et al., 2022). This is a major issue of concern because many studies find that commercial formulations are significantly more toxic than glyphosate alone, particularly to aquatic organisms (Mitchell et al., 1987; Servizi et al. 1987; Mann & Bidwell, 1999; Perkins et al. 2000; Marc et al., 2002; Everett & Dickerson, 2003; Tsui & Chu, 2003, 2004; Howe et al., 2004; Cedergreen & Streibig, 2005; Brausch et al. 2007; Brausch & Smith, 2007; Pereira et al. 2009; Moore et al. 2012; Vincent & Davidson, 2015; Bach et al., 2016; Rissoli et al., 2016; Janssens & Stoks, 2017; de Brito Rodrigues et al., 2019; Mesnage et al. 2019; Bednářová et al., 2020; Le Du-Carrée et al., 2022; Sabio y García et al., 2022).

In South America, there have also been significant changes in land use to create large-scale RR soybean farms, for example in the Rolling Pampas in Argentina and the Cerrado in Brazil, with serious negative impacts on biodiversity and water-balance (De la Fuente et al. 2006, 2010; Martinelli et al., 2010; Hayhoe et al., 2011; Macedo et al., 2013; Neill et al., 2013; Redo et al. 2013; Eloy et al. 2016; de Groot et al., 2021).

An additional issue with RR crops is that they may contribute to the development and spread of antibiotic resistant bacteria, which can make it difficult to treat human and animal bacterial infections. Some RR crops contain antibiotic resistant marker genes, which might be able to spread into the environment (Chen et al., 2012). Exposure to sub-lethal levels of the herbicide Roundup has been linked to a change in susceptibility of bacteria to antibiotics, significantly increasing the concentration of two antibiotics (kanamycin and ciprofloxacin) necessary to kill gut bacteria associated with food poisoning, *Escherichia coli* and *Salmonella enterica* (Kurenbach et al., 2015). This research suggests that spraying RR crops with RoundUp might contribute to the development of antibiotic resistant bacteria in the environment, with major implications for human and animal health (Van Bruggen et al., 2018; Raoult et al., 2021; Liao et al., 2021; da Costa et al., 2021; Daisley et al., 2022).

RR crops pose unknown risks to human health

There are significantly higher levels of glyphosate and AMPA residues in RR soybeans compared to conventionally grown or organic soybeans (Arregui et al., 2004; Bøhn et al., 2014; Bohm et al., 2014). Bøhn & Millstone (2019) estimate that glyphosate-tolerant soybeans produced on commercial farms in the USA, Brazil and Argentina accumulate in total an estimated 2,500–10,000 metric tonnes of glyphosate per year, which enter global food chains. Glyphosate has been detected in a wide variety of foods, including soy-based infant formula and honey: dietary exposure levels are generally (but not always) below permitted limits (Rodrigues & de Souza, 2018; Bøhn & Millstone, 2019; Xu et al., 2019; de Souza et al., 2021; Rodrigues et al., 2020; Louie et al., 2021; Viljoen et al., 2021). However, regulatory limits vary in different countries, there is a lack of transparency about how they are set, and some researchers believe that the risks to human health could still be underestimated (Marino et al., 2021).

Krüger et al. (2014a) showed that glyphosate that accumulates in feed can be consumed by animals and be detected in their organs and urine. Subsequently, glyphosate has been detected in the urine of adults and children, both within and outside agricultural communities (Gillezeau et al., 2020; Ferreira et al., 2021; Lozano-Kasten et al., 2021; Grau et al., 2022; Nomura et al., 2022). Farmers and other operators can be directly exposed to glyphosate-based formulations when they are spraying it onto their fields (Acquavella et al., 2004; Mesnage et al., 2012). Children may also be exposed to glyphosate-contaminated breast milk. Glyphosate was detected in all breast milk samples taken from mothers in a study in Brazil, undertaken at the peak of glyphosate application in corn and soy crops (Camiccia et al., 2022). Regulators do not currently routinely monitor levels of glyphosate in food and have not investigated reports that glyphosate may be detected in human urine samples and breast milk as a result of its presence in the food chain. Some studies suggest that spraying with glyphosate-based weedkillers may also adversely affect the nutrient composition of soybeans (Zobiole et al., 2010b,c; Bellaloui et al., 2008).

As discussed above, Roundup formulations are a mixture of glyphosate and other chemicals that have been shown to increase the toxicity of glyphosate to aquatic organisms. Many toxicological studies conducted with human, mouse and rat cells confirm these findings and suggest that looking at the effects of glyphosate alone is insufficient for a comprehensive assessment of the possible risks to human health resulting from growing and consuming RR crops (Benachour et al., 2007; Benachour & Séralini, 2009; Clair et al., 2012; Gasnier et al., 2009; Mesnage et al., 2013, 2014; Moore et al., 2012; Richard et al., 2005; Walsh et al., 2000; Young et al., 2015; Chłopecka et al., 2017; Vanlaeys et al., 2018; Dedeke et al., 2018; Defarge et al., 2018). However, regulators only consider the effects of glyphosate alone (Mesnage et al., 2019).

In March 2015, the World Health Organisation (WHO)'s cancer agency, the International Agency for Research on Cancer (IARC), classified glyphosate as "probably carcinogenic to humans" (Guyton et al., 2015). As a consequence, many countries and regions have restricted the use of glyphosate (Where is Glyphosate Banned?, 2022). Subsequent reviews of the evidence have confirmed that chronic exposure to glyphosate causes a variety of tumours in rats and mice, and that there is clear evidence of glyphosate toxicity in studies using human cells (Agostini et al., 2020; Portier, 2020).

Research in Sri Lanka and elsewhere suggests a possible link between simultaneous exposure to glyphosate and toxic heavy metals, and chronic kidney disease, with other factors (such as exposure to high temperatures and other pollutants) perhaps playing a role (Jayasumana et al., 2014, 2015; Gunatilake et al., 2019; Herrera-Valdés et al., 2019; Babich et al., 2020; Abdul et al., 2021; Upamalika et al., 2022).

There is evidence that glyphosate may act as an endocrine disrupting chemical (EDC) i.e. a chemical that interferes with female and male sex hormones (Richard et al., 2005; Benachour et al., 2007; Gasnier et al., 2009; Romano et al., 2010; Clair et al., 2012; Thongprakaisang et al., 2013; Abarikwu et al., 2015; Guerrero Schimpf et al., 2017; Varayoud et al., 2017; Anifandis et al., 2017, 2018; Cai et al., 2017; Ingaramo et al., 2017, 2020, 2022; Owagboriaye et al., 2017; Lorenz et al., 2020; Kaboli Kafshgiri et al., 2021; Lesseur et al., 2021; Milesi et al., 2021; Mohammadi et al., 2021; Muñoz et al., 2021; Serra et al., 2021; Zhao et al., 2021). Endocrine disrupters can lead to negative impacts on male and female reproductive health, even at very low doses. These effects are not adequately regulated (Kalofiri et al., 2021). Two small studies have found that glyphosate exposure (measured in urine) in pregnancy is correlated with shortened pregnancy lengths (Parvez et al., 2018; Silver et al., 2021).

Other researchers suggest that glyphosate could affect gut bacteria, killing beneficial bacteria and allowing harmful ones to cause disease (Krüger et al., 2013; Shehata et al., 2013; Pu et al., 2020, 2021; Barnett et al., 2022).

Working with glyphosate and glyphosate spray drift can affect farm workers, bystanders and people living in the surrounding area.

In the Ontario Farm Family Health Study, Arbuckle et al. (2001) observe moderate increases in risk of early abortions for preconception exposures to any herbicide, and for late abortions, preconception exposure to glyphosate is associated with elevated risk. In the same study, Savitz et al. (1997) find that combinations of farm activities using a variety of chemicals, including glyphosate, are associated with an increased risk of miscarriage in the wives of exposed farm workers. In the Red River Valley, Minnesota, USA, Garry et al. (2002) find that exposure to glyphosate is associated with an increased risk of neurobehavioral developmental effects. In the Agricultural Health Study in Iowa and North Carolina, Hoppin et al. (2008) find an increased risk of atopic asthma in farm women using glyphosate and a number of other pesticides, and Hoppin et al. (2016) find an increased risk of allergic and non-allergic wheeze in male farm workers using glyphosate and some other pesticides. In the same study, Slager et al. (2009) find an increased risk of rhinitis in farm workers who had used glyphosate in the past year.

Aerial application (spraying from planes) increases the risk of accidental exposure of neighbouring inhabitants (Schiesari and Grillitsch, 2010; Pignati et al., 2007). Epidemiological studies and reports of interviews with local people cannot prove cause and effect, nevertheless there are numerous and widespread reports of glyphosate poisonings due to aerial spraying of RR soybeans in Latin America (Benítez-Leite et al., 2007; Oliva et al., 2008; Berger and Ortega, 2010; Sineiro and Berger 2012; Rigotto et al., 2014; Oliveira et al., 2014; Silva et al., 2015; Elgert, 2016; Lapegna, 2016; Dias et al., 2020; Longhi & Bianchi, 2020). Reported effects, according to people living in sprayed areas, include vomiting, diarrhoea, respiratory problems, skin rashes, cancer, infertility, pregnancy problems, and birth defects (PAN Asia & Pacific, 2008 & 2012).

RR crops do not help to feed the world or tackle climate change

The primary reasons for hunger are poverty and lack of access to affordable food (Tscharntke et al., 2012). Conflict, weather extremes and economic shocks were the main drivers behind food insecurity in 2021, with poverty and inequality as underlying causes (EU/FAO/WFP, 2022).

RR crops are currently produced mainly for use in animal feed (soya and maize/corn) or in biofuels (corn ethanol) or fabric (cotton). Soybean and maize (corn) are the top two GM crops grown by area, the majority of which are Roundup Ready. Most soy (around 75% measured by weight in 2018) is fed to animals in livestock production systems, with around 3.8% going to biofuels and other industrial applications, and only 19.2% to direct human consumption as food (mainly as soybean oil) (Fraanje & Garnett, 2020). Similarly, around 74% of the global maize production is used for animal feed (Cassidy et al., 2013). In the U.S., 40% of the maize harvest was processed to ethanol in 2014 (Ranum et al., 2014). In 2014, production and use of corn ethanol resulted in 27 billion kg more carbon emissions than if conventional gasoline were used according to calculations by the Environmental Working Group (Cassidy, 2015a). This is because converting rainforests, peatlands, savannas, or grasslands to produce food crop–based biofuels in Brazil, Southeast Asia, and the United States releases 17 to 420 times more carbon dioxide than the annual greenhouse gas (GHG) reductions that these biofuels would provide by displacing fossil fuels (Fargione et al., 2008).

Shifting crop calories used for animal feed and biofuels to direct human consumption could, according to Cassidy et al. (2013), potentially feed an additional 4 billion people and in the U.S. alone an additional 1 billion people. Further, tackling food waste can also play a major role: many crop calories are lost during food production, transport and storage as well as in retail facilities, restaurants and at private households etc. (FAO, 2011).

It is questionable whether sparing land for nature needs higher intensity of farming to produce adequate food (Tscharntke et al., 2012). Strategies to increase yields without explicitly considering the actual and potential cost of biodiversity losses can compromise ecosystem functionality and resilience in agriculture. Rather, food security and food sovereignty need to increase in areas where the hungry live, based on robust, eco-efficient approaches. Smarter resource use, improving livelihoods of small-scale farmers, reducing food waste and small changes in diets, such as reducing meat consumption or swapping from grain-fed beef to chicken or grass-fed beef, have the potential to double calorie availability (Cassidy 2015b).

Further, in the case of RR crops, yields have not increased compared to non-GM crops (Areal et al., 2013). Cultivation of RR crops has led to significant expansion of intensive agricultural monocultures into previously diverse ecosystems (Oliveira and Hecht, 2016) and production of non-GM soybean meal has been found to be more sustainable than GM soy production (Ortega et al. 2005; Gaitán-Cremaschi et al., 2015).

Some authors have argued that the use of no-till agriculture (i.e. farming without disturbing the soil through ploughing), in combination with RR crops, has helped to mitigate climate change by keeping carbon in the soil: however, in a 41 year experiment in France, no-till agriculture led to no increase in soil organic carbon (Powlson et al., 2014). In addition, whilst the use of no-till increased in the United States from 1998 to 2016, it then shrank again, although herbicide-tolerant GM corn and soybeans still dominate the market (Yu et al., 2020). This is likely at least partly due to the increasing presence of glyphosate-resistant weeds, which have led to a return to ploughing.

Industry responses to glyphosate-resistant weeds are not sustainable

The industry's answer to the development of GR weeds is mainly herbicide-centric and includes a) developing herbicide tolerant (HT) crops with enhanced tolerance to glyphosate (allowing higher application rates), b) increasing the herbicide platform used on RR crops to include additional herbicides (e.g. in seed treatments and tank mixes); and c) developing new HT crops with tolerance to additional herbicides (Desquilbet et al. 2019).

Another aspect of the industry response is the use of other (supposedly beneficial, but likely ineffective) traits as a 'Trojan Horse' to smuggle herbicide tolerant GM traits into new crops and markets. These include HB4 GM wheat, developed by Bioceres, which is tolerant to glufosinate, but is being promoted for its supposedly drought tolerant properties (Paixão, 2020; Little, 2022); camelina (a plant also known as 'false flax') with herbicide-tolerance combined with altered oil content (Yield10 Bioscience, 2022, ACRE, 2019); and drought-tolerant GM maize for Africa, which is also being stacked with glyphosate-tolerance in some cases (African Centre for Biodiversity, 2021). These projects are consistent with the industry's awareness that, although RoundUp Ready crops are failing, there may still be opportunities to profit from expanding into new geographic areas and/or new crops before resistant weeds take hold (Green & Siehl, 2021). This PR strategy acts as a distraction from the negative consequences of growing HT GM crops, and as a means to attempt dump failing HT traits onto new markets.

Increased spraying of tank mixes of multiple weedkillers has led to grower weed control costs tripling in the USA (Vivian et al, 2013; Evans et al. 2016; Myers et al., 2016; Pratt, 2016a; Duke et al., 2018). The total applied toxicity of pesticides (not just glyphosate) has increased significantly since 2008 (Schulz et al., 2021). A 2015 survey conducted in 17 states in Brazil, revealed that 97% of respondents used tank mixtures by this date, usually with 2 to 5 products at the highest recommended doses (Gazziero 2015). A major problem remains the inadequate examination by regulators of the effects of mixtures of herbicides on human health and the environment (Sprinkle & Payne-Sturges, 2021). In addition, weeds are becoming resistant to multiple different herbicides (e.g. Benoit et al., 2020).

The US Department of Agriculture (USDA) argues that GM maize and soybeans with resistance to multiple herbicides will become the norm in future (Nandula, 2019). GM soybeans and maize with resistance to dicamba and 2,4-D are already on the market, and these are being stacked with existing GM resistance traits (to glyphosate and/or glufosinate) or other herbicides (such as isoxaflutole). In the USA, in crop year 2018, around three quarters of the soybean seed offered to farmers expressed the glyphosate-resistance gene, plus either dicamba or 2,4-D resistance genes (Benbrook, 2018). In 2019, Monsanto (now owned by Bayer) filed a petition with the USDA for determination of nonregulated status of a genetically engineered corn variety resistant to five active ingredients: glyphosate, glufosinate, dicamba, 2,4-D and quizalofop (Monsanto, 2019). These herbicide tolerant GM crops allow farmers to apply additional herbicides such as 2,4-D, dicamba, isoxaflutole or glufosinate during the whole cropping season at high rates, with the risk of detrimental effects to the environment and human health. For example:

- isoxaflutole is known to persist in the environment and to leach into and accumulate in ground- and surface waters (US EPA, 1998);

- an association between increasing 2,4-D application and human urine concentrations has already been reported (Freisthler et al., 2022); 2,4-D is classified as possibly carcinogenic by the WHO (IARC, 2018); 2,4-D is reported to be toxic to a variety of organisms, including fish, amphibians, insects, earthworms and rodents (Islam et al., 2018; da Silva et al., 2022);
- dicamba is a suspected endocrine disruptor (Zhu et al. 2015); and
- glufosinate is classified as a known or presumed reproductive toxicant and is no longer authorised for use in the EU (EFSA, 2017; European Commission, n.d.).

Moreover, 2,4-D and dicamba are prone to drift (risking damage to other farmers' crops, as well as the environment) (Murschell & Farmer, 2019; Lerro et al., 2020; Soltani et al., 2020) and it has been shown that repeated herbicide drift exposure can rapidly select for weed resistance (Vieira et al. 2020; Comont et al., 2020). Dicamba-resistant, 2,4-D resistant and glufosinate-resistant Palmer Amaranth (pigweed) have already been identified in the USA (Kumar et al, 2019; Unglesbee, 2020b; Unglesbee, 2021a). This circular process of the evolution of resistant weeds and the subsequent development of the next generation of transgenic crops, that allow for an intensified use of herbicides and thus favour the emergence of another round of resistant weeds, has been called the "transgenic treadmill" (Binimelis et al., 2009; Mortensen et al., 2012).

RR GM crops, and newer HT GM crops, use a method of genetic engineering known as transgenesis, which involves transferring new DNA from another species into plant cells (known as 'transgenes'). Newer genetic engineering techniques, using a variety of methods called 'gene editing', may allow new herbicide-tolerant GM crops to be produced which rely on mutating the crop's own genes and not on introducing foreign genes into the genome of a crop. There is commercial interest in this approach because such crops may be deregulated in some countries, so that environmental risk assessments and food labelling may not be required before they can be marketed. In particular, 'base editing' and 'prime editing' techniques can be used to mutate DNA without the need for donor DNA, although these methods are not currently efficient (Tang et al., 2020). Crops that have been gene edited to include herbicide tolerant traits remain at the experimental stage, but include wheat, rice, maize, soybean, potato, rapeseed (canola), flax, cassava, watermelon and tomato (Gosavi et al., 2022). The problems associated with existing HT GM crops will not be avoided by using gene editing techniques, since all these experimental crops are genetically engineered to withstand blanket spraying with the associated herbicides.

Lawsuits

There have been numerous lawsuits relevant to the cultivation of GM herbicide-tolerant crops in the United States.

One set of lawsuits relates to claims that exposure to glyphosate causes cancer and environmental harm. Following the IARC's classification of glyphosate as a "probable human carcinogen", in March 2015, numerous lawsuits were filed alleging that past use of Monsanto's Roundup herbicide had contributed to the plaintiffs' development of non-Hodgkin lymphoma (NHL). Three lawsuits were heard before a jury and resulted in victories for the plaintiffs. In June 2022, the U.S. Supreme Court rejected Bayer's bid to dismiss these legal claims by customers and left in place the lower court decision that upheld $25 million in damages awarded to one California resident (Hurley, 2022). In July 2021, Bayer (which bought Monsanto in 2018) took an additional litigation provision of $4.5 billion for this case, on top of $11.6 billion that the company previously set aside for settlements and litigation (Hurley, 2022). In addition, in a case brought by farmers and environmental groups, the 9th Circuit Court of Appeals in California determined in June 2022 that the EPA did not adequately consider whether glyphosate causes cancer and threatens endangered species, and ordered it to look again at the risks it poses (Stempel, 2022).

Another set of lawsuits relates to crop damage caused by farmers spraying dicamba or 2,4-D on to GM crops resistant to these herbicides. In particular, Elmore (2022) describes how, in 2021, thousands of U.S. growers reported to the Environmental Protection Agency (EPA) that dicamba sprayed by other farmers on dicamba-resistant GM crops damaged crops in fields all over the country. In February 2020, Bader Farms won the first dicamba lawsuit and was awarded U.S. $15 million in damages, plus U.S. $250 million in punitive damages. The jury also found Monsanto and BASF had engaged in a joint venture and conspiracy, knowingly risking widespread crop damage in order to increase their own profits (Davies, 2020; Gillam 2020b). In June 2020, the Ninth Circuit's three-judge panel unanimously vacated EPAs approval of dicamba based herbicides (National Family Farm Coalition v. USEPA, 2020; Unglesbee, 2020f). However, these were subsequently re-registered. In 2022, the federal judge considering a case against the EPA in the U.S. District Court for the District of Arizona ordered that the EPA should file a report on the status of its ongoing evaluation of its options for addressing future dicamba-related incidents (Unglesbee, 2022a). The environmental and farming organisations involved subsequently asked court to lift a stay and expedite their lawsuit demanding EPA vacate its 2020 dicamba herbicide registrations (Unglesbee, 2022b). Despite these developments, the companies involved aim to commercialise new dicamba tolerant traits, some with tolerances against four or five active ingredients (Unglesbee, 2020n).

Alternatives

The growing failure of RoundUp Ready crops, due to the spread of glyphosate resistant (GR) weeds, provides an opportunity to phase out the use of RR crops and adopt new methods and technologies. The priority should be to reduce and replace the use of herbicides: not to replace RR crops with other herbicide-tolerant crops, whether or not these are GM crops or produced by different methods. It is now widely recognised that herbicide dependency must be reduced (Harker et al., 2017; Beckie et al., 2019b).

Viable alternatives include:

- Increased use of agro-ecological methods, for conventional as well as organic farming, including crop rotations;
- Further development and implementation of spot spraying and precision weeding to target and reduce the use of herbicides and/or technologies to limit weed seed production during the grain harvest (Quartz, 2015; Guardian, 2015; Horticulture Week, 2015; Gonzalez-de-Santos et al., 2017; Walsh et al., 2017; Beckie et al., 2019b; Oliver, 2020; Belton, 2021; Peters, 2021).

Even advocates of GM crops now accept that RR crops – the main GM crops that are grown today - are not the future of agriculture. Former UK Life Sciences Minister, George Freeman MP (Minister for Science, Research and Innovation until July 2022) stated: "*The first generation, if you like 'GM1.0', was very crude, particularly the original Monsanto monoculture model: "Spray everything that dies apart from the thing we have protected." I do not think anyone thinks that is a particularly progressive way of doing 21st century agriculture…*" (House of Commons Science and Technology Committee, 2016). Former senior scientists at DuPont and Corteva

Agriscience conclude a recent book chapter, "*Today, glyphosate-based crop systems are still mainstays of weed management, but they cannot keep up with the capacity of weeds to evolve resistance. Growers desperately need new technologies, but no technology with the impact of glyphosate and GR crops is on the horizon. Although the expansion of GR crop traits is possible into new geographic areas and crops such as wheat and sugarcane and could have high value, the Roundup Ready® revolution is over*" (Green & Siehl, 2021).

There are significant opportunity costs associated with investing in 'next-generation' HT crops which are tolerant to more herbicides but which will not solve the long-term problem of resistant weeds and will continue to pose risks to human health and the environment. Investing in alternatives means a supporting a paradigm shift towards using less herbicide, not more, to the benefit of farmers, human health and the environment. It is particularly important that RR crops are not pushed into new countries which have so far avoided stepping onto the "transgenic treadmill".

Recommendations

GeneWatch calls for an end to the cultivation of herbicide-tolerant (HT) GM crops, including RoundUp Ready (RR) crops and 'next-generation' GM crops that are tolerant to more than one weedkiller. Protecting the environment and human health should be a priority.

The growing failure of RoundUp Ready crops, due to the spread of glyphosate resistant (GR) weeds, provides an opportunity to phase out the use of RR crops and adopt new methods and technologies. The priority should be to reduce and replace the use of herbicides: not to replace RR crops with other herbicide-tolerant crops, whether or not these are GM crops or produced by different methods.

Governments of countries where RR crops are grown should urgently develop phase-out plans for this technology and publish these for public consultation and debate.

Governments should also end subsidies for maize (corn) to be used as biofuels (corn ethanol), rather than as food.

Governments of countries where RR crops are not currently grown (for example in Europe, most of Africa and Asia, parts of Latin America and New Zealand) should maintain their *de facto* bans on this technology.

In addition:

- Food retailers should require non-GM feed for meat and dairy products, to seek to minimise environmental damage in countries where GM HT crops are grown. At minimum, labelled non-GM-fed meat and dairy products should be available to allow consumers to choose to eat such products.
- In the United States, GM food products should be labelled and food manufacturers should seek to avoid using ingredients from GM HT crops.

1. Introduction

Herbicide tolerance (HT) is the dominant trait among GM crops, with about 88% of all cultivated GM crops being herbicide tolerant, according to industry figures (166.6 million ha out of 190.4 million ha, ISAAA, 2019a). This includes 43% of commercially planted GM crops by area solely with an HT trait, plus 45% with stacked traits (HT plus insect resistant traits, also known as Bt traits). Around 8% of all cultivated GM crops consist of Bt cotton (without the HT trait) planted in India and China (15.1 million ha out of 190.4 million ha, ISAAA, 2019a). Thus, HT crops account for virtually all the GM crops grown for use in food or feed.

Glyphosate resistant, Roundup Ready (RR) crops comprise the vast majority of all HT crops (Benbrook, 2012a). RR crops are genetically engineered to survive blanket spraying with weedkiller (herbicide) containing the active ingredient glyphosate (originally sold by Monsanto with the brandname RoundUp). However, newer HT crops resistant to other herbicides such as 2,4-D and dicamba have now also entered the market, and older GM crops resistant to glufosinate have expanded market share (see Section 6. Industry response).

This reality is in sharp contrast to GM industry PR which emphasises potential new traits (not yet established on the market), including GM crops that tolerate flooding or drought. Such traits were promised more than 40 years ago (OTA, 1981; NABC, 1998), but are very difficult to deliver, even using newer genetic engineering techniques (Hüdig et al., 2022). Selling herbicide-tolerant crops with the associated herbicides remains an industry priority (FoEE, 2022).

Genetically engineered, glyphosate tolerant crops were first commercialised in 1996 and include soybeans, corn (maize), cotton, canola (oil seed rape), sugarbeets and alfalfa (Fernandez-Cornejo et al., 2014; 2016). GM soybean, which is mainly RR soybean, is the most important GM crop, accounting for 48% of all GM crop hectarage (ISAAA, 2019a). Over 90% of GM crops by area are grown in just five countries: the USA, Brazil, Argentina, Canada and India. India grows only GM cotton with an insect resistant (Bt) trait. Therefore, the majority of HT GM crops are grown in the USA, Brazil, Argentina and Canada. Paraguay, Bolivia, Uruguay and South Africa also grow some HT GM crops (mainly soybeans and maize), GM maize (some of which contains the HT trait) is also grown in the Philippines, and GM HT canola (oil seed rape) and GM cotton (some with the HT trait) is grown in Australia. In 2019, industry figures put the USA at 95% GM crop adoption in the main commodity crops (average for soybeans, maize, and canola adoption), much of which would have contained HT traits (alone or in combination) (ISAAA, 2019a). The same report cites GM crop adoption rates of 94% for Brazil (which grows mainly GM soybeans, maize and cotton), nearly 100% for Argentina (which grows mainly GM soybean, maize, cotton and alfalfa) and 90% for Canada (which grows mainly HM canola, soybeans, maize sugar beets, alfalfa). Thus, the industry describes these countries as having reached close to saturation in commercial GM crop production, and is seeking to expand markets elsewhere (ISAAA, 2019a). For example, Bayer (which now owns GM seed company Monsanto) is once again seeking to market RR cotton in India, despite its previous rejection (Bhardwaj, 2022).

U.S. farmers used herbicide tolerant (mainly RR) soybeans on 93 percent of all planted soybean acres in the USA in 2013 (Fernandez-Cornejo et al., 2014). Herbicide tolerant corn (maize) accounted for 85 percent of U.S. corn acreage in 2013, and herbicide tolerant cotton constituted 82 percent of U.S. cotton acreage (Fernandez-Cornejo et al., 2014). Some 95 percent of U.S. canola (oil seed rape) acres and over 99 percent of U.S. sugarbeet acres harvested in 2013 were planted with GM seeds containing herbicide tolerant (mainly RR) traits, whereas 13 percent of U.S. alfalfa acres were planted using GM seeds in 2013 (Fernandez-Cornejo et al., 2016).

The U.S. grows more GM crops than any other country. The hectarage planted to the three main RR crops, soybeans, corn and cotton increased from about 2.9 million hectares in 1996 to about 60.7 million hectares in 2011 (Benbrook, 2012a). RR crop adoption in single and multiple trait varieties in the U.S. had reached 94% in soybeans, 89% in corn, and 91% in cotton by 2014 (USDA

NASS, 2014) (Figure 1). An even higher adoption rate is found in Roundup Ready sugar beet that today covers 98% of the total hectarage of sugar beet in the U.S. and is the fastest ever adopted biotech crop. In Canada, RR sugar beet adoption was 96% in 2013 (James, 2013). Apart from RR crops, the U.S. and Canada also grow dicamba and 2,4-D tolerant GM crops (see Section 6. Industry response).

In Brazil, which grows the second largest area of GM crops, 83% of all GM crops were herbicide tolerant by 2014. The most important GM crop is soybean, accounting for 67% of all biotech crop hectarage in 2014. HT soybean adoption increased from 5% in 1996 to 95% in 2014 (Benbrook, 2016; Figure 2). In Argentina, which grows the third largest area of GM crops, almost all GM crops, except for 5,000 ha of insect resistant corn, were herbicide tolerant by 2014. While in 1996 only 6% of all soybean area was planted to HT soybean, adoption reached 100% in 2008 and has remained that level until today (Benbrook, 2016; Figure 2). Apart from soybeans, 100% of the total cotton plantings in Brazil are also herbicide tolerant, according to industry figures (James, 2013). RR soybean adoption is furthermore reaching saturation in Uruguay (100%), Paraguay (95%), South Africa (92%) and Bolivia (91%) (James, 2013).

In the EU, import of HT food and feed, as well as the cultivation of HT crops can be authorised. So far, several HT crops have been approved for import (these are largely used in anmal feed) but as of today, no HT crops have been approved for commercial cultivation in the EU, or the UK since leaving the EU. Most countries in the world do not grow GM crops commercially, or have not authorised GM crops with HT traits.

In this report we will elaborate the risks of Roundup Ready (RR) crops by looking back at 25 years of experience with this technology in the U.S. and South America. We first analyse the implications of adopting RR crops for farmers. Then, we look at the potential risk of this technology to the environment and to human health. Then, we consider the industry's response to growing problems with RR crops, particularly resistant weeds, including the development of HT crops with tolerance to multiple herbicides.

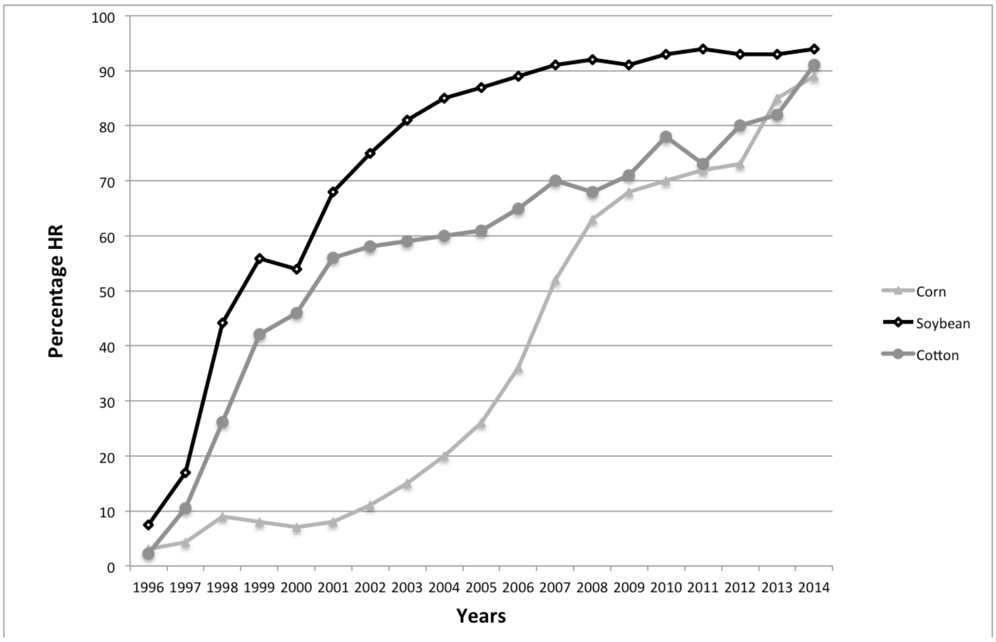

Figure 1. HR crop adoption in the U.S. from 1996-2014. Sources: U.S. Department of Agriculture, National Agricultural Statistics Service (NASS). Genetically engineered varieties of corn, upland cotton, and soybeans, by State and for the United States, 2000-14; Fernandez-Cornejo & McBride (2002). Combines percent acres planted to single and multiple trait varieties.

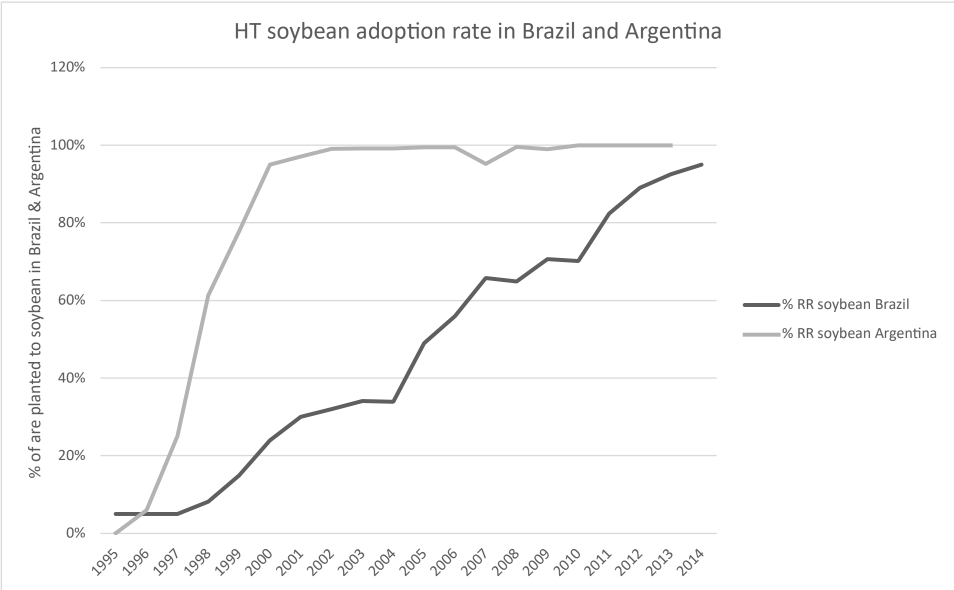

Figure 2. RR soybean adoption in Brazil & Argentina, data derived from Benbrook (2016), additional file1: Table S22

2. Background

Roundup® is a non-selective, broad-spectrum herbicide containing the active ingredient glyphosate. It was developed by Monsanto and introduced in 1974 (Monsanto, 2005a). Glyphosate was said to have a very low toxicity to mammals, birds and fish and to be environmentally sound due to rapid biodegradation and soil binding which decrease persistence in the environment and leaching (Monsanto, 1993). Further praised advantages of the herbicide were its great efficacy, being able to kill all weeds and allowing farmers to control weeds with minimal tillage, thereby not only saving time but also conserving the soil. Glyphosate based herbicides are the world's most widely used herbicides and by 2005 were registered in over 130 countries (Monsanto, 2005a). According to Glyphosate Market Outlook 2031 (n.d.), the global glyphosate herbicide market is still growing and had a market value of US $9.3 billion in 2020, when the use of glyphosate for GM crops was around 45.2% of the global market. Roundup is used in agriculture to control weeds in field crops, intercrop rows or around perennial trees and vines. It is further used to control weeds along roadside, irrigation channels, recreational areas or for woody weed control (Powles & Preston, 2006). Glyphosate controls weeds by disrupting the enzyme 5-Enolpyruvylshikimat-3-phosphate-Synthase (EPSPS). EPSPS is a key enzyme of the shikimate pathway, a biochemical metabolic pathway, that is involved in the biosynthesis of aromatic amino acids that are essential for protein synthesis and govern multiple metabolic processes in plants, fungi and some bacteria. The functionality of this pathway is therefore crucial for plant growth and the survival of plants. As the shikimate pathway or EPSPS, respectively, is not present in mammalian, avian or aquatic life forms, it has been claimed by Monsanto that glyphosate only poses a small risk to human health and the environment (Monsanto, 1993; 2005a). Risks to human health and the environment are discussed in more detail later in this report.

In the early 1980s, researchers began to look for glyphosate-insensitive EPSP synthases to develop herbicide tolerant crops. Eventually, naturally occurring glyphosate tolerant microbes (strain CP4 of *Agrobacterium tumefaciens*) were identified, that had evolved resistance in a waste-fed column at a glyphosate production plant and the first glyphosate resistance EPSP synthases could be isolated. Due to only an Alanine instead of a Glycine residue in the active site of this resistant EPSP synthase, the glyphosate molecule adopts a different form that does not inhibit the shikimate pathway (Funke et al., 2006).

In 1993, Monsanto applied for the deregulation of the first genetically modified herbicide tolerant crop, Roundup Ready (RR) soybeans at the US Animal and Plant Health Inspection Service (APHIS) (Monsanto, 1993). With the in-crop tolerance to Roundup®, these crops had the advantage that farmers could now also spray Roundup herbicides after crop emergence and throughout the growing season without risking harm to their crops. Conventional farmers have to select among a range of herbicide active ingredients and carefully manage the timing of herbicide application, also applying other nonchemical control practices. The Roundup and Roundup Ready crop technology package allows (in theory) blanket spraying with a single weedkiller. This provides for more flexibility for farmers and is easy to use, requiring less skill and knowledge (Mortensen et al., 2012). This idea was that this would lead to lower overall costs, by saving time and because, according to Monsanto, number of applications and the total herbicide use might be reduced and glyphosate was less expensive than other options (Monsanto, 1993).

3. Do farmers benefit from RR crops?

To evaluate the profitability of a system, revenue and expenses have to be balanced. According to the Agricultural Resource Management Survey (ARMS) the majority of farmers (60-77%) adopted RR crops to increase yields. Other reasons were to decrease pesticide input costs (6-20%) and to save management time and make other practices easier (12-15%) (Fernandez-Cornejo et al., 2014). In the following sections we will evaluate if the promised advantages of RR crop technology were proved right in GM adopting countries.

3.1. Impact of RR crops on inputs and farming practices

Farmers expected RR crops to decrease their overall costs by making farming practices easier and requiring less herbicide. Initially, the strategy worked. Farmers had lower weed-control costs, with glyphosate being cheaper than the mixture of selective herbicides it replaced, and fewer tractor passes and less time spent on weed identification were necessary. Other initial benefits included simplified weed management, a bigger time window and more flexibility for spraying, and abandonment of mechanical control of weeds. The economic literature, examining the effects of HT crop adoption on production and management costs and farms profits, however usually only considers short-term cost savings and ignores negative externalities (Desquilbet et al. 2019). The following section discusses the long-term impact of RR crops on overall farming prices.

3.1.1 Herbicide use

With the introduction of RR crops in 1996, a shift in the use of herbicide active ingredients was observed. Where farmers previously changed herbicides annually, or used multiple herbicides, they now began to rely more and more on a single herbicide: glyphosate. Contrary to the GM industry's promise that RR crops would reduce overall herbicide use, the already high levels of glyphosate usage increased dramatically after the introduction of RR crops, since the RR technology fundamentally changed how farmers could apply glyphosate. Before then, farmers could apply glyphosate only pre crop emergence or again after crop harvest. The RR technology however made it possible to additionally spray the herbicide after crop emergence without risking crop damage. This caused an unprecedented and fast growth in the use of glyphosate (Powles & Preston, 2006; Benbrook, 2016). This reality is in stark contrast to the industry's PR message that GM crops reduce chemical use (Kimbrell, 2016). Glyphosate use further increased after Monsanto's patent on glyphosate expired in 2000 (Duke & Powles, 2008). As a result, dozens of companies around the world began to develop generic glyphosate-based herbicides and caused glyphosate prices to fall continuously, making it even more popular. Subsequently, problems with the development of glyphosate resistant 'superweeds' (see Section 3.1.2. Superweeds) have led to increased use of glyphosate (multiple spraying) as well as other weedkillers. As a result, Schulz et al. (2021) have shown that in the two most important GM crops in the US, corn and soybean, the total applied toxicity of pesticides (not just glyphosate) has increased along with increasing GM adoption.

3.1.1.1. Global glyphosate use

Data on global glyphosate use are difficult to obtain and have uncertainties, since they are often incomplete and derived from industry production figures that are often proprietary (Benbrook, 2016). Benbrook (2016) estimate that global agricultural glyphosate use increased almost 15-fold, from 51 million kg in 1995 to 747 million kg in 2014. Of this, about 45 to 50% is used on herbicide tolerant crops, most of it in HT soybeans, followed by HT corn and HT cotton (Figure 3; Benbrook, 2016; Glyphosate Market Outlook 2031, n.d.). Today, glyphosate is the most widely used herbicide in global agriculture. Based on the figures in Benbrook (2016) paper, by 2016, around 90% of total glyphosate worldwide had been applied in the 20 years since the introduction of RR crops. Never before has a pesticide been sprayed so widely (Myers et al., 2016; Benbrook et al., 2016).

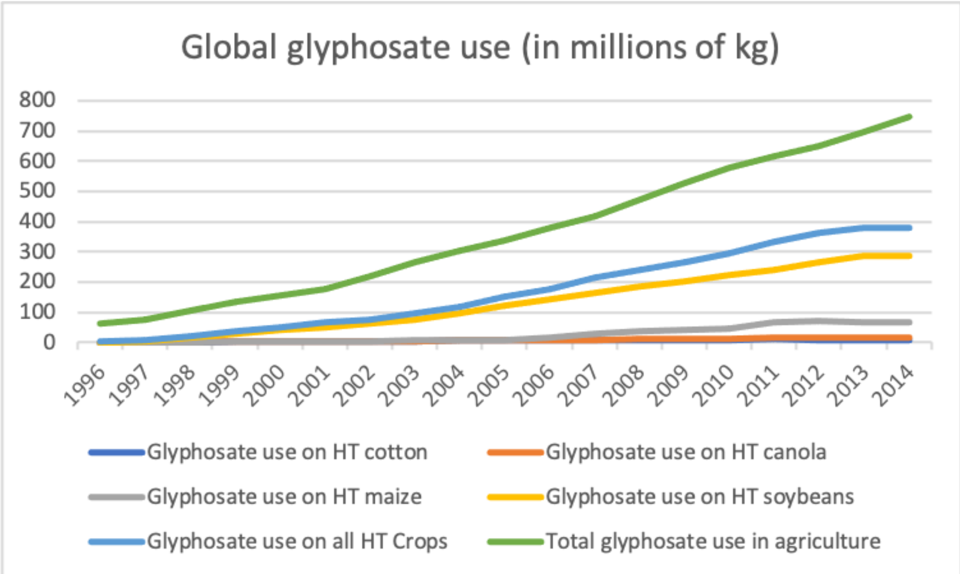

Figure 3. The trend in global glyphosate use 1996 – 2014 shows the increasing share being used on HT crops. Data derived from Benbrook (2016), additional file 1: tables S23 & S24.

3.1.1.2. Herbicide use in the U.S.

In 1995, just before the introduction of RR crops, glyphosate was only the seventh most used herbicide in U.S. agriculture according to the United States Environmental Protection Agency (EPA) (~11.3-13.6 million kg a year). Back then, usage of the most heavily applied herbicide, atrazine, was almost three times as much (~30-33.1 million kg a year). By 2001, glyphosate however already surpassed atrazine as the most widely used herbicide in U.S. agriculture (Benbrook, 2016; Grube et al 2011) and by 2007, glyphosate was used more than twice as much as atrazine (81.6-83.9 million kg a year for glyphosate versus ~32.6-35.3 million kg a year for atrazine). According to these studies, by 2016, agricultural glyphosate use in the U.S. was at 113 million kg, nine times more than before the commercialisation of RR crops (Benbrook, 2016; Myers et al., 2016). According to EPA, annual glyphsoate use has further increased to 127 million kg (US EPA, 2019a).

The largest quantity of agricultural glyphosate is applied to the three major RR crops soybean, corn and cotton. Benbrook (2016) estimates that together they account for around 80% of total agricultural glyphosate use in the U.S., while soybeans alone account for around 50%. According to this study, the introduction of RR crops in the U.S., led on the one hand to a higher amount of glyphosate applied per application (58% increase in soybeans and 43% in corn from 1995 to 2013) and on the other hand to a higher average number of applications per year (64% increase in soybeans and 16% in corn from 1995 to 2013). Thus glyphosate use increased in intensity, which is the amount sprayed per hectare multiplied by the application frequency (kg/ha/yr). From 1995 to 2013 the intensity of glyphosate use rose by 150% in soybean acres (from 0.68 kg/ha/yr in 1995 to

1.71 kg/ha/yr in 2013) and 72% in corn acres (from 0.72 kg/ha/yr in 1995 to 1.23 kg/ha/yr in 2013). As most soybean and corn acres are continuously planted with RR crops (soybean followed by corn, soybean or vice versa), they are sprayed with this amount of glyphosate every year. Glyphosate use further increased in extent (the area sprayed with glyphosate), due to a bigger area planted to RR crops. From 1995 to 2013, the hectarage of corn and soybean treated with glyphosate recorded a nine-fold increase from 6.9 to 63.5 million hectares (CFS, 2015a). CFS (2015a) found the increase of soybean and corn hectarage treated with glyphosate to closely track RR crop adoption.

The overall increase of glyphosate use in the United States in the 25 years from 1992 to 2017 is illustrated in Figure 4.

The increasing reliance on glyphosate by farmers, especially in RR crop fields, cannot be equated with a decrease in total herbicide input costs. While in the first years of adoption, herbicide use in the major HT crops was lower than in conventional crops, it steadily increased in the years since, and became much higher than in conventional crops (Figure 5, Figure 6, Figure 7). Moreover, total herbicide use (common herbicides and glyphosate-based herbicides) in soybean and cotton fields in 2011 exceeded 1996 levels by far (Figure 5, Figure 7). In cornfields, total herbicide use was lower in 2011 than in 1996 but recorded a steady increase since 2002 (Figure 6). Benbrook (2012a) calculated that the three major HT crops combined raised the total amount of herbicide usage in the U.S. from 1996 to 2011 by an estimated 239 million kilos compared to what herbicide use would have been in absence of HT crops.

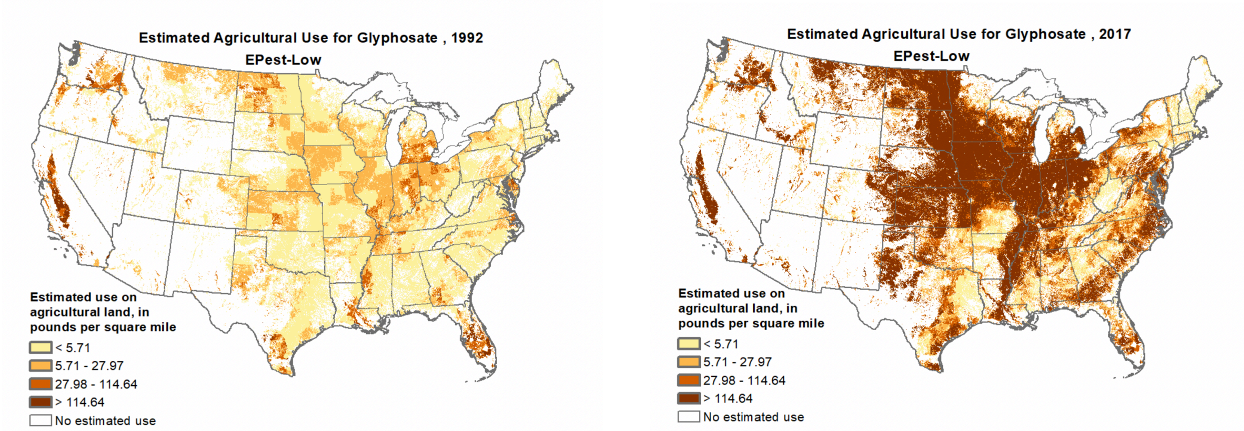

Figure 4. Estimated Agricultural Glyphosate use before (1992) and after (2017) significant adoption of RR crops. in the U.S. Credit: U.S. Geological Survey, Department of the Interior/USGS. URL: http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2012&map=GLYPHOSATE&hilo=L&disp=Glyphosate

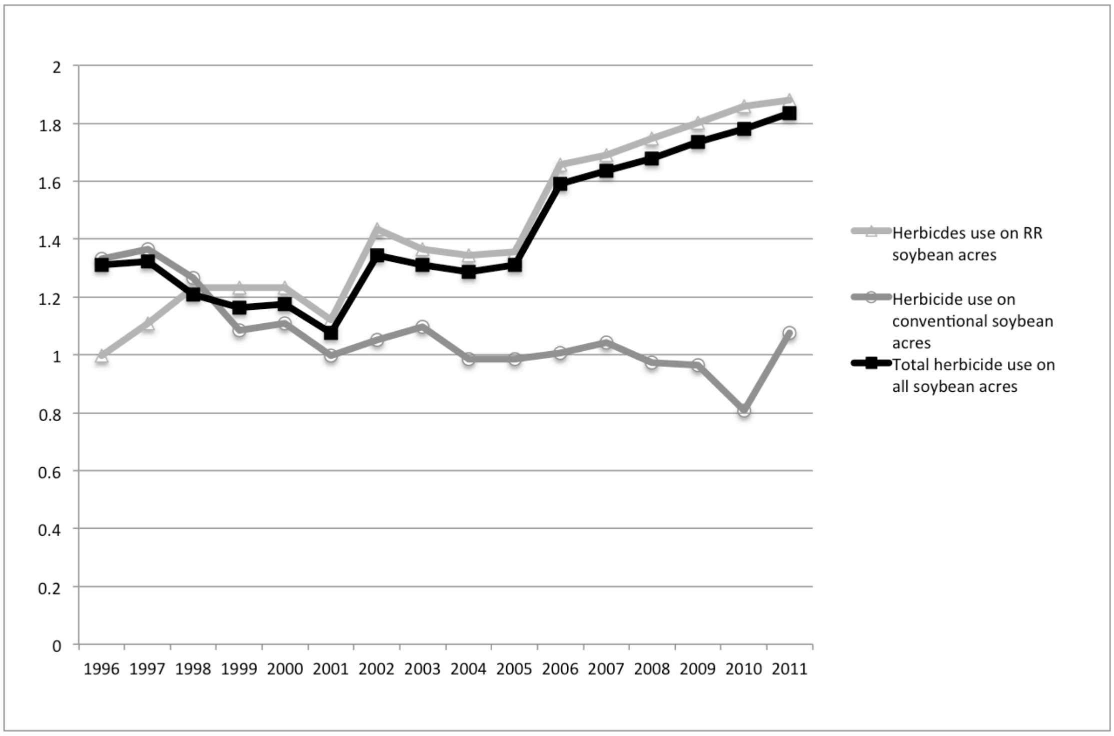

Figure 5. Total herbicide use [kg/ha] on soybean acres in the U.S. (1996-2011) and comparison between herbicide use in conventional and RR soybean production systems. Data adopted from Benbrook (2012a), based on USDA data.

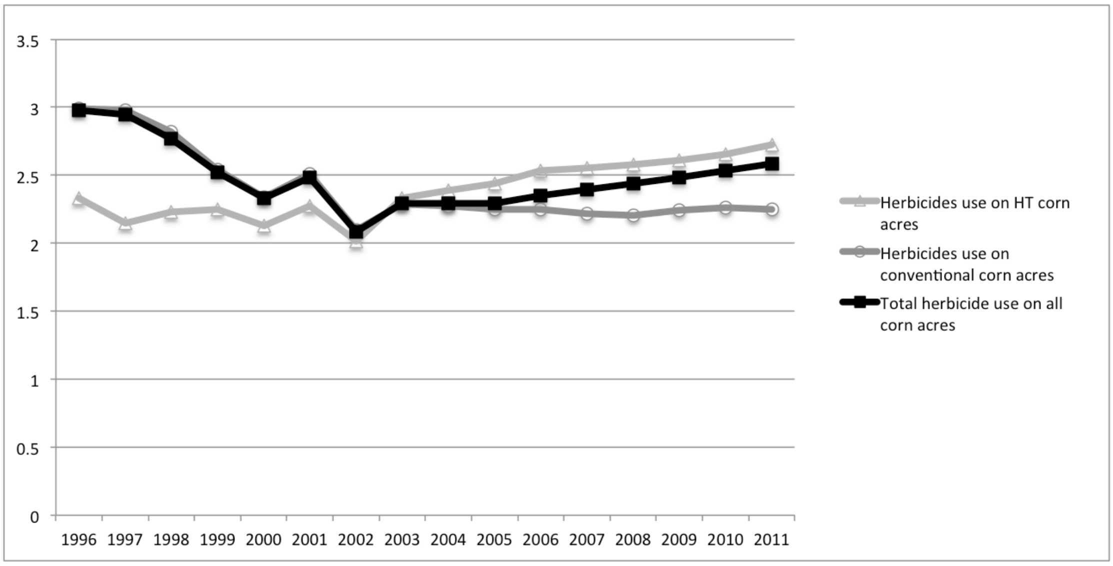

Figure 6. Total herbicide use [kg/ha] on corn acres in the U.S. (1996-2011) and comparison between herbicide use in conventional and HT corn production systems. Data adopted from Benbrook (2012a), based on USDA data.

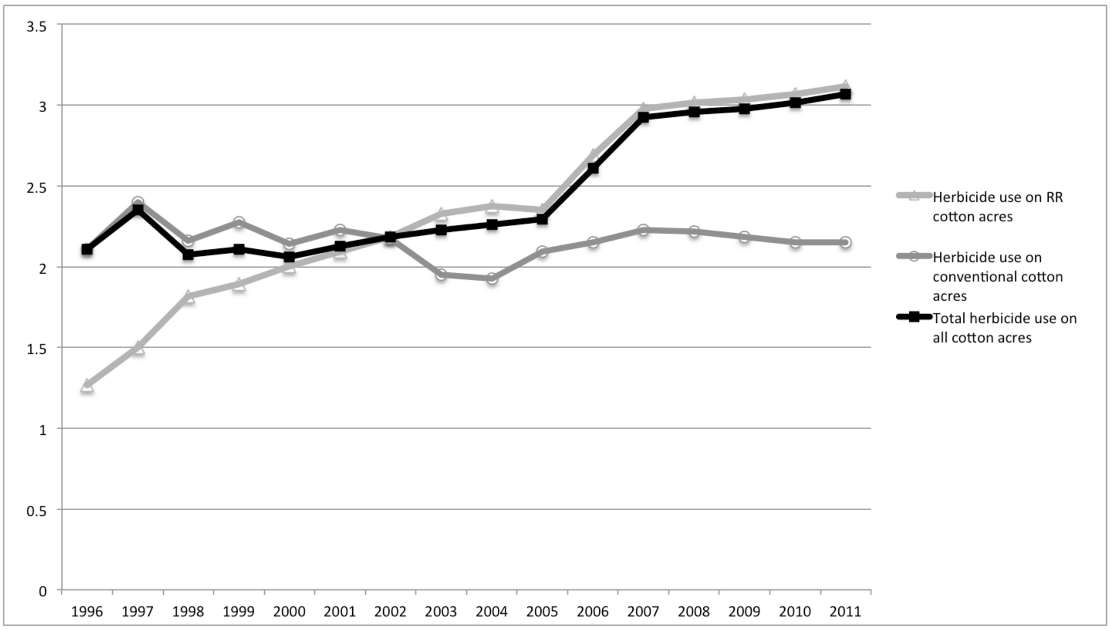

Figure 7. Total herbicide use [kg/ha] on cotton acres in the U.S. (1996-2011) and comparison between herbicide use in conventional and HT cotton production systems. Data adopted from Benbrook (2012a), based on USDA data.

Subsequently, the 2015 National Agricultural Statistics Survey (NASS), has shown that while soybean acres increased 30 percent from 3.95 million acres in 2006 to 5.15 million acres in 2015, total herbicide use increased 61 percent, with farmers spending 88 percent more on crop protectant products than they did six years before. Glyphosate resistant weeds are a major reason why herbicide usage in soybean fields is on the rise (see Section 3.1.2. Superweeds), as herbicides that rely on different modes of action have begun to be adopted by more and more producers in attempts to tackle these resistant weeds (AgWeek, 2016).

Perry et al. (2016) study pesticide use on GM crops with a large, representative sample of plot-level choices made by U.S. maize and soybean farmers from 1998 to 2011. They find that, on average, adopters of GM glyphosate-tolerant (GT) soybeans used 28% (0.30 kg/ha) more herbicide than nonadopters but adopters of GT maize used 1.2% (0.03 kg/ha) less herbicide than nonadopters: however, they note that, for both glyphosate-tolerant GM soybean and maize, adopters used increasingly more herbicides relative to nonadopters over time, consistent with the emergence of glyphosate weed resistance. In this study, increased glyphosate use came at the expense of other herbicides, although for soybeans there was also an increase in total herbicide use that began in 2007 and steadily rose through 2011. The authors conclude that there is clear evidence of increasing herbicide use by glyphosate tolerant variety adopters over time for both GM soybeans and maize, a finding that they attribute in part to the emergence of glyphosate weed resistance.

In a more recent study, Schulz et al. (2021) find that in the two most important GM crops in the US, corn and soybean, the applied toxicity of pesticides (based on total applied toxicity, TAT) increases along with increasing GM adoption. The TAT is based on the annual applied amount, weighted according to the pesticide's toxicity (based on regulatory threshold levels). Although there are uncertainties, the TAT is broadly predictive of the potential pesticide impact on the eight non-target species groups considered in the paper. In this paper, Figure 2A in this paper shows the increase in herbicide use on soybeans in the USA, and Figure 2B and Supplementary Figure S14B show how the TAT to non-target terrestrial plants for herbicides used on HT soybeans has increased with increasing HT soybean adoption. The authors note that the TAT to terrestrial plants has increased since approximately 2008 for for herbicides in HT soybean, likely due to the response to glyphosate resistant weeds (see Section 3.1.2. Superweeds). This finding contrasts with industry-funded studies such as the 2020 study by PG Economics funded by Bayer Crop Science (which now owns Monsanto). PG Economics argues that the Environmental Impact Quotient (EIQ) of herbicides used on GM HT crops is lower than that used on conventional crops (Brookes & Barfoot, 2020). However, this industry-funded conclusion is not based on actual data but on unreferenced "*opinion from extension and industry advisors across the country as to what farmers might reasonably be expected to do for pest and weed control practices, including typical insecticide/herbicide application rates*", and is thus highly susceptible to bias. In contrast, the findings of Schulz et al. (2021) are consistent with the industry response to the emergence of glyphosate-resistant weeds, which results in the extensive use of additional herbicides (see Section 6.2 Increasing the herbicide platform used on RR crops, and Section 6.3 Developing new transgenic crops with resistances to additional herbicides).

3.1.1.3. Herbicide use in South America

Rising herbicide use is also observed in South America. In Argentina, GM soybeans cover 100% of the total soya crop hectares and glyphosate comprised 62% of the total volume of pesticides sold in 2014, which is 75% of the total volume of herbicides sold (CASAFE, 2014). According to Benbrook (2016), the average single glyphosate application rate increased from 1.1 kg/ha in 1996 to 1.4 kg/ha in 2014 and the average number of glyphosate applications increased from 1.8 to 3.18 over the same time period, with as much as seven applications per year being reported. According to Warren (2013), total agrochemical use in Argentina increased nine-fold from 34 million litres in 1990 to more than 317 million litres in 2013. This article reports that Argentinean farmers applied 4.8 kg of agrochemical per hectare in 2013, much more than U.S. farmers. Catacora-Vargas et al. (2012) report that glyphosate use more than doubled in Argentina from 2000 to 2011, due to the steady increase of the cultivation area of Roundup Ready soybeans.

The increase was equally pronounced in Brazil, where pesticide sales in US$ increased 288% between 2000 and 2012 and the volume of pesticide sales increased 162% during the same time period (Carneiro et al., 2015). Since 2011, Brazil is the largest consumer of agrochemicals with a 20% share of the global market in 2017 (Alcántara de la Cruz et al. 2020). A report from Brazil's National Cancer Institute José Alencar Gomes da Silva (INCA) names the release of genetically modified seeds as one of the reasons for this (INCA, 2015). Similarly, Alcántara de la Cruz et al. (2020) name "the increase of agricultural areas destined to monoculture of transgenic crops" as reason for the increase in pesticide use in Brazil. Although overall sales of crop protection products fell in 2015 for economic reasons, there was continued growth in sales of herbicides (IEA, 2016). Data from the Food and Agriculture Organization of the United Nations (FAO) Statistics Division show a 350% increase in the use of herbicides in Brazil, from 68,131 tonnes of active ingredient (a.i.) in 1999 to 239,657 tonnes a.i. in 2013 (FAO, 2016). Glyphosate accounts for more than 50% of the national herbicide market, followed by 2,4-D (18.2% in 2017). Total sales of glyphosate increased 65% from 2009 (118.5 thousand tons a.i.) to 2018 (195.0 thousand tons a.i.) (Alcántara de la Cruz et al. 2020). According to Benbrook (2016), the average single glyphosate application rate increased from 0.8 kg/ha in 1996 to 1.4 kg/ha in 2014 and the average number of glyphosate applications increased from 2.13 to 3.18 over the same time period. Vivian et al. (2013) report that since the introduction of RR soybean technology in 2003, until 2006, there was a reduction in herbicide application on soybeans in the country, deriving mainly from the efficiency of control and range of action of glyphosate. However, they report that amount of active ingredients utilized on this crop has risen significantly since 2006, as a result of the intense use of glyphosate and other herbicides, and the development of resistant weeds (see Section 3.1.2. Superweeds). Soybean is the main consumer of pesticides in Brazil, being responsible for 52.2% of national sales (Alcántara de la Cruz et al. 2020) and occupying 56.82% of the total cultivated area of Brazil in 2016 (IEA, 2016). Given that close to 100% of this is GR soybean (95.8% in 2017), around half of all pesticides sold in Brazil are used on GR soybean. Maize and cotton account for 10.6 and 6.7% of pesticide sales in Brazil, respectively. The vast majority of this is used on GM HT varieties which occupy 89.0 and 94.0% of the total planted area of maize and cotton, respectively. The total area cultivated with glyphosate resistant crops tripled from 2009 (4.4 million hectares, equalling 31.8%) to 2018 (14.7 million hectares, equalling 89%) and more than 70% of pesticides are used in these crops (Alcántara de la Cruz et al. 2020). A study comparing the sustainability of the Brazilian GM and non-GM soybean meal chains found that the GM chain has a higher use of herbicides (Gaitán-Cremaschi et al., 2015).

3.1.1.4. Herbicide use in Europe

In Europe, where to date no RR crops are cultivated, glyphosate cannot be used to directly control weeds in growing crops. Nevertheless, it is used in a wide range of non-GM crops including cereals, maize, oilseed rape, sugar beet, field beans orchards, olive groves, vines and grassland in pre-plant, pre-emergence or post harvest applications. It is also used as harvest aid in a practice called desiccation, in which glyphosate is sprayed for a short time period onto nearly-ripe crops. This should cause the plant to quickly produce seeds, while the rest of the plant dies, aiming for a more even ripening, an earlier harvest and a reduced moisture content in the harvested grains. Thus, this practice is often used in countries such as the UK, where growing periods are wet. Desiccation also aims to reduce the number of weeds in the harvest (Friends of the Earth Europe, 2013a). Nevertheless, contrary to RR crop producing countries in North- and South America, herbicide use has declined in different European countries since the introduction of RR crops elsewhere. In France, herbicide use declined to 82% of 1995 levels by 2009. Similar trends have also been observed in other non-adopting countries like Germany and Switzerland (Heinemann et al., 2014a). This trend could however rapidly change if RR crops were to be introduced in Europe. A Greenpeace study projecting the future impact of the first 15 years of RR crop adoption (maize, soya and sugar beets) in the EU on herbicide use, were such crops to be introduced, concluded that glyphosate use would increase by 800% over all three crops if adoption were as quick and unrestricted as in the U.S (Benbrook, 2012b). According to the European Food Safety Authority (EFSA), which has argued that cultivation of RR crops should be allowed in the EU, this is purely an issue of management and the right agricultural practices. Thereby, EFSA puts all the responsibility on the farmers and neglects the wider problems of the RR cropping system. However, the Greenpeace study argues that glyphosate use would still raise by 400%, even if RR crop adoption was coupled with strict weed resistance management (Benbrook, 2012b).

3.1.2. Superweeds

One of the main reasons for the increase in herbicide use in GM adopting countries is the emergence of glyphosate resistant (GR) weeds, also referred to as ‘superweeds’ (Benbrook, 2012a). And *vice versa*, one of the main reasons for the steady increase in the evolution of glyphosate-resistant weeds worldwide, is the increase in glyphosate usage in glyphosate-resistant crops (Heap and Duke, 2018). Even enthusiasts for RoundUp Ready crops, such as Duke (2018), who argues that their introduction was an “outstanding success”, accept that evolution of glyphosate resistant weeds is now a major problem, significantly increasing the cost of weed management in some cases, and leading to increases in the use of other herbicides. Heap and Duke (2018) write in their conclusion: “*Herbicides, once seen as the final solution to weed control problems in major crops, clearly have a limited lifespan because of herbicide-resistance and concerns about environmental issues*”. Duke et al. (2018) report that, “*Currently, across large areas devoted to GR* [glyphosate-resistant] *crops, particularly in the USA, Brazil and Argentina, GR weeds have become very problematic, reducing the cost and efficacy advantages of GR crops significantly. In the Americas, GR weeds have forced farmers to much greater expenditures on herbicides for weed control. The rapid US farmer adoption of GR soybean with almost exclusive glyphosate use caused a precipitous decline in use of other herbicides from 1996 onwards for a decade. Growers relied exclusively on glyphosate for weed control in GR crops. However, as GR weed challenges emerged in US GR crop fields, growers were forced to add alternative herbicides* *to control glyphosate-resistant weeds. Grower weed control costs tripled, as evidenced by the rapid resurgence of non-glyposate herbicide use in US soybean crops*".

3.1.2.1. Development and spread of GR superweeds

In 1993, Monsanto claimed that several experts came to the conclusion that the development of glyphosate resistant weeds was 'highly unlikely'. The herbicide had already been widely used for 20 years without reports of weed resistance and the introduction of Roundup Ready crops would not significantly alter the selection pressure. Reasons given as to why this herbicide was a low-risk herbicide for the evolution of glyphosate resistant weeds were its non-selectivity, that glyphosate does not persist in the soil and that no other herbicide had the same mode of action (Monsanto, 1993). Other cited reasons were its chemical structure, its metabolism and the fact the extremely complex manipulations used to develop glyphosate-resistant crops were not able to be duplicated in nature (Bradshaw et al., 1997). Nevertheless, the first glyphosate–resistant weed, rigid rygrass (*Lolium rigidum*), was already reported in 1996 in Australia (Powles et al., 1998), the very year the first glyphosate-resistant crop was introduced in the U.S. In 1997, the evidence that in two decades of extensive use only one weed had evolved resistance to glyphosate was still considered a convincing argument for its low risk to trigger the evolution of glyphosate resistance (Heap, 1997). However, by 2003, Monsanto (now owned by Bayer) was being openly criticised by weed scientists for neglecting the problem of resistant weeds (Hartzler, 2003, 2004).

In 2021, the International Herbicide-Resistant Weed database lists 55 weed species that have evolved glyphosate resistance (Table 1, Heap, 2021) about half of which have evolved resistance in glyphosate-tolerant crop systems (Heap and Duke, 2018). Canadian horseweed, also called Canadian fleabane (*Conyza canadensis*) is the most widespread glyphosate resistant (GR) weed, found in 11 countries and 25 U.S. states (Heap and Duke, 2018). Conyza species are also the most widespread weeds in soybean farms in Brazil (Lucio et al. 2019). Palmer amaranth (*Amaranthus palmeri*), also called pigweed, is found in 27 U.S. states and is one of the most feared weeds in US row crops (Molin, 2019), The first glyphosate-resistant Palmer amaranth was detected in 2005 in Macon County, Georgia (Culpepper et al., 2006), where it spread quickly to all cotton producing counties in Georgia (Sosnoskie & Culpepper, 2014). Another important weed, *K. scoparia* has been confirmed in 13 US states and 4 Canadian provinces (Heap, 2021). Giant ragweed (*Ambrosia trifida*) spread from 15% to 39% of Indiana counties between 2006 and 2014 (Harre et al. 2017). Dias et al (2018) report differences in weed communities in glyphosate resistant versus susceptible soybean fields, with *Conyza* spp., *Commelina benghalensis* and *Digitaria insularis* dominanting in GR soybean fields. Changes in weed populations have also been observed in cotton-growing regions in Australia, where volunteer glyphosate tolerant cotton, *Echinochloa colona*, *Conyza bonariensis* and *Sonchus oleraceus* were present in the majority of fields surveyed (Manalil et al. 2017). A volunteer is a plant that grows on its own, rather than being deliberately planted by a farmer.

The U.S., where GM HT crops were first introduced and overwhelmingly adopted, has the greatest problems with GR weeds today: 17 glyphosate resistant weed species were known by 2021, 13 of which have been found in glyphosate-resistant crops (Heap, 2021; Heap and Duke, 2018). In 2012, between 21 to 33 million hectares of U.S. cropland was infested with at least one glyphosate resistant weed, accounting for one-third to fifty percent of the land planted to RR crops (Benbrook, 2012b). A survey by Stratus Ag Research conducted with about 3000 farmers across 31 U.S. states, speaks of 25 million hectares infested with glyphosate resistant weeds in 2012 (Fraser, 2013) and about 34 million hectares in 2014 (Dow AgroScience, 2015). Almost half of all interviewed farmers reported that glyphosate resistant weeds were present on their farms. The problem was more severe in the South, with 92% of growers in Georgia reporting glyphosate resistant weeds. 27% of the farmers had multiple resistant weeds on their fields. The survey also indicates that the rate at which glyphosate-resistant weeds are spreading is increasing, with a 25% increase in 2011 and a 51% increase in 2012. Jason Norsworthy, professor of weed science at the

University of Arkansas predicted, that by 2020 all U.S. row crops would be infested by glyphosate resistance (Allison, 2015).

Following the development of new GM herbicide-tolerant crops with resistance to multiple herbicides, including dicamba (see Section 6. Industry response), Geddes et al (2021) confirm the first cases of the tumbleweed kochia (*Bassia scoparia*) in Manitoba with dicamba resistance alone and in combination with glyphosate resistance. These authors conduct a randomized–stratified survey of 315 sites in Manitoba, USA, in the fall of 2018. They report that, overall, 58% of the kochia populations tested were glyphosate-resistant, while 1% were dicamba-resistant, showing a rapid increase in glyphosate resistant kochia over a five-year time frame. The potential for newer HT crops to lead to weeds that are resistant to other herbicides, such as dicamba and 2,4-D, is considered further in Section 6. Industry response).

Outside the USA, gyphosate resistant (GR) weeds are common in all RR crop producing and major exporting countries with 21 GR weeds known in Australia, 16 in Argentina, 11 in Brazil, and 6 in Canada amongst others (Heap, 2021). These are also the countries with the greatest area infested with GR weeds (Heap and Duke, 2018). The reason why Australia has the second most glyphosate resistant weeds known today, even though it only has one GM HT crop (RR canola) cultivated, may be the large number of qualified weed scientists looking for them, whereas in most other countries some GR weeds have likely been overlooked. Another reason may be that glyphosate has been used at a lower rate than in the U.S. which allows for the evolution of low-level resistance mechanisms (Heap and Duke, 2018). In western Canada, 54% of the total cropping area was infested with HR weeds by 2018 (Beckie, 2018). Nevertheless, the numbers of GR weeds found in Canada to date are still comparatively few. Beckie and Harker (2017), however, say that picture could quickly change in the future given reliance on glyphosate for weed control pre-seeding, in-crop, pre-harvest or post-harvest. They criticise the system for production of RR canola in the Canadian prairies and state that they believe the core element of a diverse weed management system is crop diversity to the extent possible, involving weed-competitive crops and agronomic practices that promote crop competitiveness against weeds. Cerdeira et al. (2011) confirm that overreliance on glyphosate in RR soybean cropping systems has resulted in the selection of resistant weed species through weed shifts and evolution of glyphosate-resistant weed biotypes, especially in Brazil, Argentina and Paraguay. According to Allison (2015), 30% of the total cropping area in Brazil was affected by GR weeds in 2015. Nine glyphosate resistant weed species have been reported in Brazil, some of which have multiple resistance to other modes of action. The selection of glyphosate resistance in these species is, with the exception of one, related to the use of RR crops (Alcántara de la Cruz et al. 2020). Vila-Aiub et al. (2008) review glyphosate-resistant weeds in South America and highlight the existence of resistant Mexican fireplant (*Euphorbia heterophylla*), hairy fleabane (*Conyza bonariensis*) and horseweed (*Conyza canadensis*) in soybean fields in Brazil. In Argentina, GR weed species evolved primarily in GM HT soybean (Heap and Duke, 2018). Vila-Aiub et al. (2007) report that whilst glyphosate initially gave good control of weeds in RR soybeans in Argentina, glyphosate-resistant Johnsongrass has resulted from an increase in the use of glyphosate from 14 million litres in 1996 to 175 million litres in 2006. Their study establishes that the failure of Johnsongrass control at commercial field rates of glyphosate (1,000g ae ha^{-1}) in the Province of Salta (Argentina) is the result of evolved heritable resistance to glyphosate, following the continuous use of this weedkiller. Ferraro & Ghersa (2013) cite evidence of glyphosate-resistant johnsongrass (*Sorghum halepense*) in Argentina and develop a model for predicting herbicide resistance risk. In 2021, the first worldwide case of glyphosate resistant *Bromus catharticus* (prairie grass) was reported in Argentina (Yanniccari et al. 2021).

Glyphosate resistant weeds have also spread beyond RR crop producing countries in countries such as Colombia, Venezuela, China, Japan and New Zealand. In eight European countries, Spain, Portugal, Greece, Czech Republic, Poland, Italy, France and Switzerland, a total of eight weeds species resistant to glyphosate are known. With five different GR weed species known in Spain, this country has the most different GR weeds, followed by Italy, Greece and Portugal that each have three different GR weed species to date (Benbrook, 2012b; Heap, 2016). This shows that the problem with GR weeds is greater in southern Europe, where the emerged cases are attributable to repeated glyphosate use in vineyards, orchards and olive groves (Benbrook 2012b, Friends of the Earth Europe, 2013a; Fernández et al., 2017). If RR crops were ever to be grown in Europe, or elsewhere, the subsequent predicted increase in glyphosate use (Benbrook 2012b) would be likely to accelerate the spread of GR weeds. One of the GR weeds that already spread into several European countries is horseweed, which is one of the most dominant GR weeds in RR fields in the U.S. Since several glyphosate resistant phenotypes are already known in Europe, it can be expected that GR weeds would spread more quickly in Europe if RR crops are grown than in the U.S. (see next section). That means that European farmers would probably benefit from the initial advantages of this technology only for a very limited time. The same applies to other countries where RR crops are currently not grown.

Pannell et al. (2017) note that herbicide-resistant (HR) weeds threaten the sustainability of herbicide-tolerant (HT) crops, pose environmental risks from increased use of alternative weed-control treatments, alter public and private research and development (R&D) programs, and necessitate new approaches to manage such resistance. They compare perspectives from Australia, the European Union, and the United States. The authors report that the rapid adoption of HT canola, corn, cotton, soybean, and sugar beet in North America since the mid-1990s was accompanied by a dramatic reduction in the diversity of weed control tactics and intensified ecological selection pressure that ushered in a new era of HR weeds. Glyphosate resistance is much lower in the EU than the United States, because RR crops have not been given regulatory approval for cultivation in the EU. The article notes that, currently, the only RR crop available to grain farmers in Australia is canola (oil seed rape). Limiting the RR gene to a single crop is helping to limit the usage of glyphosate, so that the evolution of glyphosate resistance is slower than it has been in the United States. Nevertheless, according to the authors, it seems likely that it will eventually become widespread. If additional RR crops are brought to the Australian regulator, the risk of resistance will be one of the factors that are considered. The authors note that leading weed scientists will strongly oppose the release of additional RR crops and, given their experience with resistance, many farmers would be broadly supportive of this position. They also report that it is clear that most strategies recommended to prevent herbicide resistance will not avoid it indefinitely because they do not kill all, or nearly all, surviving weeds. Further, once resistance does occur in a field, the economics of alternative farming systems can be dramatically affected, and in general, the net benefits of adopting alternative weed control methods improve. The authors conclude that decisions about approval or cancellations of herbicides and GM crops will be required to take account of implications for resistance management.

Although glyphosate-resistant weeds have been identified in non-GM crops such as orchards and vineyards and in non-GM crop adopting countries, "*it is the glyphosate resistant weeds in glyphosate-resistant crop systems that dominate the area infested and growing economic impact*" with over 90% of the area infested and the economic damage caused by GR weeds globally stemming from GR weeds in GM HT crop systems (Heap and Duke, 2018).

3.1.2.2. Causes and Mechanisms for Glyphosate resistant weeds

Glyphosate resistant weeds became a huge problem in a short amount of time, despite Monsanto stating that it was highly unlikely for glyphosate resistant weeds to evolve at all. Despite warnings, what was not accounted for was the unprecedented selection pressure exerted due to monocultural production systems, the reliance on a single herbicide, and the very fast adoption of RR systems that allow for multiple applications during the growing season. Additionally, crop rotations of different RR crops exposed weed populations to annually repeated glyphosate selection pressure. Simultaneously, farmers adopted zero tillage, which further increased the risk of glyphosate resistance evolution (Powles & Preston, 2006). On the other hand, repreated exposure to low doses of herbicides due to herbicide drift can also rapidly select for weed resistance (Vieria et al. 2020). Hormesis is a biological phenomenon whereby a beneficial effect (improved health, stress tolerance, growth or longevity) results from exposure to low doses of an agent that is otherwise toxic or lethal when given at higher doses. Brito et al. (2017) review the hormetic effects of glyphosate on plants, including evidence that low rates of glyphosate application can increase plant growth. Glyphosate rates that cause hormesis and phytotoxicity are very close, making it difficult to use glyphosate to increase crop yields. However, the authors speculate that glyphosate hormesis may play a role in the evolution of and success of glyphosate-resistant weeds. Subsequently, based on pot trials in Australia, Mobli et al. (2020) report that the sublethal doses of glyphosate produced hormetic effects on growth and seed production of common sowthistle (*Sonchus oleraceus*) that change the dynamics of weed–crop competition. Additionally, the spread of resistance genes from glyphosate-resistant to susceptible weed species due to pollen-mediated dissemination can greatly accelerate the distribution of existing glyphosate resistance traits and has been reported in different weed species (Ganie and Jhala, 2017; Sarangi et al. 2017; Yanniccari et al., 2018). Nevertheless, pollen-mediated gene flow is usually neglected, under-estimated and under-appreciated (Beckie, 2018; Beckie et al. 2019a). Gene flow from GM crops to wild relatives is discussed further in Section 3.4.2.5. GM contamination threatens biodiversity).

Several different mechanisms of glyphosate resistance in weed species have been found, more than for any other herbicide mode of action (Gaines et al. 2019). On the one hand, several weed species have been reported that are inherently more resistant to glyphosate than most other weeds (Table 1). Due to the commercialisation of Roundup Ready crops, naturally resistant species could occupy vacant ecological niches in Roundup Ready crop fields, which leads to a weed shift (Nandula et al., 2005). On the other hand, different cases of evolved glyphosate resistance are also known. These include resistance mechanisms at the target-site in the genome of the plant, either by modifying the EPSPS enzyme or by duplicating it, as well as resistance mechanisms that reduce the amount and rate of glyphosate accumulating at the target site (non-target-site mechanisms) These have been demonstrated in many weed species and populations across the globe, as discussed below.

i) target-site mutation

The first reported examples of evolved glyphosate resistance involving EPSPS-alteration were Malaysian populations of goosegrass (*Eleusine indica*). The resistance was attributed to a single mutation in the DNA of this weed, namely an amino acid substitution in the EPSPS gene, changing Pro106 to Ser or Thr (Baerson et al., 2002; Ng et al., 2003). Mutations of Pro106 to Ala, Leu have also been reported (Sammons and Gaines, 2014). The glyphosate resistant EPSPS from goosegrass has been patented for the potential creation of glyphosate resistant crops (Nandula et al., 2005). The mutation of Pro 106 has also been found in glyphosate resistant ryegrass (*Lolium spp.)* (Perez-Jones et al., 2005; Wakelin & Preston, 2006; Tehranchian et al. 2018), *Amaranthus tuberculatus* (rough-fruited water-hemp), *Echinochloa colona* (jungle rice), *Digitarias insularis* (sourgrass), *Conyza sumatrensis* (tall fleabane) and *Chloris virgata* (feather fingergrass) (Amaro-Blanco et al., 2018; Heap and Duke, 2018; Nandula et al. 2018; Sammons and Gaines, 2014). A single base pair target-site mutation confers a low level of glyphosate resistance (two to six-fold resistance). There is however also a known double mutation, called TIPS double mutation (due to a Thr102Ile change in addition to the Pro106Ser change) that has evolved in glyphosate-resistant *E. indica* (Indian goosegrass) and confers a 180-fold resistance factor (Yu et al. 2015). The TIPS form of EPSPS makes plants as, or even more, resistant to glyphosate than GR crops and has also been used in commercial GR maize varieties (Chen et al. 2015; Heap and Duke, 2018; Yu et al. 2015). More recently, a triple mutation, TIAVPS (due to an additional Ala103Val mutation) has been documented in an *Amaranthus hybridus* (green pigweed) population from Argentina (García et al. 2019; 2020; Perotti et al. 2019). It is not clear yet, how much the Ala103Val mutation adds to the resistance (Gaines et al. 2019). Target-site mutations may decrease the catalytic activity of the EPSPS enzyme and could thereby pose a plant fitness cost (Vila-Aiub et al. 2019).

ii) EPSPS gene amplification

Another glyphosate resistance mechanism is increased EPSPS expression. An increase in EPSPS means that the amount of glyphosate needed to inhibit enough EPSPS to effectively kill the plant needs to be increased (Heap and Duke, 2018). A study conducted with GR Palmer amaranth in

Georgia attributed increased EPSPS expression to EPSPS gene amplification on multiple chromosomes. Genomes from GR plants contained 5-160-fold more copies of the EPSPS gene than did genomes of susceptible plants (Gaines et al., 2010). Today, duplication of EPSPS has been reported in several population of Palmer amaranth throughout the U.S. (Heap and Duke, 2018). EPSPS gene amplification has since also been found in spiny amaranth (*Amaranthus spinosus*) from Mississippi, U.S. (Nandula et al., 2014), common waterhemp (*Amaranthus tuberculatus*) from Missouri, Kansas and Illinois, U.S. (Chatham et al., 2015; Lorentz et al., 2014; Dillon et al., 2016), *Amaranthus rudis* from Nebraska U.S. (Sarangi et al. 2017), ripgut brome (*Bromus diandrus*) from South Australia and Victoria, Australia (Malone et al., 2015), kochia (*Kochia scoparia*) from Kansas, Colorado, North Dakota, South Dakota, Wyoming, Nebraska, and Montana, U.S. (Wiersma et al., 2014; Gaines et al., 2016), indian goosegrass (*Eleusine indica*) from China (Chen et al. 2015), windmill grass (*Choris truncate*) from Australia (Ngo et al. 2018) and italian ryegrass (*Lolium perenne ssp. multiflorum*) from Arkansas, U.S. and Argentina (Salas et al., 2012; Yanniccari et al. 2017). There is a linear relationship between EPSPS gene amplification number and glyphosate resistance level (Gaines et al., 2016; Kumar & Jha, 2015; Vila-Aiub et al., 2014). Amplification generally results in higher resistance levels compared to single base pair mutations (Heap and Duke, 2018).

iii) altered glyphosate sequestration and translocation

Studies with the first glyphosate resistant species, rigid ryegrass (*Lolium rigidum*), showed that the patterns of glyphosate translocation (its movement from the leaves to other parts of the plant) were different between resistant and susceptible populations. Compared with susceptible plants, the resistant population had an increased glyphosate accumulation in the treated leaf and a decreased accumulation in the stem, stem meristem and roots (Lorraine-Colwill et al., 2002; Wakelin et al., 2004). Experiments on the mechanism of glyphosate resistance in Italian ryegrass (*Lolium multiflorum*) and horseweed (*Conyza canadiensis*) also found a reduced translocation of glyphosate to the roots and an accumulation at the site of application (Feng et al., 2004; Koger & Reddy, 2005; Perez-Jones et al., 2005). Translocation can, for example, be reduced by rapid sequestration of the herbicide into parts of the plants such as vacuoles (Heap and Duke, 2018). Reduced absorption and/or translocation was also found in further *Conyza* species (Amaro-Blanco et al. 2018), Johnsongrass (*Sorghum halepense*) (Vila-Aiub et al. 2012), *Digitaria insularis* (de Carvalho et al. 2012), *Chloris elata* (Brunharo et al. 2016), *Leptochloa virgata* (Alcántara-de la Cruz et al., 2016) and *Echinochloa colona* (Nandula et al. 2018). A reduced cellular transport of glyphosate from the site of absorption to the growing parts of the plant is thus considered the cause of resistance to glyphosate in these species. This resistance mechanism usually confers low levels of resistance (Heap and Duke, 2018).

Other resistance mechansims include rapid cell death, which has been demonstrated in *Ambrosia trifida* (giant ragweed) (Moretti et al., 2018; Van Horn et al. 2018), and enhanced metabolism of glyphosate to AMPA (Heap and Duke, 2018; Gaines et al. 2019). The latter however still lacks robust evidence. The fact that about 60% of GR *Amaranthus* species plants from Ohio could not be explained by known resistance mechanisms, may also indicate that there are yet other resistance mechanisms (Murphy et al. 2019). Some species exhibit different resistance mechanisms among separate populations or genetic lineages. It is currently unclear why particular populations seem to be more likely to evolve target site or non-target site resistance mechanisms, respectively (Baucom, 2019). Furthermore, accumulated evidence about glyphosate-resistance mechanisms in common ragweed (*Ambrosia artemisiifolia*) from Ohio suggests that multiple mechanisms of glyphosate resistance are possible within a single common ragweed population and likely also within individual plants (Parrish, 2015). It seems to be a common trend for different glyphosate resistance mechanisms to combine within populations and individuals and result in a higher fold resistance than either mechanism alone (de Carvalho et al. 2012; Chen et al. 2015; Murphy et al. 2019; Sammons and Gaines, 2014).

Table 1. Summary of weed species with natural and evolved resistances to glyphosate. Derived from Nandula et al. (2005) and the International Survey of Herbicide Resistant Weeds (Heap, 2016).

Weed Species		First Appearance
	Natural Resistance	
Asiatic dayflower	*Commelina communi*	2005
Birdsfoot trefoil	*Lotus corniculatus*	1990
Chinese foldwig	*Dicliptera chinensis*	2002
Common lambsquarters	*Chenopodium album*	2005
field bindweed	*Convulvulus arvensis*	1984
Tropical spiderwort	*Commelina benghalensis*	2004
Velvet lead	*Abutilon theophrasti*	2005
	Evolved Resistance	
Smooth Pigweed	*Amaranthus hybridus*	2013 (Argentina)
Palmer Amaranth	*Amaranthus palmeri*	2005 (USA)
Spiny Amaranth	*Amaranthus spinosus*	2012 (USA)
Tall Waterhemp	*Amaranutus tuberculatus (= A. rudis)*	2005 (USA)
Common Ragweed	*Ambrosia artemisiifolia*	2004 (USA)
Giant Ragweed	*Ambrosia trifida*	2004 (USA)
Capeweed	*Arctotheca calendula*	2020 (Australia)
Saltmarsh Aster	*Aster squamatus*	2021 (Mexico)
Hairy Beggarticks	*Bidens pilosa*	2014 (Mexico)
Wild Oat	*Avena fatua*	2018 (Australia)
Sterile Oat	*Avena sterilis ssp. Ludoviciana*	2018 (Australia)
Hairy Beggarticks	*Bidens pilosa*	2014 (Mexico)
Greater Beggarticks	*Bidens subalternans*	2018 (Paraguay)
Sweet Summer Grass	*Brachiaria eruciformis*	2014 (Australia)
Birdsrape Mustard	*Brasica rapa (=B. campestris)*	2012 (Argentina)
Rescuegrass	*Bromus catharticus*	2017 (Argentina)
Ripgut Brome	*Bromus diandrus*	2011 (Australia)
Compact Brome	*Bromus diandrus*	2011 (Australia)
Red Brome	*Bromus rubens*	2014 (Australia)
Downy Brome (Cheatgrass)	*Bromus tectorum*	2021 (Canada)
Plumeless Thistle	*Carduus acanthoides*	2019 (Argentina)
Swollen Fingergrass	*Chloris barbata = (C. inflate)*	2018 (Mexico)
Tall Windmill Grass	*Chloris elata*	2014 (Brazil)
Windmill Grass	*Chloris truncata*	2010 (Australia)
Feather Fingergrass	*Chloris virgata*	2015 (Australia)
Hairy Fleabane	*Conyza bonariensis*	2003 (South Africa)
Horseweed	*Conyza canadiensis*	2000 (USA)
Sumatran Fleabane	*Conyza sumatrensis*	2009 (Spain)
Gramilla mansa	*Cynodon hirsutus*	2008 (Argentina)
Sourgrass	*Digitaria insularis*	2005 (Paraguay)
Junglerice	*Echinochloa colona*	2007 (Australia)
Barnyardgrass	*Echinochloa crus-galli car. crus-galli*	2019 (Argentina)
Goosegrass	*Eleusine indica*	1997 (Malaysia)
Wild Poinsettia	*Euphorbia heterophylla*	2019 (Brazil)
Woody borreria	*Hedyotis verticillata*	2005 (Malaysia)
Common Sunflower	*Helianthus annuus*	2015 (USA)
Smooth arley	*Hordeum murinum ssp. glaucum*	2016 (Australia)
Hare Barley	*Hordeum murinum ssp. leporinum*	2018 (Spain)
Kochia	*Kochia scoparia*	2007 (USA)
Willow leaved lettuce	*Lactuca saligna*	2017 (Australia)
Prickly Lettuce	*Lactuca serriola*	2015 (Australia)
Tropical Sprangletop (Juddsgrass)	*Leptochloa virgate*	2010 (Mexico)
Perennial Ryegrass	*Lolium perenne*	2008 (Argentina)
Italian Ryegrass	*Lolium perenne ssp. multiflorum*	2001 (Chile)
Rigid Ryegrass	*Lolium rigidum*	1996 (Australia)
Ragweed Parthenium	*Parthenium hysterophorus*	2004 (Colombia)
Arrocillo	*Paspalum paniculatum*	2010 (Costa Rica)
Buckhorn Plantain	*Plantago lanceolata*	2003 (South Africa)
Annual Bluegrass	*Poa annua*	2010 (USA)
Wild Raish	*Raphanus raphanistrum*	2010 (Australia)
Russian-thistle	*Salsolsa tragus*	2015 (USA)
Annual Sowthistle	*Sonchus oleaceus*	2014 (Australia)
Johnsongrass	*Sorghum halepense*	2005 (Argentina)
Coat Buttons	*Triday procumbens*	2016 (Australia)
Liverseedgrass	*Urochoa panicoides*	2008 (Australia)

3.1.2.3 Economic damage caused by GR weeds

While the post-emergence application of a broad-spectrum herbicide initially lowered weed control costs, the subsequent spread of weed resistance lowered the profitability of herbicidal weed control again (Desquilbet et al. 2019) Glyphosate resistant weeds undermine agricultural productivity and profitability. The emergence of GR weeds forces farmers to increase their herbicide application rates, apply additional herbicides and go back to costly, time- and labour-intensive weed control measures like ploughing, deep tillage and manual weeding. Nevertheless, weed resistance has received less attention in the economic literature compared to other types of market failure associated with HT crops, such as costs of coexistence with non-GM crops. Economic literature, examining costs and benefits of HT cropping systems for farmers, mostly considers the short-term cost savings only (Desquilbet et al. 2019). It is estimated that glyphosate resistant weeds have increased overall costs for weed management by 50-100% (Benbrook, 2012a). By 2009, it was reported that weed infestations in some parts of the USA were sometimes so severe, that farmers had abandoned cultivation of some fields (Caulcutt, 2009).

Cotton growers have experienced more problems with weed resistance than growers of other major row crops because a) cotton emergence after planting is slower compared with other crops and b) there are fewer registered herbicides available for cotton than for other crops (Zhou et al. 2015). Riar et al. (2013) sent a survey questionnaire to cotton consultants of Arkansas and Mississippi through direct mail and Louisiana and Tennessee consultants through on-farm visits in fall of 2011. The survey was returned by a total of 22 Arkansas, 17 Louisiana, 10 Mississippi, and 11 Tennessee cotton consultants, representing 26, 53, 13, and 38% of total cotton planted in these states in 2011, respectively. Collectively, the area planted to RR cotton was 97%, glyphosate plus glufosinate-resistant (Widestriket Flex, WRF) cotton was 30%, and glufosinate-resistant (Liberty Link, LL) cotton was 2.6% of the total cotton surveyed in 2011. Seventy percent of the area in all states was still under continuous RR/WRF cotton. The average cost of herbicides in RR systems was $114 per hectare and in LL systems was $137 per hectare. Palmer amaranth, morning glories, and horseweed were the most problematic weeds of cotton across Arkansas, Mississippi, and Tennessee. In Louisiana, however, morning glories were the most problematic weed followed by Palmer amaranth and common waterhemp. Glyphosate-resistant (GR) Palmer amaranth infested 13% of the scouted cotton area in Louisiana compared with 75% in the remaining three states, and consequently, hand-weeding to control GR Palmer amaranth was practiced on 2.5% of th total scouted area of Louisiana and 49% of the scouted area of the remaining three states. Hand-weeding added an additional $12 to $371 per hectare to weed-management costs. In a survey conducted in 2012 with 2500 potential cotton farmers in 13 southern U.S. states, over two thirds of the 307 farmers who responded to the relevant question reported herbicide resistance on their farms, mostly resistance to glyphosate (Zhou et al., 2015). The survey further suggests that farmers who responded to the survey significantly decreased no-till practice in cotton acres after weed resistance emerged. Besides chemical and mechanical practices to manage weed resistance, they relied heavily on labour-intensive practices, mainly hand hoeing or pulling weeds. The survey reports that these farmers spent an increased amount of money on weed control after weed resistance emergence. These farmers reported that Palmer amaranth was the dominant resistant weed problem (61%), followed by horseweed (24%), ragwed (5%) and other weeds (10%) (Zhou et al., 2015). Lambert et al. (2017) use the Zhou et al. (2015) survey of upland U.S. cotton producers to determine the factors contributing to changes in weed management costs (WMCs) after the identification of herbicide-resistant weeds. Post-resistance WMCs for surveyed cotton farmers ranged between $25.37 and $53.19 million. Average costs of managing weeds increased by $98 per hectare following the establishment of herbicide-resistant weeds. Post-resistance changes in WMCs ranged between $85 and $138 per hectare, depending on the combination of adopted practices.

Wechsler et al. (2016) model herbicide demand and glyphosate resistance on U.S. corn (maize) farms. Their preliminary results suggest that glyphosate resistance may have decreased weed control by 11% from 2005 to 2010 (where 5 resistant weeds are present), although they note that no highly-accurate data on weed pressure among U.S. corn fields exists. In Brazil, the potential ecomomic cost of glyphosate resistant weeds on soybean producers was estimated to be 40 to 322% higher, depending on the glyphosate resistant weed species. The total cost for resistance management and yield loss by weed competition is estimated to exceed R$ 9 billion annually in soybean cultivation alone (Alcántara de la Cruz et al., 2020). In addition, Albrecht et al. (2020) report that higher doses of glyphosate-based herbicides, often applied in response to resistant weeds, cause crop damage that can cause significant reductions in farmers' incomes from RR soybean crops. In 2015, the USDA reported that, since the commercial introduction of RR crops in 1996, glyphosate use in soybean production has promoted the spread of GR weeds more than its use in corn (maize) production (Livingston et al., 2015). In surveys of crop production practices, growers were asked to report their concerns about glyphosate resistance, either as the presence of "GR weeds" in corn (maize) or "declines in glyphosate effectiveness" in soybeans. They reported GR-weed infestations on 5.6 percent of the corn acres in 2010 and declines in glyphosate effectiveness in about 40 percent of soybean acres in 2012, with the majority of those acres in the Corn Belt and Northern Plains. Corn growers who reported GR weeds and soybean growers who reported reduced glyphosate effectiveness realized lower returns than similar corn and soybean growers who did not report them. Computer modelling in this report suggests that corn growers who had reported a GR-weed infestation in 2010 realized significantly lower operating (-$60.19/acre) and total (-$67.29/acre) returns than similar corn growers who had not reported such an infestation. Similarly, soybean growers who had reported a decline in the effectiveness of glyphosate as of 2012 received lower total (-$22.53/acre) returns than soybean growers with similar characteristics who had not reported such a decline. The estimates suggest that lower yields and higher chemical costs might have contributed to the lower returns, although the difference in yields is not statistically significant at the 10-percent level. These findings suggest that glyphosate resistance contributed to a 14-percent reduction in returns to affected soybean growers. Simulations in the report also show that weed-seed dispersal from a field where crop growers ignore resistance when managing weeds could reduce the returns on nearby fields.

Palmer amaranth (*Amaranthus palmeri*) is the most economically damaging GR weed globally (Heap and Duke, 2018). In 2017, it was voted the country's most troublesome weed by the Weed Science Society of America (Bomgardner, 2019). It is an invasive weed, native to the Sonoran desert and southwest United States. Several traits make this weed a strong competitor against field crops: it is a prolific seed producer that starts germinating early in the growing season and grows very fast (> 6 cm day^{-1}) and very tall (≥ 2.5 m), so that it can completely obscure and smother low-growing and young crops. With its woody stem that can grow up to 15 centimetres in diameter, this weed can also damage harvesting equipment. Further it competes efficiently for nutrients, is drought-resistant, tolerates heat extremes and has very diverse genetics (Benbrook, 2009; Caulcutt, 2009; Nature, 2014; Eurekalert, 2014; Molin, 2019). Moreover, Pamer amaranth has developed resistances to several other herbicides, in addition to glyphosate (Molin, 2019) and does not appear to suffer from fitness costs associated to herbicide resistance (Bomgardner, 2019; Vila-Aiub et al., 2014). How fast Palmer amaranth can spread was shown in a study conducted in Arkansas. 20,000 GR Palmer amaranth seeds were sown into a $1m^2$ circle at different cotton fields with no prior Palmer amaranth infestation to simulate one GR female Palmer amaranth plant. Within 3 years, this led to more than 95% infestation with GR Palmer amaranth, causing complete crop failure. The high density of Palmer amaranth made cotton harvest impossible due to potential equipment failure and competition from high densities of Palmer amaranth resulted in little to no cotton to harvest (Norsworthy et al., 2014). Further, 20,000 seeds per plant is a conservative estimate, as Palmer amaranth can produce more than 1.5 million seeds per plant (Smith et al., 2012) and the seed may be viable in the soil for a few years (Molin, 2019). The spread of Palmer amaranth in Macon County Georgia forced farmers to abandon over 4,000 hectares in 2007 (Delta Farm Press, 2008). As a consequence of its spread in Georgia, costs for herbicide input more than doubled and costs for hand weeding increased by 475% compared to the years prior to resistance (Sosnoskie & Culpepper, 2014). According to Culpepper, these farmers hand-weeded 45% of their severely infested fields in 2008 (Caulcutt, 2009) and Southeast Farm Press reported that Georgia spent at least US$ 11 million in 2009 to manually remove Palmer amaranth from 1 million acres

(Haire, 2010). Besides Georgia, glyphosate-resistant Palmer amaranth has been confirmed in another 27 U.S. states (Heap, 2021; University of Nebraska CropWatch, 2015). Murphy et al. (2019) observed glyphosate resistance in all populations of *Amaranthus* spp. collected from 51 soybean fields in Ohio. Interestingly, the molecular screening generally underestimated the phenotypically observed resistance. Shimono et al. (2020) report that glyphosate resistant Palmer amaranth has likely been established in Japan via contamination in internationally traded grain commodities.

Amaranthus tuberculatus, the economically next most important GR weed, is found in 18 U.S. states. Both *amaranthus* species are particularly worrisome as they have already evolved resistance to most of the other herbicides used to control them, with some plants having evolved resistances to four or more sites of action. Glyphosate resistant crops were, amongst other reasons, rapidly adopted to control weeds that had evolved resistance to other herbicides, such as ALC-, ACCase- and triazine herbicides. The fact that no new herbicide modes of action have been developed, and only few new chemistries have been introduced, in the past 30 years, makes the increasing number of GR weeds an even more serious problem (Heap and Duke, 2018). Results from a large-scale survey in the Mississippi Delta region of eastern Arkansas demonstrate the prevalence of multiple-herbicide resistance in roadside Palmer amaranth populations. About 89 and 73% of the surveyed populations showed more than 90% survival to pyrithiobac and glyphosate, respectively (Bagavathiannan & Norsworthy, 2016). The development of newer herbicide tolerant GM crops, with resistance to additional herbicides (see Section 6. Industry response), increases concerns regarding the spread of weeds with resistance to multiple herbicides.

Kochia scoparia is the first weed to evolve glyphosate resistance in sugar beet in the western US, where it is one of the most troublesome broadleaf weeds, with low weed densities being able to cause big yield reductions (Kumar et al. 2018). Gaines et al. (2016) describe how widespread adoption of RR sugarbeet systems in the US has resulted in significant glyphosate selection pressure, and increasingly sugarbeet growers are reporting reduced control of *Kochia scoparia* grass with glyphosate. In their study, glyphosate resistance was confirmed in *K. scoparia* populations collected from sugarbeet fields in Colorado, Wyoming, and Nebraska, and Montana. Kumar et al. (2018). confirm glyphosate resistant *K. scoparia* in fields that had for more than 7 years, repeatedly been cultivated with glyphosate tolerant crops (corn-sugar beet rotation) with two to three glyphosate applications per year. The glyphosate resistant kochia populations were 2.0- to 9.6-fold more resistant to glyphosate than the glyphosate susceptible groups of plants (accessions). The authors also point out that with recent evolution of kochia accessions with resistance to multiple herbicides including glyphosate, ALS inhibitors, PS II and dicamba and if glyphosate resistance spreads in sugar beet, *"there will no longer be any herbicides registered for sugar beet that will control this weed"*.

Horseweed (*Conyza canadensis*) shows very high levels of resistance in Ohio and Iowa (40-fold resistance) (Beres et al. 2018a). The resistance level as well as the frequency of GR horseweed is higher in agricultural sites in Iowa and Ohio, compared to non-agricultural sites. Moreover, there does not seem to be a fitness cost related to the glyphosate resistance, including very strong resistance, making it likely that glyphosate resistance will persist in horseweed populations even if selection pressure from exposure to glyphosate were to cease (Beres et al. 2019). A study of glyphosate resistant *Conyza bonariensis* (hairy fleabane), in Brazil, also found it had no fitness penalty, so the glyphosate resistant weeds can persist in the environment and outcompete non-resistant weeds, regardless of further glyphosate selection pressure (Kaspary et al., 2017). Zhang et al. (2022a) conduct a 3-year pot experiment to investigate the agronomic performance of different generation hybrids between genetically modified (GM) glyphosate-tolerant soybean and wild soybeans. They find the presence and absence of EPSPS or the copy number of the EPSPS gene are not significantly correlated with vegetative growth and fecundity. However, they conclude that GM and wild soybean hybrids may have competitive advantages, allowing hybrids to obtain some similar growth characteristics to female wild soybean, such as seed dormancy, a higher stable grain weight, and greater pod and seed numbers per plant. The authors conclude that these growth characteristics could increase the possibility of dispersal of transgenes through seed systems and may adversely affect genetic and species diversity of wild soybean.

Jacobs and Kingwell (2016) use a dynamic simulation model that evaluates the profitability of ryegrass (*Lolium rigidum*) control methods in rainfed mixed enterprise agricultural land-use over 10 years with 7 types of crops and 3 types of pastures, including rotations which include canola (oil seed rape), which is available as a RR crop in Australia. They find that, without harvest weed-seed control, and given a high initial weed seed density, resistance to non-selective hebicides such as glyphosate would reduce farm profit in Western Australia by roughly 37%; with additional harvest weed-seed control, the reduction in profit due to glyphosate resistance would still be around 13%.

Little research has been done on the implications of glyphosate resistance for the other properties of plants. However, Kuester et al. (2017) use a combination of laboratory and greenhouse studies of 32 natural populations of the common agricultural weed, *Ipomoea purpurea*, to show that herbicide-resistant populations self-fertilise more than susceptible populations.

Thus, GR superweeds not only counteract the initial advantages of RR crops on farming practices (like no-till), they also lead to severe economic damage for farmers, that can be attributed to RR crop technology. Nevertheless, the herbicide-centric approach to weed control persists (see Section 6. Industry response). Desquilbet et al. (2019) analyse the current herbicidal 'lock-in' in countries where GM HT crops are grown, showing different barriers to a more sustainable weed management, including changes in farm size, equipment and crop rotation that were triggered by the HT cropping system, which are less suited for ecological weed management and difficult to reverse; a lack of regulation for HT crops; faith in companies offering new solutions; and the lack of incentive for private companies (that conduct a major share of agri-food R&D) to abandon the herbicide-centric approach. In some countries, another factor contributing to 'lock-in' is that the most popular seeds (for example, bred to have higher yields) are released only as GM herbicide-tolerant versions (Benbrook, 2018; Brunharo et al., 2022). Binimelis et al. (2009) and Mortensen et al. (2012) describe the resulting "transgenic treadmill": a spiralling process of the evolution of resistant weeds and the subsequent development of the next generation of transgenic crops, that allow for an intensified use of herbicides and thus favour the emergence of another round of resistant weeds (see also Section 6. Industry response). As Pannell et al. (2017) note, because of the mobility of resistant weeds, the susceptibility of weeds to a specific herbicide is a resource shared in common by all operators in the community. Under such conditions, the collective long-term interest of farmers is to conserve the herbicide's usefulness. Yet, farmers have an individual short-run incentive to use the herbicide without considering effects on resistance because they are unsure their neighbours will reciprocate with sound stewardship. Simulations in the 2015 USDA report on the Economics of Glyphosate Resistance Management in Corn and Soybean Production (Livingston et al., 2015) also show that weed-seed dispersal from a field where crop growers ignore resistance when managing weeds could reduce the returns on nearby fields.

3.1.3 Impact of fertilisers on glyphosate efficacy

The simultaneous application of pesticides with other agrochemicals such as fertilisers, is a common practice that aims to reduce production costs as well as soil compaction since the number of trips made across the fields can be reduced (Bailey et al., 2002). This practice can, however, reduce glyphosate efficacy. Glyphosate is known to act as a chelating agent that forms insoluble, stable complexes with hard-water cations or with cationic nutrients found in fertilisers. Glyphosate was initially even patented as metal chelator (Stauffer Chemical Co, 1964).

Studies of the effects of micronutrients on the herbicidal effectiveness of glyphosate have shown impaired leaf penetration and limited translocation of glyphosate within the plant due to the formation of such stable, insoluble complexes (Eker et al., 2006; Bailey, 2002; Bernards et al., 2005a; Hall et al., 2000). In greenhouse bioassays, Bernards et al. (2005a; b) have found that several manganese (Mn) fertilisers antagonise glyphosate efficacy against different weed species including velvetleaf, giant foxtail and common lambsquarter. The antagonism depended on the glyphosate salt, the weed species treated, as well as upon the Mn formulations applied. The authors estimate that in tank mixtures with either of two fertilisers (Mn-LS and $MnSO_4$), less than 10% of the applied glyphosate entered the plants and moved towards actively growing tissues. Fertilisers that antagonised glyphosate efficacy contained chelates or complexing agents with stability constants lower than glyphosate, such as citric acid or lignin sulfonate for example. This means that glyphosate is the stronger chelator and some fertilisers may lose manganese ions (Mn^{2+}) to glyphosate (Bernards et al., 2005b). On the other hand, fertilisers may even increase glyphosate control if they have a higher chelate stability constant for Mn^{2+} than glyphosate and can bind Mn tightly enough to prevent it from forming a complex with glyphosate.

Glyphosate solutions may exert greater herbicidal activity the more acidic they are. Bailey et al. (2002) found that adding manganese formulations to glyphosate solutions reduced the acidifying effect of glyphosate salts as well as the herbicidal activity against four weeds, common lambsquarter, larger crabgrass, morningglory and smooth pigweed. The antagonism varied depending upon the Mn formulation applied and upon the species treated. The most severe reduction in control was observed with common lambsquarters. The authors suggest that higher glyphosate application rates could restore control in some species.

Thus, the reduced efficacy of glyphosate when combined with fertilisers may be another reason for increased glyphosate use.

Bernards et al. (2005 a; b) and Hall et al. (2000) recommend that certain adjuvants such as ammonium sulphate, that compete with Mn^{2+} for binding sites on the glyphosate molecule, should be added to the tank mixtures to reduced or overcome the antagonism. This method could however not eliminate the antagonism for all fertilisers on all species. The authors further recommend not to use excessive Mn application and that glyphosate and Mn should be applied on separate days.

3.1.4. Impact of climate change on glyphosate efficiency

It is predicted that climate change will significantly impact weed management strategies. Changing environmental conditions, such as precipitation or the rise in concentrations of greenhouse gases in the atmosphere, can affect the physiological and growth processes of weeds. Elevated carbon dioxide (CO_2) can, for example, enhance growth, biomass and yield of crop plant as well as weeds, through greater carbon availability and increases in photosynthesis and water use efficiency, respectively (Cowie et al., 2020; Mollaee et al., 2020). Changing environmental conditions can also affect weed response to herbicides. A recent study suggests that increasing atmospheric CO_2 levels reduce the efficacy of glyphosate against the invasive weed *Parthenium hysterophorus* (Cowie et al, 2020). Mollaee et al. (2020) find water-stress to decrease glyphosate efficacy against both glyphosate resistant and susceptible *Echinochloa colona*. The authors suggest that increased vegetative growth due to rising CO_2 levels, combined with water stress, may decrease herbicide uptake, absorption and translocation and ultimately decrease herbicide efficacy. Using high doses of glyphosate in these conditions may, however, increase the risk of resistance evolution. Further studies need to be conducted to understand whether rising CO_2 levels and water stress generally reduce herbicide efficacy against different weeds and how other climate change factors such as radiation or temperature influence herbicide efficiency.

3.1.5. Seed prices, patents and corporate control

To fully reflect the costs associated with RR crop technology, the increasing costs for herbicides noted above have to be added to the increasing costs for RR seeds. The development of a GM trait was estimated to cost about $136 million in 2011 (Phillips McDougall, 2011) and thus much more than a similar conventional trait that cost about $1 million in 2002 (Goodman, 2002). It makes sense that the industry wants a reward for its investment. The introduction of GM crops created the possibility of claiming intellectual property rights for crop varieties, the most restrictive of which is the patent. This development further triggered the enormous market concentration that we observe in the seed sector (Howard, 2009), with only three companies (Monsanto, DuPont and Syngenta) owning more than 50% of the commercial seeds market by 2013 (ETC Group, 2013). The US company Monsanto was the market leader in GM crops until it was bought by Bayer in 2018. The other major companies involved are now Corteva Agriscience (formed from the agricultural parts of DuPont, Dow and Pioneer and spun out as a separate company in 2019), BASF and Syngenta (Real Money, 2016). A takeover of Syngenta by China National Chemical Corp. (ChemChina) occurred in 2017. Thus, Syngenta, Bayer Crop Science, BASF and Corteva were the top four global agrochemical firms in 2020 (Yuan, 2021).

Clapp (2021) describes the problem with growing corporate concentration and power in the global food system, detailing how concentrated firms can shape markets, shape technology and innovation agendas, and shape policy and governance frameworks. She describes how just four large firms (Bayer, Corteva, ChemChina-Syngenta, and BASF), which control around 70% of the global pesticides market and 60% of the global seed market, can exert power within the global food system, both directly and indirectly. This allows these powerful firms to shape the policy agenda (spending significant sums on lobbying and PR) and also influence technology and innovation pathways, with a particular focus on genetically modified seed and agrochemical packages (selling both the herbicide-tolerant GM crop and the associated herbicide). Vanloqueren & Baret (2009) describe how this leads to research and innovation systems that develop genetic engineering but lock out alternatives, such as agroecological innovations. Because these seed companies have such control over the market, they typically release some seeds only as GM herbicide-tolerant versions in countries growing GM crops, restricting farmer choice (Benbrook, 2018; Brunharo et al., 2022). In Brazil, in 2010, Monsanto introduced an 85/15 rule, which allowed farmers to buy only 15% non-GM seeds, while the other 85% had to be GM seeds (E.O.S. Intelligence, 2016).

In a highly concentrated market, competition does not regulate price and can thus lead to an increase in seed prices. In the U.S., seed prices rose rapidly since the introduction of GM crops. According to Zilberman et al. (2010), overall seed prices in the U.S. had risen by 140% compared to 1994. Soybean seed prices in the U.S. rose about 63% in the 25 years from 1975 to 2000 and over 200% in the subsequent 12 years (Benbrook, 2012b). In 2010, a bushel of RR soybean seed was 47% more expensive than a bushel of conventional soybean seed (Benbrook, 2012a). Gaitán-Cremaschi et al. (2015) report a higher price for GM soybean seeds than for non-GM soybean seeds in Brazil. For corn (maize), GM corn seed is more expensive than non-GM corn seed and its price increases at a faster rate than the price of non-GM corn seed. Between 1996 and 2005, the price of GM corn seed varieties doubled (Benbrook 2012b). In 2010, GM corn seed cost about twice as much than non-GM corn seed (Benbrook, 2012a). Moreover, biotech companies have implemented a 'technology' or 'trait fee', that is charged in addition to basic seed costs. This trait fee rose from $4.50 per bag in 1996 to $17.50 in 2008 (Hubbard, 2009). Royte (2013) reports that the ratio between GM and non-GM seed prices might even be distorted in that non-GM seed prices are artificially elevated by large seed companies to encourage farmers to continue buying GM crops.

In Brazil, trait fees for GM seeds are not collected from individual farmers: a royalty system is used instead. In the mid-2000s, Monsanto implemented a nationwide private mechanism of royalty collection for RR soybeans that virtually eliminated the right to freely save seeds for those growing RR varieties (Filomeno, 2013). Since the implementation of the system, soy growers using RR seeds have had to make payments to seed companies twice. First, when they purchase the seeds, they pay a royalty implied in the price of each bag. Second, when rural producers sell the harvest that originated from the cultivation of those seeds, they pay royalties corresponding to RR technology. This payment, which can also be made in advance, is regulated by the Law of Industrial Property and is based on Monsanto's patents in Brazil. The soy grower can declare his or her harvests are free of RR soybeans, but if their presence is detected by tests applied during the harvest sale, a fine will be charged. A royalty system also applies in Paraguay. Conflicts regularly emerge over Monsanto's attempts to charge royalties on RR soybeans throughout South America (e.g. Reuters, 2015b; Buenos Aires Herald, 2016; Peschard, 2019).

Afidchao et al. (2014) report seed costs in the Philippines for RR maize of US $354.51 per hectare, compared to US $262.84 per hectare for conventional maize, meaning a 35% premium for the GM variety.

The increase in seed price is not compensated by rising prices for crops. Between 1994 and 2010 overall crop seed prices more than doubled relative to market prices farmers received for their agricultural commodities (Fuglie et al., 2011). Soybean seed to soybean market price ratio was 2.02 in 1995 before the commercialisation of RR soybeans and thus consistent with the historic norm. In 2005 it was 6.1 for GM soybeans and 3.4 for non-GM soybeans. Although farmers are supposed to be compensated for higher seed prices and/or royalty fees by lower costs of production, these short-term benefits are eroded over time as resistant weeds develop (see Section 3.1.2. Superweeds). For example, in cotton grown in the USA, Nichols (2018) reports that "*the costs of weed control in tillage, trait costs, increased herbicide use, and hand weeding have greatly increased with respect to those of 10 years ago*". Furthermore, the so-called transgenic treadmill locks farmers into escalating costs as they are trapped into buying ever more expensive seeds and weed control options (Binimelis et al., 2009; Mortensen et al., 2012). In her anthropological studies of Canadian farmers, Müller (2021) describes glyphosate as "*like an entry drug to chemical dependency*", based on a series of simplifications promoted by a handful of transnational corporations as an easy solution for complex problems.

Another consequence of GM seeds and the affiliated strict intellectual property (IP) instruments is that they prevent farmers from exercising their customary habit of seed saving (Mascarenhas & Busch, 2006). Instead, they have to purchase new seed every year from the biotech companies. This additionally results in higher costs for seed. Although not all non-GM seeds can be saved (hybrid seeds do not breed true), seed saving still plays an important role for many farmers. Monsanto (now owned by Bayer) has tried to obtain recognition and protection for IP rights on the RR technology around the world. Unlike hybrid maize, soy can reproduce through self-fertilization, and its seeds retain their agronomic qualities from one generation to another. This allows rural producers to save soybean seeds for future cultivation, which Monsanto regards as a breach of its intellectual property rights (Filomeno, 2013). In Argentina, the corporation has unsuccessfully tried to obtain recognition for the IP rights it claims to have over RR soybeans: seed saving is allowed and Monsanto was refused a patent in 2019 (Fries et al., 2019). However, Monsanto's patents are strictly enforced in the USA and the company threatens to sue farmers it suspects of saving GM seeds (EcoWatch, 2012). Such lawsuits continue to this day (Carignan, 2021).

3.2. Impact of RR crops on yield

The majority of farmers adopted GM crops to increase their yield. However, studies about yield differences between GM and non-GM crop varieties have been controversial, with some studies finding that GM crops increase, decrease or have the same yield compared non-GM varieties (see for example Fernandez-Cornejo et al., 2006; Gurian-Sherman, 2009 and Zilberman, 2010). These differences in study results can have several causes. On the one hand, they could result from different background genetics rather than the transgene. If high-yielding GM crops are compared with average-yielding non-GM crops or vice versa, this would bias the results. And it is very difficult to separate the yield effect from the crop variety that the genes are inserted into from the effects of the transgene. Therefore, background genetics between the GM and non-GM varieties should be as identical as possible. On the other hand, study results depend on the definition of 'yield'. Herbicide tolerant crops are designed to reduce crop losses in the presence of weeds, to approach the highest possible yield that the genetics of the crop allow when grown under ideal conditions (this is known as 'potential yield'). This means they ideally would increase the actual yield (i.e. the potential yield minus pest damage) but not the potential yield itself (Gurian-Sherman, 2009). There are no GM crops available today that increase the yield potential of a hybrid variety (Fernandez-

Cornejo et al., 2006; Gurian-Sherman, 2009) and the value of GM traits depends on pest pressure (Nolan & Santos, 2012). This was also experimentally shown by Bruns (2014) who found no decisive yield or economic benefit of multiple trait GM crops compared to non-GM crops in the absence of pest pressure. In addition, with the development of herbicide resistant weeds, the actual yield of RR crops is also declining. For example, Norsworthy et al. (2014) (as discussed in Section 3.1.2.3 Economic damage caused by GR weeds) showed clearly how fast GR weeds can spread and lead to complete crop failure. A modelling study conducted by Nolan & Santos (2012), using 163,941 experimental field studies conducted between 1997 and 2009 in the most important maize producing U.S. states, reported a positive impact of GM traits on corn yield. But this effect on the one hand could only explain about 25% of the yield increase in corn during this time (Gurian-Sherman, 2013) and on the other hand only concerned GM pest resistant (Bt) crops and stacked trait varieties. For single herbicide tolerant traits no yield benefit was found (Nolan & Santos, 2012). Shi et al. (2013) addressed the same question, using field studies that have been conducted in the U.S. state of Wisconsin from 1990-2010. They were surprised not to find strong positive transgenic yield effects. For RR maize, the average yield was even lower than for conventional maize.

A global meta-analysis of studies by Areal et al. (2013) reports no significant differences in yields between RR and conventional crops. In Brazil, only minor differences in RR and conventional soybean yield are reported by Bohm et al. (2014); and Hungria et al. (2014) find that yield parameters were more affected by location, cropping season and cultivar than by the transgene, herbicides, or weed-management strategy.

In 2009, the Union of Concerned Scientists (UCS) published a report evaluating the yield effects of GM crops after 20 years of research and 13 years of commercialisation. They found that herbicide tolerant crops failed to increase actual crop yields (Gurian-Sherman, 2009). They attributed the recorded increase of crop yields over the last 15 years mainly to traditional breeding, improvements of agricultural practices and more extensive crop rotations that not only include soybeans and corn but many other crops as well. Similarly, Brian Rossnagel, a retired oat and barley breeder from the University of Saskatchewan, stated that the big increase in corn yields was primarily due to improved plant architecture, such as upright plant growth, that is achieved by conventional plant breeding and not GM technology (Pratt, 2014a). A study comparing different RR, multiple trait GM and non-GM corn crops found that environmental parameters such as early season drought or reduced solar radiation at critical growth stages had also a much bigger influence on yield than the type of hybrids used (Bruns, 2014). According to agronomic and soils specialist Dr Heather Darby from the University of Vermont, RR corn had no effect on yield in a cropping system field trial with GM and non-GM corn varieties. The non-GM varieties performed as well or even better than the GM varieties. More important for production and yields were good rotation and soil management (Roseboro, 2015a).

Schütte et al. (2017) note that the actual yield reduction in Roundup Ready soybean observed in some studies cited by Gurian-Sherman (2009) might be due to several causes: (i) the present resistance gene in the first generation of Roundup Ready line (40-3-2) and (ii) reduced nodular nitrogen fixation upon glyphosate application and/or a weaker defence response. They note that the second generation RR2Y soybean (MON 89788) was introduced to provide better yields, but when tested in the greenhouse, different cultivars of RR2Y performed less well than RR 40-3-2 (Zobiole, 2010d).

When looking at USDA NASS (National Agricultural Statistics Service Information) data, it becomes evident that crop yields in the U.S. have been continuously increasing since long before the commercialization of genetically engineered crops and that the commercialisation of GM crops in the mid-1990s has not led to an obvious leap in yield increase (Figure 7). Moreover, wheat yields, for which there are no commercialised transgenic crops, increased by the same magnitude as soybean yield since 1930 (Figure 8.). Gurian-Sherman (2013), estimated that 86% of the total increase in yield in corn from 1996 to 2008 reported by the USDA was due to other factors than GM, such as crop breeding and improved agronomy.

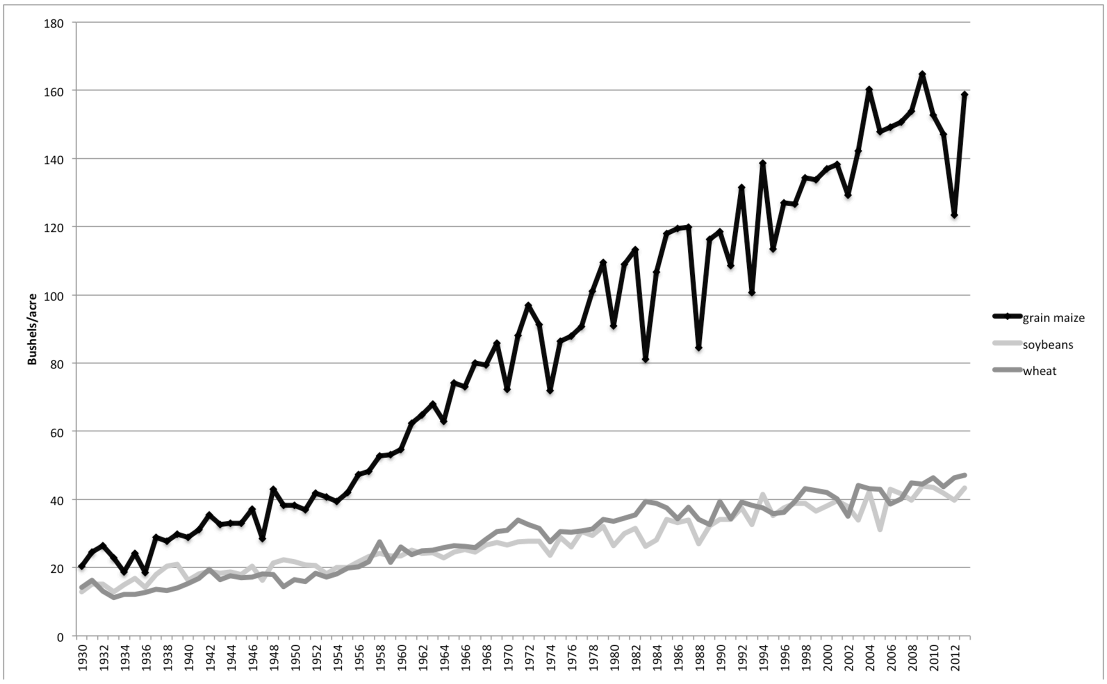

Figure 8. Grain maize, soybean and wheat crop yield started to increase continuously decades before the introduction of genetically modified crops. Source: USDA NASS Statistics by Subject: http://www.nass.usda.gov/Statistics_by_Subject/index.php?sector=CROPS.

A study that compared maize, rapeseed and wheat yield data from North America and Western Europe found that Western Europe, where to date no herbicide tolerant crops are grown, had a greater yield increase between 1961 and 2010 than North America for all three species and had an overall higher yield of rapeseed and wheat. Maize yields were similar or even slightly higher in Europe in recent years, according to the authors (Heinemann et al., 2014a). In an article published later that year, Heinemann et al. (2014b) further included newly published maize yield data. They revealed that in 2011 and 2012 maize yields in Western Europe were higher compared to those in the U.S., thereby confirming and further pronouncing the trend observed by Heinemann et al. (2014a). Similarly, Hilbeck et al. (2013) reported that maize yields in European non-adopting countries (Austria, France, Germany, Netherlands and Switzerland) had been similar and even slightly higher than maize yields in Spain (where a small amount of GM Bt maize is grown) and the USA. Despite the introduction of GMOs in North America, yield benefits did not exceed those of Western Europe in either absolute number or in their yield growth per year, also indicating that conventional breeding methods are more efficient than genetic engineering at increasing yield.

Rizzo et al. (2022) conclude that climate and agronomy, not genetics, underpin recent maize yield gains in favorable environments. They analyse an extensive database collected from the largest irrigated maize production domain in the world located in Nebraska (United States) from 2005 to 2018. In this study, 48% of the yield gain was associated with a decadal climate trend, 39% with agronomic changes, and only 13% with improvement in genetic yield potential. Agronomic changes that appeared to increase yields included increased seeding rates and greater use of fertilizer, fungicide and insecticide, and more use of maize-soybean rotations. A small yield penalty was associated with the use of conservation tillage (see 4.6. Can RR crops help to mitigate climate change?). Genetic yield potential in this study includes the use of new (conventionally bred) maize hybrids as well as GM traits (which include insect-resistant traits, as well as herbicide-tolerance). The authors highlight that this finding is consistent with the view that yield gains become more difficult to achieve in cropping systems in which average farm yield is near yield potential, as is the case for irrigated maize in the United States. They conclude, "*Our study shows that previous predictions of sharp increases in maize yield potential (2 to 3.6% p.a.) with the advent of* *biotechnology and molecular techniques have fallen short of reality… Indeed, we found the rate of genetic gain in maize yield potential to be less than a third of the yield gain due to management (0.17 versus 0.51% p.a.), suggesting that the rate of yield increase of maize grown in favorable environments will slow markedly over coming decades*." These authors suggest that opportunities to increase yields on existing farmland in irrigated and favorable rainfed environments will more likely come from increased cropping intensity (more crops per year) rather than higher yields per crop.

3.2.1. Impact of glyphosate on plant health and crop productivity

Glyphosate controls weeds by disrupting the enzyme 5-Enolpyruvylshikimat-3-phosphate-Synthase (EPSPS), a key enzyme of the shikimate pathway. RR crops are genetically modified to produce glyphosate-insensitive EPSPS so they survive glyphosate treatment. However, several reports show higher incidence of many soil-borne diseases in RR crops upon glyphosate treatment, as well as a decrease in plant nutrient content and photosynthetic parameters, with effects on plant biomass. This may subsequently impact plant health and rises concerns regarding the impact of glyphosate on crop productivity and the economic benefit of the RR cropping system. Freitas-Silva et al. (2022) review evidence showing that indirect effects of glyphosate-based herbicides (GBHs) on plant physiology can also lead to plant death and conclude that GBHs promote plant death not only through EPSPS inhibition but also through other biochemical, physiological, and structural changes.

Several studies show that glyphosate alters rhizosphere microbial communities, shifting the balance of beneficial and detrimental plant-associated microorganisms. Positive impacts on certain plant pathogens such as *Fusarium spp.* that cause disease in many crops, are frequently reported. The effect might be increased by the negative impact of glyphosate on some beneficial soil micro-organisms such as *Fluorescent Pseudomonas* that antagonise pathogens (see Section 4.5. Impact on soil microbial communities). According to Sanogo et al. (2000), supressed plant defence and enhanced disease susceptibility caused by glyphosate reduces the benefit of herbicide tolerance. As a response, Monsanto enhanced the second generation of RR soy with a proprietary fungicide coating. Such measures can however lead to a chemical treadmill, which is costly to farmers.

A change in the soil microbial community composition can also change soil nutrient dynamics and cause nutrient deficiencies in plants. Different studies have shown that glyphosate reduces the ratio of manganese (Mn) reducers to Mn oxidisers upon release in the rhizosphere (see Section 4.5. Impact on soil microbial communities). This suggests that soil Mn is immobilised by glyphosate and not available for plant uptake and active defence reactions, which potentially detrimentally affects plant growth. Glyphosate has also been shown to exert toxic effects on nitrogen-fixing organisms in the rhizosphere (see Section 4.5.1. Impact on bacterial communities and beneficial fungi). Several studies indeed suggest that glyphosate at label use rate reduces nodulation in soybeans (Zobiole et al. 2012). King et al. (2001) found a negative impact of glyphosate application on growth, nitrogen (N_2) accumulation and N_2 fixation of different RR soybean cultivars. Early application of glyphosate decreased shoot biomass and nitrogen accumulation in both roots and shoots at day 19 after emergence. By day 40 plants had however recovered. Continuous application of glyphosate between days 19 and 40 prevented this recovery and also affected root growth in some cultivars. Biomass and nitrogen content were also decreased when RR soybeans were grown with available soil nitrogen. N_2 fixation was more sensitive to water deficits in glyphosate-treated plants compared to untreated plants. Data also suggests that RR soybeans treated with glyphosate have smaller nodules but a similar total nodule mass as non-treated RR soybeans due to an increased number of nodules. This is in contrast to the study of Zobiole et al. (2012), where glyphosate application significantly decreased not only nodule mass but also nodule number.

Bellaloui et al. (2008) study the effect of glyphosate application on the nitrogen metabolism and seed composition in RR soybeans in a two-year field experiment. They find a significant effect of glyphosate application on nitrogen assimilation and seed composition. For soil nitrate to be used by plants, it has to be reduced to nitrite. This is done by the enzyme nitrate reductase. After a first application of glyphosate, nitrate reductase activity in leaves, roots and nodules of the soybeans decreased compared to untreated plants, probably because of a reduced or limited nitrate uptake by the roots and subsequent translocation to the shoots. A second application of glyphosate, resulted in a significant decrease of the nitrate reductase activity in the leaves and nodules but a significant increase in the roots up to full potential. The authors suggest this was probably to compensate for the previous reduction in leaves and nodules. Glyphosate application at a higher rate than suggested, representing a "worst case scenario", further resulted in a higher protein percentage, a higher oleic acid percentage and a lower linolenic acid percentage compared with the non-treated soybean. The increase in protein percentage may be a result of the nitrate translocation from root to leaves, the main site of nitrogen assimilation. The changed oil percentages may suggest a possible alteration to carbon metabolism namely a reduction in photosynthesis and carbon substrate availability due to the glyphosate application. They conclude that glyphosate application may alter nitrogen and carbon metabolism. Johal and Huber (2009) suggest that regular inoculation of legume crops with nitrogen-fixing organisms may be required for maximal productivity where glyphosate applications have eliminated them from the soil.

Moreover, the stable, insoluble complexes between glyphosate and cationic nutrients not only antagonise glyphosate efficacy but also plant uptake and translocation of essential minerals (Eker et al., 2006). This is problematic because micronutrients can activate or inhibit many critical physiological functions and are essential for many metabolic pathways. A change or reduction in availability of micronutrients can greatly affect plant growth and also resistance to diseases and pests.

Studying the effects of spraying sublethal doses of glyphosate on sunflowers, Eker et al. (2006) showed that glyphosate treatment decreased uptake, translocation and accumulation of iron (Fe) and manganese (Mn) in sunflower plants. In one experiment Fe concentration in non-treated leaves was almost 3-fold higher than in treated leaves. The authors concluded that the formation of poorly soluble glyphosate-metal complexes is possibly the main factor for the antagonism between glyphosate and cationic micronutrients. Glyphosate that is transported to the roots upon spraying may form immobile complexes with essential metal nutrients and consequently impair translocation to the leaves. And glyphosate that leaks into the soil solution may accordingly impair root uptake of those nutrients. Impaired nutrient uptake and translocation can have negative impacts on plant health and growth.

This antagonistic effect of glyphosate on micronutrient uptake and plant growth was also demonstrated in RR crops tolerant to glyphosate. Bott et al. (2008) showed that glyphosate decreased the Mn concentration and total Mn in RR soybean leaves by approximately 50-60%. Glyphosate further significantly reduced root dry matter production of a RR soybean in a hydroponic experiment with sufficient Mn supply. A similar trend was also observed with low Mn supply and for shoot biomass of glyphosate treated soybeans, although the differences were not significant. Glyphosate further reduced root length by approximately 30% and the number of root tips. In an experiment in soil culture, glyphosate significantly reduced the concentration of zinc (Zn) in young RR soybean leaves depending on the soil.

Zobiole et al. (2010b; 2010c; 2012) found glyphosate not only to decrease micronutrient- but also macronutrient content in RR soybean leaf tissues. In the study of Zobiole et al. (2010b), there were however differences in reduction between the RR cultivars, with the early maturity crop being most affected. Interestingly, the concentration of shoot macro- and micronutrients was also decreased in the RR soybeans not treated with glyphosate, compared to their respective non-RR parental lines, suggesting that the RR gene itself also reduces the plant's nutrient efficiency. Application of glyphosate had an additive negative impact on nutrient accumulation. In the study of Zobiole et al. (2012), macro- and micronutrient content was proportionally reduced with increasing rates of glyphosate. However, except for copper, nutrient concentrations were within the nutrient-sufficiency ranges for soybeans. Zobiole et al. further observed glyphosate to reduce photosynthetic parameters such as photosynthetic rate, stomatal conductance and transpiration rate (Zobiole et al., 2010a; b; c; 2012). Photosynthetic rate was more reduced with increasing rates of glyphosate (Zobiole et al., 2010a). One reason for the observed reduction in photosynthetic parameters could be the observed reduction in essential micronutrients, such as Mn, by glyphosate. Since the chloroplast is sensitive to Mn deficiency for example, a decrease in essential micronutrients might affect the chloroplast and hence photosynthesis. Another reason might be that accumulation of one of the main metabolites of glyphosate, AMPA, in the glyphosate treated plants may cause plant injury and chlorosis (Zobiole 2010b; c). Since plant injury also occurred several weeks after herbicide application, the authors suggest that either glyphosate or AMPA exert long-term effects on plant physiology. Zobiole et al. (2010a; b; c; 2011) further found glyphosate to reduce shoot and root biomass of RR soybeans. The effect increased with increasing glyphosate rates (Zobiole et al., 2011). Zobiole et al. (2010b; c; 2012) suggest that the additive effect of decreased photosynthetic parameters and the lower nutrient concentration may cause the reduced plant biomass. Zobiole et al. (2011) further suggested that glyphosate-based suppression of plant growth promoting bacteria contributes to the decreased biomass. According to Zobiole et al. (2012) a decrease in dry biomass could also mean a decrease in the production of grain, since dry biomass and grain yield are closely linked for soybean crops. Zobiole et al. (2010b) suggest that the reduced nutrient efficiency of RR crops needs to be considered for fertiliser recommendations. According to Zobiole et al. (2012), even higher levels of nutrients may be required to achieve physiological sufficiency in RR soybeans upon glyphosate treatment.

Krenchinski et al. (2017) investigate reports of visual injuries to RR soybeans after glyphosate application. In greenhouse experiments, they find a significant linear decline in the chlorophyll index with rising glyphosate dose for all four Intacta RR2 soybean cultivars tested. However, they find that, in general, RR2 soybeans have the ability to recover from visual intoxication injuries and reestablish the normal chlorophyll production and photosynthetic parameters after glyphosate application.

Bomfim et al. (2017) observe that the application of glyphosate in RR soybeans moderately affects nitrogen fixation and assimilation.

Helander et al. (2019) find that glyphosate residues in soil affect crop plant germination and growth. They study the effects of the glyphosate-based herbicide (GBH) Roundup Gold, and of pure glyphosate. The seed germination of faba bean, oat and turnip rape, and sprouting of potato tubers was delayed in the greenhouse experiments. However, total shoot biomass varied between greenhouse and field experiments. Potato tubers tended to accumulate low amounts of glyphosate (0.02 mg/kg) and its metabolite AMPA (0.07 mg/kg). In addition, grazing by barnacle geese was three times higher in oats growing in the GBH soils compared to control oats in the field.

Fan et al. (2017) also report that glyphosate appears to exert stress on the glyphosate-resistant (GR) soybean cultivar used in their greenhouse experiments. In these experiments, glyphosate-treated GR soybean had lower chlorophyll content, root mass, nodule mass, total plant nitrogen, and nitrogenase activity than the untreated conventional cultivar, and glyphosate also inhibited the growth of rhizobia isolated from root nodules.

Soares et al. (2019) evaluate oxidative damage and antioxidant responses in tomato plants grown for 28 days under different concentrations of a commercial formulation of GLY (Roundup® UltraMax) - 0, 10, 20 and 30 mg kg^{-1} soil. The exposure of plants to increasing concentrations of GLY caused a severe inhibition of growth (root and shoot elongation and fresh weight), especially in the highest treatments. The evaluation of the antioxidant system showed that GLY interfered with several antioxidant metabolites and enzyme activities. The authors conclude that soil contamination with glyphosate, applied as part of its commercial formulation Roundup® UltraMax, impairs the growth and physiological performance of tomato plants, and likely of other non-target plant species, after 28 days of exposure.

Fuchs et al. (2022) seek to determine the effect of GBH residues in soil on phytohormone pools of three different crop species (oat, potato and strawberry). They argue that central role of phytohormones in regulating plant growth and responses to abiotic and biotic environment has been ignored in studies examining the effects of glyphosate residues on plant performance and trophic interactions. They find that residues of GBH in soil modulate plant hormonal homeostasis, plant size and herbivore damage, with results that vary among crop species.

3.3. Profitability of marketing RR crops versus non-GM crops

In addition to production costs and yield it is crucial for farmers to be able to sell their products for a good price. However, some uncertainties exist regarding the marketing of RR crops, such as different and changing policies regarding GM crops from country to country and increasing demand for non-GM seeds and foods.

3.3.1. Effects of different and changing policies regarding GM crops on RR crop marketing

Detected unauthorised GM seeds or the presence of an unauthorised GMO in food or feed can be a reason to either recall products or reject imports at national borders (Price & Cotter, 2014). Issues of GM contamination can lead to expensive rejections of shipments, or product recalls, particularly if some markets have not authorised a particular GM crop, or if crops labelled as non-GMO or as organic crops command higher prices. Examples of GM contamination incidents and the associated costs are given in Section 3.4.2. Consequences of GM contamination.

3.3.2. Effects of the increasing demand for non-GM seeds and foods on RR crop marketing

Farmers worldwide need to consider the increasing demand for non-GM ingredients. Although predictions vary, significant market growth is forecast by all analysts. According to Mordor Intelligence (n.d.), the non-GMO foods market is projected to witness a compound annual growth rate (CAGR) of 9% during the forecast period 2020 to 2025. According to a Grand View Research (2019), the global non-GMO food market size is expected to reach USD 2.76 billion by 2025 registering a CAGR of 16.5%. According to Fortune Business Insights (2022), the global non-GMO food market is projected to grow from USD 623.96 billion in 2021 to USD 1,231.13 billion in 2028 at a CAGR of 10.20% in the forecast period. Driving factors are reported to include a significant increase in certified non-GMO producers (to augment market share), and rising investment.

The current market for non-GM soybean in the EU is relatively high compared with other parts of the world and considered more than a niche market. For example, the fast-food chain, McDonalds, abandoned GM soy in their products in France in 2015 (Smagghe, 2015). In 2015, about 8.3% and 11.3% of the soybean and soybean meal imported by 14 EU countries that together account for 91% of the total soybean and soybean meal imports in the EU, was segregated as non-GM according to a report by the European Commission's Joint Research Centre, (Tillie & Rodríguez-Cerezo, 2015). Despite the higher price, demand for GM-free soya is high (Hungary Today, 2015). The situation is however very mixed between EU member states. While in some countries like Poland and Portugal, the demand for non-GM soy is virtually non-existent, others like Hungary and Sweden import exclusively non-GM soy from outside the EU (Tillie & Rodríguez-Cerezo, 2015). In Hungary, the government provides subsidies to promote GM-free soya production (Hungary Today, 2015). The Danube Soya Association aims to increase Europe's self-supply with GM-free protein and counts an increasing area planted to GM-free soya in the Danube region. In June 2015, Europe's biggest soy producer, the Ukraine, signed the Danube Soya Declaration (Donau Soja, 2015a; b). Europe also imports a lot of non-GM canola from Australia, which pays Australian farmers on average $40 a tonne more than GM canola (Gribbin, 2013). Such price premiums for non-GM crops reflect the preference of European consumers for non-GM products (Gaitán-Cremaschi et al., 2015) and are a clear incentive for farmers to produce GM-free crops. Fortune Business Insights (2022) notes that Europe is one of the leading customers of GM-free food and this is forecast to continue to grow.

Although GM foods are required to be labelled in the EU (and hence consumers reject them), meat and dairy products from GM-fed animals are not required to be labelled (see Section 5.2. Consumers' reluctance to eat GM crops). To address this issue with animal products, retailers and food manufacturers in Germany can make use of the "GMO-free"-seal, issued by the industry association VLOG. To use the label, retailers have to ensure that all ingredients, including pharmaceuticals and feed supplements are GMO-free and provide an appropriate certification from suppliers. With a growing demand for GM-free products, this effort is certainly worthwhile. Similar labels exist in some other European countries (Michail, 2015). In Germany, there is a continuing shift towards non-GM material in animal feed. In 2015, Germany's largest dairy company decided to transition to GM-free feeding of their dairy cows and TÖNNIES Holding, Germany's largest pork marketer, began to convert to non-GM soybean meal. Moreover, the vast majority of retailers demand more GM-free raw materials for their private label products (Breloh et al., 2015). Demand for non-GM soybean meal has also increased in other European markets such as France, Austria, Switzerland, Hungary, Italy or the Scandinavian region (Breloh et al., 2015; Byrne, 2015). A 2016 report in Germany highlighted the ability to secure increased supplies of non-GM feed from Brazil, provided the food retail sector is willing to pay the higher costs for segregation (VLOG, 2016). By 2021, around 60-70% of all milk egg, poultry and meat production in Germany was certified according to the VLOG standard (Southey, 2021). Consumers spent around 13.2 billion euros on "Ohne Gentechnik" (Non-GMO) products in Germany in 2021, 4.3 percent more than in the previous year (VLOG, 2022a).

In Brazil, ProTerra certification requires soybeans to be non-GM and ensures that farms practice sustainable use of soil, pesticides, and water and do not convert native forests or other high conservation value areas (HCVAs) to cropland. More specifically, soybeans may not be grown on HCVA land that was cleared after 2004. This standard requires certified products to be segregated and traceable from farm to fork. Compliance with the ProTerra standard is evaluated according to a uniform certification protocol, by a third-party (independent) certification body that is accredited according to ISO/IEC standards. The premium for ProTerra certified soybeans is roughly $4 per ton, which is added to the standard premium for non-GM soybeans (Garrett et al., 2013). Brazil has increased its import share faster in countries with a strong non-GM preference versus other countries. This is explained statistically by Brazil's level of non-GM soybean production rather than by changes in prices. More specifically, Garrett et al. (2013) find that the Netherlands, Italy, Spain, and Belgium increased imports from Brazil and simultaneously decreased imports from the United States, even as Brazil's currency increased in value in the late 2000s, which should have made Brazilian soybean producers less competitive than their North American counterparts on a pure cost basis. The non-significant finding for direct imports from Brazil to Germany is likely related to the large amount of non-GM soybeans that Germany imports indirectly via the Netherlands: and similarly, Japan also imports non-GM soybeans from China. Brazil produced the majority of the globally certified non-GM soybeans in 2012: 4.3 million tons, while India, China, the US and Canada together provided less than 2 million tons. Approximately 79% of Brazil's certified non-GM soybeans were also certified under ProTerra standards for environmental and social responsibility. The advanced soybean supply chains of central Brazil are well illustrated by the case of the Brazilian soybean agribusiness giant Grupo Andre Maggi, which produces non-GM soybeans certified by the ProTerra Foundation, has continued to produce non-GM soybeans on its farms and has maintained private ports specialized in non-GM soybeans. These ports, located in Itacoatiara, Amazonas and Porto Velho, Rondônia, allow for a direct shipping route to Europe through the Amazon river. This vertically integrated export pathway not only prevents GM contamination, but also reduces the costs of segregation and aids traceability. In contrast, other South American countries that did not develop segregated supply chains for non-GM soybeans now face smaller opportunities to access non-GM markets. Fortune Business Insights (2022) reports that the South

American non-GMO food market continues to grow (retail sales were around USD 30.5 billion in 2020, and are projected to grow to USD 61.81 billion in 2028), with Brazil expected to have the biggest market. According to figures from Brazil's Instituto Soja Livre (ISL), Brazil plans to increase non-GMO soybean acreage by 24 percent for the 2022/23 crop to meet demand from Europe (VLOG, 2022b).

In the U.S., farmers are also increasingly demanding non-GM and organic seed. Among US farmers, interest in growing non-GM varieties reportedly started increasing around 2012, with seed companies reporting strong demand for non-GM seed sales and some even reporting they had sold out of non-GM seeds due to the rapidly increasing demand (Bunge, 2015; Roseboro, 2015b). eMerge Genetics' non-GM soybean and corn (maize) seed sales for example tripled from 2012 to 2015 (Doering, 2015). One reason is the continuous and accelerating growth of the non-GM and organic food market due to consumer demands. In 2014, non-GM food products were among the fastest growing U.S. food segments. According to Packaged Facts, non-GM foods and beverages generated $200 billion in sales in the U.S. in 2014 (Heneghan, 2015; Packaged Facts, 2015). Retail sales of products verified by the Non-GMO Project rose dramatically from $248.8 million in 2010 to $8.5 billion in 2014 and 13.5 billion in 2015, with sales now over $26 billion (Non-GMO Project, 2014; 2015; 2022). The Wall Street Journal reported an almost 30% increase of sales of food that is labelled as "non-GM" in 2013 (Case, 2014). Data from the Natural Marketing Institute shows that use of food labelled as non-GM rose to 59% of the general U.S. population in 2014, which was up from 53% the year before and 37% in 2012. GM-free product launches in the U.S. also rose, from 551 in 2012 to 1992 in 2014 (Gelski, 2015). Moreover, sales of organic food in the U.S., that is certified as free of synthetic chemicals or genetic engineering, increased 11% from 2013, reaching $35.9 billion in 2014, which accounts for about 5 percent of U.S. grocery spending (Bjerga, 2015; OTA, 2015). According to Packaged Facts, the U.S. organic food market tripled from 2005 to 2015 (Heneghan, 2015; Packaged Facts, 2015). Fortune Business Insights (2022) reports that North America is projected to dominate the global market in terms of revenue from GMO-free foods, supported by increasing resistance by consumers to GM foods.

Due to consumer demand, U.S. food companies and retailers increasingly provide voluntary consumer information about the presence of GMOs in their food products. In January 2016, Campbell Soup Co. announced it would cite GMOs on its packaging and advocates for labelling all food products and beverages regulated (Gasparro, 2016). Some companies are abandoning single GMO products or ingredients, others are committed to become totally GM-free. Whole Foods Market for example commits to full GMO transparency. In 2013, it stated that by 2018, all products sold in its U.S. and Canadian stores would be labelled to indicate if they contain genetically modified ingredients (Whole Foods Market, 2013). Also in 2013, the retailer Target introduced its new brand Simply Balanced, aiming to eliminate all GMOs by the end of 2014 (Renter, 2013). General Mills removed GMO ingredients from its original cheerios, Post from Grape Nuts (Lindholm, 2014), Abbott offers a GM-free version of its commercial baby formula Similac Advance (Strom, 2015), Ben & Jerry's removed all GM ingredients from its ice-cream (Lindholm, 2014) and Hershey's promised to remove GM sugar beet from its most popular chocolates by the end of 2015 (Devine, 2015). In spring 2015, the fast-food chain Chipotle announced that it would remove GM ingredients from its food in stages (Alesci & Gillespie, 2015). Reasons for this decision by Chipotle include concerns about environmental and human health risks associated with the heavy use of glyphosate in RR crop fields (Chipotle, 2015). In 2020, Chipotle announced it had officially reached its goal of going 100 percent GMO-free for all of its ingredients at all United States Chipotle and ShopHouse location (Jones, 2020). In June 2015, US meat producer Applegate removed GMO ingredients from all of its products and in 2016 promised to take GMOs out of its entire supply chain and to seek third-party verification for all its products (AgWeb, 2016): this has been proceeding step by step. In 2016, the global agribusiness Bunge added Non-GMO Project Verified milled corn ingredients and Non-GMO Project Verified oils to the products it supplies, to meet growing demand for non-GM ingredients (Business Wire, 2016).

The reasons why farmers increasingly demand non-GM seeds are the failing effectiveness of GM crops due to resistance development, and declining commodity prices for corn and soybeans, higher seed costs and technology fees for GM seeds, as well as premium prices for non-GM and organic grains. In the USA, demand for non-GM seeds has reportedly been increasing due to the problems caused by herbicide-resistant weeds, associated with growing RR crops (Kuphal, 2017). As prices for organic grains are about double those of conventional grains, some farmers go beyond non-GM food production and convert to organic food production (Case, 2014; Lucht, 2014; Bunge, 2015; Doering, 2015; Roseboro, 2015b; Selman, 2015). As a consequence, research into conventional soybean varieties at the University of Arkansas System Division of Agriculture has started to expand. Their biggest challenge is the scarcity of seed (Hightower, 2015).

The non-GM corn and soybean supply in the U.S. is relatively small. Of the 87.2 million soybean acres planted in the U.S. in 2021, 4.4 million were non-GMO. Around 2.6 million acres were food-grade non-GMO soybeans, whilst the other 1.7 million acres of non-GMO soy were feed-grade (Twellman, 2021). Growing demand for non-GM and organic foods can force the U.S. to import those crops from nations that are largely free of GM crops. U.S. corn (maize) imports from Romania, for example, increased more than 20-fold from 2013 to 2014 (Bjerga, 2015). Countries where GM crops have not been grown could continue to dominate the non-GM market in future, surpassing countries such as the U.S. where non-GM agricultural production has become more and more difficult.

3.4. Economic and regulatory implications of RR crop cultivation on coexistence with conventional crops

The purpose of co-existence rules is to allow GM crops to be grown whilst protecting non-GM crops from contamination so that they can be sold in GM-free markets (including organic markets), which consumers generally prefer. However, cases of GM contamination are known worldwide, including in Europe (Price & Cotter, 2014), and the concept of coexistence, using GM and non-GM cropping systems in parallel, and its technical measures and feasibility, remain a topic of controversy (Binimelis, 2008) .

Due to the lack of systematic global monitoring of GM contamination incidents, GeneWatch UK and Greenpeace International established the GM Contamination Register, a searchable database of recorded incidents of GM contamination that covered the period from 1997 to 2013. The GM Contamination Register contains almost 400 incidents of GM contamination across 63 countries from 1997-2013 (Price & Cotter, 2014). As only the incidents that have been publicly documented are recorded, the real number of global contamination incidents is probably much higher. This is also supported by the fact that the countries reporting the highest number of contamination incidents, Germany, France, USA and the United Kingdom, are (with the exception of the USA) currently not even cultivating GM crops and are probably not the countries with the highest degree of GM contamination. It is more likely that there is more frequent testing and a more effective mechanism to report such incidences in those countries.

There are a number of ways in which a GM crop may cause contamination of non-GM crops and/or end up in harvested material, feed and foodstuffs. These include cross-pollination of non-GM crops and co-mingling of seeds or grains during harvest, transportation, storage, processing and distribution. The hazard of cross-pollination depends on a variety of factors, many of which are crop specific, such as whether or not it is a cross-pollinating crop and what vectors (wind-borne or insect borne) it depends on to spread its pollen. According to Zhang et al. (2018a), honeybee-mediated gene flow in rapeseed plays a greater role at smaller distances and wind-mediated gene flow becomes a greater contributor at greater distances. While soybean is, for example, mainly self-pollinating, maize and sugar beet are cross-pollinating crops (European Commission, 2003). Other important factors that determine the hazard of cross-pollination include the duration of pollen viability and the degree of overlap of flowering periods. How far the pollen can ultimately travel by wind depends on landscape and weather-related factors. In insect-pollinated crops, numerous factors including crop characteristics, pollinator species, pollinator density, pollinator foraging behavior, field size, planting management practices, topographical factos, and environmental factors, such as water availability and rainfall etc., all affect gene flow (Kesoju et al. 2021).

There are considerable uncertainties about how far pollen may be spread by wildlife, including pollinators, such as bees. Vallaeys et al. (2017) cite evidence that bees do not spread in the same way as a gas (Brownian motion) but make a different type of motion, consisting of frequently occurring short displacements with more occasional longer displacements (known as Lévy flight). Using a computer model, they show that the isolation distances required to keep outcrossing levels below a certain threshold are substantially increased if the bees spread through Lévy flight, by comparison with the original predictions (based on Brownian motion). They suggest that isolation distances between GM and non-GM crops may need to be much larger than originally thought.

In the end, it is important to note, that even with great care being taken by producers, GM contamination may occur accidentally, for example if seeds remain stuck in farming equipment. Moreover, there exists no harvesting system capable of containing all the seeds produced on a plot of land (Smyth et al., 2002). Seeds that are inadvertently left in a field after harvest can germinate in the following seasons, depending on the germinability of the crop, and lead to the establishment of RR volunteer plants. The potential to form RR volunteers also depends on the crops and the time their seeds remain viable in the soil. The risk of RR volunteers is for example greater in oilseed rape than in maize whose seeds might not survive frost (European Commission, 2003). To control RR volunteer plants, older and more toxic pesticides, such as 2,4-D are often used. With reports of field evolved resistance to 2,4-D and other herbicides (see Section 6. Industry response), the control of volunteers may require the application of more and more expensive chemicals.

Cases of GM contamination are not restricted to countries that commercialise these crops (Price & Cotter, 2014). Cases of spilled grains of transgenic oilseed rape and even established plants are also known in countries where cultivation is prohibited and only import is allowed such as Japan or Korea (see for example Aono et al., 2006; Han et al., 2014; Kawata et al., 2009; Nishizawa et al., 2009; Saji et al., 2005). Seeds and established plants form imported transgenic oilseed rape were found at major grain ports, in storage facilities, near the feed processing plants or along transporting routes. Even in Switzerland where import of GM plants that are capable of propagation, as well as plant parts and seeds that are intended for agricultural, horticultural or forestry use in the environment are prohibited, feral genetically modified oilseed rape has been found (Hecht et al., 2014; Schoenenberger & D'Andrea, 2012; Schulze et al., 2014). Sohn et al. (2021) conduct a review of the unintentional release of feral genetically modified rapeseed into the environment. They find that the unintentional release of GM rapeseed mainly occurs due to seed spillage during harvesting, storing in soil seed banks, and seed spillage during importation of the GM rapeseed and its transportation along road verges.

RR alfalfa is another crop that has dispersed into the environment beyond cultivated fields. Occurrence of feral alfalfa in alfalfa growing areas is widely recognised. Greene et al, 2015, for the first time also detected RR plants in feral alfalfa populations in the U.S. (see also Section 3.4.2. Consequences of GM contamination). Spot checks of seed and crop shipments also frequently reveal GM-contamination and lead to the elimination of the seeds or crops (Hungary Today, 2015).

Paull (2018) argues that coexistence with non-GM varieties is a fiction and categorises genetically modified organisms as invasive species. He concludes: *"If GMOs are regarded as invasive species, or potential invasive species, then they can be evaluated appropriately as a threat to health and wealth and dealt with on a risk assessment, biosecurity and quarantine basis. The onus is then on the promoters to prove, manage and be responsible for containment, risk and escape, and to maintain alerts at all points of the foodscape. Under such a scenario, the secrecy of GM crops is replaced with transparency, farms with GMOs are declared, neighbours are aware, foods with GMOs are declared, there are labelling and traceability protocols in place, and the present practices of GM-invisibility is replaced with consumer awareness and clear declarative labelling."*

3.4.1. Preventing GM contamination

Some countries have specific guidelines or regulations in place to prevent GM contamination. These often rely on isolation distances. Kesoju et al. (2021), demonstrate that other factors, such as size of GM pollen pool within the pollinator foraging range and the foraging behaviour of pollinators, are also important variables to consider when trying to minimize GM contamination in outcrossing plants. Similarly, Lu et al. (2019) argue that increasing isolation distance alone will not prevent gene dispersal and name human activities including cultivation methods, agricultural practice, transportation, trade and seed-sharing as posing greater potential risks that can cause large-scale gene dispersal. In other countries such regulations or appropriate labelling of GM products are still entirely lacking. Preventing contamination might be especially difficult in smallholder agricultural systems where seed saving and exchange is a daily practice. Iversen et al. (2014), for example, found transgenes in local maize varieties of small-scale subsistence farmers in South Africa, outside the formal seed system. Those included the Roundup Ready maize NK603. They attributed the contamination to seed saving, seed exchange and lack of knowledge from both retailers, about the seeds they were selling, with unclear or even incorrect labelling of seeds, and from farmers about the seeds they were buying, planting, saving or sharing.

3.4.1.1. Regulation in the EU

In the European Union (EU), where there is currently very limited cultivation of GM crops, and no cultivation of GM HT crops, there is a legal obligation for coexistence of GM and non-GM agricultural production. The aim is that on the one hand, farmers can freely choose between conventional, organic and GM crop production, and on the other hand, consumers have a choice between GM and non-GM food products. To facilitate producer and consumer choice, food or feed containing more than 0.9% of EU-authorised GMO-resources need to be labelled as containing GMOs. Food and feed containing detectable traces of unauthorised GM events cannot be legally marketed in the EU. Food and feed products that contain less than 0.9% GMO-resources do not have to be labelled if the presence of the GMO was adventitious or technically unavoidable. (Directive 2001/18/EC; Regulation (EC) No 1829/2003; Regulation (EC) no. 1830/2003).

In the EU, coexistence measures are the responsibility of the Member States, since farming conditions such as farm and field size and management practices as well as other regional aspects such as climatic conditions, topography or pollinator behaviour vary enormously across Europe and need to be taken into account when developing and implementing coexistence measures. In developing and implementing national strategies and best practices for co-existence, Member States should follow the guidelines provided by the European Commission (European Commission, 2010) and the European Coexistence Bureau (ECoB). These guidelines are, however, non-binding recommendations. The Network Group for the Exchange and Coordination of Information concerning Coexistence of Genetically Modified, Conventional and Organic Crops (COEX-NET) should facilitate the exchange of information among the Member States and the Commission. Where no other measures are sufficient to prevent GM contamination, the Commission notes, it may be necessary to exclude GMO cultivation from large areas (European Commission, 2010).

By February 2009, 15 Member States had adopted specific legislation on coexistence and three further Member States had notified draft legislation to the Commission. In some Member States the development of a regulatory framework is not envisaged since the cultivation of GM crops on their territory is considered unlikely (European Commission, 2009). As from 3 April 2017, Member States in which GMOs are cultivated are required to "*take appropriate measures in border areas of their territory with the aim of avoiding possible cross-border contamination into neighbouring Member States in which the cultivation of those GMOs is prohibited, unless such measures* *are unnecessary in the light of particular geographical conditions*". Four Member States have done so (EC, n.d. a). Eighteen Member States have also introduced national measures to restrict GM crop cultivation on all or part of their territory (EC, n.d. b). Since only one GM crop is grown in the EU at present (Bt maize, grown mainly in parts of Spain), and this is not a GM HT crop, co-existence measures are largely untested even where they have been adopted.

Among the Member States that have adopted specific legislation on coexistence, the measures vary greatly from country to country. In most Member States, farmers who wish to grow GM crops are legally obliged to priorly inform their intentions to neighbours and/or competent authorities (Verrière, 2014). They further might have to negotiate a mutual agreement with neighbouring farmers and landowners on their respective cropping intentions (Devos et al., 2009). Further coexistence measures implemented by member states include spatial and/or temporal isolation of GM crops on the field, as well as prevention of contamination during harvest, transport, storage or the cleaning of tools amongst others (European Commission, 2009; Verrière, 2014). Defining appropriate isolation distances or buffer zones for example is non-trivial and remains a disputed topic. In the EU for example, member states proposed isolation distances from a couple of meters to several kilometers (Munro, 2008; Verrière, 2014). In order to establish appropriate isolation distances to prevent cross-pollination it is important to understand gene-flow and to know how far pollen of a certain GM crop can be deposited. Hofmann et al. (2014) analysed data on maize pollen deposition collected from 2001 to 2010 in Belgium, Germany and Switzerland to model pollen deposition in relation to distance from the nearest field. They concluded that a power function described the decrease in pollen deposition with increasing distance from the nearest pollen source better than the exponential model currently used in EU risk assessment and management. With the exponential curve, pollen deposition is underestimated for distances greater than 10 m, with increasing inaccuracy over longer distances. Hofmann et al. (2014) concluded that maize pollen is not restricted to close distances of less than 100 meters but can travel up to the kilometre range. Brunet et al. (2003) even observed maize pollen dispersal over dozens of kilometres. Based on their results, Hofmann et al. (2014) questioned the current buffer zone distances of 20-30 meters between GM maize and protected habitats, as suggested by the European Food Safety Authority (EFSA). To prevent exposure of non-target organisms, buffer distances should instead be in the kilometre range. Hofmann et al. (2014) suggest that *previous risk assessments and conclusions regarding distances, potential exposure, and effects on non-target organisms should be revised in the light of these findings*. In response, the EFSA GMO panel announced in December 2014, that they would re-evaluate their risk mitigation measures reducing exposure of non-target organisms to GM maize (EFSA, 2014). In their revision, completed in July 2015, the EFSA GMO panel controversially concludes that their previous recommended isolation distance of 20-30 meters still remains valid. They recommend further studies to estimate the effective exposure of non-target organisms to maize pollen (EFSA, 2015a). However, not only the effects on non-target organisms should be revised, but also the current risk mitigation measures preventing conventional and organic fields from GM contamination. Kruse-Plass et al. (2017) respond to EFSA point-by-point and confirm the need for specific environmental impact assessments for GM maize with respect to protected habitats within isolation buffer distances in the kilometre range. Keeping in mind that large isolation distances might not always be feasible in practice (Devos et al., 2009), the results of Hofmann et al. (2014) show that the cultivation of RR crops in Europe would come with a great risk of GM contamination.

3.4.1.2. Regulation in the U.S.

In contrast to Europe, there exists no legislation governing the co-existence of GM and non-GM agricultural production in the U.S. and labelling of food and feed containing GMOs is not required, although manufacturers will be required to label some products containing GMOs (using a 5% ingredient threshold) by 2022 under a new National Bioengineered Food Disclosure Standard (NBFDS) (Berry, 2021). It is estimated that processed food in the U.S. contains 70 - 80% GM ingredients (Paull, 2018). In 2011, the U.S. Department of Agriculture convened the Advisory Committee on Biotechnology and 21st Century Agriculture (AC21) to address the feasibility of coexistence in agriculture, to design a compensation mechanism (i.e. to address liability) and to issue recommendations. They claimed that there was insufficient data to determine if contamination was occurring. Thus, the AC21 recommends that the USDA should fund and/or conduct research to quantify the economic loss incurred by farmers as a result of GM contamination and assess the efficacy of existing GM contamination mitigation techniques. If needed, the USDA should develop improved mitigation techniques. The USDA should further fund a comprehensive education and outreach initiative to strengthen understanding of the importance of coexistence and provide tools and incentives to promote coexistence. Primary strategies for coexistence emphasised are good stewardship practices and communication and collaboration between neighbouring farmers (AC21, 2012). According to farmer statements, communication between GM, non-GM and organic farmers has however rather deteriorated since the introduction of GM crops. Good practice alone is sometimes not enough to prevent GM contamination (FWW & OFARM, 2014). Moreover, the Office of General Counsel has indicated that the USDA lacks the legislative authority to implement a program to incentivise the development of joint coexistence plans by neighbouring farmers (AC21, 2015). Accomplishing coexistence of GM and non-GM agricultural production in the U.S. seems difficult in the light of these findings and given the fact that GM crop adoption already reaches saturation in the main GM crops. By 2016, at least, ten GM maize (corn) contamination events had occurred in the U.S. (Han and Garcia, 2016).

3.4.1.3. The costs of contamination prevention

It is important to note that in order to have coexisting GM and non-GM agricultural production, costs to implement appropriate coexistence measures arise prior, during and after cultivation. The European Commission (2010) notes that additional costs might be incurred by farmers if they have to adopt monitoring systems and measures to minimise the admixture of GM and non-GM crops. It is however difficult to find reliable data on coexistence cost in food supply chains. In the EU, the question of coexistence is still a theoretical one in most supply chains and thus the database to calculate the costs of coexistence systems is uncertain. Generally, it can be said that every actor and level of a supply chain will be economically affected under a coexistence scenario and that costs of coexistence of GM and non-GM agricultural production systems are influenced by multiple, dynamically changing factors and have to be calculated on a case-by-case basis (Gabriel & Menrad, 2015).

Coexistence measures are extensive on the different levels of the supply chain. At the producer level they include costs for cleaning of machinery and equipment, buffer zones of uncultivated land around the edge of non-GM fields, monitoring costs (such as testing of seeds or crops), and building additional farm storage facilities. Regarding the food-processing level, Gabriel & Menrad (2015) present three possible general strategies to prevent contamination: spatial specialisation or temporal specialisation within one factory or segregation of the production lines in spatially separated factories. Depending on the strategy, costs to prevent contamination include: costs for testing of the incoming commodity as well as the produced outgoing goods, greater transportation distances to the next GM or non-GM plant respectively, building of additional storage facilities, creating a complete second production line in an existing plant, cleaning or flushing of repositories, investment in additional personnel and equipment and training programs for workers (Gabriel & Menrad, 2015). Gabriel & Menrad (2015) show that ensuring coexistence has a significant economic impact on actors on the different levels of the non-GM supply chains of rapeseed oil and maize starch. Depending on assumed segregation strategies, the total additional costs of coexistence and implemented product segregation systems can amount up to 14% of the total product turnover at the gates of rapeseed oil mills or companies processing maize starch, respectively. Costs for insurance policies or compensation funding were not included in these estimates.

In Switzerland, Agroscope names the crop, the size of the farm, the allocation of the GM fields, the number of neighbours that must be consulted, the number of fields that must be tested for GM presence and how strict the demanded coexistence measures are, as parameters the costs of coexistence depend on. They calculated that under unfavourable conditions, costs for coexistence measures could amount to 5-20% of the total costs for conventional production in Switzerland (Albisser Vögeli et al., 2011). In this study, under unfavourable conditions, the field size is small, the two GM fields have a distance of 1500 meters from one another; the GM field has 6 neighbours, the gene flow potential of the crop is high and the coexistence measures are strict.

Thus, allowing GM cultivation in countries that do not currently cultivate GM crops, would increase the cost of food supplies, because of the added costs of segregation (assuming that at least some famers and consumers wish to maintain access to GM-free markets, which generally command a higher price).

It is also important to note that according to Munro (2008), there can be no market equilibrium in which all land is cultivated and GM and non-GM crops types coexist. Otherwise, some non-GM crops would be grown within a distance to GM crops at which contamination occurs. In that case the crop could only be sold at the lower price for GM crops, which would not be profit maximising. If non-GM farmers have to sell their crop for the lower price of the GM variety, due to GM contamination, they might face elimination from the market or be forced to switch to GM production. Thus, there are only three possibilities for market equilibria: either only GM crops are cultivated, only non-GM crops are cultivated, or not all land is cultivated. This means that coexistence comes at the cost of leaving some uncultivated land. Further costs to regulate planting patterns have to be taken into account. Munro (2008) calculated that when only 10% of an area is devoted to GM farming, over 60% of the area could be denied to non-GM crops, even if the distance of gene flow is small. How much land is lost for non-GM crops very much depends on the pattern of planting. If for example GM fields are allocated so that the number of adjacent non-GM fields are minimised, the area unavailable for non-GM varieties is up to 3.7 times smaller than if the GM fields are chosen at random. This study concludes that coexistence may be impossible without strong regulation on planting patterns. In some cases, enforcing planting patterns would, however, mean that some farmers are not able to choose between GM and non-GM agricultural production. Munro (2008) estimates that, if the distance in which contamination occurs is large enough, it will be economically optimal to ban the GM variety. Munro (2008) further suggests introducing a subsidy for non-GM farmers that operate in a zone in which GM contamination occurs, that covers the price difference between the GM and non-GM crop to the farmers. Additionally, he argues that there should be a licensing scheme for GM crops that ensures that a crop is only approved when the resulting pattern of land use is externality minimising, i.e. crop types are efficiently planted in clusters to minimise the area unavailable for non-GM varieties.

The costs to prevent GM contamination might be especially high for organic producers, since global organic farming standards do not allow GMOs in either seed or food (IFOAM, 2002). The European Commission (2010) notes that since organic production is often more costly, stricter segregation efforts to avoid GM contamination may be necessary to guarantee the associated price premium. In the EU, the organic sector argues that, following the polluter-pays-principle, the costs of coexistence should be borne by the companies that place GMOs on the market, and not by the organic and GMO-free sectors (Oehen et al., 2018). In the U.S., organic farmers are responsible for making certain that they do not grow GM crops, thereby bearing the burden of avoiding GMO presence from crops planted by neighbouring GM farmers. Certain preventative measures to minimise the risk of GM contamination are required by the USDA organic standards. Those include maintaining a buffer zone. Buffer zones represent financial losses to organic farmers, since the buffer takes up space that otherwise could be cultivated. In cases where conventional crops are planted as pollen barriers, the financial loss comes in the value of the organic premium for those acres. Other preventative measures that farmers take, in addition to what is required by the USDA, include delayed planting so that their crops pollinate later than their neighbours', seed testing, flushing out equipment more often, abandoning crops prone to GM contamination and spending more on purer seeds. Median annual costs for preventative measures were estimated at $6,532 to $8,500 per farmer in 2014. Adding to this are median costs of $520 for record-keeping to prevent GM contamination (FWW & OFARM, 2014).

Fernandes et al. (2022) discuss the challenges regarding the coexistence of GM and non-GM crops based on transgene flow detection in maize landraces in Brazil. In this participatory transgene-flow-monitoring process, 1098 samples of maize landraces were collected in the Brazilian Semi-arid Region between 2018 and 2021 and analyzed using immunochromatographic strips (known as strip tests). GM proteins were detected in 34% of samples. Of these, in 2018-19, 98% had insect resistance (from GM Bt crops), 53% had glyphosate tolerance (mostly stacked with the Bt trait as well) and 3% glufosinate tolerance (all stacked with Bt). In 2020-21, 75% had insect resistance (from GM Bt crops), 62% had glyphosate tolerance (mostly stacked with the Bt trait as well) and 9% glufosinate tolerance (mostly stacked with Bt and/or glyphosate tolerance). The authors conclude that, "*Effective measures are needed to confine GM seeds in the areas and agricultural systems for which they were designed, thus preventing the social sectors responsible for on-farm conservation from assuming the burden of monitoring actions and the threat of losing their rights and their seeds*".

3.4.2. Consequences of GM contamination

Preventing GM contamination may not always be possible, regardless of how effective regulations are or how much care is being taken by producers. Where GM contamination does occur, despite preventative measures being taken, the consequences are numerous and costly, including product recall, loss of crops, GM-free fields, sales, markets, certifications, premium prices, reputation, consumer trust, non-GM seed supply and genetic diversity as well as lawsuits and fines. In the US, farmers can be accused of intellectual property infringement by seed companies if patented GM plants inadvertently grow in their fields (Barker et al., 2013; Hoyle, 1999; Reuters, 2014). In 2014, the U.S. Supreme Court dismissed a case filed by the Organic Seed Growers and Trade association et al. that meant to stop Monsanto from suing farmers for patent infringement in case their land gets contaminated with Monsanto's seeds. Between 1997 and 2016, Monsanto had already settled around 700 cases and filed at least 140 lawsuits against farmers for allegedly planting their patented seeds (Chow, 2016) (see also Section 3.1.5. Seed prices, patents and corporate control).

In the EU, products intended for entry into the human or animal food chain that contain GMOs above the tolerance threshold of 0.9% are subjected to mandatory labelling (see Section 3.4.1.1. Regulation in the EU). Thus, contamination of non-GM food or feed with GM food or feed could cause a loss of income, due to lower market prices and difficulties in selling the product (Devos et al., 2009; European Commission, 2010). The economic loss does not only depend on the price difference between GM and non-GM products. Even if the price difference is small, there are still costs to identify contamination, re-label and re-market the crop. It is important to note, that costs of GM contamination do not only affect the farm level but also the marketing level, as well as food companies and food processors. Grazina et al. (2017) detected RR soybean in 9 out of 90 samples of processed foods commercialised in Portugal. Of these samples, 5 were identified as being the GTS-40-3-2 event, 3 the MON89788 event and one contained both events. The estimated RR soybean contents of 8 samples ranged between 0.01 and 0.39%, but the sample containing both events accounted for 23.9% of GM ingredients. The authors conclude that the identification of a sample with high level above the threshold for labelling regulations suggests the need for more strict control of GMOs in foods. Areal and Riesgo (2021) find that the probability of finding imported products containing GMOs above the threshold varies among member states and years but could be quite high, as a result of limited human and financial resources allocated to inspections and analysis of import samples.

The following examples illustrate some consequences of GM contamination.

3.4.2.1. Contamination incidents can lead to the destruction of crops or entire fields

- In Switzerland in 1999, many cornfields had to be burnt or destroyed due to the contamination of two of Pioneer Hi-Bred's non-GM corn (maize) seed varieties with GM corn. Moreover, the Swiss seed importer Eric Schweizer Samen AG had to pay affected farmers 700 Swiss Francs per hectare in compensation (Furst, 1999).

- When, in 2000, the EU found 0.4% unapproved GM traits in canola seed imported by Advanta, France ordered that all 600 hectares planted had to be ploughed down. The contamination incident occurred despite growers following isolation rules (Smyth et al., 2002).

3.4.2.2. Contamination incidents can cause rejection of shipments, product recalls and loss of market

- In 1998, Aventis's GM StarLink corn (maize) with traits of herbicide and insect resistance, was approved for commercial production of animal feed, but not for human consumption, in the United States. Subsequently, the corn was required to be grown in segregated areas, surrounded by a buffer crop, which also was supposed to be marketed as animal feed. Nevertheless, in late 2000, the StarLink corn found its way into the human food chain across the U.S., Japan, South Korea and Canada. It is estimated that the StarLink trait contaminated 10% of all foods containing corn meal. As a consequence, many food manufacturers had to recall whole product lines and Aventis had to pay more than U.S. $1 billion to withdraw StarLink and compensate producers (Smyth et al., 2002; Schaefer & Carter, 2015). The Starlink contamination incident had a large negative effect on U.S. maize (corn) prices (Han and Garcia, 2016).

- Triffid flax, a genetically modified flax resistant to soil residues of sulfonylurea-based herbicides, was developed in Canada and authorised for commercial use in Canada and the United States in the late 1990's. Canada, the global leader in flax production, has a flax export value averaging over $200 million CAD. Canada's biggest export market for flax is Europe, receiving more than 70% of Canada's flax production. Thus, it is not surprising that Triffid flax was officially deregistered in 2001 and all remaining stocks were supposedly destroyed after Europe threatened to stop importing Canadian flax should GM flax enter into commercial production. Nevertheless, in 2009, Triffid flax was detected in EU food products, with over 100 reported incidents (Ryan and Smyth, 2012). The transgene was also detected in flax shipments from Canada to Japan and Brazil (Booker et al. 2017). This led to an immediate halt of Canadian flax imports and severe economic losses for the Canadian flax industry. Following the contamination incidents, a testing protocol was developed to manage the situation in Canada. Samples that tested positive at levels ≥ 0.01% for Triffid would not be accepted for import into the EU. Regular testing of flax all along the value chain put a burden not only on grain companies but also on farmers, who had to bear the costs for the Triffid tests themselves. When eventually two flax varieties that tested positive at 0.01% for Triffid were determined as a source of the Triffid contamination, their seed stores were subsequently destroyed. Other varieties, that showed trace levels of Triffid contamination, were reconstituted in a lengthy and expensive procedure (Ryan & Smyth, 2012). Ryan & Smyth (2012) estimate the total costs for quarantine, testing, segregation etc. in the first 1-2 years alone to be $ 29 million CAD. This does not include costs to the EU flax industry. Testing costs between 2009 and 2014 were estimated at $3.34 million CAD from 2009 to 2014. Thereafter, testing costs for producers are estimated at $500,000 CAD. Numbers are not known for the flax industry (Booker et al. 2017). In the long term, Canada lost some market share to Russia and Ukraine, who increased flax production to service short supplies in the EU flax market. Total costs for the EU's value chain were calculated at more than $50 million CAD (Ryan and Smyth, 2012). Prior to the Triffid flax incident, the EU imported an average of 80% of Canada's flax production. Twenty years later, the international flax trade between Canada and the EU was still adversely affected with the EU only importing one-third of the flax produced in Canada, while China replaced the EU as most valuable export market for Canadian flax. Furthermore, flax commodity shipments to the EU continued to be tested for transgene presence: *"The political sensititvity of testing has now become embedded within the flax trade between Canada and the EU and is likely to be viewed as entrenched. Therefore, this cost will likely have to be borne by producers and the flax industry going forward"* (Booker et al. 2017).

- In 1999, the EU detected pollen from a GM canola not yet approved for consumption in the EU in a honey shipment from Canada. As a result, honey shipments to the EU dropped by 55% between 1998 and 2000, with a monetary loss of C$4.8 million, reaching the lowest level in over ten years (Smyth et al., 2002).

- RR wheat not approved for cultivation was found on an Oregon farm in May 2013, causing Japan and South Korea to temporarily reject some U.S. wheat imports and the EU to call for tougher testing of shipments into the EU. This led to a class action law suit which was settled by Monsanto paying $ 350,000 (NBC News, 2015). RR wheat not approved for cultivation was again found in Montanta in 2014 and Washington state in 2016 (Reuters, 2016c). In August 2016, this contamination incident led Japan and South Korea to announce that they would defer new purchases of U.S. wheat until they could implement a new test for genetically engineered wheat (Capital Press, 2016). Ultimately this RR wheat strain contaminated non-GM wheat supplies throughout the U.S. (Capps and Babula, 2019). Capps and Babula estimate that U.S. farmers producing red hard wheat lost receipts ranging from US$32.77 million to US$131.06 million and suffered a drop in wheat prices of 3.83% (US$0.27 per bushel) in the wake of the May 2013 contamination event. This would amount to U.S. $4,807 in lost receipts for an individual farmer.

- Glufosinate resistant rice, which escaped into the supply chain from field trials conducted from 1999 to 2001 in Louisiana State University, was detected in a rice shipment to the EU in 2006. As a result, the EU greatly reduced imports from the U.S., costing U.S. rice farmers at least U.S.$ 1.2 billion (Schaefer & Carter, 2015).

- In 2005, the USDA deregulated RR alfalfa for cultivation. Since alfalfa is an insect-pollinated, outcrossing species that has high potential for gene flow, many seed producers became concerned that cultivation of RR alfalfa would lead to the contamination of organic and conventional alfalfa. In 2007, an injunction was passed, barring further planting of RR alfalfa. In 2010, the Supreme Court granted the USDA the authority to establish conditional deregulations with coexistence measures. Nevertheless, RR alfalfa was deregulated a second time in 2011, without any conditional coexistence measures. The short and limited duration of the first deregulation period of RR alfalfa, allowed Greene et al. (2015) to assess transgene penetration into feral alfalfa populations during that time. In a survey conduced between 2011 and 2012 in alfalfa seed production areas in the U.S., they detected transgenic plants in 27% of all sites surveyed where feral alfalfa plants were detected. There was also evidence that the populations may be self-sustaining and that gene flow is likely. The authors suggest that minimising seed spillage during production and transport, as well as eradicating feral alfalfa along road sites, would be the best strategies to decrease transgene dispersal of alfalfa to a minimum. A study by Boyle (2015), however, highlights the importance of pollinator-mediated gene-flow between glyphosate-tolerant and conventional alfalfa crop fields. Studying the foraging range of the alfalfa leafcutting bee *Megachile rotundata* and its influence on RR trait expression in harvested conventional seed, Boyle (2015) suggests that current AOSCA (Association of Official Seed Certifying Agencies) isolation standards for the alfalfa leafcutting bee may be inadequate to ensure that harvested seed will fall under the 0.1% threshold for adventitious presence. Moreover, economic impacts from the adventitious presence of RR alfalfa were seen in 2014 when China, which had not approved GM alfalfa, rejected all shipments containing GM material upon testing of hay imports from the U.S. This resulted in a drop in U.S. hay prices (Schaefer & Carter, 2015).

- Starting in November 2013, China rejected more than 850,000 metric tons of U.S. maize (corn) containing GM MIR162 maize (corn) produced by Syngenta under its Viptera brand, which was not approved for import to China. According to analysis by the U.S. National Grain and Feed Association (NGFA), this trade disruption cost between $1 billion and $2.9 billion in economic losses, although more recent analysis has questioned whether other U.S. market factors had a greater effect on the drop in U.S. maize (corn) prices at the time (Han and Garcia, 2016). As a result of these major losses, Syngenta faced almost 1,800 consolidated lawsuits as of May 2015. As of June 2015, Hecker Law Group represented over 10,000 clients that had field lawsuits against Syngenta. Lawsuits were filed from farmers and commodity traders, such as Cargill and Archer Daniel Midland, against Syngenta for launching US sales of MIR 162, despite the fact that it was not yet approved for import by China. Reportedly, there were lawsuits pending against Syngenta in 22 states and more than 50,000 farmers across the U.S. had filed suit by 2016, with a class-action lawsuit expected to go ahead in 2017 (Muscatine Journal, 2016; Davies, 2016). In June of 2017, a federal grand jury in Kansas awarded nearly $218 million to around 7,300 growers who had sued Syngenta and a $1.5 billion settlement was then reached for the remaining cases (WNAX, 2018). In November 2015, Syngenta on the other hand sued Cargill and Archer Daniel Midland, saying that it was the exporters that failed to keep MIR 162 corn separate from approved strains and for shipping it to China, even though they should have known the strain was not approved by China (Polansek, 2015). In 2019, Archer Daniels Midland Company then filed a lawsuit against Syngenta, alledging negligence and false statements regarding whether or not major corn purchasers like China would accept a new gene in GMO corn (Strom, 2020). Either way, the National Grain & Feed Association estimated that US farmers suffered combined losses of over $1 billion due to trade disruptions linked to the rejections. Other sources spoke of economic damages between $1 and almost $3 billion. The economic damage may be substantially higher, as U.S corn exports to China were slow to recover. In 2014, exports of U.S. corn were 85 percent lower than in 2013 and accordingly the price of US corn dropped (AP, 2014; Grant, 2014; Plume, 2014; Polansek, 2014a; 2014b; Turner, 2015a). In the first five months of 2015, China purchased nearly 90% of their total corn imports in the Ukraine, which grows non-GM, and thus surpassed the U.S. as top corn exporter to China (Terazono, 2015).

3.4.2.3. Contamination incidents result in fines

- GM farmers can be punished for failure to comply with national coexistence measures, such as failure to respect isolation distances. Depending on the country, this can result in fines of up to €150,000 and prison sentences up to two years (Verrière, 2014).

- Glyphosate-tolerant creeping bentgrass was developed in order to help controlling weeds in superior quality turf on golf courses. But the grass has been found growing wild since its first approved field trials in 2002, leading to a fine of $500,000 for Scotts Miracle-Gro, developer of the grass. Monsanto and Scotts subsequently sought deregulation for the grass, although according to the companies they do not plan to commercialise it or licence it to other entities (Kaskey, 2016; USDA APHIS, 2016a).

3.4.2.4. GM contamination threatens the organic sector

Whereas in the above cases, single crop varieties, fields or product lines were affected, GM contamination poses a threat to the whole organic sector. Since global organic farming standards do not allow for GMOs in both seed and food (IFOAM, 2002), GM contamination can lead to product recalls and the withdrawal of organic certification. The associated loss of price premiums, reputation and trust in organic products are serious issues not only for organic farmers but also on the marketing level. Without the organic label, companies are forced to sell their products at a lower price on the conventional market or on lower-premium markets, such as the animal feed market. Adding to this is extra labour to find new buyers if a load is rejected and shipping costs to move a load back to the farm and to a new buyer (FWW & OFARM, 2014).

In a survey conducted by FWW & OFARM (2014) with organic farmers, median loss of loads rejected due to GMO presence in one season was $4,500, with one organic farmer reporting losses of $367,000 in one year. Upon rejection of their crops, contaminated farmers must often also pay for the transportation of that load back from the buyer, estimated at $1,000 to $2,000 per rejected load. With some crops getting rejected more than once, this can become very costly and time-consuming. The 2015 USDA Organic Survey revealed that 92 U.S. organic farms suffered combined monetary losses of over $6 million between 2011 and 2014 due to GMO contamination (USDA NASS, 2015). Others have estimated that contamination of the total organic maize crop could costs U.S. organic farmers $90 million annually (Hewlett & Azeez, 2008). In Brazil, farmers lost higher premiums for organic products because of GM contamination of organic soybeans (Hewlett & Azeez, 2008). In Spain, GM contamination of organic maize has caused economic losses to farmers that had their organic certification withdrawn upon contamination. As a result, some organic farmers have given up cultivating maize because of the impossibility of preventing GM contamination and organic maize is progressively disappearing in regions with dense cultivation of GM maize (Cipriano et al., 2006; Hewlett & Azeez, 2008; Verrière, 2014). In Canada, organic farmers have largely stopped growing canola because of GM contamination that prevented farmers from growing, selling and exporting organic canola (CBAN, 2008; Holmes, 2002; Hoyle, 1999; The Sydney Morning Herald, 2008). Smyth et al. (2002) estimate that this lost market amounts to between C$100,000 and C$200,000 annually. However, this is a conservative estimate and the organic market has grown considerably since then. IFOAM speaks of ‘millions of dollars of damage to businesses’ (Hewlett & Azeez, 2008). This has also become a problem for organic canola growers in the U.S. (FWW & OFARM, 2014) and Australia. In 2014, a lawsuit case became popular in the media in which an organic farmer from Western Australia sued his neighbouring farmer, whose GM canola contaminated his property. Following the contamination, the farmer lost his organic certification. After a three-week hearing, the Western Australia Supreme Court decided in favour of the GM farmer (Supreme Court of Western Australia, 2014). The organic farmer who had to pay the court costs of about $804,000 appealed the decision with no success (Chow, 2016). This landmark case highlights gaps in GM legislation and the potential negative impacts on organic farmers.

In Hawaii, organic farmers suffered economic losses due to GM contamination of organic papaya (Greenpeace International, 2006). While the papaya ring spot virus is mostly a problem for large-scale production, organic farmers say that it is less damaging on organic papaya farms that are run by some of the only small-scale family farmers left in Hawaii. GM ring spot virus resistant papaya however, threatens organic papaya farmers’ markets. According to this report, since the introduction of GM papaya in Hawaii total papaya production declined and fewer papayas are harvested in Hawaii now than during the years when the outbreak of papaya ringspot virus was at its worst. Since traditional buyers rejected the GM papayas, the Hawaiian papaya industry has lost export markets and prices of GM papaya dropped. Simultaneously, other papaya producing and exporting countries, such as Mexico or Brazil, showed steady increases in production. On average, farmers earn 35% less per kilogram for their fruit than they did before the GM papaya was released (Greenpeace International, 2006).

3.4.2.5. GM contamination threatens biodiversity

A further concern is that GM crops could spread into a crop’s wild or weedy relatives, traditional varieties or landraces. If that GM crop confers a trait that benefits the plant, such as herbicide tolerance, the resulting hybrids may have increased ecological fitness. This could boost the extinction probability of wild populations within a local econsystem, thereby threatening genetic diversity that is the basis for crop breeding and the development of new crops. Crop wild relatives and landraces are today increasingly used in breeding programs because they are well adapted to their environment and pests and therefore often possess valuable traits.

The chance of establishment of feral populations of GM crops or of interbreeding with wild relatives, depends on the one hand on the spread of pollen or seed and, on the other hand, on the extent to which the crop is competitive in the wild and the genetic closeness and abundance of its relatives. Oilseed rape, for example, has a number of close relatives, including wild and crop plants, while wheat has only few potential partners for hybridisation (Munro, 2008). Feral populations of oilseed rape and alfalfa are widely known today (see Section 3.4. Economic and regulatory implications of RR crop cultivation on coexistence with conventional crops).

Fernandes et al. (2022) discuss the challenges regarding the coexistence of GM and non-GM crops based on transgene flow detection in maize landraces in Brazil (see Section 3.4.1. Preventing GM contamination).

Mexico is recognised as one of the 12 megadiverse countries and considered the centre of origin and diversity of cotton and maize (Burgeff et al., 2014). Maize is mainly produced by smallholders in Mexico, using landraces that are very well adapted to the local growth conditions. Contamination of these landraces, could threaten preservation of this very important maize genetic diversity (Snow, 2009). GM transgenes have already been reported in at least some maize landraces in Mexico (Agapito-Tenfen et al., 2017; Dyer et al. 2009; Piñeyro-Nelson et al., 2009; Quist & Chapela, 2001; Serratos-Hernández et al., 2007; Snow, 2009). Seed management practices and social characteristics of the communities engaged in maize farming play an important role in the extent and frequency at which transgenes can be found in Mexican maize landraces. Controlling the spread of transgenes will be particularly difficult for communities sharing seeds within and outside the community in informal markets and purchasing seeds from grain stores in the formal market. As seed saving, sharing and purchasing practices can vary from season to season, even for individual farmers, sampling the same fields over different years using the same method can obtain different results for transgene frequency. A further explanation for studies reporting inconsistent results on transgenes in Mexican maize, is the fact that even validated methods for transgene detection are not specifically developed for the purpose of detecting transgenes in landraces and wild relatives (Agapito-Tenfen et al., 2017).

Rendón-Aguilar et al. (2019) investigated whether transgenes are still present in Oaxaca, Mexico, nearly 20 years after the first report by Quist and Chapela (2001). From 2008 to 2018 they collected 1,412 samples of maize landraces (and some hybrid varieties) in different municipalities in Oaxaca that are important for the conservation of biodiversity (Priority Terrestrial Regions). 1.69% of the samples analysed were positive for the presence of transgenes at low levels. The presence of transgenes flucturated through the years and farmers' responses indicate that there is a high movement of seed among municipalities and from outside Oaxaca. Traditional management, mechanisms for seed acquisition, as well as government seed distribution policies via municipalities or peasant organisations are named as sources of introcution of foreign material. These findings are in line with the results from Agapito-Tenfen et al. (2017). González-Ortega et al. (2017), report a high abundance of transgenes in a wide variety of maize food products consumed in Mexico, with 82% of all food samples analysed containing at least one transgenic marker and at least 60.8% of all food samples analysed containing transgenic maize. This also includes food products labeled as GMO-free. While industrially produced maize-derived food products revealed a greater chance of transgene presence than artisan products, which are putatively derived from local maize landraces, the frequency of transgenic markers detected in artisan products analysed was still between 55.6 and 59.3%, respectively. While artisan products are putatively derived from local maize landraces, the authors suggest it is more likely that the source of transgenes in these products stems from using industrialised flour. In order to contribute to food security and sovereignty and as a special measure to protect native corn and human health, amongst other things, the Mexican government has decided to revoke or refrain from granting permissions for the environmental release of GM corn and its dietary use as of January 31st 2024 (DOF, 2020).

Wild populations of the most widely cultivated cotton species in the world, *Gossypium hirsutum*, have also been contaminated by GM varieties, the majority of which are geographically located over 300 km away from all wild cotton populations (Wegier et al., 2011). In Spain, GM contamination of organic maize reportedly led to the loss of farmers' maize varieties adapted to the local climate (Cipriano et al., 2006). Burgeff et al. (2014) suggest that such events could limit the future availability of high-value germplasm in breeding programs. This could threaten innovation in plant breeding and decrease farmers' freedom of choice.

Gene flow from transgenic to wild soybean is a major environmental concern in China, Japan, Korea, and far eastern Russia, where wild soybean is extensively distributed (Liu et al. 2021a). There is evidence for outcrossing from transgenic to wild soybeans in studies conducted in both Japan (Nakayama & Yamaguchi, 2002; Mizuguti et al., 2009; 2010) and China (Chen et al., 2006; Liu et al. 2008; 2012; 2020a), where wild soybean is extensively distributed (and GM soybeans are not cultivated commercially). In these experiments, the resulting transgenic hybrids either exhibit lower, similar or greater performance compared with that of their wild relatives for some traits (Guan et al., 2015; Kan et al., 2015; Liu et al., 2021a). Liu et al. (2021a) show that the herbicide resistance gene from the transgenic soybeans was highly conserved in the F1 hybrids. Crossed seeds had significantly lower vegetative and reproductive fitness (with one exception) than the wild relatives but were viable. That means F1 hybrids can still germinate and backcross with wild soybeans. Thereby, the transgene could introgress into the wild soybean and create herbicide resistant wild soybean. This could be accelerated under glyphosate pressure, when the transgene confers a selective advantage. Introgression from cultivated into wild soybean is known and has led to the establishment of the semi-wild type (Wang et al. 2010). The authors conclude: *"Our results suggest that more attention should be paid to the escape of genetically modified genotypes to safeguard the biosafety of wild soybean gene pool, if GM soybeans are released in China, the place of origin of cultivated soybeans".* Liu et al. (2022a) study how pollen-mediated gene flow may alter the fitness of wild soybean relatives. The fitness of the first generation F1 hybrid between transgenic and wild soybeans was significantly lower than that of its parent. However, as the F2 generation of transgenic and wild soybeans had no fitness cost and the flowering stages overlapped, the foreign gene (EPSPS protein) might still spread in the wild soybean population. A two-year field study in Korea, also confirmed that pollen-mediated gene flow from glufosinate-ammonium resistant genetically modified soybean to wild soybean could occur under natural field conditions (Yook et al., 2021). Their results suggest that transgenes of glufosinate resistant soybeans may disperse into wild populations and persist in the environment, as the hybrid progeny showed greater fitness than the glufosinate resistant soybean. Notably, the hybrid progeny had almost 3 times greater seed productivity, 4 times greater pod shattering, and over 18 times greater seed dormancy.

Brassica napus (oilseed rape/canola) has many wild and weedy relatives in agricultural and natural ecosystems and there are numerous reports in the scientific literature of transgenic oilseed rape hybridising with many of those relatives such as *Brassica rapa* or *Brassica juncea* (see, for example, references in Song et al. 2010). Studies analysing the fitness of outcrossed hybrids between genetically engineered herbicide tolerant *B. napus* and wild brown mustard *B. juncea* suggest a potential rapid introgression of herbicide resistance genes to the wild relative and highlight the weedy potential of the hybrids (Di et al., 2009; Song et al. 2010). The maximum potential gene flow from herbicide tolerant *B. napus* to B*. juncea* has been reported at 21.95% (Zhang et al. 2018a). In addition, herbicide tolerant oilseed rape itself can act as a problematic weed in herbicide tolerant cropping fields. Pandolfo et al. (2016) report the presence of glyphosate-resistant oilseed rape (canola) populations in Argentina, as weeds in RR soybeans and other fields. This study identifies Monsanto's GT73 GM oilseed rape as the source of the contamination, although its cultivation is prohibited in Argentina. The authors speculate that the contamination could come from unauthorized GM oilseed rape crops cultivated in the country, or as seed contaminants in imported oilseed rape cultivars or other seed imports. The authors raise concerns about the potential for hybridization with wild related species, which was the main reason for the ban on cultivation and import of GM oil seed rape in Argentina.

Weedy rice is a serious problem in one of the world's most important food crops (Delouche et al. 2007). Since cultivated rice and weedy rice belong to the same species, they are also both killed by the same herbicides. It is thus attractive to cultivate herbicide tolerant rice in order to selectively control weedy rice. On the other hand, belonging to the same species also increases the danger of gene flow between the cultivated rice and the weedy rice. Indeed, the commercialization of the conventional imidazolinone (IMI) herbicide tolerant rice (Clearfield rice), has led to the quick introgression of the IMI-resistance genes into weedy rice populations wherever this rice is grown and led to more complications in managing weedy rice in some countries (Sudianto et al. 2013; Zhang et al. 2006)[1]. Gene flow from different herbicide resistant rice to weedy rice relatives can results in hybrid progeny with lower, similar or greater performance compared with that of their weedy relatives (Chun et al., 2011; Liu et al. 2016; Nam et al. 2019; Song et al. 2011; Wang et al., 2014; Zhang et al. 2003). Liu et al. (2016) demonstrate that potential of gene flow from transgenic to weedy rice, as well as the fitness of the resulting hybrids, depends on the genotype of both transgenic and weedy rice and whether they are of the same or different subspecies. In the study of Wang et al (2014), the transgenic crop-weed rice hybrid progeny, derived from a glyphosate resistant cultivar and different weedy rice populations, had a very strong and consistent increase in fitness compared with their non-transgenic counterparts, even without exposure to glyphosate. Zhang et al. (2003) demonstrate that glufosinate resistance can be transferred from transgenic crop lines to weedy rice. In their study, glufosinate resistance did however not increase fitness in hybrids or subsequent progeny. Nam et al. (2019) quantified gene flow from herbicide resistant to weedy rice at 0.025% - 0.139%. The resulting hybrids and subsequent progeny had significantly more and heavier grains. Moreover, the F3 progeny showed resistance to a PPO-inhibiting herbicide, indicating that the herbicide resistance gene is dominantly inherited. Despite the low rate of hybridization, the authors conclude that: "*These results suggest that transgenes that could escape from PPO-inhibiting herbicide-resistant rice and be transferred to weedy rice might persist and disperse into weedy populations over several generations due to herbicide resistance and improved reproductive traits in the hybrids.*" Zhang et al. (2018b) warn that the potential risk of 'reverse' gene flow, weedy rice traits introgressing into hybrid rice, must not be underestimated and demonstrate that glufosinate resistant weedy rice can also rapidly arise by pollen-mediated gene flow from weedy to transgenic hybrid rice. In their study, the composite fitness of the weed-rice-like (feral) progeny was significantly higher than that of the transgenic hybrid rice and many also had higher relative fitness than the weedy rice parents. Moreover, all the feral plants found had the glufosinate-resistance gene: *"The high relative (both vegetative and reproductive) and composite fitness, weediness traits, and glufosinate-resistance of the feral plants suggest that they could be potentially harmful and difficult to control in paddy fields, particularly if glufosinate-resistant transgenic rice is grown sequentially*". The authors conclude: *"Our findings suggest that there is a need to revise the transgenic rice safety assessments and management regulations that were originally established based on the premise of unidirectional gene flow, and to consider the relevance of gene flow from weeds to transgenic crops."*

Fang et al. (2018) assess the fitness effects of transgenes overexpressing EPSPS in *Arabidopsis thaliana* (thale cress). They conclude that their results provide a strong support to the hypothesis that transgenic plants overproducing EPSPS can benefit from a fecundity advantage in glyphosate-free environments. Beres et al. (2018b) also conclude that that overproduction of EPSPS in *Arabidopsis* does not have a fitness cost and might confer a fitness benefit under the examined growth conditions.

[1] Resistance to ALS inhibitors, such as IMI herbicides may also evolve from spontaneous mutations in the ALS gene of weedy rice. Gene flow has however accelerated the evolution of ALS-resistance in weedy rice (Sudianto et al. 2013).

3.4.3. Liability & costs for compensation

If a non-GM farmer suffers economic losses due to GM contamination, the question arises whether or not they will be compensated for the loss and who will be liable.

3.4.3.1. Regulation in the EU

In the EU, liability and financial compensation regimes for economic damage caused by GM contamination are the exclusive competence of member states (EU Commission, 2010). Some EU member states adopted specific rules on liability and compensation if contamination occurs (Verrière, 2014; Koch, 2007). Those vary greatly between member states[2]. A minimum of protection in cases of GM contamination is provided under the regular conditions of tort law (which involves lawsuits seeking to obtain civil remedies) in all national jurisdictions (EU Commission, 2010; Koch, 2007). Tort law requirements vary substantially throughout Europe. Some countries maintain traditional tort law rules based on fault liability, others have introduced special strict liability regimes, which apply specifically to GM contamination. Under strict liability regimes, those that take advantage of a risk must compensate any losses in case the risk materialises, independent of the individual behaviour or fault. Thus, GM farmers are more likely to be held liable for economic losses than under traditional tort law, where defendants can only be held liable due to faulty behaviour, for example if they did not maintain the required isolation distances (Koch, 2007).

In member states such as Spain, that exert fault liability, affected farmers have to prove causation and fault by identifying the farmer responsible for the contamination and by proving his or her culpability for the damage caused (Binimelis, 2008). Given the various sources that can contribute to GM contamination it can however be very challenging to prove a causal link between the damage and the source of the damage. This issue gets even more complicated if there are causal uncertainties, for example if several farmers in the neighbourhood grow GM crops, or in cases of cross-border contamination. In such cases it might be impossible to determine whom to hold liable for the contamination and the question arises how to refund affected farmers. In countries like Germany and Austria, that have adopted special liability regimes, GM crop farmers are jointly liable for the incurred losses caused by contamination (Devos et al., 2009). Another option might be to redirect the claims against the seed producers. In that case, they might however pass these costs back to their customers, for example by increasing seed prices (Koch, 2007).

Insurance might be an alternative to tort law. Liability insurance would however only be available if the insured is actually liable, meaning that all substantive requirements of tort law are met. Alternatively, non-GM farmers could be insured against losses from GM contamination. However, non-GM farmers may not know that they are at risk or not be willing to pay insurance if the risk is brought about by GM farmers. Neither liability, nor first party insurance products covering GM contamination risks, are available on EU markets today. One reason for this is that there is currently not enough data available to predict likelihood and extent of possible losses due to GM contamination (Koch, 2007). Moreover, many insurance companies have already announced that risks linked to GMOs will not be covered by them (Verrière, 2014).

Some Member States have established compensation funds to cover losses resulting from GM-contamination. The money is to be collected from GM farmers or seed producers. In some cases, this is supposed to happen via a levy for GM crop cultivation or a seed tax (European Commission, 2009; Koch, 2007). Because GM cultivation in the EU is currently limited, these liability regimes have not been fully tested.

In the end, it is most likely that farmers and not seed producers have to bear the costs resulting from GM contamination, unless appropriate liability regimes are adopted and enforced in future.

[2] For the detailed special liability or compensation regimes implemented in each member state, please refer to Koch (2007).

3.4.3.2. Regulation in the US

In the U.S., the Department of Agriculture convened the Advisory Committee on Biotechnology and 21st Century Agriculture (AC21) to design a compensation mechanism for farmers that are economically harmed by GM contamination. Even though they were unable to estimate the costs associated with GM contamination on non-GM and organic farms due to lack of data, they suggested that non-GM farmers pay a premium as a form of crop insurance. Non-GM farmers should furthermore receive incentives for the development of joint coexistence plans with neighbouring farmers in the form of a reduced insurance premium.

To obtain compensation, a farmer would need to demonstrate that they had suffered an actual financial loss (AC21, 2012; FWW & OFAEM, 2014). In 2014, the USDA created the Contract Price Addendum, that allows organic farmers to use their contract price, rather than USDA-established prices to establish crop insurance guarantees. The contract price addendum is available for 73 crop types, including corn, cotton and soybeans (USDA RMA, n.d.; 2013; 2016). Since 2016, the USDA can also offer farmers insurance under Whole Farm Revenue Protection, if they wish to insure every commodity on the farm. A survey conducted by FWW & OFARM (2014) with organic farmers however revealed that nearly half of respondents would not purchase crop insurance and that most farmers that would purchase insurance for GMO contamination-related losses believe that GMO patent holders and farmers should pay the added premium. Moreover, there is doubt that a crop insurance mechanism is feasible for organic growers. The Office of General Counsel has indicated that the USDA lacks the legislative authority to implement a crop insurance program that addresses economic losses farmers suffered from GM contamination. AC21 Member, Charles Benbrook argues that for a crop insurance program to work, a threshold of GM contamination that triggers payments is needed. Yet no threshold or guidance on how to set one has been suggested. He further criticises the fact that between 50% and 75% of the total cost of crop insurance is paid by taxpayers, via the USDA budget (AC21, 2012).

It is evident that many uncertainties evolve around the question of compensation for non-GM farmers in the U.S. and that ultimately non-GM farmers, as well as taxpayers, pay the burden and costs of GM crop contamination.

<u>3.4.4. Summary</u>

In summary, coexistence measures are costly and not sufficient to prevent GM contamination. Thus, in countries where GM crops are grown, non-GM farmers, including organic farmers, bear risks and costs associated with protecting their crops from GM contamination and certifying their supply chain as GM-free for consumers. Commercialising RR crops in new countries in Africa, Asia, Europe, or elsewhere, would increase the hazard of GM contamination, which in turn would pose legal and economic uncertainties to farmers and be prone to create tensions among neighbouring farmers. Ultimately this would result in increased costs for food production. According to the IFOAM EU Group (Verrière, 2014), banning GMO cultivation altogether would be the most efficient and cost-effective way to prevent contamination.

3.5. Impact of RR crops on farmers’ choice, land rights and indebtedness.

Intellectual property (IP) rights associated with GM crops, and the resulting increasing market concentration (Howard, 2009), lead to restricted access to breeding material for farmers and breeders and thus hinder innovation in plant breeding and impede farmers’ freedom of choice (Then & Tippe, 2014; see also Section 3.1.5. Seed prices, patents and corporate control). A study comparing seed availability in GM adopting (Spain) and non-adopting (Switzerland, Germany, Austria) European countries found that in adopting countries the maize seed market is more concentrated with fewer available maize cultivars for farmers than in the non-adopting countries (Hilbeck et al., 2013). Apart from an overall decrease in seed cultivars, it has become more and more difficult to find non-GM seeds in GM adopting countries (Roseboro, 2008). In the U.S. for example, already more than 90% of all soybean, corn and cotton cultivars are GM (USDA NASS, 2014: see also Section 1. Introduction). Thus, the widespread adoption of GM cultivars can also decrease the choice of farming practice, as it gets more difficult to find conventional or organic seed. And vice versa, the lack of conventional varieties in the local seed markets are also a reason for the high adoption rates of GM crops in some countries (Burgeff et al., 2014). This questions again whether coexistence of GM and non-GM agricultural production is feasible and highlights concerns about the 'transgenic treadmill', in which farmers are trapped into paying the increasing costs of GM seeds and the associated chemicals.

Whilst selling GM HT seeds and the associated herbicides has been profitable for large agrochemical companies, there have not been the same benefits for farmers, or for taxpayers (who pay for subsidies). In the USA, rising input costs, volatile production values, and rising land rents have left farmers with unprecedented levels of farm debt, low on-farm incomes, and high reliance on federal programs (Burchfield et al., 2022). According to Burchfield et al. (2022), "*In nine of the last 10 years, the United States Department of Agriculture (USDA) has reported that the average funds generated on-farm for farm operators to meet living expenses and debt obligations have been negative*". Subsidies are largely directed at commodity production, including soy and corn, which are typically GM crops, and for which per acre costs tripled between 1990 and 2020.

3.5.1 Impacts on smallholders in South America

Leguizamón (2016) explores how agriculture in Argentina has transformed from a food-producing activity into a commodity and, eventually, to a stock in the financial market. She argues that the expansion of GM soy monocultures has been associated with violent peasant displacements; increased cancer rates in rural and peri-urban populations due to agrochemical exposure; food insecurity; deforestation; soil nutrient depletion; and water, air and soil pollution. The Argentine soybean seed market is not particularly profitable because certified seed sales are low and farmers do not make royalty payments, unlike in Brazil. Nevertheless, the adoption of new technologies, including the use of RR seeds, has transformed labour by replacing workers with machines, leading to rural displacement and depopulation in conjunction with the specialization and concentration of rural labour. Soy production in Argentina is now highly concentrated by large agribusinesses that farm vast tracts of land: in 2010, only 2.6 percent of producers (approximately 1600 farmers) controlled more than 50 percent of soybean production, farming 9.34 million hectares in plots larger than 5000 hectares. There is a shift to leasing land, rather than owning it, which reduces the farmer's incentive to use sustainable practices by removing his or her stake in future productivity. According to this analysis, the GM soy model has entailed – contrary to the rhetoric of agribusiness – an intensification of fossil fuel- and chemical-powered agroindustrial practices, whilst labour-replacing technologies in reality decrease social benefits and increase ecological risk.

Lapegna (2013) documents a number of cases where activists of peasant and indigenous organizations have been killed in the context of land conflicts in northern Argentina. These conflicts are associated with the expansion of genetically modified soybeans in the area, which has resulted in, sometimes violent, enclosures of peasant land and also destroyed thousands of hectares of native forests.

Goldfarb and van der Haar (2016) show how the process of soy and cattle expansion into the new frontiers in Argentina happens through a group of different mechanisms which range from voluntary purchase to violent evictions. Soy expansion mostly affects forest areas, indigenous communities, and small-scale farmers (campesinos) with vulnerable land rights. Based on field-based research in Santiago del Estero, the researchers observe different mechanisms of land control, mainly in the direction of dispossession and enclosure.

McKay and Colque (2016) document a similar process in Bolivia, where GM soybeans were legalized much later (in 2005). Small farmers in Bolivia are becoming more and more subject to the terms of their unequal relations of production, and dependent on external inputs and international markets.

Similarly, Paraguay's soy boom has resulted in increasing soy production on fewer, larger farms, increasingly excluding peasant farmers from the rural landscape whilst providing them with few livelihood alternatives (Elgert, 2016). Elgert's research is based on two years of fieldwork, between 2004 and 2008, in Canindeyú, a department in the North-East of Paraguay, where small-scale subsistence and cash-crop farming on parcels of around 10 hectares sit uncomfortably beside soy farms 10 to more than 100 times their size. She argues that most of Paraguay's 6.8 million people receive few benefits from the country's soy boom and that alternatives to 'more soy on fewer farms', that include rather than exclude small-scale producers in Paraguay's agricultural development trajectory, are likely to be more sustainable and equitable. During her research, she interviewed three small-scale producers, living and farming along the perimeters of soy fields, who reported their entire subsistence crop eradicated by a neighbour's glyphosate application.

Phélinas and Choumert (2017) document how planting GM soybeans in Argentina initially increased farm productivity and reduced the costs per unit produced: however, they question whether this is sustainable. They note that economic benefits arose in Argentina partly because Monsanto's patents were not enforced (see Section 3.1.5. Seed prices, patents and corporate control) and thus GM seeds were cheaper than elsewhere. Using data from a 2011 field survey, they find a mixed picture of changing land distribution patterns and labour displacement resulting from GM soybean expansion, with former farm labourers likely losing out and few if any benefits for the poorest segments of the rural population. They note that the expansion of GM soya in Argentina has caused major concerns regarding environmental impacts, particularly the expanse of crop land at the expense of natural areas and forests, and created dependence on the foreign exchange revenue generated by export earnings. These authors question whether the short-term economic advantages of GM soya can be sustainable. It is worth noting that soy exports from Argentina fell from a high of $5.25 billion in 2011 (when the field survey was undertaken), briefly rebounding to $4.27 billion in 2015, before falling steeply afterward to $1.89 billion in 2018 (when 95% of total exports were to China) (Davis, 2020).

Schmidt et al. (2022) document social and environmental conflicts caused by agrochemical use in Salta, Santiago del Estero and Santa Fe, Argentina, in an area dominated by use of genetically modified seeds and agrochemicals, including glyphosate sprayed on glyphosate-tolerant GM crops. They highlight how conflicts and disputes over the environmental and health consequences of exposure to agrochemicals have surged in society and conclude that there is no official recognition of the health and environmental damage.

Garrett and Rausch (2016) argue that federal investment in the soy industry in Brazil has largely excluded the poorest farmers, particularly in the North and Northeast regions, to the benefit of large multinational agribusiness firms, small farmers from the South, and well-capitalized entrepreneurs from the Southeast. In addition, counties with high levels of soybean production tend to have higher income inequality than counties dominated by other land uses. These authors conclude that soy production has created substantial but exclusive economic benefits without reducing domestic food security, since it has not replaced other crops. However, the expansion of soy cropland into native savannas has endangered future generations' well-being by contributing to irreversible climate change and biodiversity loss in ways that are uncertain and immeasurable.

Nevertheless, many family farms still exist in Brazil, with a variety of farming practices, including organic and conventional production (Vennett et al. 2016; Cacho, 2016), so not all Brazilian soy production is large-scale GM soy. Garrett et al. (2013) provide empirical evidence that Brazil's continued production of non-genetically modified (GM) soybeans has increased its competitive advantage in European countries with preferences against GM foods. Brazil's strong trade relationship with European consumers has facilitated an upgrading of the soybean supply chain. Upgraded soybean supply chains create new conservation opportunities by allowing farmers to differentiate their products based on environmental quality in order to access premiums in niche markets in Europe. These interactions between GM preferences, trade flows, and supply chain structure help to explain why Brazilian soybean farmers have adopted environmental certification programmes on a larger scale than Argentinian, Bolivian, Paraguayan, and Uruguayan soybean producers.

Dreoni et al. (2022) present a systematic literature review of the direct and indirect social-economic impacts of soybean agricultural production for trade. They find clear evidence clear of negative impacts associated with soybean production due to land use changes and deforestation, and agricultural intensification. However, they also find that that the empirical evidence for direct social impacts of soy production is scarce and mixed in terms of direction of impact. Income, nutrition and living standards are more often positively impacted by soy trade, while more intangible dimensions such as freedom of choice and cultural value are found to be negatively affected. These authors also find that more attention to equity and power issues is required, such as actions to avoid land appropriation, and to empower smallholders in supply chains.

3.5.2. Increasing indebtness in the Philippines

In the Philippines, GM corn (maize) rapidly increased in area from 2002, initially with the insect resistant Bt trait. In 2011, 96% of all GM corn contained the RR trait. Farmers were promised increased incomes from growing GM crops. However, the farmer-led network MASIPAG argues that they have instead experienced increasing indebtedness, unemployment, loss of ownership of their lands and control over their seeds, as well as food insecurity from loss of biodiversity (MASIPAG, 2013).

While the introductory price for GM corn (maize) was not much higher than the price for conventional corn, it subsequently rose dramatically. According to MASIPAG, in 2000, in Carataya, Cuartero for example, a 18-20 kg bag of RR corn cost 60% less than a 9 kg bag in 2008. In 2012, costs for RR corn were about 2.5 times as much as for hybrid seed. Moreover, Roundup is the most expensive herbicide brand. Combined costs for GM corn seed and Roundup accounted for 22-26% of total farmers' production costs in 2011. Before the introduction of RR corn, farmers saved their seeds and hence also saved the costs for expensive seeds. Intellectual Property Rights (IPRs) (i.e. patents) on the RR seeds however prevent farmers from replanting and re-using the seed for cross breeding with other varieties without paying royalties to the patent holder (MASIPAG, 2013). Afidchao et al. (2014) report seed costs in the Philippines for RR maize of US $354.51 per hectare, compared to US $262.84 per hectare for conventional maize, meaning a 35% premium for the GM variety.

Farmers in all case areas in the MASIPEG study reportedly complain of not being able to plant vegetables, fruits and rootcrops near their GM cornfields because herbicide drift negatively affects them. As a result, families now have to buy vegetables. Moreover, farmers reportedly lost the staple crop white corn due to GM contamination. Farmers also complain about soil erosion, landslides, destroyed crop fields and heavy rainwater runoff from cornfields planted with RR corn. According to MASIPEG, in 2009, corn (maize) farms had the highest rate of soil loss (MASIPAG, 2013). In a survey of farming households on the Philippine island of Mindanao, Bequet (2020) finds a correlation between herbicide tolerant corn cultivation and landslide occurrence. He argues that more aggressive weed control via broad-spectrum herbicide is a likely mechanism.

Many smallholder farmers in the Philippines are greatly indebted today. One reason for this is that traders charge farmers with 5-10% monthly interest on the farmers' loans. The inputs are also priced higher when bought on a loan basis. Moreover, the farmers are bound to sell their produce to the traders at a price usually lower than the prevailing market price, since traders control the price of inputs and the buying price for corn. Indebted farmers loose control over their lands and the decisions over what crops, which variety and brand to plant to traders. If they wanted to plant other corn varieties, traders could deny loans for their corn production and consumption needs.

According to MASIPAG, the introduction of RR crops further contributed to rural unemployment, since many farm workers lost their livelihood as weeders (MASIPAG, 2013).

3.6. Conclusions

In North and South America, the initial benefits from RR crops for farmers have declined quickly, mainly due to the emergence of GR weeds which force RR crop adopting farmers today to apply additional, older and higher risk herbicides, making weed control more difficult, more expensive and more environmentally damaging. With 55 evolved GR weed species already known worldwide and new GR weed species evolving at an increasing rate, this technology is becoming obsolete. Applying ever increasing amounts of more and more toxic herbicides is detrimental to the environment and human health and locks farmers into a system where they heavily rely on technological improvements by the industry to keep up with the evolution of weeds. Moreover, the adoption of RR crops brings about legal uncertainties for farmers and states that do not want to grow GM crops and decreases overall seed choice. Patents on GM seeds give companies monopoly control and have led to significant increases in seed prices. Farmers buying RR seeds are locked into a "transgenic treadmill" in which they are forced to pay for hikes in seed prices and for increasing amounts of herbicides and labour to tackle weed resistance. The biggest winners are the multinational biotech companies, selling not only the seeds but also the corresponding herbicides.

4. Environmental impacts of RR crops and associated glyphosate-based herbicide regime

The economic literature, examining the effects of HT crop adoption on profit for farms, seed and herbicide suppliers and consumers, usually ignores negative environmental externalities (Desquilbet et al. 2019). The European Food Safety Authority (EFSA) has acknowledged that the cultivation of RR crops and the associated use of glyphosate may have potential adverse environmental effects such as glyphosate resistant weeds, subsequent changes in weed community diversity (as mainly glyphosate tolerant species will be selected), a reduction in farmland biodiversity and changes in soil microbial communities (see, for example, EFSA, 2012). We already described the development of GR weeds above (See Section 3.1.2. Superweeds) and will in this section discuss the other potential environmental effects. Unfortunately, reliable and independent data on the long-term environmental impact of the cultivation of RR crops are scarce globally. The major RR crop cultivating countries fail to systematically monitor the impact of non-selective herbicides such as glyphosate on the environment (Hilbeck et al., 2008). The largest field trials ever conducted with HT crops are the Farm-scale Evaluations (FSEs) in the UK (see Section 4.2.1 Farmland biodiversity and the UK Farm Scale Evaluations (FSEs)), which explored impacts of growing such crops on farmland biodiversity, and informed the UK decision not to grow such crops.

Adverse environmental impacts associated with the use of glyphosate in agriculture are of two kinds: (i) indirect impacts, for example due to the loss of habitats for wildlife; and (ii) direct impacts due to adverse effects of glyphosate-based hericides on living organisms. Although glyphosate is used as a weedkiller in many different applications, its use on RoundUp Ready GM crops involves blanket spraying of agricultural fields and has resulted in a significant increase in the volume of glyphosate-based herbicides in countries where RoundUp Ready GM crops are grown (See Section 3.1.1 Herbicide use).

When glyphosate was approved for use in 1974 it appeared to be safe because its acute toxicity (i.e., the immediate effect on an organism, following a single dose of glyphosate) appears to be low. However, subsequently attention has shifted to the effects of long-term exposure to low doses (Shaw, 2021). Mechanisms of harm can include oxidative stress, caused by the accumulation of toxic oxygen reactive species (ROS) in cells and tissues (Wang et al., 2022a), and endocrine disruption (see also Section 5.5.4. Endocrine disruption and reproductive health). Another major limitation of most early studies was the lack of consideration of other chemicals, mixed with glyphosate to form glyphosate-based herbicides (Martins-Gomes et al., 2022). Regulators focus only on the supposed ‘active’ ingredient, not on the harmful effects of mixtures (Sprinkle & Payne-Sturges, 2021).

The US Environmental Protection Agency (EPA) released its final Biological Evaluation (BE) assessing risks to listed species from labeled uses of glyphosate in November 2021 (US EPA, 2021a). The term "listed species" refers to those that are federally listed as endangered or threatened, as well as experimental populations and species that are proposed and candidates for listing. The EPA identified that glyphosate was ‘likely to adversely affect’ (LLA) 93% of the species assessed (including mammals, birds, amphibians, reptiles, fish, plants, aquatic invertebrates and terrestrial invertebrates) and 96% of their habitats. This was a total of 1676 species and 759 critical habitats. According to the EPA, most of these adverse impacts had moderate evidence. Strong evidence was found for one bird species (the California clapper rail, *Rallus longirostris obsoletus*), and six critical habitats (for the Mississippi sandhill crane, *Grus canadensis pulla*; and the plants Hoover's spurge, *Chamaesyce hooveri*; Gypsum wild-buckwheat, *Eriogonum gypsophilum*; Greene's tuctoria, *Tuctoria greenei*; Willamette daisy, *Erigeron decumbens*; and Large-flowered woolly Meadowfoam, *Limnanthes floccosa ssp. Grandiflora*).

Many studies have now identified chronic toxicological effects of glyphosate in a wide variety of animals (Gill et al., 2018). These authors note that toxicological effects have been traced from lower invertebrates to higher vertebrates. Their review of toxicological effects of glyphosate and metabolites notes that effects have been observed in annelids (earthworms), arthropods (crustaceans and insects), molluscs, echinoderms, fish, reptiles, amphibians and birds. They document how toxicological effects like genotoxicity, cytotoxicity, nuclear aberration, hormonal disruption, chromosomal aberrations and DNA damage have also been observed in higher vertebrates like humans.

Singh et al. (2020) review evidence of glyphosate toxicity on different ecosystems. They find that experiments reveal that excessive glyphosate use induces stress on crops and on non-target plants, and is toxic for mammalians, microorganisms and invertebrates. They conclude that the long half-life period of glyphosate and its metabolites under different environmental conditions is a major concern.

Barbosa Lima et al. (2021) review the environmental effects of glyphosate on a wide variety of species and express concern about glyphosate contamination of water resources and soil in Brazil. Marques et al. (2021) also review environmental impacts of glyphosate from a Brazilian perspective. They highlight studies that show that the intensive use of glyphosate has the potential to cause harmful effects on soil microorganisms, leading to changes in soil fertility and ecological imbalance, as well as impacts on aquatic environments, nontarget species and the contamination of the atmosphere.

This section will look at such existing data and case studies to approach the question what impact the cultivation of RR crops, including the use of glyphosate-based herbicides like Roundup, has on the environment. Impacts of new 2,4-D and dicamba-tolerant crops that have been developed as a response to GR weeds are likely to add to environmental harms (see Section 6. Industry response and Section 7. Environmental and health effects of other herbicides).

Production of glyphosate requires the mining of phosphate (also used to make fertilizer), which can have adverse impacts on the environment, such as destruction of soil and vegetation, contamination of watercourses and noise and air pollution (Wozniacka, 2019). However, these impacts are not considered further here.

4.1. Increased environmental occurrence of glyphosate and AMPA

The introduction of RR crops and the corresponding increase in the use of glyphosate-based herbicides has obviously also increased environmental exposure to those herbicides. Glyphosate binds strongly to soil and is very water-soluble. Its half-life (the time taken to reduce its concentration by half, as it breaks down into other chemicals) is said to range from 2 - 215 days in soil and from 2 – 91 days in water (Battaglin et al., 2014). Myers et al. (2016) argue that the half-life of glyphosate in water and soil is longer than previously recognised. One of glyphosate’s primary metabolites (the main substance produced when glyphosate breaks down), aminomethyl phosphanic acid (AMPA), is also very water-soluble but degrades more slowly than glyphosate. AMPA finally degrades into inorganic phosphate, ammonium and CO_2 (Battaglin et al., 2014).

Mamy et al. (2016) consider that a significant fraction of pesticides sprayed on crops may be returned to soils via plant residues. In experiments using oil seed rape (canola) they find that the trapping of herbicides in plant materials provides protection against degradation, so that crop residues may increase the persistence of glyphosate in soils. Glyphosate was still detected after 80 days when an entire leaf was left on the soil surface. This pattern appeared more pronounced for glyphosate-tolerant crops, which accumulated more non-degraded glyphosate in their tissues. These authors conclude that the increase in extractable glyphosate and AMPA following soil degradation of glyphosate contained in oilseed rape leaves could increase the potential risk of groundwater contamination.

Battaglin et al. (2014) detected glyphosate and AMPA in 39.4% and 55%, respectively, of 3,732 environmental samples ranging from precipitation, streams, rivers, lakes, ponds, wetlands, soil water and ground water to soil and sediment. The samples were collected from 2001 – 2010 in 38 US states. Medalie et al. (2019) test 70 streams throughout the United States, from 2015 to 2017, and find glyphosate and AMPA in all regions and all size watersheds. Bollani et al. (2018) find concentrations of glyphosate and AMPA, with maximum values of 13.6 and 9.75 μg L^{-1}, in water samples water from an area of the Pampean region (Argentina).

Pesticides can become airborne through volatilization, spray drift or wind erosion of soil particles to which they are attached and be carried by wind in unintended environments where they can then be deposited by precipitation. Majewski et al. (2014) found glyphosate and AMPA in more than 75% of air and rain samples collected in the Mississippi delta in 2007. Glyphosate was detected over the entire growing season and accounted for 55% of the total herbicide flux. Chang et al. (2011) detected glyphosate and AMPA in more than 60% and more than 50%, respectively of all air and rain samples collected in agricultural areas in Mississippi, Iowa and Indiana during the growing seasons of 2004, 2007 and 2008. In 2004 in Indiana, both glyphosate and AMPA were detected in 92% of the rain samples. The detection frequency and median glyphosate concentrations in air were comparable to other highly used herbicides, however the maximum concentrations of glyphosate were greater. For rain, both median and maximum concentrations of glyphosate were substantially greater than those of other currently used herbicides even though other herbicides are more volatile than glyphosate.

Bento et al. (2016) study the persistence of glyphosate and AMPA in ‘loess’ soil (windblown dust and silt). They find that glyphosate and AMPA dissipate rapidly under warm and rainy climate conditions. However, they conclude that repeated glyphosate applications in fallows or winter crops in countries where cold and dry winters normally occur could lead to on-site soil pollution, with consequent potential risks to the environment and human health.

Bohm et al. (2014) find that two applications of glyphosate to RR soybeans in Brazil at 960 g a.i. ha^{-1} brought about a residue of 4.33 mg kg^{-1} in soil. AMPA residues were significantly higher in the areas where glyphosate was applied twice (11 mg kg^{-1}) compared with the area of only one application (5 mg kg^{-1}). In their study of glyphosate and AMPA in topsoil in Brazil, da Silva et al. (2021) find glyphosate (GLY) and AMPA at peak concentrations of 66.38 and 26.03 mg/kg soil respectively. This study collected soil from three different farming areas and nearby forest patches to perform a pesticide screening. GLY was strongly associated with forest soil properties, while AMPA associated more with no-tillage soil properties. According to the authors, the glyphosate concentrations are the highest ever reported in the world. They recommend that future studies investigate the possible mechanisms and transport pathways of GLY and AMPA from agricultural land to forest areas.

Ramirez Haberkon et al. (2021) report the first evidence of glyphosate and AMPA in breatheable dust particles (PM10) emitted from unpaved rural roads of Argentina. They find that actual PM10 emission was 11.5 g ha^{-1} $year^{-1}$ in agricultural soils and 4711.4 g ha^{-1} $year^{-1}$ in unpaved roads, partly due to higher wind erosion. The content of glyphosate in the PM10 ranged from 59 to 359 μg kg^{-1} in agricultural soils, from 382 to 454 μg kg^{-1} in unpaved roads inside farm fields, and from 39 to 639 μg kg^{-1} in unpaved roads outside farm fields. Content of AMPA in the PM10 ranged from 387 to 7228 μg kg^{-1} in agricultural soils, from 900 to 4138 μg kg^{-1} in unpaved roads inside farm fields, and 98 to 500 μg kg^{-1} in unpaved roads outside farm fields. They highlight the importance of considering the risk of PM10 dust particles emitted by unpaved roads and agricultural fields.

Cristofaro et al. (2021) assess glyphosate concentrations in six reservoirs of the Paraíba do Sul and Guandu River Basins in southeast Brazil. Glyphosate was detected in all six reservoirs and in three of them concentrations were above the limit imposed by Brazilian legislation. Barbosa Lima et al. (2021) and Clasen et al. (2019) also highlight glyphosate contamination of water resources and soil in Brazil. Brovini et al. (2021a) perform a systematic review of quantitative studies of glyphosate, atrazine, and 2,4D in Brazilian freshwater. In this analysis, regarding environmental risks, 94% of Brazilian states had a medium to high risk to glyphosate and 80% of Brazilian states evaluated showed a high environmental risk considering a mixture of the three pesticides. The authors state that most of the environmental concentrations registered were below the allowed limits but could still pose a high risk for aquatic ecosystems. They strongly recommend a revaluation of the maximum allowed values of these pesticides in Brazilian legislation.

Aparicio et al. (2013) demonstrate that glyphosate and AMPA are present in agricultural soils in Argentina. Sixteen agricultural sites and forty-four streams in agricultural basins were sampled three times during 2012. In cultivated soils, glyphosate was detected in concentrations between 35 and 1502 µg kg^{-1}, while AMPA concentration ranged from 299 to 2256 µg kg^{-1}. In the surface water studied, the presence of glyphosate and AMPA was detected in about 15% and 12% of the samples analyzed, respectively. In suspended particulate matter, glyphosate was found in 67% while AMPA was present in 20% of the samples. In streams sediment glyphosate and AMPA were also detected in 66% and 88.5% of the samples respectively. In stream samples the presence of glyphosate and AMPA was relatively more frequent in suspended particulate matter and sediment than in water. The authors conclude that surface run-off can cause the movement of soil particles which carry adsorbed glyphosate and end up in surface water courses where the glyphosate can also be desorbed, biodegraded and accumulate in the bottom sediment. Iturburu et al. (2019) attempt to develop an Environmental Risk Assessment for pesticides in the surface water of the Pampas region of Argentina. They find that 29% of reported sites showed high risk for current use pesticides, including glyphosate. DeMonte et al. (2018) find glyphosate and AMPA in 15% and 53% of analyzed samples from livestock wells waters from 40 dairy farms located in the central region of Argentina, with concentrations ranging from 0.6–11.3 µg/L and 0.2–6.5 µg/L respectively. These authors report greater concentrations of glyphosate in waters from open-reservoir tanks, which are directly exposed to the farm environment, with glyphosate and AMPA occurrence quantified in 33% and 61% of samples, with values ranging 0.6–21.2 µg/L and 0.2–4.2 µg/L respectively.

Alonso et al. (2018) collect 112 rainwater samples in urban areas of the Argentine pampas having different degrees of land use and with extensive crop production, plus 58 subsurface-soil samples. They report glyphosate, AMPA, and atrazine in 80% of the rainwater samples. In the soil samples, glyphosate was found in 41%, atrazine in 32% and AMPA in 22%. These authors highlight the ubiquitouness of these herbicides in the atmosphere and in rainfall, at concentrations higher than those detected in other countries and warn that this might constitute a source of exposure of the population to these pollutants from the air. Lupi et al. (2019) study glyphosate runoff and its occurrence in rainwater and subsurface soil in Argentina. Their experimental results demonstrate that 88.1% of the applied glyphosate was retained in the surface soil layer (0–9 cm). Glyphosate leaching was negligible compared to its runoff (3.9%) and spray drift (6.9%). Thus, the risk of groundwater pollution would be lower in comparison to that of both surface waters and rainwater. Moreover, under field conditions, glyphosate and AMPA were detected in 52% of the rainwater samples and glyphosate was detected up to 1 m in both soil profiles. Spray drift was the main source of glyphosate off-site transport, degrading air quality and rainwater for human consumption and glyphosate and AMPA in rainwater exceeded the limit set for safe human consumption in drinking water in the European Union (this is 0.5 µg/l for total pesticides, or 0.1 µg/l for any single pesticide). The highest glyphosate concentrations in rainwater were detected in periods with intensive pesticide application (summer and autumn-winter months).

Pesticides can reach water bodies by direct application to aquatic weeds but also by agricultural runoff and leaching processes or by precipitation. In 2002, Battaglin et al. (2005) found glyphosate and AMPA in 40% and 83%, respectively, of 51 streams in nine Midwestern states with a maximum concentration of 8.7 µg/l and 3.6 µg/l respectively. As a comparison, the maximum level of glyphosate allowed in drinking water in the EU is 0.1 µg/l. (Directive 98/83/EC). Struger et al. (2008), reported a considerably higher maximum concentration of glyphosate of 40.8 µg/l in surface waters of southern Ontario, Canada. Coupe et al. (2012) found measurable concentrations of glyphosate and AMPA in the majority of 7 analysed streams in four different agricultural basins.

They found maximum concentrations of glyphosate as high as 250 μg/l in Iowa, 430 μg/l in Indiana and 73 μg/l in Mississippi and 86 μg/l in France. The highest observed glyphosate concentration in runoff was 5.2 mg/L one day after application (Edwards et al., 1980). Zheng et al. (2018) study agricultural fields in the Midwestern United States, which are are commonly tile-drained to remove excess water from the soil. They monitor glyphosate and AMPA in tile drainage and their receiving watersheds (e.g., the Spoon River and Salt Fork). In this study, glyphosate and AMPA were frequently detected in river water samples at concentrations ranging from 0.13 to 2.85 μg/L and 0.13 to 1.30 μg/L, respectively, with much lower levels in subsurface tile drainage. This suggests that surface runoff and soil erosion could be major transport pathways for glyphosate and AMPA into watersheds. Montiel-León et al. (2019) find widespread occurrence of pesticides in the St. Lawrence River (SLR) and tributaries in Quebec, Canada. Glyphosate was one of the most recurrent compounds (detection frequency: 84%) in surface waters. Surface water samples were compliant with guidelines for the protection of aquatic life (chronic effects) for glyphosate and atrazine. However, 31% of the samples were found to surpass the guideline value of 8.3 ng L^{-1} for the sum of six priority neonicotinoids.

Bonansea et al. (2017) study glyphosate and AMPA in the Suquía River basin, Argentina. Compared to levels found in the water, levels ranged from 12 to 20 times higher for glyphosate and AMPA in sediment and suspended particulate matter (SPM). The most polluted area was situated within a green belt zone of the city; while in second place were sites located in areas of extensive agriculture. The authors conclude that aquatic organisms inhabiting areas both inside and outside agricultural areas are threatened by water glyphosate concentrations.

Fernandes et al. (2019) monitor the occurrence of glyphosate and AMPA residues in epilithic biofilms occurring in a watershed. Epilithic biofilms are communities of microorganisms composed mainly of microbial cells, substances from the metabolism of microorganisms, and inorganic materials. For this study, epilithic biofilm samples were collected in the Guaporé River watershed in southern Brazil, in the fall and spring seasons of 2016 at eight points. This study reports that the concentrations of glyphosate and AMPA detected in epilithic biofilms vary with the season and are strongly influenced by the amount of herbicide applications. One site was protected but at the other seven sites, glyphosate was detected in concentrations ranging from 10 to 305 μg kg^{-1}, and AMPA in concentrations from 50 to 670 μg kg^{-1}.

Lutri et al. (2020) study glyphosate and AMPA in groundwater and surface water in Córdoba, Argentina (the eastern slope of Las Peñas Mountain and its adjacent oriental fluvio-aeolian-plain). From the total water samples collected, glyphosate was detected in 66% of surface water samples (0.2 to 167.4 μg/L), in 15.8% of the groundwater samples (1.3 to 2 μg/L) and in the harvested precipitation sample (0.2 μg/L). AMPA was found in 33% of surface water and 15.8% of groundwater. These authors highlight that detection of glyphosate and AMPA in the unconfined aquifer (the primary water resource) shows that the application of glyphosate in agriculture in this region exceeds the degradation potential of the soil and the unsaturated zone, causing groundwater contamination. In a subsequent review, Carretta et al. (2022) highlight detectable groundwater contamination by glyphosate and AMPA in several countries, with many cases exceeding European groundwater quality standards.

Wang et al. (2016a) show that sediment plays a key role in the microbial degradation of glyphosate via both the sarcosine and AMPA pathway. Their findings demonstrate the key role of sediments in the degradation of glyphosate. These authors warn that accumulation of the main metabolite of glyphosate, AMPA, may be a cause for environmental concern and argue that further investigation of the fate of AMPA in water-sediment systems is needed.

Munira et al. (2016) show that phosphate fertiliser impacts on glyphosate sorption by soil, suggesting that, under moderately acidic to slightly alkaline conditions, glyphosate may become mobile by water in soils with high phosphate levels.

Mendez et al. (2017) document glyphosate and AMPA in dust emitted by an agricultural soil in Argentina. They find that glyphosate and AMPA are found in the respirable dust (RD) emitted by different sources (bulk soil and aggregate-size fractions), even 12 months after the last glyphosate application. Aminomethylphosphonic acid (AMPA) content in the RD is higher than glyphosate content. Glyphosate contents in RD were from 4 to 17 times higher than in the soil and aggregate source and AMPA contents in RD were from 4 to 9 times higher than in the source. The authors conclude that this suggests that glyphosate accumulates in RD, even when it is not detected in the source. This indicates that glyphosate and AMPA are accumulated in the respirable dust and it can potentially be a source of air contamination in the studied region.

Aparicio et al. (2018) study glyphosate and AMPA concentrations in wind-blown material under field conditions in three areas in Argentine semiarid regions (Chaco, La Pampa, and San Luis). The wind-blown material carried by the wind at a height of 150 cm had concentrations of 247 and 218 µg kg^{-1} of glyphosate and AMPA, respectively. This material was enriched 60 times in glyphosate and 3 times in AMPA as compared with the original soil. The authors conclude that this shows that the eroded material can, potentially, have a negative impact on the ecosystem and also on human health, depending on the proportion of this material released into the atmosphere in suspension as particulate matter.

Okada et al. (2018) study seasonal variations of glyphosate and AMPA seasonal in soil, groundwater, surface water, and sediments within a rural agricultural basin in Argentina. They report that all of the studied compartments had variable levels of glyphosate and AMPA. The highest frequency of detections was found in the stream sediment samples (glyphosate 95%, AMPA 100%), followed by surface water (glyphosate 28%, AMPA 50%) and then groundwater (glyphosate 24%, AMPA 33%). Despite glyphosate being considered a molecule with low vertical mobility in soils, they found that its detection in groundwater was strongly associated with the month where glyphosate concentration in soil was the highest. The maximum levels of glyphosate in soil and groundwater were detected in the autumn (fall).

By linking a pesticides database and a computer model, Maggi et al. (2020) find that low but pervasive contamination with glyphosate occurs in croplands globally, whilst a few geographic hotspots have mid to high contamination hazard. Glyphosate was found to be a persistent contaminant at relatively low values in about 30% of global croplands but AMPA was found to be persistent in about 93% of croplands. Hotspots found in South America, Europe, and East and South Asia were mostly correlated to widespread glyphosate use in pastures, soybean, and corn (maize). Soil residue accumulation and leaching below the root zone contributed locally to the hazard in hotspots. These authors note that the environmental persistence of glyphosate contradicts the earlier perception of rapid degradation "*and rather indicates extended periods of time during which residues may be remobilized such as by wind erosion, runoff, and leaching and cause exposure to non-target organisms and ecosystems*".

Botten et al. (2021) collect plant tissues from five forest understory perennial species growing in two distinct biogeoclimatic regions of northern British Colombia (Canada). Samples of roots and shoots were collected from four species of plants: *Salix spp.* (willow), *Cornus sericea L., syn. C. stolonifera* (red-osier dogwood), *Rubus idaeus L.* (red raspberry), and *Chamaenerion angustifolium* (L.) Scop. (fireweed) and fruits were also collected from *R. idaeus* and *Vaccinium caespitosum Michx*. (dwarf blueberry) plants. In this study, glyphosate residues persisted for up to 12 years in some tissue types, and root tissues generally retained glyphosate residues longer than shoot tissue types. Samples from the colder, more northern biogeoclimatic zone retained significantly higher levels of glyphosate for longer than samples collected from the warmer biogeoclimatic zone. The authors conclude that their study clearly demonstrates that surviving plants in forest cutblocks treated with glyphosate-based herbicides (GBH) may contain glyphosate residue in their roots, shoots and fruits for the first full year or more after treatment, and many also contain AMPA, with some plants retaining these residues for twelve years or more.

Yan et al. (2022) report that glyphosate, AMPA and glufosinate occurred widely in surfacewater, sediment and organisms (grasscarp, crayfish and crab) in aquaculture ponds from Honghu, China, with AMPA the most likely to accumulate in the intestine of aquatic products.

These results indicate that glyphosate and AMPA occur widely in the environment, are mobile and that their median concentration in the environment increases over time. Increasing environmental exposure of a pesticide can have direct toxic effects to non-target organisms or an indirect impact by altering habitat and resource availability, competition or predator abundance.

4.2. Impact on farmland biodiversity

Farmland biodiversity has declined substantially in recent decades due to agricultural intensification. Widespread use of herbicides in agriculture reduces weed seeds in the soil bank. Arable weeds play an important role in supporting farmland biodiversity and agro-ecosystem functioning. A decline among arable weeds can threaten invertebrates, small mammals and seed-eating birds that depend on the weeds for food resources, foraging, shelter or nesting habitats (Chamberlain et al., 2000; Donald et al., 2001; Fried et al., 2009; Fuller et al., 1995; Marshall et al., 2001; Moreby et al., 1994; Robinson & Sutherland, 2002; Stoate et al., 2001; Storkey et al., 2011). Concern has been expressed that broad-spectrum herbicides, like Roundup used with HT crops, would exacerbate the observed long-term steady decline in farmland biodiversity (Buckelew et al., 2000; Hails, 2000; Krebs et al., 1999; Marshall et al., 2001; Watkinson et al., 2000).

In a review of published evidence, Schütte et al. (2017) show that the adoption of herbicide-resistant crops impacts agronomy, agricultural practice, and weed management and contributes to biodiversity loss in several ways: (i) many studies show that glyphosate-based herbicides, which were commonly regarded as less harmful, are toxic to a range of aquatic organisms and adversely affect the soil and intestinal microflora and plant disease resistance; further, the increased use of 2,4-D or dicamba, linked to new herbicide-resistant crops, causes special concerns (see also Section 6. Industry response and Section 7. Environmental and health effects of other herbicides); (ii) The adoption of herbicide-resistant crops has reduced crop rotation and favoured weed management that is solely based on the use of herbicides; (iii) the intensive use of glyphosate over the last 20 years have led to the appearance of at least 34 glyphosate-resistant weed species worldwide. Although recommended for many years, farmers did not counter resistance development in weeds by integrated weed management, but continued to rely on herbicides as the sole measure of weed control. Despite the occurrence of widespread resistance in weeds to other herbicides, industry prefers to develop transgenic crops with additional herbicide resistance genes. (iv) Agricultural management based on broad-spectrum herbicides as in herbicide-resistant crops further decreases diversity and abundance of wild plants and impacts arthropod fauna and other farmland animals. The authors conclude that, taken together, adverse impacts of herbicide-resistant crops on biodiversity, when widely adopted, should be expected and are indeed very hard to avoid.

4.2.1 Farmland biodiversity and the UK Farm Scale Evaluations (FSEs)

The UK Farm Scale Evaluations (FSEs) of genetically modified herbicide tolerant crops arose out of concern that such crops would harm farmland biodiversity. The FSEs aimed to study the environmental impact of HT crops and their associated management practices. The research that started with a series of pilot studies in 1999, was commissioned by the government and overseen by an independent Scientific Steering Committee. The FSEs studied maize, spring-sown and winter-sown oilseed rape and beet in 273 field trials around England, Wales and Scotland. This broad coverage aimed to avoid possible bias due to local variations. Each experimental field was split in half, with one side being cultivated with a conventional variety and managed according to the then current normal practice, and one side being cultivated with HT varieties and controlled by a broad-spectrum herbicide. For HT maize, winter oilseed rape and spring oilseed rape the broad-spectrum herbicide used was Liberty (glufosinate-ammonium) and for beet it was Roundup (glyphosate). The field trials were carried out by conventional farmers who were free to manage the crops themselves, deciding when and how to plough the fields and to apply herbicides. The large number of field trials should reduce the chance of differences among the farmers affecting the overall results. The researchers monitored several indicators of farmland biodiversity such as weed density, weed biomass, the number of seeds that fell from the weeds on to the soil surface (seed rain) and the number of seeds left in the soil after harvest (the seedbank) in and around the crops. These indicators should help to determine food resource availability, whether the weeds would reproduce well and whether they were able to grow again the following year. They further monitored invertebrates present in the fields, including pollinators, herbivores, detritivores, predators and parasitoids. The data was collected several times a year before, during and after the crops were grown (Burke, 2003; 2005; Firbank et al., 2003).

The researchers found treatment effects in all the crops. In HT spring oilseed rape and RR beet, they found overall fewer weeds and weed seeds than in the conventional varieties. The researchers stressed that the differences they found do not arise from the genetically modified crops per se, but rather from different crop management practices. Whereas in conventional crops farmers often applied specific herbicides to the field before weed emergence to prevent seeds from germinating and then different herbicides after the weeds had emerged but were still small, in HT crops they were able to leave weeds to grow around the crops before spraying. They concluded that the broad-spectrum herbicide is a more effective weed killer than the combination of herbicides used on conventional crops, leaving fewer weeds in those GMHT crops, and that in the long term, seed stores could get depleted beyond recovery.

In winter oilseed rape, overall weed number did not differ between the treatments. However, the researchers found fewer broad-leaved and flowering weeds and weed seeds in the GMHT crops. On the other hand, they found more grass weeds and weed seeds in the GMHT field halves compared to the conventional field halves. The researchers attributed these results to the fact that the particular broad-spectrum herbicide used with this GM crop was relatively better at controlling broad-leaved weeds and less efficient at controlling grass weeds than the conventional herbicides.

In all three crop fields, there were more butterflies and bees in and around the conventional crops, probably because there were more flowering weeds to attract them. Flowering weeds are particularly important not only to insects but also to birds and small mammals. Growing GMHT beet and oilseed rape on a large-scale may thus disadvantage wildlife that depend on weeds and weed seeds. Springtails that live in the soil and feed on decaying and dead weeds, were however more abundant in the HT crop field halves compared to the conventional field halves. The researchers concluded that they benefit from farmers being able to apply the broad-spectrum herbicides post-emergence in HT cropping systems. Thus, the weeds can grow bigger before they are killed, leaving more rotting biomass to feed on for the springtails. More abundant springtails would further benefit their predators such as certain beetles and spiders. The researchers however speculated that this effect might only be short-lived, as from year to year there could be fewer weeds left for the herbicide to kill and for the springtails to feed on.

In maize, the treatment effect was different with more weeds, weed seeds, bees, butterflies and springtails found in HT fields compared to the conventional fields. The reason was that the broad-spectrum herbicide used on the HT maize fields was not as effective as the triazine herbicides, mostly atrazine, used on conventional fields (Burke, 2003; 2005; EFSA, 2011). Here it has to be noted that atrazine was withdrawn from approved lists of EU chemicals in 2004 (Commission Decision, 2004/248/EC). Perry et al. (2004), predicted that the comparative benefits for arable biodiversity of HT maize cropping versus conventional cropping would be reduced, but not eliminated, by this withdrawal. These conclusions are however only based on assumptions made in 2004 about future herbicide regimes. Furthermore, application of glufosinate-ammonium based herbicides in HT maize crops was limited to a single spray (at dose rates lower than 0.8 kg/ha in most cases) and might thus not fully reflect real agricultural practice. Especially, in case of emergence of weed resistance, herbicide application is likely to increase in number and dosage. It has also to be noted that while glufosinate-ammonium based herbicides were used in HT maize cropping in the FSE, glyphosate tolerant maize varieties are more widely used in countries which grow GM HT crops. Glyphosate-based herbicides reportedly provide more consistent and effective weed control than glufosinate-ammonium in particular cases (EFSA, 2011). Thus, the results of the FSEs for maize may not be sufficient to predict the effects of cultivation of RR crops on farmland biodiversity, because the impacts of RR crops on biodiversity might be expected to be worse.

Overall, the results of the FSEs were remarkably consistent from year to year and from area to area, even though there was a wide range of species abundance, geographic location and crop management across the field sites (Burke, 2003). As a consequence of the FSEs, the UK government stated that it would oppose commercial cultivation of HT beet and spring oilseed rape in the European Union, if farmers managed the crops as in the trials (Burke, 2005).

Research by Morandin & Winston (2005) in Canada supports the findings of the FSEs. Pollination deficit (the difference between potential and actual pollination) and bee abundance were measured in organic, conventional, and herbicide-resistant, genetically modified (GM) oil seed rape (canola) fields (*Brassica napus* and *B. rapa*) in northern Alberta, Canada, in the summer of 2002. Bee abundance data were collected using pan traps and standardized sweep netting, and pollination deficit was assessed by comparing the number of seeds per fruit from open pollinated and supplementally pollinated flowers. There was no pollination deficit in organic fields, a moderate pollination deficit in conventional fields, and the greatest pollination deficit in GM fields. Bee abundance was greatest in organic fields, followed by conventional fields, and lowest in GM fields. Overall, there was a strong, positive relationship between bee abundance at sampling locations and reduced pollination deficits. Seed set in *B. napus* increased with greater bee abundance. The authors speculate that the use of RoundUp in the fields growing GM crops may have reduced bee abundance.

Glyphosate spray drift may also damage nontarget plants outside agricultural fields (Cederlund, 2017). Golt & Wood (2021) cite evidence that low-dose glyphosate-based herbicide applications can cause male sterility in plants and report that glyphosate-based herbicides (GBHs) alter the reproductive morphology of *Rosa acicularis* (Prickly Rose), changing petal colour, petal shape, pollen viability, pollen size and shape, and anther development. These authors also report persistant GBH residues in flowers two years after applications.

In two-year field trials, Pereira et al. (2018a) observe lower densities of arthropods in soils planted with transgenic soybeans and given three applications of glyphosate compared to other treatments (mechanical weeding, or one application of glyphosate), especially the predators *Achaearanea* sp. (Araneae: Theridiidae), *Oxypodini* sp. (Coleoptera: Staphylinidae), *Solenopsis* spp. (Hymenoptera: Formicidae), the detritivorous *Entomobryidae* (Collembola), *Hypogastrura* sp. (Collembola: Hypogastruridae) and *Xyleborus* sp. (Coleoptera: Scolytidae). They also compare with non-transgenic soybeans and state that their results indicate that the insertion of the glyphosate resistant gene does not affect the richness and abundance of the arthropods, however the use of glyphosate reduces the densities of predators and detritivorous (organisms that eat dead or decaying plants or animals) on the soil surface.

Pereira et al. (2020) evaluate the impact of glyphosate-resistant soybean and its management with glyphosate on the canopy arthropod community in an experiment undertaken in Coimbra, Minas Gerais, Brazil, during the 2007/2008 and 2008/2009 growing seasons. These authors note that most studies on the impact of glyphosate have shown that this effect is due to the habitat change where arthropods live and not necessarily to the toxicological effect of the compound itself. They find that glyphosate application reduced the richness of predators and chewing and sucking phytophagous arthropods in treatments with three herbicide applications. In the second season, total arthropod density was the lowest in blocks growing GM soybean with three glyphosate applications, with varying impacts on the different species studied.

4.2.2 Land use and biodiversity

Although there have been no studies equivalent to the FSEs in other countries, a few other studies have looked at the impacts of RR crops on biodiversity. For example, De la Fuente et al. (2006) survey RR soybean fields in the Rolling Pampas in Argentina. They find a loss of local and regional diversity, associated with the adoption of RR crops. In a later study, De la Fuente et al. (2010) show that weed richness and non-herbivore arthropod richness both decrease with the increasing percentage of soybean in the surrounding landscape.

When a pasture or a soybean farm replaces natural ecosystems in Brazil, approximately 200–300 species per hectare are replaced by very few species. The impact on Brazilian biomes has had additional deleterious consequences for Brazilian fauna: the number of endangered animal species in Brazil has increased from less than 100 in 1963 to more than 600 in 2004 (Martinelli et al., 2010). Landscape-scale conversion to soy also substantially alters water-balance, potentially altering the regional hydrology over large areas and increasing stream temperatures (Hayhoe et al., 2011; Macedo et al., 2013; Neill et al., 2013). In Argentina, researchers have reportedly warned that the change of land use from forest to soybean fields is a key to explaining why floods are becoming more continuous and serious (Página 12, 2016).

In the mid-2000s, the Cerrado – Brazil's central savannah - overtook Amazonia as the leading area of deforestation in Brazil. Eloy et al. (2016) analyse how agricultural and environmental policies play out at the ground level in the Cerrado in western Bahia state, the main area of rapid expansion of high-input soybean agriculture in the Cerrado. They show that despite the strengthening of environmental regulations, the soybean frontier is still advancing. They argue that selective environmental policies put a disproportionate strain on smallholders and traditional populations, whilst continuing to allow large-scale soybean plantations. Redo et al. (2013) map vegetation change in Brazil's three largest dryland ecoregions – the Cerrado, Caatinga, and Mato Grosso seasonal forests from 2001 to 2009. South America's dryland ecoregions cover 46% or 8,282,217 km^2 of available land surface, yet have received much less media, research, and conservation attention in comparison with other tropical forests. The overall area planted in cropland and tree plantations increased by 34,822 km^2 from 2002–2003 to 2007–2008, although changes in the extent and distribution among the various crop types differed considerably. Among crops, soybeans experienced the largest increase with 17,880 km^2.

De Groot et al. (2021) argue that large-scale soybean monoculture has reduced honey yield in Argentina. Their results indicate that the expansion of the area cultivated with soybean since 1996, which involved the replacement of natural habitats with extensive cultivated fields, planted with GM soy and sprayed with glyphosate, is associated with a reduction in honey yield of around 60%.

In the U.S., wild bees have also declined in areas of intensive agriculture, such as the Midwest Corn Belt. Koh et al. (2016) suggest that conversion of land to grow corn for biofuel production might be responsible for the decline. They didn't exclude the possibility that pesticides are having an impact on wild bees (McGrath, 2015). See also Section 4.2.5. Pollinators.

4.2.3. Farmland Birds

Farmland birds have declined over past decades (Chamberlain et al., 2000; Donald et al., 2001; Fuller et al., 1995; Gregory et al., 2004). Intensive agriculture leaves fewer nesting places, weed seeds and insects as food supplies for the birds (Burke, 2005). Gibbons et al. (2006) use FSE data on weed seed rain and information on bird diets to determine how GMHT cropping might change the food resources available to farmland birds. They calculate the total abundance of all weed seeds important in the diet of each bird species in each crop and half-field. In beet and spring oilseed rape they found that the rain of weed seeds important in the diets of all 17 bird species was less in the GMHT compared to conventional halves, with an approximately threefold difference. These differences were significant for all but one species in each crop. In winter oilseed rape, the rain of seed weeds important in bird diets was also lower in GMHT treatments, but this effect is less pronounced. In maize, the rain of weed seeds important to bird diets was however higher in the GMHT compared to the conventional halves for all 17 bird species, although this effect was only significant for seven species. However, as noted above, the conventional maize in this trial was treated with atrazine, which has now been banned in the EU. Since seeds from different weed species vary greatly in size and composition the researchers further used weights and compositions of seeds to determine the true resource availability to foraging birds. Overall, treatment effects for seed rain abundance and seed energy were strongly correlated. Total energy available from weed seeds important in the diets of all 17 bird species was also lower in GMHT beet and oilseed rape and higher in GMHT maize compared to conventional halves. The only systematic difference between these two measurements was that the treatment effect for weed seed energy in beet and spring oilseed rape was slightly but significantly more pronounced than for seed rain. According to Gibbons et al. (2006) that suggests that for those two GMHT crops the energetic resource available to birds would be reduced even further than suggested from the simple reduction in seed numbers. Gibbons et al. (2006) concluded that introduction of beet, spring and winter rape crops in the UK could, if managed as in the FSEs, markedly reduce important food resources for farmland birds, many of which declined during the last quarter of the twentieth century.

As well as indirect adverse effects on birds (as a result of damage to their habitat), evidence of direct adverse effects of glyphosate on birds also needs to be considered.

Kissane & Shephard (2017) note that a mounting number of studies in wildlife and humans indicate that there are concerning effects with even sub-lethal exposure concentrations of glyphosate-based herbicides. They argue that the rise in glyphosate due to the introduction of GMOs and glyphosate resistant crops makes it necessary that more research be done on the effects of exposure, particularly at sub-lethal levels, and that, as proven indicators of environmental toxicity, birds may well hold the key to some of the unanswered questions relating to chronic exposure of glyphosate. Birds are exposed to pollution through numerous pathways and their potential for exposure to glyphosate is high, given its application and known presence in wetland, agricultural, and urban environments, which contribute contaminant runoff to coastal and marine systems. These authors argue that, in particular, wetland birds may be excellent species for study as their biology and ecological roles in the functioning of wetland ecosystems is well understood, and glyphosate residues, and AMPA, are known to be present. However, very limited relevant research has been conducted to date. They note that the inhibition of the enzyme AChE has been reported in wild ducks exposed to glyphosate sprayed on rice crops in Mexico (Osten et al. 2005). These ducks are consumed by humans throughout the year. In addition, Oliveira et al. (2007) have reported harmful effects of RoundUp on the male genital system of mallard drakes.

In the first long-term experiment testing the parental effects of glyphosate-based herbicides (GBHs) in birds, Ruuskanen et al. (2020a) expose a parental generation of Japanese quails (*Coturnix japonica*) to GBHs (200 mg/kg feed) or respective controls. Glyphosate residues were found in eggs (ca 0.76 kg/mg) and embryonic development tended to be poorer in the eggs of GBH-exposed parents (76% of eggs showed normal development) compared to control parents (89% normal eggs). Embryonic brain tissue from GBH-exposed parents tended to express more lipid damage (20% higher), however other biomarkers showed no apparent differences and there were no observed differences in egg quality. The authors argue that more studies are needed. Ruuskanen et al. (2020b) conduct further experiments in which they expose Japanese quails to GBHs from the age of 10 days to 52 weeks. They find that GBH exposure decreased the activity of an intracellular antioxidant enzyme (catalase) in the liver, but did not influence other intracellular oxidative stress biomarkers. They also report that GBH exposure altered overall gut microbiome composition, especially at a younger age and in females, and suppressed potentially beneficial microbes at an early age. GBH exposure decreased male testosterone levels both at sexual maturity and at 52 weeks of exposure, but did not clearly influence reproduction in either sex. They conclude that their results suggest that cumulative GBH exposure may influence health and reproduction-related traits, which is important in predicting their effects on wild populations and the global poultry industry. In an earlier study, Ruuskanen et al. (2020c) show that female quails prefer GBH-contaminated food compared to control food. In females, exposure to GBHs caused delayed plumage development, and GBH residues were present in eggs, muscles, and liver.

Jarrell et al. (2021) report negative effects of RoundUp exposure on broiler breeder rooster reproductive health (reductions in sperm mobility, viability and count).

Fathi et al. (2020) investigate the toxic effects of pure glyphosate or Roundup on the liver and small intestine of chick embryos. In their experiments, a total of 180 fertile eggs were injected with deionized water (control group), 10 mg pure glyphosate, or 10 mg of the active ingredient glyphosate in Roundup/kg egg mass. They find that exposure to glyphosate caused increased liver function enzymes, histopathological alterations in the liver and small intestines, and induced oxidative stress in chick embryos. They also find that glyphosate and RoundUp may cause dysfunction of the liver and intestinal enzymes system in chick embryos, which they conclude may increase the potential health risks to animals and humans.

In a study that has not yet been peer reviewed, Lehel et al. (2021) treat chicken embryos with single and simultaneous doses of glyphosate (Amega Up, 360 g/L, 4%) and copper sulphate (0.01%), by injection or immersion. The report an additive interaction was between the copper sulphate and glyphosate "*that may result in reduced vitality of the embryos and thus the number of offspring of wild-life birds*".

4.2.4. Butterflies

Butterflies rely on nectar from flowering crops, weeds and wildflowers. The UK Farm Scale Evaluations (FSEs) show a decreased abundance of butterflies in herbicide tolerant sugar beet and oilseed rape fields compared to conventional fields, thought to be due to a reduction in flowering weeds in those fields. Butterflies can fly long distances to find the plant they need, they do not have to be immediately impacted by a decline in flowering weeds in single GMHT fields. However, if weeds die away over large areas over several years, which could happen when RR crops are cultivated continuously on a large scale, this could have adverse impacts on butterflies. The UK FSEs suggested that growing conventional crops might thus be especially important in regions with few suitable flowers and nectar resources for butterflies. In such areas, a long-term reduction in weed populations could exacerbate the decline in butterfly populations (Burke, 2003; 2005). In the U.S., where large-scale cultivation of RR crops and associated spraying of Roundup is abundant, serious negative impacts of RR cropping systems have been found on the famous Monarch butterfly.

Monarch Butterflies (*Danaus plexippus* L.) undergo a multi-generation annual cycle that includes migration from central Mexico to their breeding areas in North America and back. During spring, adults that overwintered in Mexico begin migration to North America. In this time about three generations of larvae are produced that continue the journey north. Females lay their eggs exclusively on milkweed plants (*Asclepias),* which is the sole food source of the monarch butterfly larvae. In fall, adult monarchs enter a state of reproductive diapause and begin migrating back to central Mexico, where they overwinter. There is also a smaller overwintering population in western California.

Monarch butterfly surveys are undertaken in Mexico (of the overwintering population) and of the overwintering 'Western' population in the U.S.A. These surveys show significant declines from historic numbers over the past decades, despite some small signs of partial recovery in recent years:

- The International Union for the Conservation of Nature (IUCN) estimates that the population of monarch butterflies in North America has declined between 22% and 72% over 10 years, depending on the measurement method, and added the monarch butterfly to its "red list" of threatened species and categorized it as "endangered" for the first time in 2022 (Larson, 2022).

- More than 1.2 million Monarch butterflies were recorded in the Western population in 1997, and scientists estimate that this population has decreased by 95% since the 1980s (Kimbrough, 2022). Other reported estimates are that the population of monarch butterflies he studies in the eastern United States has declined between 85% and 95% since the 1990s (Larson, 2022).
- According to an annual survey by WWF of the area of forest occupied by overwintering monarch butterfly colonies in Mexico from 1993-1994 to 2021-2022, during the second half of December 2021, ten colonies of Monarch Butterflies were registered covering 2.835 hectares (ha) of forest, which represents a 35% increase in relation to the area registered in 2020 (2.10 ha) (Rendón-Salinas et al., 2022). Six colonies covering 2.174 ha were located inside the Monarch Butterfly Biosphere Reserve (MBBR) and four covering 0.661 ha were located outside the MBBR. The occupied area appears to have recovered from a historic low of 0.67 hectares in 2013-14, but is still significantly lower than the 6.23 hectares recorded in 1993-94, and the peak of 18.19 hectares recorded in 1996-97.
- According to a count managed by the Xerces Society, the Western USA population of Monarch butterflies (overwintering in California) reached a historic low of 2,000 in 2020, but has since rebounded to 247,000 in 2022: however, this is still a dramatic decline from historic numbers and is not necessarily a sign of long-term recovery (Kimbrough, 2022).

The Eastern population in the USA is made up of the butterflies east of the Rocky Mountains and accounts for roughly 99% of all North American monarchs. According to the Center for Biological Diversity (CBD), Monarch butterflies remain at risk of extinction in 2022 (CBD, 2022).

Studies have implicated a number of factors in the historic decline in Monarch butterfly populations, including a significant loss of milkweed habitat in the USA, where Monarchs lay their eggs, due to to blanket spraying of RR GM crops with glyphosate.

From 1994-2011, a statistically significant decline in the area occupied by overwintering monarchs was observed (Brower et al., 2012). Vidal & Rendón-Salinas (2014), reported a particular decline during the last seven seasons with a 20-year low reached during the 2013-2014 season, when the long-term average of about 350 million butterflies overwintering in Mexico dropped to a mere 33.5 million butterflies (Fallon, 2014). In only 20 years, there had thus been a 90% decline in overwintering monarchs, putting them at risk of extinction (Monarch ESA Petition, 2014). In the 2014-2015 season the number of monarchs rose again to approximately 56.6 million individuals but this is still the second lowest number ever observed (Fallon, 2015). A modelling study by Semmens et al. (2016) concluded that this population of monarch butterflies has a substantial probability of quasi-extinction (meaning the loss of a viable migratory population of monarchs in eastern North America). They calculate that an approximately 5-fold increase of the monarch population size (relative to the winter of 2014–15) is necessary to halve the risk. Loss of overwintering sites due to illegal logging in Mexico, severe weather conditions and the loss of milkweed plants associated with increased glyphosate use in RR crop fields, have been named as probable reasons for the population decline (Brower et al., 2012).

For a long time, it was believed that the main reason for the decline was deforestation and degradation of the monarchs' overwintering sites (Brower et al., 2002; 2004). To address these problems, the Monarch Butterfly Biosphere Reserve, today a World Heritage site (UNESCO, 2008), was established in 2000. Subsequently, a monarch butterfly conservation trust fund was created to provide economic incentives to landowners and agrarian communities to conserve their forests. Together with stringent law enforcement by Mexican authorities, payment for environmental services, and the creation of alternative incomes and employment for local communities, a decrease of illegal logging was observed from 731 ha affected in 2005-2007 to none affected in the 2011-2012 (Vidal et al., 2014; Vidal & Rendón-Salinas, 2014). Since then there was a slight increase in illegal logging, resulting in degradation of 5.18 ha in 2013-2014 (Vidal & Rendón-

Salinas, 2014; WWF Mexico & Fondo Monarca, 2013). Thus, illegal logging might not be completely halted but the improvement is nevertheless substantial. Still, monarch numbers are worryingly low.

A subsequent study challenges the view that deforestation on the overwintering grounds is the main reason for the decline in monarch butterflies (Flockhart et al., 2014). This population model predicts that milkweed loss on the breeding grounds of monarchs has a much stronger negative impact on them. Between 1995 and 2013 the model estimated a 21% decline in milkweed abundance. Such a big decline in milkweed abundance is not only detrimental for monarch larvae feeding on it. A modelling study, conducted by Zalucki & Lammers (2010) found that decreasing milkweed density can also reduce lifetime potential fecundity of monarch females by about 20%, due to increased search time for host plants. With increasing energy invested for searching for host plants, the butterflies' body fat depletes and as a consequence they lay fewer eggs or die before reproduction (Wines, 2014). Flockhart et al. (2014) attributed the huge milkweed loss predicted by their population model to herbicide-resistant corn (maize) and soybeans that are increasingly cultivated in the U.S. Midwest, which is also the major breeding ground for monarchs. They concluded that mitigating the negative impacts of GM crops on host plant abundance was the highest conservation priority. Semmens et al. (2016), as described above, argue that Flockhart et al. (2014) have underestimated the risk of quasi-extinction of this monarch butterfly population, particularly because the population is not only in decline but also fluctuating wildly.

Common milkweed is a perennial plant with a deep and extensive root system that allows re-sprouting in the spring or after disturbance (e.g. mowing or herbicide application). That is why common milkweed establishes best in disturbed areas, such as ploughed or some cultivated fields, pastures, along rails, railroads tracks and roadways, and why common herbicides do not have a big effect on milkweed as they only kill the above-ground plant while leaving the reproductive root system intact. They can even be beneficial to milkweed, in that they kill competing weeds. In fact, row crops like corn and soybeans with heavy use of milkweed-ineffective herbicides are a favourable habitat for milkweed - more favourable than crops and plants that grow more densely and tend to supress milkweed, such as wheat, alfalfa or grassland or unmown pasture. Despite its ability to survive in row crops treated with common herbicides and its wide distribution therein, common milkweed has rarely posed a threat to crop yields (CFS, 2015a). Glyphosate however, is toxic to milkweed. Upon spraying, glyphosate is absorbed by the leaves and stems of the plant and then translocated to its growing tissues such as the roots (Duke & Powles, 2008). In this way it can prevent regrowth the following year and thus is capable of killing milkweed. Applied with RR crops, it is particularly lethal because it is sprayed at a higher extent, at higher rates, higher frequencies and later in the season during milkweed's most vulnerable flowering stage of growth. As RR crops are often cultivated continuously (due to crop rotations of different RR crops), this leads to one or more applications of glyphosate every year (CFS, 2015a).

Decline in milkweed has also been shown in experimental field studies. A comparison between milkweed infestations in crop fields and adjacent roadsides in Iowa in 1999 and 2009, revealed, that within this 10 year-period, the percentage of infested sites raised slightly at roadsides and declined vastly (more than 6-fold) in crop fields. Whereas in 1999, milkweed was found in half of the surveyed corn and soybean fields, in 2009 only 8% of surveyed sites contained milkweed. According to CFS (2015a) only 1% thereof is estimated to have remained by 2013. The area infested with milkweed declined by approximately 90% (Hartzler, 2010). The observed time period is coincident with the increase in glyphosate use due to the adoption of RR crops and was named as the probable primary reason for the decline of milkweed in crop fields. This is also supported by the fact that at the roadsides, where the number of infested sites rose, herbicide use declined since the establishment of an integrated roadside vegetation management program in 1988. With additional data from Pleasants, who observed the change in milkweed density in cropfields in Iowa from 2000 to 2008 in a more limited survey, Pleasants & Oberhauser (2012) were able to make an assumption about the shape of the decline between 1999 and 2009. According to them, an exponential decay function fits the observed decline best and is also consistent with the increase in cultivation of RR crops. They find that milkweed declined 81% in crop fields in Iowa between

1999 and 2009. In non-agricultural habitats, including roadsides, pastures and Conservation Reserve Programs (CRP), the decline of milkweed was lower (31%). Their finding that Monarch females lay four times more eggs on agricultural milkweeds than on non-agricultural milkweeds makes the milkweed decline in crop fields even more devastating. Possible reasons why more monarch eggs are laid on agricultural milkweeds are that either more females find patches of agricultural milkweed or that individual females lay more eggs on agricultural milkweed. The first could be explained by a stronger milkweed chemical signal, against the monoculture background of the crop field and the latter by a preference of agricultural milkweed due to its higher nitrogen content, which potentially makes them more nutritious for larvae (Pleasants & Oberhauser, 2012). Whilst agricultural milkweed provided for 78% of U.S. Midwest monarchs in 1999, it only provides for 5% today. Thus, milkweed outside of crop fields, such as pastures, CRP and roadsides today provides for 95% of U.S. Midwest monarchs. But the small area outside cropland where milkweed grows cannot support viable monarch populations. Pastures, which are the most abundant habitat for monarchs outside of agricultural land, have only a low milkweed density, possibly because of the high competition with other grasses (CFS, 2015a). Moreover, milkweed density in pastures declined by 50% since 1999. The same is true for CRP land, which is the major provider of monarchs today (Pleasants & Oberhauser, 2012). In addition, the hectarage enrolled in Conservation Reserve Programs is sharply declining as many U.S. Midwest farmers are converting their CRP lands to cropland and the U.S. Congress has vastly reduced the maximum hectarage that can be enrolled in the program. On roadsides, milkweed density does not seem to have declined, but roadside habitats are simply too small to ensure a viable monarch population (CFS, 2015a). Milkweed decline is not only reported in Iowa. Other weed surveys and observation by credible witnesses such as grain farmers and scientists, conducted in other Midwestern United States, also confirm that common milkweed, which was once quite prevalent, has been virtually eradicated from their soybean and corn fields (CFS, 2015a). Pleasants & Oberhauser (2012) estimate that between 1999 and 2010 monarch egg production was reduced by 81% throughout the U.S. Midwest.

Some authors have argued that the decline in the overwintering Monarch butterfly population is not connected with the summer and early fall population size and that there has been no decline in the summer monarch population in the United States (Davis and Dyer, 2015, Inamine et al., 2016 and Agrawal & Inamine, 2018). They suggest that instead of milkweed limitation, increased mortality during fall migration (mainly due to increased parasite load and decreasing nectar availability) has been responsible for the decline in the overwintering population (migration mortality hypothesis). Saunders et al. (2019) however find no association between disease rate and colony sizes. Although they do find autumn greenness along the Midwest migratory route (as indicator of nectar availability) to explain some of the variation in overwintering population size, they don't find a significantly decreased of autumn greenness during the period of monarch decline. Furthermore, they do find a significant relationship between summer breeding population size and winter arrival dynamics. Using tagging and recovery data, from 1998 to 2015, Taylor et al. (2020) further disproved the migration mortality hypothesis on multiple counts concluding: "*the main determinant of yearly variation in overwintering population size is summer population size with migration success bein a minor determinant*". They suggest that increasing milkweed habitat would be the most effective conservation measure. Moreover, Pleasants et al. (2016) argue convincingly that problems with the three papers cited by Davis and Dyer undermine their conclusion of no decline in the summer monarch population. Stenoien et al. (2016) review the processes that may have affected the decline in the eastern population of the monarch butterfly in North America. They accept there are likely multiple contributing factors, such as climate and resource-related effects on breeding, migrating, and overwintering populations, however they conclude that the key landscape-level change appears to be associated with the widespread use of genetically modified (GM) herbicide tolerant crops that dominate the extensive core summer breeding range. These authors convincingly dismiss Davis and Dyer (2015) and Inamine et al (2016) as based on logically flawed misinterpretations of the summer adult count data, because they consider only the counts per milkweed patch, rather than the fact that the number of milkweed patches is declining. Pleasants et al. (2017) also question the use of counts of adult butterflies or eggs per milkweed stem to estimate population size, because this does not account for the shift of monarch activity from agricultural fields to non-agricultural sites over the past 20 years, as a result of the loss of agricultural milkweeds due to the use of glyphosate herbicides on GM crops. They show how corrected summer monarch counts, which account for these changes, do show a decline over time. Stenoien et al. (2016) also highlight that egg densities within the remaining patches of milkweed have been found to be declining over the most recent 7 years, suggesting that many of the remaining sites are found by fewer or no females as the overall monarch butterfly population has declined. Reinforcing their argument, they note that annual herbicide resistant GM crop acreage is a useful predictor of the area occupied by overwintering monarchs.

Thogmartin et al. (2017) investigate climatic and habitat-related factors influencing monarch population size from 1993 to 2014. They find that climatic factors, principally breeding season temperature, are important determinants of annual variation in abundance. However, their results also indicate strong negative relationships between population size and habitat loss variables, principally glyphosate use, and also weaker negative effects from the loss of overwinter forest and breeding season use of neonicotinoids. Cumulative glyphosate application was strongly negatively associated with overwinter population size, and these authors found a strong positive causal relationship of milkweed resource on overwinter monarch butterfly population size. These authors conclude that, given that more than 92% of corn and soy agriculture in the northern USA is now glyphosate-tolerant, there will likely be relatively little additional loss of agricultural fields as habitat for monarch butterflies in the future, as the major losses have already taken place.

Malcolm (2018) sums up the threats to both the Eastern migrant population of monarchs in North America, which overwinter in high-elevation forests in Mexico, and the western monarchs which overwinter in trees on the coast of California. He states that both populations face three primary threats to their viability: (a) loss of milkweed resources for larvae due to genetically modified crops, pesticides, and fertilizers; (b) loss of nectar resources from flowering plants; and (c) degraded overwintering forest habitats due to commercially motivated deforestation and other economic activities. Secondary threats to population viability include (d) climate change effects on milkweed host plants and the dynamics of breeding, overwintering, and migration; (e) the influence of invasive plants and natural enemies; (f) habitat fragmentation and coalescence that promote homogeneous, species-depleted landscapes; and (g) deliberate culture and release of monarchs and invasive milkweeds. He notes that both the abundance and migratory behavior of monarch butterflies both east and west of the Rocky Mountains are a product of the diversity and abundance of larval milkweed host plant. Their population declines are associated with dramatic losses of milkweed resources in and near agricultural fields, associated with the increased use of herbicides and cultivation of herbicide-tolerant GM crops.

Pleasants (2017) estimates that since 1999, 850 million milkweeds have been lost from GM maize (corn) and soybean fields in the Midwest USA. In addition, since 2008, over 11 million milkweeds have been lost from grasslands due to their conversion into cropland, an annual loss rate of about 2 million milkweeds. Of the estimated 2.2 billion milkweeds present on the landscape in the Midwest in 1999, only 1.34 billion remained in 2014, a decline of almost 40%. Pleasants (2017) concludes that, because each milkweed stem in an agricultural field averages 3.9 times more monarch eggs than a milkweed stem in non-agricultural habitats, the potential monarch support capacity loss has been 71%.

In their mini-review, Belsky & Joshi, 2018 explore the role of major drivers in the recent decline of monarch butterflies in North America, concluding that: "*Many scientists attribute the increased planting of genetically modified crops and herbicide spray applications in the mdiwestern United States to reductions of milkweed in agricultural crop fields. As a result, the food supply in monarch breeding habitats has subsequently been diminished*". They further conclude that habitat destruction due to logging in the overwinterning sites in Mexico and inconsistent climatic conditions have also contributed to the decline of Monarchs, but to a lesser extent. They recommend further studies to investigate the direct impact of pesticide mixtures applied to herbicide tolerant GM crops on monarchs (including possible synergistic toxicity) and to determine whether pesticide exposure can change monarch behaviour. They also name protozoan parasite infestation as possible contributor to the decline of monarch butterflies, suggesting that protozoan parasites primarily affect monarchs at their summer breeding locations. They recommend investigating whether sub-lethal pesticide exposure and increased stress resulting from diminishing milkweed abundance may render monarchs more vulnerable to protozoan parasites.

In 2019, the leading hypothesis that HT GM crops are the driving force in the decline of monarchs was challenged again by Boyle et al. These authors claimed that monarchs and milkweed already began to decline around 1950, predating the the introduction of HT GM crops, concluding that herbicide resistant crops, therefore, are clearly not the only culprit and, likely, not even the primary culprit. Systematic monitoring of monarchs began in 1993, not long before the introduction of GM HT crops. To test their hypothesis that monarch decline began before the introduction of GM HT crops, Boyle et al. (2019a) used natural history collections to look at the 117-year period from 1900 to 2016, assuming that number of museum specimens collected in a given year is proportional to population size: “we divided the number of milkweed and monarch speciems collected each year by the total number of vascular plant and lepidoptera [butterflies and moths] specimens, respectively, collected within the same geographic range and year”. Their results showed an increase in monarch and milkweed abundance early in the century, peaking around 1950 and a respective decline thereafter. The authors hypothise that the decline of milkweed during that period correlates to the mid-century agricultural revolution in the U.S. which saw greatly increased mechanisation, chemical inputs to farmland and a consolidation of farms. The authors themselves pointed to several possible biases in their method (such as the increase in the number of monarch specimen records being due to an increase in scientific interest in monarchs or even certain rare species, rather than a true increase in population size) and concluded: “it is almost certain that our dataset contains error attributable to these biases.” In a letter, Wepprich (2019) argues that using museum records for tracking abundance is of limited use due to spatial and temporal biases. He shows that the trend observed by Boyle et al. (2019a) changes with the choice of taxa to standardise monarch records. When reassessing the data for monarch abundance as a proportion of butterflies only, there is no mid-century peak and subsequent decline in monarch abundance. This is because Lepidoptera collection methods changed over the last century, with increasingly more light traps being used around the mid-20th century, favouring the collection of moths. This led to a respective rise in moths in museum collections beginning in the 1950s. Thus, moth records should not be used to correct for butterfly species analyses, as their collection method differs substantially (light trapping at night for most moths versus net captures during the day for butterflies). Moreover, the corrected trend by Wepprich (2019) does not correspond with the real-world observed population decline, further affirming that museum records are unreliable for abundance estimates. Additionally, Ries et al. (2019) address the problem of spatiotemporal bias, stating: “*One way to reduce this bias is to restrict analysis to the core range and time of year when the speices is most evenly distributed and consistently abundant*”, which is the summer breeding season in the case of the eastern population of migratory monarchs. As in Wepprich (2019), they find no-mid-20th-century peak in monarch abundance when using the corrected data. Ries et al. conclude: “…*using digitized museum records to track monarch butterfly populations over the last century is currently not possible*.” In their reply to Wepprich (2019) and Ries et al. (2019), Boyle et al. (2019b) accept some merit in these arguments, stating that “*the monarch trend presented in our original study may or may not represent the true trend in monarch abundance over the 20th century*”. Nevertheless, they stick to their original conclusion that GM HT crops are not the main driver in the monarch decline observed today, arguing that the decades-long declines in across milkweed species have not been questioned by either Wepprich (2019) or Ries et al. (2019) and are likely more robust than monarch trends. However, even if the decline of milkweed started much earlier due to farm consolidation and the increase in chemical inputs etc., it is evident that the introduction of HT GM crops added an unprecedented threat to weeds in arable land.

As the population declines, other threats, such as extreme weather events, have become a bigger danger to Monarchs, as the population is much smaller and more vulnerable. The winter storm of

2002, for example, that killed about half a billion monarchs could today eradicate the whole population (Brower et al., 2004).

The significant decline in Monarch butterflies has caused great concern among environmental organisations, scientists and politicians, amongst others, and even led Monsanto to take action to restore the monarchs' breeding habitat. In September 2014, Monsanto claimed that it would do its part to protect the butterfly. This includes restoring monarch-breeding habitat outside of cropland (Monsanto, 2014). In March 2015, Monsanto promised investments of $4 million over the next three years for monarch research, education and habitat restoration, mainly to the National Fish and Wildlife Foundation's (NFWF) Monarch Butterfly Conservation Fund, which was newly established in 2015 (NFWF & Monsanto, 2015; Sachs, 2015). However, as discussed above, milkweed in cropland is much more valuable in producing monarchs and non-agricultural land alone is unlikely to be enough to save the monarch.

The Center for Food Safety reviewed the work of milkweed and monarch biologists, weed scientists and other researchers to provide a detailed analysis of how herbicide use triggered by genetically modified, herbicide-tolerant crops has been a major driver in the dramatic decline of milkweeds and monarchs and list policy recommendations to protect monarch butterflies, that have been proposed by organisations and scientists to the FWS, USDA, EPA and U.S. Congress (CFS, 2015a). According to them "*phasing out the use of herbicide-resistant crops would be the best means to restore milkweed and therefore monarchs*". They demand that "*weed management according to agroecological principles and methods must replace herbicidal weed eradication*". Alternatives are crop rotation, cover crops, intercropping, fertilisation methods that favour the crop over weeds and closer plant spacing among other methods. These solutions are of course not in the interest of companies like Monsanto (now Bayer) that sell herbicide-resistant crops.

Nevertheless, demands to restrict glyphosate use became widespread. In March 2015, 52 members of the U.S. Congress expressed their concern about the monarch butterfly in a letter to President Barack Obama, naming the widespread spraying of herbicides in agricultural areas as the main reason for the decline in milkweed in the U.S. Midwest. They state: "*without a sea-change in how the federal government addresses the use of herbicides, especially as applied to herbicide-resistant crops, vital monarch habitats will simply continue to disappear*." They further encourage the U.S. administration as well as the president to spare no expense in order to restore the monarch butterfly (Pingree, 2015). In light of the rapid decline of the monarchs, the Natural Resources Defense Council (NRDC) filed a petition with the United States Environmental Protection Agency (EPA) in February 2014, asking them to take immediate steps to undertake an interim administrative review for glyphosate and to restrict glyphosate use. The rules for glyphosate were last updated in 1993, before the rapid spread of RR crops and the associated increase of glyphosate use. Thus, the EPA greatly underestimated glyphosate use in its 1993 re-approval of glyphosate. The petition argues that the EPA should take responsibility in ensuring that the pesticides it approves do not harm the environment and impose restrictions to glyphosate use, now that harmful effects on monarchs have been identified. Farmers should be required to set up herbicide-free buffer zones around or other milkweed-friendly zones within their agricultural area. Glyphosate should further be banned along roads, power-lines or other rights-of-way where milkweed could grow freely. The EPA should also ensure that these restrictions on glyphosate use do not lead to an increased use of other herbicides (NRDC, 2014). As the EPA did not respond to this petition within a year, the NRDC filed a lawsuit in February 2015 in order to force EPA to evaluate glyphosate's effects on monarchs and enact appropriate mitigation measures (Fallon, 2015). In June, 2015 the EPA finally reached an agreement with the Centre for Biological Diversity (CBD) to assess effects of glyphosate on 1,500 endangered species in the United States, a task long overdue (CBD, 2015). In the report, the US EPA (2021a) eventually identified that glyphosate was 'likely to adversely affect' (LLA) 93% of the species assessed (including mammals, birds, amphibians, reptiles, fish, plants, aquatic invertebrates and terrestrial invertebrates) and 96% of their habitats. In June 2022, the 9th Circuit Court of Appeals in California determined that the EPA did not adequately consider whether glyphosate causes cancer and threatens endangered species, and ordered it to look again at the risks it poses (Stempel, 2022). Legal cases are discussed further in Section 8. Lawsuits. Unfortunately, there is still no special legal status at the federal level for monarch butterflies in the USA. However, the International Union for the Conservation of Nature (IUCN) added the monarch butterfly to its "red list" of threatened species and categorized it as "endangered" for the first time in 2022 (Larson, 2022).

In Canada, the monarch butterfly has been listed as a species of special concern since 2003 by Canada's Species at Risk Act. In Mexico, monarchs are also protected by the Species at Risk Norm (Vidal & Rendón-Salinas, 2014). In August 2014, the Center for Biological Diversity (CBD) and the Center for Food Safety (CFS), joined by the Xerces Society and the well-known monarch scientist Dr. Lincoln Brower, filed a legal petition to the U.S. Fish and Wildlife Service (FWS) to protect the monarch butterfly as a threatened species (Monarch ESA petition, 2014). This petition was supported by more than 40 leading monarch scientists and over 200 organisations and businesses that urged Secretary of the Interior Sally Jewell to protect these butterflies under the Endangered Species Act in November 2014 (CFS, 2014b). According to the Centre of Food Safety (CFS, 2015a) listing the monarch as threatened species under the ESA would be followed by development of a recovery plan and also provide resources to restore the monarch's breeding habitat. Furthermore also 52 members of the Congress who expressed their concern about the monarch butterfly in a letter to president Barack Obama, expressed the opinion that the ESA "is one of the most successful and powerful tools that can restore the monarch butterfly" (Pingree, 2015). Monsanto however dismissed listing the monarch under the ESA as of no help to solve the problem (Monsanto, 2014). If the monarchs are listed under the ESA, it is possible that restrictions on the use of glyphosate or RR crops are the consequence, and thus reduce Monsanto's (now Bayer's) profits. Nevertheless, in December 2014, the FWS stated that they will conduct a one-year status review on monarch and that the Endangered Species Act may be warranted (CBD, 2014). In January 2016, the Center for Biological Diversity and the Center for Food Safety filed a notice of intent to sue the FWS for failing to make 12-month finding required under the Endangered Species Act (CFS, 2016; CFS & CBD, 2016). As of 2022, the FWS still is due to put the monarch butterfly under the federal Endangered Species Act, arguing that its resources are limited and that other species are in greater need of help. The decision will only be revisited in 2024 (Pennisi, 2021; CBD, 2022).

There is also a demand to list the Monarch Butterfly Biosphere Reserve as site considered in danger. According to the International Union for Conservation of Nature and Natural Resources' (IUCN) 2014 World Heritage Outlook, that assesses the conservation status of all natural World Heritage sites, the Monarch Butterfly Biosphere Reserve's conservation outlook is "Critical". This is the lowest of four possible conservation outlook categories (Osipova et al., 2014). Subsequently, non-governmental organisations from Mexico, Canada and the United States asked the UN World Heritage Committee to include the Monarch Butterfly Biosphere Reserve on a list of sites considered in danger, in the hope that governments take greater effort to protect the butterflies' habitat (AP, 2015; Report on the Status of the Monarch Butterfly Migration, 2015). In response, the UN World Heritage Committee asked the United States and Canada to join Mexico in producing a report to inform on their actions to protect the monarch migration (Riley, 2015).

To effectively reverse the trend of population decline, protective measurements and policies have to be taken in all countries concerned, Canada, the United States and Mexico. In February 2014, a tri-national letter from Grupo de los Cien, Make Way for Monarchs and the well-known monarch scientist Dr. Lincoln Brower, signed by over 100 international monarch butterfly scientists, writers, artists, scientists and environmentalists was sent to President Peña Nieto, President Obama and Prime Minister Harper, asking them to discuss the future of the monarch butterfly during the North American leaders' Summit in February 2014. As well as Mexico addressing issue of illegal logging, the United States and Canada must also address the effects of their current agricultural policies. The letter also makes suggestions on how to restore habitat for the monarch butterfly, such as the establishment of a milkweed corridor through the three countries along the monarchs' migratory route (Grupo de los Cien & Make Way for Monarchs, 2014). In response, President Peña Nieto, President Obama and Prime Minister Harper agreed to launch a tri-national High Level Working Group to work on monarch conservation and each government agreed to convene a high-level task force in their country. Nevertheless, insufficient action has been taken so far to restore the monarch population back to a secure level. The Canadian government has not yet publicly announced any plan for how they intend to assist in monarch butterfly conservation. In the U.S., the Fish and Wildlife Service (FWS) launched a U.S. $3.2 million effort towards habitat enhancement but they have not addressed the need to strengthen the regulation of glyphosate herbicides or phase-out herbicide-resistant crops (Report on the Status of the Monarch Butterfly Migration, 2015).

Bøhn & Lövei (2017) cite the situation with monarch butterfly populations in the USA as one example of how GM plants associated with simple pesticide-solutions are unable to solve complex agricultural problems and overlook important ecological and evolutionary factors.

Furthermore, additional threats are already on the horizon: next-generation HT crops, with additional resistance to 2,4-D and dicamba, that were developed due to the evolution of glyphosate resistant weeds (see 6. Industry response) will probably exacerbate the decrease of common milkweed because: a) 2,4-D and dicamba both partially supress regrowth of common milkweed; b) most growers would supplement the selective herbicides 2,4-D and dicamba with glyphosate to effectively kill non-glyphosate resistant weeds; and c) 2,4-D and dicamba are expected to harm nectar-producing flowers that adult butterflies feed on (CFS, 2015a).

The specific case of the monarch butterfly is also relevant for Europe, were RR crops ever to be grown there, as they inhabit Portugal and southern Spain along the Iberian Peninsula, and the Mediterranean habitat offers a suitable environment for monarch butterflies to proliferate (MonarchLab, 2014). Milkweed is naturalized in cultivated ground and dry grassland in various parts of central and southern Europe (CABI, 2011). Moreover, impacts on other species could occur in Europe through similar impacts on their habitat. For Germany, Hilbeck et al. (2008) identified 21 lepidoptera species that only feed on one or a few specific weed species whose populations would be strongly influenced by the application of non-selective herbicides such as glyphosate and glufosinate associated with HT crops. One example is the Queen of Spain fritillary (*Issoria lathonia*) that is reported to exclusively feed on *Viola arvensis*.

4.2.5. Pollinators

About 75% of agricultural staple crops rely on pollination by insects, especially honeybees (Klein et al., 2007), making their preservation a critical issue for our food security. Agricultural intensification reduces the diversity and abundance of native bees (Kremen et al., 2002).

A phenomenon called bee Colony Collapse Disorder (CCD) occurs when the majority of worker bees in a honey bee colony disappear. It has been documented all over the world (Potts et al., 2010; Van der Zee et al., 2012; Van Engelsdorp et al., 2008). Exposure to insecticides has been named as one probable cause of this phenomenon, alongside other stresses on bee colonies, such as pathogens and climate change. It has been shown that insecticides such as neonicotinoids can contribute to colony weakening (see for example Sandrock et al., 2014). Consequently, in 2013, the EU commission tightly restricted the use of three neonicotinoids for a three-year period as a consequence of a risk assessment on the effects of neonicotinoids on honeybees conducted by the European Food Safety Agency (Regulation (EU) No 485/2013). In this section, we document evidence regarding the effects of glyphosate on pollinators, including bees.

In addition to potential direct harmful effects of glyphosate-based herbicides on bees, damage to habitat should also be considered. For example, Strandberg et al. (2021) find that glyphosate spray-drift has a significantly negative effect on the cumulative number of flowers on *Trifolium pratense* (red clover) and *Lotus corniculatus* (bird's-foot trefoil). The authors warn that lack of floral resources is known to be of major importance for pollinator declines. Fuchs et al. (2021) describe how glyphosate residues can substantially interfere with plant resistance and the attraction of beneficial insects, both of which are essential elements in integrated pest management and healthy ecosystems. These authors review evidence showing how sublethal doses of glyphosate, in the form of persistent glyphosate residues in soils, can alter many physiological plant processes, including the regulation of plant defence responses by plant hormones. This substantially changes how plants interact with their biotic environment. See also Section 4.2.1 Farmland biodiversity and the UK Farm Scale Evaluations (FSEs) and Section 4.2.2 Land use and biodiversity.

Tan et al. (2022) summarize research on the direct effects of glyphosate on honeybees, including effects on their behaviours, growth and development, metabolic processes, and immune defence.

Research on other (non-pollinator) insect species is considered in Section 4.4. Impact on terrestrial organisms.

The main observed effects on pollinators are discussed further below.

i) Effect of glyphosate on survival and development of honey bees

In a laboratory experiment, Dai et al. (2018) find chronic exposure to glyphosate at environmentally relevant concentrations to significantly decrease larval weight (0.8 or 4 mg/L) and larval survival (4 mg/L) of honey bees. However, glyphosate had no effect on the developmental rate. Vázquez et al. (2018) confirmed the findings that chronic exposure to glyphosate at environmentally relevant levels decreases larval weight of in vitro reared honey bee larvae. A decreased larval weight is evidence of malnutrition. Contrary to Dai et al. (2018), they however find glyphosate, at 1.25-5.0 mg/L of food, to affect development, with a higher proportion of larvae experiencing delayed moulting. They also found a varying susceptibility to glyphosate among colonies. The authors conclude: *"Even if the in vitro procedure cannot be considered to completely reflect toxicity to larvae inside a hive, it can be considered as a reliable tool in a first step to determine subtle adverse effects. The impact of GLY-based herbicide formulations on the honey bee and the interaction with multiple factors such as pathogens, other pesticides or adverse environmental conditions, are unknown. However, our results suggest that the exposure to the active ingredient of these herbicides could affect brood development with unpredictable long-term consequences at the colony level."* In their subsequent study, Vázquez et al. (2020) again found a significant delay in development of larvae after being fed a sublethal dose of glyphosate in a chronic in an in vitro exposure experiment. They also found the 29% of bee larvae that displayed no observable signs of toxicity still showed transcriptional changes in multiple genes. They suggest an *"enhanced catabolism and oxidative metabolism in honey bee larvae as a consequence of the sub-lethal exposure to GLY, even in absence of observable symptoms*" and conclude: *"A maladaptive physiological response in early stages in life cycle could lead to long-term negative effects on bee populations."* A recent meta-analysis, evaluating sixteen papers with 34 data-sets on bee mortaility, comes to the conclusion that glyphosate in ecologically relevant doses, or in doses recommended by the manufacturer for agricultural settings, is toxic to bees and might cause lethal effects. Chronic exposure seems to be more harmful (Battisti et al., 2021).

ii) Effect of glyphosate formulations on mortality of various insect pollinators

Several studies also looked at the effect of glyphosate-based formulations that are used in the field on insect pollinators. Abraham et al. (2018) find mortality of two social bee species (*Apis mellifera* and *Hypotrigona ruspoli*) to increase upon contact with the glyphosate formulation Sunphosate 360 SL, freshly sprayed at the recommended concentration. Increasing the dose to twice the recommended concentration further increased mortality. Bees exposed to air-dried filter paper soaked with the glyphosate formulation, had a significant elevated mortality at twice the recommended concentration. The authors point out the importance of the timing of glyphosate application to avoid insects getting in direct contact with the herbicide and keeping to label instructions.

Seide et al. (2018) find that Roundup, at the highest dose commonly applied for weed control in Brazil, kills larvae of the stingless bee *Melipone quadrifasciata*, which are important pollinators for various crops in Brazil. Mortality was 100%, which is why no statement on potential effects of Roundup on developmental time could be made. Survival time in Roundup treatments was significantly lower than in the positive control with the neonicotinoid insectide Imidacloprid. A study from Iran suggests that both glyphosate and Roundup exhibit mortality in honey bees when fed sublethal concentrations over 10 days. The mortality rate of the Roundup treatment was on average twice as large as in the glyphosate treatment. The authors suggest, that the herbicide *"may contribute to the phenomenon"* of colony collapse disorder (Faghani and Rahimian, 2018).

Straw et al. (2021) test direct spraying of bumble bees with Roundup products at recommended concentrations and below. They report high levels of mortality with different Roundup products. These findings are relevant because as the authors point out, "*the guidance in the product's UK Environmental Information Sheet stating, "Roundup ProActive is of low toxicity to honeybees; there is no requirement to avoid application of the product when bees are foraging on flowering weeds in treated crops". This means that on-label guidance explicitly allows application directly onto bees, along with spraying onto flowering weeds, which are frequently visited by bees (…). This means that the exposure bees will face is incredibly high, with no attempt being made to mitigate their exposure".* They further point out that exposure through herbicide tolerant GM soybean is probably significantly higher than through flowering weeds, as soybean flowers are an attractive resource for bees and spraying throughout the flowering period is allowed. As the high levels of mortality were not observed when applying glyphosate alone, the authors point out the importance of surfactance in the toxicity of herbicides to non-target organisms. Therefore, it is important to always test the actual herbicides used in the fields and not only the active ingredient, in this case glyphosate: *"We suggest that the necessity to properly test pesticide effects on wildlife outweighs company rights to with- hold proprietary information."* See also Section 4.3.6. Impact of adjuvants on aquatic non-target organisms.

iii) Sublethal effects of glyphosate and Roundup on honey bees and solitary wild bees

A study conducted by Herbert et al. (2014) has investigated whether the herbicide glyphosate could also have sub-lethal effects on honey bees in chronic and acute exposure experiments. The glyphosate concentrations used were based on recommended levels for spraying and those measured in the environment. In the chronic exposure experiments laboratory reared bees were exposed to glyphosate during the first 15 days of the adult stage. The results showed that a prolonged exposure to sub-lethal concentrations of glyphosate led to a lower sensitivity to a nectar reward and impaired the ability to establish an association between an odour and a reward. The researchers concluded that glyphosate promotes an increase in sugar response threshold. Acute exposure to sub-lethal concentrations of glyphosate not only led to an impaired associative learning but also impaired retention of olfactory memory. The authors concluded that field-realistic doses of glyphosate could reduce sensitivity to nectar reward and lead to cognitive deficits on honeybees. As Herbert et al. (2014) found no effect on forage activity they speculated that glyphosate present in nectar would be constantly brought to the hives, accumulate and be fed to the larvae and young bees, having long-term negative consequences on colony performance. Goñalons & Farina (2018) study the effect of chronic joint exposure to field-realistic concentrations of the neonicotinoid insecticide imidacloprid and glyphosate on young adult honey bees. Young worker bees receive cues from outside the hive, especially through taste and smell. For example, honey bees extend their proboscis as a reflex in response to an appetitive stimulus such as nectar. In olfactory conditioning, bees are trained to associate an initially neutral odour with a sucrose reward and finally exhibit a conditioned response towards the odour alone. This study reports that both pesticides reduced sucrose responsiveness and had a negative effect on olfactory learning, confirming the findings of Herbert et al. (2014). Glyphosate also reduced food uptake during rearing. The glyphosate concentration used in the study – which is equivalent to 2.08 mg kg^{-1} – is similar to the highest found in agricultural environments. Luo et al. (2021) used Roundup rather than pure glyphosate, creating a more realistic exposure scenario. Honey bees were chronically exposed to Roundup at 1/2x, 1x and 2x the recommended concentration. Luo et al. (2021) were able to confirm the findings of Herbert et al (2014) and Goñalons & Farina (2018) regarding reduced sucrose responsiveness, olfactory learning and memory ability. They also found a significant decline in water responsiveness and climbing ability of honey bees upon chronical exposure to Roundup. These obervations were all made at or below the recommended concentration.

According to Helmer et al. (2014), field-realistic sublethal doses of glyphosate may also alter carotenoid or retinoid metabolism in honey bees. They found some diet-derived antioxidants such as β-carotene, a precursor of vitamin A, to decrease with increasing doses of glyphosate. These metabolic products are essential for biological functions such as vision, reproduction, larval development or immune system response. An imbalance could therefore affect honey bee health.

Solitary wild bees of the genus *Megachile*, which are relevant for crop pollination, have been shown to not consider the presence of a glyphosate commercial formulation (Roundup® ControlMax) when selecting their nesting sites in an agroecosystem located in the Pampean region in Buenos Aires, Argentina (Graffigna et al., 2021). However, the number of brood cells per nests was significantly lower in traps treated with field relevant field relevant doses of the glyphosate formulation compared to the control. Furthermore, larvae completed their development four times less in nests treated with glyphosate formulation. The authors suggest that cognitive failure of nesting females, due to glyphosate exposure, could lead females to abandon established nests because they don't find their way back after forage trips and/or that they die before finishing their nests

Faita et al. (2018) found sublethal concentrations of Roundup to negatively affect the royal jelly-producing glands of honey bees. Royal jelly is essential for feeding the offspring in their first larval days, as well as the queen throughout her entire life. The hypopharyngeal glands of bees fed with a sugar syrup mixed with pollen and Roundup, sustained physiological as well as mitochondrial damage. The authors discuss how the observed alterations could trigger damage to the development, maintenance and survival of bee colonies. Although the average weight of royal jelly was lower in the hives exposed to Roundup than in the control hives, the difference was not statistically significant. The reduction of royal jelly production in hives treated with Roundup, has however since been confirmed by Chaves et al. (2021). The authors suggest that the reduction in royal jelly "*would certainly compromise the hive's nutrition and social immunity*". Faita et al. (2018) suggest that long-term studies on the nutritional quality of the royal jelly produced should be conducted. They also alert that in the field honey bees are exposed to multiple pesticides simultaneously which could potentially increase damage to the hypopharyngeal glands and royal jelly. They conclude: "*Considering the importance of pollinators for the maintenance of the balance of different ecosystems (…), as well as for the production of food in agroecosystems and bee products, it is urgent that regulatory agencies and public policies take into account the evidence-based adverse effects on bees that have been obtained by the independent scientific community."*
Faita et al. (2022) conduct proteomic profiling of royal jelly produced by bees (*Apis mellifera* L.) exposed to food containing herbicide-based glyphosate (RoundUp). They report that glyphosate-based herbicides down-regulate MRJP3 synthesis, which performs functions related to immunity, in royal jelly.

Weidenmüller et al. (2022) find that whereas environmentally realistic exposure levels of glyphosate are not directly lethal to bumblebees, they decrease the ability of colony members to maintain required hive temperatures, which could lead indirectly to decline.

iv) Effects of glyphosate on gut microbiota and pathogen defence

Bees rely on a specific gut microbiota for growth, detoxifying harmful molecules, immune system regulation and defence against pathogens and parasites. Since most bee gut bacteria contain the EPSPS enzyme, it is relevant to analyse the effects of glyphosate exposure on the bee gut symbionts and overall bee health. Dai et al. (2018) find glyphosate at 20 mg/L to siginifcantly decrease the intestinal bacterial diversity of honey bees. Similarly, Motta et al. (2018) find that glyphosate exposure at environmental relevant concentrations alters the honey bee gut microbiota, decreasing relative and absolute abundance of dominant gut microbiota species, and increasing mortality of bees exposed to the opportunistic pathogen *Serratia marcenses*. Bacterial species varied in susceptibility to glyphosate, with some species being able to tolerate high concentrations of glyphosate due to the presence of a class II EPSPS enzyme. Blot et al. (2019) confirmed the finding that glyphosate alters honeybee gut microbiota. In both studies, growth of *Snodgrassella alvi* was the most strongly affected. Blot et al. (2019) also confirmed that strains producting a glyphosate-resistant EPSPS are not negatively affected by glyphosate. Glyphosate had no effect on infection by the intestinal parasite *Nosema ceranea*. Almasri et al. (2021) however show that overlapping exposure to glyphosate and the fungicide difenoconazole at environmental concentrations, synergistically increase the adverse effect of *N. ceranea* infection on honey bee longevity and induced higher mortality. The authors suggest that the fungicide *"may enhance the toxicity of glyphosate by inhibiting its metabolism".* These studies show that gut microbiota are important for protection against pathogens and glyphosate may enhance susceptibility of honey bees to some pathogens. Motta et al. (2020) further show that different routes of exposure to glyphosate-based herbicide can affect honey bees and their gut microbiota. They investigate the oral and topical effects of variable concentrations of glyphosate in herbicide formulation on the honey bee gut microbiota and health under laboratory and field conditions and find that the formulation, dissolved in sucrose syrup or water, affects the abundance of beneficial bacteria in the bee gut in a dose-dependent way. In their field experiments, glyphosate was detected in honey collected from exposed hives, and bees exposed to the formulation were more likely to disappear from the colony, once reintroduced after exposure. The authors report that, under field conditions, a single oral exposure to the herbicide formulation was enough to reduce the abundance of the beneficial bacteria *Snodgrassella* in the bee gut. This effect persisted in subsequent weeks during the experiments, regardless of whether further exposures occurred. They note that, in some trials, the effects of the formulation extended to other beneficial bacteria, such as *Bifidobacterium*, and persisted even one month after treatments ended. The authors conclude that glyphosate may affect the bees' gut microbiota, with negative consequences for bee health, and that adjuvants in glyphosate-based herbicides may also enhance undesired effects. Motta et al. (2022) also report that exposure of honey bees to glyphosate can reduce the abundance of beneficial gut bacteria and lead to immune dysregulation.

v) Combinatorial effects

Almasri et al. studied how interactions of glyphosate with other pesticides and pathogens impact honey bee health. Almasri et al. (2020) show in a chronic 20-day exposure experiment that glyphosate at concentrations found in beehive matrices or lower, significantly reduces survial of winter honey bees. As in the study of Seide et al. (2018), exposure to the neonicotinoid insecticide imidacloprid was associated with a higher survial rate than exposure to glyphosate. Binary exposures to glyphosate and imidacloprid as well as the ternary mixture of glyphosate, imidacloprid and the fungicide difenocanzole further increased bee mortality in a synergistic, or subadditive manner (depending on the mixture and concentration). The authors also found impacts on the physiological state of honey bees, namely perturbations in the detoxification process, nervous system, metabolism, defence against oxidative stress, and immunity. They conclude: *"These results demonstrate the importance of studying the effects of chemical cocktails based on low realistic exposure levels…".* Disruptions of the nervous system, detoxification system and immunity were also found when exposing honey bees infected with *Nosema ceranae* (a small, single-cell parasite) to environmental concentrations of glyphosate, the fungicide difenoconazole or both (Almasri et al., 2021). The authors conclude: *"…the interactions of Nosema with pesticides could contribute over time to colony collapse due to alterantions in the behavior, foraging performance* *and homing flights of honey bees"* Almasri et al. (2022) chronically expose newly emerged honey bees to imidacloprid, glyphosate and difenoconazole, individually and in a ternary mixture, at an environmental concentration of 0.1 µg/L. In these experiments, the pesticides induced physiological disruption by directly altering the detoxification system, the antioxidant defences, and the metabolism of the host. In their review of the non-insecticide pesticide impacts on bees, Iwasaki & Hogendoorn (2021) point out that pollinators are rarely exposed to a single pesticide and that chemical interactions may enhance toxicity. However, most chemical combinations have only been studied once. They suggest: "*To limit toxic effects on bees in agricultural landscapes, the potential for interactive effects through co-application should be available on pesticide labels wherever reasonable and possible, and taken into account in both research and industrial usage*."

Pal et al. (2022) study the toxicity to winter honey bees of the pesticides imidacloprid, difenoconazole and glyphosate alone and in binary and ternary mixtures. They find that the toxicity of the pesticides greatly increased when they occurred as mixtures, and the highest mortalities were recorded at intermediate exposure concentrations of 0.1 and 1 µg/L.

4.3. Impact on aquatic biodiversity

Whilst agricultural soil is the main recipient for pesticides such as glyphosate-based formulations, water bodies adjacent to agricultural areas are usually the ultimate recipient for pesticide residues (Pereira et al., 2009). Pesticides can enter aquatic ecosystems via run-off, leaching processes, spray drift or by precipitation. Several studies indicate that glyphosate-based herbicides and their primary metabolite AMPA are abundant in water bodies in countries where RR crops are grown (see Section 4.1. Increased environmental occurrence of glyphosate and AMPA). Thus, environmental risk assessment of pesticides requires examination of effects on aquatic non-target species as well as terrestrial ones.

In the scientific literature, adverse impacts of glyphosate, commercial glyphosate-based formulations and AMPA on a wide number of aquatic non-target organisms are known. Studies show direct toxic effects, as well as implications for the aquatic biodiversity and the functioning of the aquatic ecosystem at environmentally relevant concentrations. Although evidence is continually growing, it has been clear for many years that glyphosate-based herbicides harm aquatic ecosystems. For example, an outdoor mesocosm experiment, including algae and 25 species of animals, simulated the impact of direct overspray of insecticides and herbicides on a wetland. Roundup decreased overall species richness by 22%, as well as predator and large herbivore biomass when added at the recommended maximum application rate (3.8 mg a.i./L) (Relyea, 2005a).

Focusing on European Union regulation of pesticide and water policy affecting aquatic environments, Hendlin et al. (2020) argue that the effects of glyphosate on fresh and ground water, and on aquatic biodiversity, have not received sufficient attention as legitimate rationales for regulating the chemical. Glyphosate may also impact aquatic environments in other ways. A study led by Ohio Northern University chemistry professor Christopher Spiese, presented at a 2016 conference, links farmers' use of glyphosate to dissolved phosphorus in soils (No-Till Farmer, 2016). Mobilization and runoff of phosphorus to streams and lakes is associated with toxic algae blooms in Lake Erie and elsewhere. More research is needed to confirm these findings.

Pérez et al. (2012) review a vast number of studies on direct toxicity of different glyphosate-based formulations on different groups of aquatic organisms (algae, aquatic plants, protozoa, crustaceans, molluscs, amphibians and fish), each playing a pivotal role for the functioning of an aquatic ecosystem. They conclude that glyphosate-based formulations are hazardous to the aquatic environment, with several of the reviewed studies reporting significant effects at concentrations lower than the estimated expected environmental concentration of 2.6 mg a.i./L (milligrams of active ingredient per litre). Snails and worms for example showed significant effects in growth, reproduction and metabolism at concentrations below 1 mg/L of glyphosate and crustaceans showed lethal effects at concentrations lower than 3 mg a.i./L of Roundup.

Gonçalves et al. (2019) also review the ecotoxicological effects of glyphosate-based herbicides (GBHs) on aquatic environments. They discuss how glyphosate in the aquatic environment can cause the death of aquatic plants (the macrophyte community), which provide a habitat for plankton and algae and act as a refuge and feeding habitat for fish. The damage caused by glyphosate on the aquatic plant community ranges from the death of the plant itself to the reduction of biodiversity and imbalance in ecosystems. Aquatic invertebrates vary in their sensitivity to GBH. Microinvertebrates (less than 35 µm in size) play a key role in aquatic ecosystems and GBHs can cause negative impacts on the process of recolonization from resting egg banks as well as shifts in community composition. Fish species are particularly vulnerable to GBH and in general, the surfactant and the commercial formulation in GBHs show higher toxicity than glyphosate alone. Amphibians, reptiles and aquatic birds and mammals may also be impacted. These authors note that under Brazilian law, populations of yellowtail tetra fish (*A. lacustris*) are not safe since sperm cells of this species are dead in lower concentrations than 65 µg L^{-1} (the legal limit for relevant water bodies), whereas the USA allows a much higher lmit of 700 µg L^{-1} in water bodies, and Canada allows 280 µg L^{-1} in drinking water.

In a systematic literature review of glyphosate concentrations in freshwater ecosystems worldwide, Brovini et al. (2021b) identify 73 articles on freshwater ecosystems from 21 countries. These authors find that glyphosate may pose a moderate to high risk in 95% of the countries investigated, reaching a maximum concentration of 105 mg L^{-1}. In their risk analysis, glyphosate concentrations below 0.1 µg L^{-1} represent a low risk, whereas glyphosate concentrations above 1 µg L^{-1}, which is below the limit established by some countries' legislation, represent a high risk to aquatic organisms.

Yu et al. (2021) study the effects of microplastics and glyphosate on the aquatic plant species *Salvinia cucullate* (a warm-water floating fern), finding evidence of ecotoxic effects, physical damage and oxidative stress. They conclude that pervasive microplastics and herbicide contamination in freshwater may potentially affect the growth of aquatic plants.

Tresnakova et al. (2021) conduct a further review of the effects of glyphosate and AMPA on aquatic organisms. They find that the toxic effect of glyphosate and its major metabolite AMPA has been found to influence growth, early development, oxidative stress biomarkers, antioxidant enzymes, haematological, and biochemical plasma indices and also caused histopathological changes in aquatic organisms. The results of the studies summarized in this review indicate that glyphosate (GLY) mainly caused oxidative stress, and affected antioxidant enzymes, blood parameters, and caused several histopathologic changes in the gills, liver, and kidneys, genotoxicity, immunotoxicity, and cardiotoxicity in fish and oxidative stress, antioxidant enzymes, and haemocyte parameters in mussels. These authors note that there are many gaps in the scientific literature. AMPA may cause genotoxicity and immunotoxicity in fish, adverse changes in haemolymph parameters, effects on mussels' antioxidant enzymes, and developmental delay and survival of tadpoles.

In a broader review of reproductive toxicity due to herbicide exposure in freshwater organisms (which includes, but is not limited to glyphosate), Yang et al. (2021) highlight the reproductive toxicity of herbicides found in a variety of freshwater environments. They note that, in freshwater, mussels, snails, frogs, and fish, are exposed to various types and concentrations of herbicides. Invertebrates are sensitive to herbicide exposure because their defence systems are incomplete, whereas fish show high bioaccumulation of herbicides because they are at the top of the food chain. They conclude that herbicide exposure causes reproductive toxicity and population declines in freshwater organisms and further contamination of fish used for consumption poses a risk to human health.

Demirci (2022) evaluates the toxic effect of the herbicide glyphosate together with an insecticide and fungicide, alone and as a mixture, on the aquatic organism *Gammarus lacustris* (which lives as a scavenger in ponds), using biochemical markers. The results of this study show the potential for increased toxicity in organisms exposed to pesticide mixtures. However, little research has been done on the effects of mixtures of pesticides on aquatic organisms.

In the following sections, we highlight evidence regarding the adverse effects of glyphosate-based herbicides on various aquatic species.

4.3.1. Amphibians

41% of amphibians face the threat of extinction, making them the most endangered vertebrates in the world (Monastersky, 2014). Due to their particular life-cycle (aquatic external fertilisation, eggs without shell, metamorphosis) and high skin permeability, amphibians are more vulnerable to aquatic contaminants and depend on water ecosystem quality. Therefore, amphibians are key bioindicator organisms for diagnosing the state of an ecosystem (Slaby et al. 2020; Riaño et al. 2020) and it has been suggested that pesticide pollution is one of the major causes for declines in anurans (frogs and toads) (Davidson, 2004; Mann et al. 2009; Sparling and Fellers, 2009). Amphibians may be particularly susceptible because they often breed in shallow fresh waters, which can contain higher pesticide concentrations, and surveys of natural populations have shown correlations between population declines and proximity to agricultural lands (Mann et al., 2009). Brodeur et al (2011) for example found reduced body size and significant enzymatic alternations in four adult anuran species inhabiting GM soy production areas in the humid pampas of Argentina, compared to uncultivated natural reserves not receiving agricultural pesticides. Although it remains difficult to causatively link pesticide use to the observed effects in survey studies, the observed correlation has pointed to the urgent need for more research on the subject.

Amphibians exploit both aquatic and terrestrial habitats, therefore exposure to glyphosate in either of these habitats may be relevant.

4.3.1.1. Impact of glyphosate on amphibians

A number of studies have considered the effects of glyphosate and glyphosate-based herbicides on amphibians, finding direct toxic as well as sublethal effects, including developmental, physiological, morphological and behavioral effects.

In their review on the potential impacts of glyphosate-based herbicides on amphibians, Wagner et al. (2013), conclude that the impact of glyphosate on amphibians generally depends on the herbicide formulation, the taxa and life stage. Therefore, amphibian risk assessment has to be conducted in a case-specific way (Wagner et al. 2013).

In an outdoor mesocosm experiment, Roundup had a direct toxic effect on tadpoles, reducing overall tadpole richness by 70%, completely exterminating two tadpole species (Leopard frogs, *Rana pipiens* and Gray tree frogs, *Hyla versicolor*) and reducing one species (Wood frogs, *Rana sylvatica*) to two percent. As no negative impact of Roundup on the tadpoles food resources (periphyton) was found and much of the tadpole mortality occurred within the first 24 hours, it was concluded that Roundup had a direct toxic effect on tadpoles and an indirect negative impact on predators through the trophic cascade (Relyea, 2005a). Direct toxic effects on tadpoles were confirmed in further outdoor mesocosm experiments. Relyea (2005b) recorded only 2% frog and toad tadpole survival after Roundup application at 3.8 mg a.i./L for 3 weeks. When Roundup application rate was reduced to approximately one third of the preceding study (1.3 mg a.i./L), the authors still found a 40% decrease of total tadpole survival and biomass in the absence of predators. In the presence of newts, Roundup caused an additional 21% reduction in leopard frog survival (Relyea et al., 2005). The authors conclude that substantially lower than the maximum expected concentrations of Roundup can still have a major impact on tadpole survival. Estimating the median lethal dose of Roundup for 6 tadpole species, (Relyea, 2005c) find in a laboratory experiment that Roundup is moderately to highly toxic to these amphibians. They also suggest a synergistic interaction of predatory stress and Roundup. Roundup is twice as lethal in the presence of predators compared to without predators against wood frog tadpoles. This is relevant because predators are usually present in the wild. However, dynamics are more complex in the wild. Relyea (2012, 2018), shows that the presence of predators could lead some tadpoles to avoid surface waters, where herbicide concentration is higher when temperature stratification occurs. Gabor et al. (2019), on the other hand, found evidence that environmentally relevant concentrations of glyphosate in combination with the glucocorticoid stess hormone, corticosterone (CORT) may act as an infodisruptor and prevent adaptive antipredator repsonses in tadpoles of the Gulf coast toad *Inicilius nebulifer*. Environmental pollutants such as glyphosate often act as endocrine disruptors that affect hormones and internal communication in organisms (see also Section 5.5.4. Endocrine disruption and reproductive health). CORT may become elevated in amphibians when exposed to pollutants and in the presence of predators. This may lead to altered immunosuppression and ultimately population declines. In some cases, impacts of lethal predators may also exceed those of herbicides. In the presence of uncaged lethal predators, the mortaility of three tadpole species was similar to or higher than that caused by the herbicide alone (Relyea, 2018). The author however stresses that it is important to note that a) the predators used in this experiment belong to the most lethal invertebrate predators in wetlands and b) that there are some wetlands that contain few or no predators. Under such circumstances, the mortality caused by higher herbicide concentrations are likely to exceed the mortality caused by other species of lethal predators.

It is known that predators induce morphological changes in a wide range of amphibian tadpoles, such as deeper tails, that help them to better escape from predators (Van Buskirk et al. 1997, Van Buskirk 2002). Relyea (2012) discovered that glyphosate can induce similar morphological defence changes in two tadpole species (wood frogs and leopard frogs). The effects were additive when combining predator cues and the herbicide, such that even larger morphological defences were produced. Another defence mechanism is behavioral adaptation. Jones et al. (2011) report that competitive stress can make Roundup more deadly to larval amphibians. They use outdoor mesocosms containing three tadpole species that were exposed to a factorial combination of three glyphosate concentrations and three tadpole densities (low, medium, or high). They find that increased tadpole density caused declines in tadpole growth, but also makes the herbicide significantly more lethal to one species, bullfrogs (*R. catesbeiana*).

Leeb et al. (2020) find evidence that juvenile common toads (*bufo bufo*) avoid the glyphosate formulation Taifun® forte at maximum recommended field rates for vine. The authors suggest that such avoidance behaviour might lead to chemical landscape fragmentation and associated reduced gene flow between amphibian populations.

Wagner et al. (2017) find that larvae of European Common Frogs (*Rana Temporaria*) from forest populations are more sensitive to a commonly used glyphosate-based herbicide compared with individuals from agrarian land. Effects of the glyphosate-based herbicide were stronger for earlier larval stages compared with later larval stages, suggesting higher risk of mortality in the spring (when early larvae are present in breeding ponds). Nearly all test concentrations caused retarded growth. Burraco and Gomez-Mestre (2016) study the physiological stress response in spadefoot toad tadpoles (*Pelobates cultripes*) to three levels of a series of stressors: salinity (0, 6, and 9 ppt), herbicide (0, 1, and 2 mg/L acid equivalent of glyphosate), water acidity (pH 4.5, 7.0, and 9.5), predators (absent, native, and invasive), and temperature (217, 257, and 297C). They find that salinity and herbicides cause dramatic physiological changes in tadpoles and pose serious threats to larval amphibians even at nonlethal concentrations. Krynak et al. (2017) study the effects of the glyphosate-based herbicide Rodeo (produced by Dow AgroSciences) on the Blanchard's Cricket Frog (*Acris blanchardi*), a declining North American amphibian species. They find a 37% decrease in survival of larvae exposed to an environmentally relevant concerntration of 2.5 mg L^{-1} (acid equivalent) compared to controls. This effect is not predicted by the results of acute analyses of glyphosate toxicity. They also find that glyphosate-based herbicide use may indirectly contribute to disease-related amphibian declines by altering the skin bacterial community that can provide pathogen resistance.

In Colombia, where glyphosate is the most used agrochemical, environmentally plausible concentrations of the commercial formulation Roundup Active®, led to concentration dependent-histopathological alterations in the liver of the Colombian endemic frog *Dendropsophus molitor* after one month of exposure (Riaño et al. 2020). The authors conclude that chronic exposure to sublethal concentrations of glyphosate-based herbicides can affect liver function, which is the most important organ in detoxification processes. Slaby et al. (2020). investigated the effects of glyphosate and its commercial formulation Roundup® GT Max on an essential and early step of amphibian reproduction, oocyte (egg) maturation. Their results show that this hormone-dependent process was seriously disturbed by both pure glyphosate and the formulation in *Xenopus laevis*. The authors also observed a number of severe and particular abnormalities, such as double spindle formation, which may prevent fertilisation. Herek et al. (2021) report cytotoxic and genotoxic damage of Roundup at environmentally relevant concentrations on tadpoles of two native South American amphibian species, *Physalaemus cuvieri* and *Physalaemus gracilis*. Moutinho et al. (2020) report 15% mortaility of *Boana pardalis* tadpoles after exposure to glyphosate at a concentration relevant for Brazilian sugar cane production sites.

Babalola et al. (2021) expose embryos of the African clawed frog (*Xenopus laevis*) to three glyphosate-based herbicides. The exposure concentrations ranged between 0.2–0.6 mg/L, 0.9–28 mg/L and 90–280 mg/L for Roundup, Enviro Glyphosate, and Kilo Max, respectively. This study reports reproductive malformations including mixed sex, translucence, aplasia, segmented hypertrophy and segmented aplasia and translucence. These authors conclude that their results indicate that some of the glyphosate formulations have the capacity to cause widespread reproductive malformations in a way that could reduce the reproductive fitness of this species. They suggest that the observed impaired gonadal development in this study is possibly associated with endocrine disruption by the glyphosate formulations (see also Section 5.5.4. Endocrine disruption and reproductive health).

4.3.1.2. Impact of multiple environmental pollutants on amphibians

To address the problem of glyphosate resistant weeds, the industry has developed new GM herbicide tolerant crops with resistances to 2,4-D, dicamba, and isoxaflutole in addition to glyphosate (see Section 6. Industry response and Section 7. Environmental and health effects of other herbicides). It is thus important to also assess the combinatorial effects of herbicide mixtures as well as other aquatic pollutants to amphibians.

Soloneski et al. (2016) study the effects of a mixture of glyphosate- and dicamba-based herbicides on the larvae of a species of toad found in Argentina (*Rhinella arenarum*). This study is relevant to the cultivation of newer herbicide-tolerant crops, which have been genetically engineered to be tolerant to both glyphosate and dicamba. It provides the first experimental evidence of acute lethal and sublethal effects exerted by dicamba on this species. In the mixture, both herbicides induced DNA damage in the cells assayed at higher frequencies than those observed for each pesticide alone, thereby indicating that these herbicides act synergistically when applied together. The authors conclude that because mixtures of dicamba and glyphosate herbicides produce synergistic DNA damage, they could magnify these effects inside freshwater amphibian populations and harm the tadpoles' survival.

The first study to look at chronic effects caused by glyphosate plus 2,4-D mixtures on amphibians, finds that concentrations found in natural environments and allowed in Brazilian waters affected swimming activity, and caused nuclear alternations and damage to body structures (mouth and intestine) in *Boana faber* and *Leptodactylus latrans* tadpoles, two species widely distributed in South America and found close to agricultural areas. The effects were species-specific with *L.*

latrans being more sensitive to the mixture than *B. faber*. In *L. latrans* body length and mass was also decreased (Pavan et al. 2021).

Peluso et al. (2021) find environmentally realistic non-equitoxic mixtures of the glyphosate-based herbicide ANTANOR® and and the 2,4-D-based herbicide Así Max 50® to have additive or synergistic effects on larvae of *Rhinella arenarum* (a species of toad), depending on the concentration and exposure time. The authors also point out that the herbicide interactions further depend on the compound form. They conclude: "*This fact highlights the need to assess mixture toxicity not only at different proportions of each compound and at different effect level but also at chronic exposure times since they are more environmentally accurate*." An observational study in the central Brazilian Amazon finds malformations in three species of Leptodactylus frogs and local extinctions of *Scinax ruber* (red-snouted treefrog) and *Rhinella marina* (cane toad) from reproductive sites close to a 3.6-ha area of pasture after 2L of Roundup (200 mL per 20 L of water) and 120 mL of Disparo, a herbicide containing 2,4-D and Picloram (60 ML per 20 L of water), were applied (Ferrante and Fearnside, 2020). A smaller area of the pasture was also treated with an additional herbicide. The authors exclude alternative hypotheses to explain the morphological anomalities and warn of long-term effects on amphibian populations. Although the contribution of each individual active ingredient to the observed effects is not known, this study adds to the warning signs that the cultivation of newer herbicide-tolerant crops, which have been genetically engineered to be tolerant to both glyphosate and 2,4-D, may have additional negative impacts on amphibian species. Further studies also find combinatorial and synergistic effects, including genotoxic effects, disruption of gut microbiota, morphological abnormalities and several further sublethal developmental effects of glyphosate and different environmental pollutants (including herbicides, insecticies and antibiotics) on tadpoles of *Rhinella arenarum* (Carvalho et al., 2019a; Boccioni et al. 2021).

Microplastics have been reported to exacerbate the problems of pesticide exposure. They can carry pesticides through long distances in wetlands, acting as pesticide vectors. Lajmanovich et al. (2022) study the combined exposure of microplastics and glyphosate or glufosinate (GA), respectively on tadpoles of the Striped-snouted tree frog, *Scianx squalirostris*. They find polyethylene microplastic particles to increase ecotoxicity of both formulations, especially in the case of glufosinate. They conclude: *"There is an urgent need to transform the current agro-industrial model based on the use of herbicides such as GLY and GA for transgenic crops, which generates thousands of tons of grains that are accumulated due to financial speculation in plastic silo-bags, into an agroecological model that could safeguard the health of ecosystems."*

Some studies indicate that commercial pesticide formulations are more toxic to amphibians than the active ingredient alone: these studies are discussed in Section 4.3.6. Impact of adjuvants on aquatic non-target organisms).

4.3.2. Fish

Fish are considered particularly sensitive to environmental pollutants and are a crucial indicator of the ecological integritiy of aquatic systems (Chovanec et al., 2003; Atamaniuk et al., 2013). Zebrafish, *Danio rerio* is a model organism classically used in ecotoxicology to study acute lethal and chronic sub-lethal effects of xenobiotics in fish (Davico et al., 2021; Faria et al., 2021; Fiorino et al., 2018). Another good biological model for toxicological investigations related to pesticide toxicity is the goldfish, *Carassius auratus L.* (Atamaniuk et a., 2013).

4.3.2.1. Impact of glyphosate on fish

A number of studies have investigated the effects of glyphosate and/or glyphosate-based herbicides, such as Roundup, on fish. A variety of negative effects including developmental toxicity, reproductive toxicity and neurotoxicity have been demonstrated in the model organism *Danio rerio*, as well as in many other fish species, including some important food species and endangered species.

Zhang et al. (2021a) find glyphosate and AMPA, one of its primary degradation products, at typical environmental residual concentrations, to exert developmental toxicity in zebrafish embryos and larvae. Exposure to 10, 100 and 700 μg/L glyphosate or AMPA significantly reduced survival and hatching rates of zebrafish embryos and induced a series of developmental malformations. With increasing exposure dose, defects in cardiac development and function, as well as percentage of apoptotic cells (cells programmed to die) appeared. These were related to changes changes found in expression of several genes that are involved in cardiac development and apoptosis (programmed cell death), *"Our results suggest that more attention be given to the toxicity of AMPA along with that of GLY, and their corresponding synergy requires further study."* Similarly, Sulukan et al. (2017) find that glyphosate (GLY) exposure causes several types of developmental malformations in zebrafish in a dose-dependent manner. They associate the observed body malformations with cellular apoptosis (cell death) caused by reactive oxygen species (ROS) and inhibition of the carbonic anhydrase enzyme (CA), as a result of glyphosate treatment. Fiorino et al. (2018) show increased mortality and some occurences of malformations in early stages of zebrafish and common carp (*Cyprinus carpio*) at glyphosate concentrations as low as 0.005 mg/l. The authors find common carp to be more sensitive to acute exposure to glyphosate than zebrafish, with higher malformation rates and a delay in development. Another study on early development on common carp, finds low concentrations of Roundup to reduce egg swelling, survival of embryos and quality of fish larvae (Lugowska, 2018).

Liu et al. (2022b) study the developmental toxicity of glyphosate on embryo-larval zebrafish (*Danio rerio*). The study indicates that glyphosate treatment can cause significant developmental toxicity, including premature hatching, decreased heartbeats, pericardial and yolk sac oedema (swelling), swim bladder deficiency, body malformation, and shorter body lengths. The authors conclude that their findings show that glyphosate affects the early life stages of zebrafish and provide insight into the mechanisms of glyphosate toxicity in fish.

Kelly et al. (2010) investigate the independent and combined effects of exposure to glyphosate and the trematode parasite *Telogaster opisthorchis* on the survival and development of spinal malformations in juvenile *Galaxias anomalus*, a New Zealand freshwater fish. Survival of juvenile fish was unaffected by exposure to glyphosate alone (at an environmentally relevant concentration; 0.36 mg a.i. L^{-1}) or by *T. opisthorchis* infection alone. However, simultaneous exposure to infection and glyphosate significantly reduced fish survival. Zebral et al. (2017) study the South American fish known as pejerrey (*Odontesthes Humensis*). They report that exposure to high concentrations of Roundup (5.43 mg a.e./L) for 96 h causes high mortality rates of fish embryos, but lower ecologically relevant concentrations have the potential to produce morphological alterations. Roundup exposure for up to 72 h did not induce developmental disturbances or retardation in this study but exposure to the herbicide for a longer period of time (96 h) induced morphological effects. Zebral et al. (2018) find that Roundup exposure leads to negative outcomes in reproduction, embryonic development and embryonic upper thermal tolerance in the fish *Austrolebias nigrofasciatus*, an endangered annual fish species endemic to Southern Brazil. Annual fish live in Central and South America in ephemeral wetlands that completely dry out annually. During the periods of drought, all the adult individuals die and the fish populations are maintained by embryos that can survive drying out whilst buried in the mud. This study demonstrates that 96 h exposure to the low and environmentally relevant Roundup concentration of 0.36 mg a. e./L can reduce fish fertility and embryonic thermal tolerance. This is important because the embryos of annual fish need to survive high temperatures and the adult fish need to continually reproduce until they die in the next dry season.

Pompermaier et al. (2022) report impaired initial development and behavior in zebrafish exposed to environmentally relevant concentrations of widely used pesticides. In these experiments, exposure to GBH decreases survival of embryos, causes hypermobility and anxiolytic behaviour in embryos and larvae, negatively affects the anti-predatory behavior of the larvae, and increases acetylcholinesterase activity.

As a major site of gas exchange, fish gills are in contiuous close contact with the aquatic environment and its pollutants. Santos-Silva et al. (2021) find Roundup alone or in combination with the organosphophate Temephos and/or Sodium Dedecil Sulfate to cause adaptive changes in zebrafish gills. Pesticide concentrations were based on environmental findings. Severe alterations in gill ultrastructure were also demonstrated in pejerrey fish (*Odontesthes bonariensis*) upon subchronic exposure to a glyphosate-based herbicide at 1 and 10 mg/L, respectively (Menéndez-Helman et al., 2020). De Moura (2017) study the effects of RoundUp on the hybrid fish jundiara (*Leiarius marmoratus × Pseudoplatystoma reticulatum*), finding significant alterations in metabolic and hematological processes. Dos Santos et al. (2017) find that a glyphosate-based herbicide induces histomorphological and protein expression changes in the liver of the female guppy *Poecilia reticulate*. The results indicate that the GBH at 1.8 mg of glyphosate L^{-1} induce the development of hepatic damage in *P. reticulata*, which is exposure-time dependent. They conclude that glyphosate-based herbicides cause inflammatory, regressive, vascular and progressive disorders in the liver of guppies. Bonifacio et al. (2016) study the river fish *Cnesterodon decemmaculatus*, from the Pampean region of South America. They study the toxicity of Clorfox and Roundup Max, the commercial formulations of chlorpyrifos and glyphosate, respectively, alone and in combination. They also report impacts of RoundUp on the liver, plus complex interactions and combined effects of the two pesticides on the liver and the brain. These authors conclude that the presence of these pesticides in freshwater systems could impose a risk for populations of this river fish. Similarly, Li et al. (2016a) report adverse effects of glyphosate on the brain, liver and kidney of goldfish (*Carassius auratus*). Significant perturbations in neurotransmitter equilibrium, energy metabolism as well as amino acid metabolism were observed in glyphosate dosed fish, which were associated with the toxicity of glyphosate. Uren Webster & Santos (2015) characterise and compare the global mechanisms of toxicity of glyphosate and Roundup in the liver of brown trout (*Salmo trutta*). They expose juvenile female brown trout to 0, 0.01, 0.5 and 10 mg/L of glyphosate and Roundup (glyphosate acid equivalent) for 14 days, and sequence 6 replicate liver samples from each treatment. They report transcriptional changes consistent with generation of oxidative stress and the widespread induction of compensatory cellular stress response pathways. The mechanisms of toxicity identified were similar across both glyphosate and Roundup treatments, including for environmentally relevant concentrations.

Pesticide exposure, in general, can generate oxidative stress (a build up of potentially damaging oxygen reactive species) in animals. To determine whether glyphosate causes oxidative stress in the model organism *Danio rerio* (zebrafish), the effects of its exposure were evaluated by Lopes et al. (2016). They conclude that exposure to glyphosate promotes a physiological response in male *D. rerio* tissues (brain, muscle, and gills). In this study, glyphosate exposure caused an imbalance in the oxidative status and altered the cholinergic system in a tissue-dependent manner. The authors state that these results are consistent with the toxicity mechanisms previously described for the commercial formulation. Velasques et al. (2016) find that zebrafish exposure to Roundup alters oxidative status and causes a response in terms of antioxidant defence system gene expression. Specifically, Roundup exposure causes an alteration of the antioxidant status in zebrafish gills and liver. The glyphosate formulation Scout® (0.065 and 1.0 mg/L) was found to induce neutrotoxic effects in zebrafish, including mitrochondrial dysfunction in brain cells, reduced brain cell viability and reactive species production. Mitochondrial dysfunction and oxidative stress play and important role in neurodegenerative diseases. The formulation also induced behavioral impairments at the lowest concentration. Exploratory activities were altered (position of the fish in the aquaria) (Pereira et al., 2018b). Similar behavioural changes upon exposure to a glyphosate-based formulation were also found by da Costa Chaulet et al. (2019) however at higher concentrations (3 and 5 mg/L). The authors argue that such altered activity patterns influence the fishes' ability to avoid or evade predators and may result in significant repercussions for the species. The effects seemed to be augmented when fish were additionally exposed to a fipronil-based insecticide. Faria et al (2021) tested much lower, environmentally relevant concentrations of glyphosate (0.3 and 3 μg/L) in a chronic exposure trial and also find glyphosate to have neurotoxic effects on zebrafish, including impairment of exploratory and social behaviors, that indicate increased anxiety. They further report evidence of changes in the antioxidant defence system and oxidative stress in adult zebrafish. Roundup-exposed adult zebrafish further demonstrated impairment in memory. These authors raise concerns about the potential for glyphosate and Roundup to affect wild fish populations, even at concentrations that are found in the environment and conclude: *"Aggressive behavior and memory are very important regarding resources dispute, nesting sites dispute and mate dispute and this impairment could be very harmful to fish living in the wild"* (Faria et al., 2021). Bridi et al. (2017) find that both glyphosate and Roundup below 1 mg/L alter behaviour in zebrafish such as swimming performance and aggressiveness. Similarly, Forner-Piquer et al. (2021) also find glyphosate to significantly decrease swimming performance and to cause neurophysiological defects in zebrafish larvae at 1 mg/L or higher. In addition, exposure to a low dose of 1 μg/L changed expression of several genes involved in biological processes and molecular functions, indicating glyphosate-induced molecular vulnerability. For example, gene pathways directly involved in neuronal physiology and synaptic transmission were deregulated, which is in accordance with the observed negative neurophysiological outcome. The results also indicated morphological microglia modifications, as sign of neuro-inflammation. Furthermore, several genes related to mitochondria were altered, in accordance with previous findings of glyphosate-induced oxidative stress in zebrafish. Since zebrafish are used as a vertebrate model in human neurobehavioral studies, these results are also relevant for understanding risks of glyphsoate and glyphosate-based formulations on human health (see Section 5.5. Health effects of Glyphosate and Roundup).

Sobjak et al. (2017) detect an acute effect of glyphosate throughout the early development of silver catfish (*Rhamdia quelen*), with a decrease in the antioxidant system control and neurotoxic effects. However, they observe a higher survival rate in the larvae of the treated group, possibly due to the effects of glyphosate on pathogens. Roundup was also found to greatly affect behavioral patterns in the livebearer *Jenynsia multidentate,* indicating a neurotoxic action of Roundup on *Jenynsia multidentate* (Sánchez et al., 2021). This fish naturally inhabits agricultural areas in southern Brazil and Argentina where the concentration used in this experiment (0.5 mg/L) is environmentally relevant in waterbodies. In this study, different Roundup formulations negatively affected swimming performance, long-term memory consolidation and the sexual activity of males in *Jenynsia multidentate.* One formulation negatively affected social interaction and two formulations increased time spent by the fish in the center of the open field test apparatus, which the authors consider as an indication of depression. The results show that different Roundup formulations varied in the severity of the effects indicating that the adjuvants present in the formulations have different targets of toxicity (see also Section 4.3.6. Impact of adjuvants on aquatic non-target organisms). Giaquinto et al. (2017) analyze the effects of commercial formulation of glyphosate on feeding behaviour in Pacu (*Piaractus mesopotamicus*), a South American freshwater fish. Fish were exposed to three glyphosate concentrations (0.2, 0.6, and 1.8 ppm) for 15 days. At concentrations of 0.2 and 0.6 ppm, food intake decreased on day 13 and then returned to normal on day 15. At the highest glyphosate-based herbicide concentration, 1.8 ppm, food consumption decreased dramatically and did not recover on day 15. The authors conclude that this study shows that glyphosate-based herbicide at sub-lethal concentrations can affect feed intake in pacu and consequently inhibits its growth. Tapkir et al. (2019) argue that anthropogenic alterations in water chemistry, due to environmental contaminants such as glyphosate, has the potential to impair recognition of predators, which is based on odour signatures. They show that exposure to a sublethal concentration (0.5 mg/L) of Roundup for 3h or 15 days, respectively, impaires the recognition of conspecific alarm cues and subsequent alarm response in the prey fish spiny loach (*Lepidocephalichthys thermalis*). The authors further showed that Roundup deactivates conspecific alarm cues and dimishes associative learning for detection of predators. The behavioral suppression to detect conspecific alarm cues was time-dependant (fish exposed for 15 days showed higher levels of behavioral suppression than fish exposed for 3h) and transient, with fish recovering after two days. The authors discuss the possibility that the effect may be permanent with higher exposure levels and warn that *"...due to the worldwide occurrence of glyphosate in* *water bodies, glyphosate mediated behavioral suppression exposes the prey animals to a considerable risk of predation, both by native and non-native predators."*

Lopes et al. (2014) find exposure to pure glyphosate for 24 and 96h at concentrations of 5 and 10 mg/L to decrease sperm motility in model organisms *Danio rerio* (zebrafish). They conclude: *"The results showed that glyphosate can induce harmful effects on reproductive parameters in D. rerio and that this change would reduce the fertility rate of these animals."* Davico et al. (2021) further find Roundup WG® (0.065 and 6.5 mg/L) to adversely affect ovarian maturation in zebrafish, which can lead to reproductive toxicity and ultimately comprise population dynamics. Decreased sperm quality upon glyphosate exposure has also been shown in other fish species. Akça et al. (2021) find glyphosate to disrupt sperm quality in rainbow trout (*Oncorhynchus mykiss*) and increase DNA fragmentation in sperm cells, at similar concentrations (2.5, 5 and 10 mg/L) to the study of Lopes et al. (2014). More concerning, are the findings of Gonçalves et al. (2018) who exposed yellowtail tetra fish (*Astyanax lacustris*) to environmental relevant concentrations (50, 300 and 1800 μg/l) of a glyphosate-based herbicide. They also find the herbicide to affect sperm quality. In particular, the herbicide reduced sperm viability and motility. They conclude: *"...environmental protection agencies must review regulations of glyphosate-based herbicdes on water bodies".* In the study of Mohapatra et al. (2020), exposure to sublethal doses of glyphosate for 45 days resulted in deleterious alterations in testis, ovaries and liver structure, as well as haematological parameters of the climbing perch *Anabas testudineus*, an edible and commercial fish. Furthermore, a reduction in spawning performances (fertilization and hatching rate) was observed. The authors conclude that the herbicide could deleteriously impair reproductive fitness and could ultimately result in a reduction in growth and population size. They state: *"Its* [glyphosate's] *indiscriminate use might lead to an alarmingly reduced population or even extinction of many aquatic organisms. The consumption of contaminated fish could also result in health hazards in humans. Therefore, new regulatory mechanisms, judicious applications and public awareness are necessary for better survival of aquatic organisms."* (Mohapatra et al. 2020).

A study conducted with rainbow trout (*Oncorhynchus mykiss*), finds transgenerational and intergenerational toxicity of an environmentally relevant concentration (1 μg/L) of glyphosate and two glyphosate-based formulations on rainbow trout. Exposure to previous generations negatively affected the early development of the F2 generation (the second filial generation, generated through inbreeding of the first filial, F1, individuals). Intergenerational exposure to pure glyphosate increased viral susceptibility of juveniles (Le Du-Carrée et al., 2021).

Jia et al. (2022) study the livers of tilapia (*Oreochromis niloticus*) under chronic exposure to glyphosate. They find potential toxicity, mainly manifested as redox imbalance (imbalance between oxidants and antioxidants) and dysregulation of metabolism function, in the liver of tilapia after long-term glyphosate exposure at 2 mg/L.

De Maria et al. (2022) report endocrine, immune and renal toxicity in male largemouth bass after chronic exposure to glyphosate and the glyphosate-based herbicide Rodeo®. Using four fish in each tank, they expose adult male largemouth bass for 21 days to two doses of glyphosate and Rodeo® (chemically equivalent concentration of glyphosate) at 0.5 mg L^{-1} and 10 mg L^{-1} and to a clean water control. In these experiments, endocrine disruption was corroborated at the hormone and gene expression levels (see also Section 5.5.4. Endocrine disruption and reproductive health).

4.3.2.2. Impact of glyphosate on reptiles

Some studies have considered the impact of glyphosate may have on caimans (reptiles which live in marshes, swamps, rivers and lakes), often as part of a mixture of pesticides.

López González et al. (2019) demonstrate genotoxicity of pesticide mixtures, including glyphosate, under conditions that simulate the real situation of exposure suffered by caiman and other wild species in Argentina. A subsequent two-month exposure experiment with broad-snouted caiman (*Caiman latirostris*), simulating natural pesticide degradation in water, revealed that glyphosate-based formulations alone or in mixtures with different insecticides induce genotoxicity, immunotoxicity and oxidative stress in hatchlings. The authors highlight that: "*Under field conditions, organisms can be exposed, in many cases, to different xenobiotics and other stress factors simultaneously, probably increasing the effects observed in controlled studies*." (López González et al., 2021).

Odetti et al. (2020) conduct two similar experiments in consecutive years, in which broad-snouted caiman (*C. latirostris*) eggs were exposed to pesticide formulations, including glyphosate, separately and in different mixtures through application on the incubation material. In blood samples taken after hatching, results indicated the presence of DNA damage, oxidation of purines and pyrimidines, and increased frequency of micronucleus, in the case of glyphosate and the other formulations, as well as in all the mixtures tested, with respect to the control groups. These authors conclude that they have demonstrated that the pesticides generated genotoxicity at concentrations and combinations recommended for application in agricultural activities, associated mainly with soybean crops.

4.3.3. Aquatic invertebrates

Matozzo et al. (2020) review the effects of glyphosate and its commercial formulations, such as Roundup, on marine invertebrates. Most studies in this review relate to marine molluscs, such as oysters (*Crassostrea gigas* and *Crassostrea virginica*), mussels (*Mytilus galloprovincialis* and *Perna perna*), clams (*Ruditapes philippinarum* and *Ruditapes decussatus*) and sea snails (*Haliotis tuberculate*). There are also some reported studies in crustacea (*Artemia salina*, *Acartia tonsa*, and the crabs *Callinectes sapidus* and *Neohelice granulata*), echinoderms, corals and polychaetes (bristle worms). The reviewers find that, generally, data obtained in acute toxicity tests indicate that glyphosate and its commercial formulations are lethal at high concentrations, which are not environmentally realistic, whereas results of long-lasting experiments indicate that glyphosate at lower levels can markedly affect biological responses of marine invertebrates. They argue that more efforts should be addressed at evaluating chronic or sub-chronic effects of such substances to marine invertebrate species. For example, Matozzo et al. (2018) demonstrate that glyphosate can affect both cellular and biochemical parameters in mussels, highlighting a potential risk for aquatic invertebrates. Similarly, Milan et al. (2018) find significant effects on gene expression in Mediterranean mussels (*Mytilus galloprovincialis*) even at low glyphosate concentrations of 10µg/L.

Iori et al. (2020) assess the effects of glyphosate (GLY), its degradation product AMPA, and a mixture of both, on the mussel *Mytilus galloprovincialis* in a controlled experiment, using next-generation sequencing to evaluate such effects at the molecular level in both the mussel and its microbiota. They report variable capacity of bacteria to proliferate in the presence of glyphosate and find a compromised physiological status of the mussel following exposure to AMPA and GLY, which may lead to significant microbiota modifications, as well as changes in response to pathogens. They conclude that, in addition to the direct toxicity on host-physiology, changes occurring in the host-microbial community must also be taken into consideration when considering adverse effects. Further illustrating the complexity of freshwater ecosystems, Lu et al. (2020) find that the addition of glyphosate in artificial freshwater microcosms did not strongly affect the aquatic microbial community composition but did alter the community's transcription levels. Metatranscriptomic analyses indicated that the transcriptions of some cyanobacteria were significantly influenced by glyphosate. The authors suggest this might be potentially explained by the possibility that some microbes could alleviate glyphosate's toxicity by utilizing glyphosate as a source of phosphorus (P). This is consistent with the findings of Wang et al. (2017a), who study marine, rather than freshwater, algae. These authors observe that, after more than 60 days, *Prorocentrum donghaiense*, a dinoflagellate known to cause major harmful algal blooms in the East China Sea, can grow in a medium with glyphosate as the sole P source. This study demonstrates that glyphosate could selectively promote the growth of particular groups of bacteria within an algal culture and that in glyphosate enriched coastal waters, this interaction may potentially further facilitate the growth of algae. Xu et al. (2021) report that combined exposure to glyphosate and antibiotic contaminants promotes cyanobacterial growth at no-effect concentrations of single exposure. They conclude that this suggests an increased threat from combined contamination to aquatic ecosystems through promoting the formation of cyanobacterial bloom.

It is important to evaluate not only lethality but also sub-lethal effects of glyphosate-based formulations, such as effects on growth, reproduction or metabolism, as they seem to be more sensitive indicators of effects and give more insights into pattern of toxicity (Battaglin, et al., 2014). Avigliano et al. (2014a) studied the effects of sub-lethal concentrations of glyphosate on chronically exposed early juvenile crayfish, *Cherax quadricarinatus*. In Argentina most farms of freshwater crayfish are close to agricultural crops and subject to contamination by glyphosate-based herbicides. The crayfish show reduced weight gain and protein and lipid reserves and the authors assign this to the chronic stress attributed with the herbicide exposure.

Estuarine crabs (*Neohelice granulata*), that inhabitat the coast of Samborombón Bay in Argentina, are exposed to glyphosate and other herbicides via several rivers and channels that cross extensive agricultural areas and reach the Bay. Avigliano et al. (2014b), exposed egg-carrying females of the estuarine crab to both glyphosate and Roundup Ultramax at sub-lethal concentrations they assume could be found in runoff water from crop fields sprayed with glyphosate. This is relevant, because the crabs are known to be most severely exposed to these chemicals in summer during their reproductive period. Roundup exposure led to a significant reduction in the number of hatched larvae, indicating a clear embryonic mortality of the Roundup formulation. As these effects were not found for pure glyphosate, the authors assumed that Roundup compounds other than glyphosate may be responsible for the embryonic mortality (see Section 4.3.6. Impact of adjuvants on aquatic non-target organisms). Additionally, several abnormalities were reported in larvae hatched in both glyphosate and Roundup. The observed stimulation of egg maturation by glyphosate led the authors to assume that exposure to glyphosate disrupts the hormonal system that controls reproduction (see also Section 5.5.4. Endocrine disruption and reproductive health). Canosa et al. (2018) subsequently studied the effects of chronic Roundup exposure on ovarian growth over the 3-month pre-reproductive period in *N. granulata* crabs. They report significant impairments. Both concentrations used in the study were within the environmental range of glyphosate reported for several water bodies of Argentina. *In vitro* experimental results also showed an effect of glyphosate on ovarian growth. Additionally, Avigliano et al. (2018) find that exposure to pure glyphosate at concentrations relevant for Argentinian water bodies, harms ovarian growth during the pre-reproductive period in *N. granulata* in vivo (at 1 mg/l) and in vitro (at 0.2 mg/L). In accordance with Avigliano et al. (2014a), glyphosate also reduced weight gain of adult females at a low concentration (0.02 mg/L). Canosa et al. (2021) further investigate the possible interference of Roundup (0.2 mg/L) on the endocrine control of ovarian growth in *N. granulata*. They provide evidence that Roundup could stimulate the progesterone secretion exerted by the ovary and conclude that it is a possible endocrine disruptor affecting the functionality of progesterone-like hormones produced by the ovary of crustaceans. Rodríguez et al. (2021) review the evidence about the effect of glyphosate, both technical and formulated, on the ovarian maturation of *Neohelice granulata* female crabs, and the effects of glyphosate on sperm production in males. The concentrations used in the in vivo assays reported were within the environmental range of glyphosate reported for several water bodies of Argentina. In females, both formulated and technical glyphosate were able to produce a significant incidence of oocyte reabsorption in the ovary: despite this, glyphosate stimulated oocyte growth, suggesting that glyphosate could be acting as an endocrine disruptor. In male crabs, several reproductive imbalances were noted, such as a significant decrease of the sperm count, abnormal spermatophores, and possible disrupting effects of glyphosate on the androgenic gland.

In a study of the effects of low concentrations of Roundup WG® on the shrimp species *Macrobrachium potiuna*, de Melo et al. (2019) found impacts on the endocrine systems of males, in the form of altered gene expressions.

Zhou et al. (2022) report that glyphosate disturbs coral calcification, meiosis and symbiont nutrient export in the coral *Pocillopora damicornis*.

Ferreira-Junior et al. (2017) study the effects of Roundup on the freshwater insect *Chironomus xanthus*. They show that concentrations of glyphosate caused delayed emergence of females (at 1.53 mg/L) and induced fast emergence of males (at 0.49 mg/L), compared to control treatment. They conclude that negative effects of environmentally relevant concentrations of glyphosate (0.7 mg/L) occur on this insect's growth and development. Females of *C. xanthus* were more sensitive to low concentrations of glyphosate.

Gutierrez et al. (2017) find that the application of a glyphosate-based pesticide selectively affects the hatching dynamic of zooplankton egg banks, which suggests that these resting structures are highly sensitive to the toxicity of the pesticide. Andrade et al. (2021) suggest that adverse effects of glyphosate on zooplankton may be synergistic: in a mesocosm experiment, they found that the acute toxicity of a mixture of glyphosate and cypermethrin was 3 and 4 times higher than the isolated toxicities, respectively.

Various studies also show negative impacts on the model organism *Daphnia magna.* In chronic exposure testing over the whole life-cycle of the fresh water flea species *Daphnia magna,* Cuhra et al. (2013) find a significant reduction of juvenile size at a concentration (from 0.05 mg/l) which is far below the current accepted maximum contaminant level for glyphosate in surface waters in the U.S (which is 0.7-1.0 mg/l), for both glyphosate and Roundup. They further show that chronic exposure to glyphosate at concentrations of 1.35 mg/l and Roundup at 0.45 mg/l could result in serious reproductive damage. These are levels close to or below the current US maximum contaminant level for glyphosate and RoundUp respectively. Cuhra el al. (2013) also observed negative impacts on growth, which became more evident with progressing time, emphasising the need to study the whole life cycle of non-target organisms. In a subsequent life-long feeding study with RR, conventional and organic soybeans, Cuhra et al. (2014) find *D. magna* fed with RR soybeans to consistently perform less well in terms of survival, growth and fecundity, than the animals fed either conventional or organic soybeans. They conclude that this was due to a difference in feed quality either because of the compositional differences between the soy types and/or because of the glyphosate and AMPA residues found in RR soy that were lacking in the conventional or organic soy samples (see also Bøhn et al., 2014 in Section 5.3. Impacts of GM crops and foods on the health of humans and farmed animals). To further investigate the effects of glyphosate and AMPA residues found in RR crops on the life-history traits of *D. magna*, Cuhra et al. (2015) conducted another life-long feeding study with soymeal diets containing a range of glyphosate residues. They find that high levels of glyphosate residues in the soybean feed tested correlated with 1) higher mortality, 2) reduced growth and fecundity in some parts of the life-cycle, 3) delayed reproduction, and a reduced total number of offspring (Cuhra et al., 2015). Those residue levels are still below the current maximum residue level (MRLs) in the U.S. and found in "ready to market" soybeans. Still, evidence of the toxicity of glyphosate to non-target organisms often remains inconclusive. For the model organism *Daphnia magna* for example, different studies reported median lethal concentrations of glyphosate ranging from 13 mg/l up to 2000 mg/l (Cuhra et al., 2013). Cuhra et al. (2013) tested whether these differences can be attributed to varying sensitivities between *D. magna* with different backgrounds and levels of exposure to pesticides. However, they find a relatively uniform susceptibility to glyphosate and Roundup between all *D. magna*, with older individuals being more resistant. They attributed the varying results in scientific literature to different testing protocols, especially the glyphosate formulations. Some studies used the technical grade glyphosate, which is non-soluble in water. In fact, many studies on aquatic organisms suggest that variations in toxicity levels result from differences in the glyphosate formulations used (see Section 4.3.6. Impact of adjuvants on aquatic non-target organisms).

Negative impacts may also be influenced by other pollutants in the environment. In a study of behavioural responses of juvenile *Daphnia magna* after exposure to glyphosate and glyphosate-copper (Cu(II)) complexes, Hansen and Roslev (2016) report that glyphosate-Cu(II) complexes were more toxic to *D. magna* than glyphosate alone. Sublethal concentrations resulted in decreases in swimming velocity, acceleration speed, and distance moved and the inactive time of *D. magna* increased. They note that glyphosate is a chelating agent that can form stable complexes with copper ions (see Section 3.1.3 Impact of fertilisers on glyphosate efficacy) and conclude that environmental metals can play a role in apparent glyphosate toxicity. Rodríguez-Miguel et al. (2021) further warn about multigenerational adverse effects on freshwater zooplankton. Since impacts on the parental generation can further impact the behaviour and health of the next generation, multigenerational exposure aims to investigate the long-term impact of pollutant on non-target organisms. In their study, Rodríguez-Miguel et al. (2021) find that the observed negative effects on *Daphnia exilis* upon exposure to sublethal concentrations of the glyphosate-based formulation Faena®, are significantly higher in the first progeny than in the parental generation. Exposure to the glyphosate formulation for example almost completely inhibited reproduction in the progeny. The authors suggest that such an increased toxic response could contribute to the extinction of populations and recommend: *"The frequently claimed low toxicity of glyphosate must be revised to control the indiscriminate use of this herbicide."*

In a further study in *Daphnia*, Suppa et al. (2020) report that chronic exposure to ecologically relevant concentrations of glyphosate and Roundup, at the approved regulatory threshold for drinking water in the US, induce embryonic developmental failure, induce significant DNA damage (genotoxicity), and interfere with signaling. In addition, they find that chronic exposure to the weedkiller alters the gut microbiota functionality and composition. They conclude, "*The impact of the weedkiller on this keystone species has cascading effects on aquatic food webs, affecting their ability to deliver critical ecosystem services*".

Ramsdorf et al. (2021) highlight adverse transgenerational effects (on survival, reproductive capacity and oxidative stress) of a mixture of glyphosate and atrazine on *Daphnia magna*. They highlight the difficulties of assessing mixtures of herbicides, and the importance of considering effects across generations.

4.3.4. Algae and periphyton

Periphyton is the material growing under freshwaters, consisting of a community of algae, bacteria, fungi, and various invertebrates. Phytoplankton are microscopic algae which usually float in the upper part of oceans, or freshwater, where they are exposed to sunlight.

Wang et al. (2016b) study the physiological effects of glyphosate on fourteen species of marine phytoplankton, representing five major coastal phytoplankton phyla (haptophyta, bacillariophyta, dinoflagellata, raphidophyta, and chlorophyta). They conclude that glyphosate could be used as nutrient (phosphorus) source by some species, is toxic to some other species and has no effects on others. Glyphosate could significantly inhibit the growth of the twelve out of the fourteen species. The authors suggest that the increasing concentration of glyphosate in coastal waters will likely exert significant impact on coastal marine phytoplankton community structure.

Pizarro et al. (2016) explore the joint impact of glyphosate and the invasive golden mussel *Limnoperna fortunei* on freshwater phytoplankton, bacterioplankton and periphyton, and on the physical and chemical properties of the water. They find that the ability of mussels to reduce glyphosate in water may be valued as positive, but their results allow them to predict that the invasion of *Limnoperna fortunei* in natural freshwater systems contaminated by glyphosate will accelerate the negative impact of the herbicide associated with eutrophication (i.e. when the water becomes enriched with nutrients, which can cause harmful algal blooms).

Carles et al. (2019) investigate the relationship between biofilms, phosphorus and glyphosate in French rivers. Seasonal fluctuations in glyphosate, AMPA and phosphorus concentrations were correlated, peaking in spring/summer shortly after pesticide spreading. They find that phosphorus not only is a key driver of river eutrophication but also can reduce complete glyphosate degradation by biofilms and favour the accumulation of AMPA in river water. These authors conclude that the predominant role of biofilms and the trophic status of rivers must therefore be considered in order to better assess the fate and persistence of glyphosate.

Vera et al. (2010) investigate the impact of Roundup on the periphyton (freshwater organisms attached or clinging to plants and other objects projecting above the bottom sediments). The experiment was carried out over 42 days in ten outdoor mesocosms of different typology in Argentina: ‘‘clear’’ waters with aquatic macrophytes and/or metaphyton and ‘‘turbid’’ waters with great occurrence of phytoplankton or suspended inorganic matter. The herbicide was added at 8 mg L^{-1} of the active ingredient (glyphosate) in five mesocosms while five were left as controls (without Roundup addition). Total phosphorus significantly increased in treated mesocosms due to Roundup degradation what favored eutrophication process. It was observed that glyphosate produced a long-term shift in the typology of mesocosms, ‘‘clear’’ turning to ‘‘turbid’’, which is consistent with the regional trend in shallow lakes in the Pampa plain of Argentina. Gattás et al. (2018) study the joint impact of the glyphosate-based commercial formulation Roundup Max® and the invasive mussel *Limnoperna fortunei* on phytoplankton and water quality the Salto Grande reservoir in Argentina, in a 7-day experiment using 400 litre enclosures. A decrease in species diversity was observed in the enclosures treated with RoundUp Max and with mussels, with respect to controls. In the enclosure where invasive mussels and glyphosate were both applied, species diversity showed a significant decrease due to the explosive growth of a small and opportunistic Chlorophyta (green algae), *Spermatozopsis exsultans*. The concentration of RoundUp Max applied (5 mg L^{-1} of active ingredient (a.i.)) was relatively high, but the authors argue this represents a worst-case scenario and that their results may reflect short-term effects of an input of glyphosate into a water body after a fumigation event, and the joint presence of *L. fortunei*, an invasive species widely spread along the reservoir and the Río de la Plata basin.

Tolerance to glyphosate is common among cyanobacteria (blue-green algae found in water), including harmful algal bloom-forming species. Dabney (2018) reports that at low concentrations, glyphosate stimulates growth of the harmful algae *Prymnesium parvum* through mechanisms caused by its degradation and consequent release of phosphorus. In this study, glyphosate and glyphosate-based herbicides show hormetic effects (low-dose stimulation and high-dose inhibition) on *P. parvum* growth at environmentally relevant concentrations, although the effect is reduced for forumlations containing a high proportion of inactive ingredients. This research suggests that glyphosate-contaminated runoff potentially contributes to incidences of algal bloom (Dabney & Patiño, 2018). Berman et al. (2020) survey 52 Pampean lakes and 24 Patagonian lakes. Lakes in the Pampas region of Argentina have been exposed to glyphosate for more than 30 years. The authors conclude that long-term agricultural practices relying on glyphosate-based technologies have had important effects on freshwater microbial communities, particularly by promoting increases in picocyanobacteria abundance. Picocyanobacteria are the smallest cyanobacteria, and may be a source of toxins.

4.3.5 Aquatic mammals

Manatees are large marine mammals, sometimes known as sea cows. The Florida manatee (*Trichechus manatus latirostris*) is a subspecies of the West Indian manatee (*Trichechus manatus*). Chronic exposure to glyphosate in Florida manatee has been studied by de Maria et al. (2021), who find that glyphosate and AMPA are ubiquitous in Florida water bodies. They note that Florida manatees were chronically exposed to glyphosate and AMPA, during and beyond the glyphosate applications to sugarcane in the area, possibly associated with multiple uses of glyphosate-based herbicides for other crops or to control aquatic weeds. This is the first study to quantify glyphosate and AMPA in marine mammals.

4.3.6. Impact of adjuvants on aquatic non-target organisms

With the expiration of Monsanto's patent on glyphosate in 2000 (Duke & Powles, 2008), many new glyphosate-based herbicides that all differ slightly in composition entered the market (Howe et al., 2004). Pesticide ingredients are a mixture of active and inert ingredients (Cox & Surgan, 2006). In glyphosate-based herbicide formulations, glyphosate is the active ingredient that is supposed to kill the target weeds. Those formulations also contain various adjuvants, the so-called inert ingredients, whose function within the formulation is to enhance the chemical and physical efficacy of the active ingredient in diverse manners. This includes increasing the solubility, stability and half-life of the active ingredient and protecting it from degradation as well as supporting mixing, dilution and application and facilitating cell penetration (Cox & Surgan, 2006; Mesnage et al., 2014; Pereira et al., 2009). The most common adjuvants in herbicide formulations are surfactants such as polyethoxylated tallow amine (POEA) which is found in Roundup (Brausch & Smith, 2007). POEAs promote penetration of the active ingredient into plant cuticles (Relyea, 2005b). Because adjuvants are not *per se* toxic to the target weeds they are called inert ingredients. Despite their name, they may however be biologically or chemically active (Cox & Surgan, 2006). The first generation of POEA surfactants (POE-tallowamine) in Roundup are markedly more toxic than glyphosate (Mesnage et al. 2019). Glyphosate-based herbicide (GBH) formulations containing POAE surfactants are progressively being phased out in Europe and replaced by a new generation of surfactants, but this is not happening in the USA. Although newer formulations can have reduced toxicity there is no regulatory requirement to disclose surfactants and only the active ingredients are assessed by regulators. Currently, the risk assessment of pesticides in the European Union and in the United States focuses almost exclusively on the stated active ingredient (Mesnage & Antoniou, 2018).

The exact composition of herbicide formulations is generally not declared on product labels (Cox & Surgan, 2006) and is often protected as proprietary information of the manufacturer (Howe et al., 2004). This is one of the reasons why ecotoxicological assessment of pesticides usually focuses on the effects of the active ingredient rather than on commercial formulations like Roundup that are actually used in the field, and explains why studies comparing the effects of the active ingredient, the inert ingredients and the formulation are uncommon. However, toxicity testing of both is likely to provide a more realistic picture of the overall impact of pesticides on non-target organisms (Cox & Surgan, 2006; Pereira et al., 2009).

Existing toxicity studies with aquatic organisms (including fish, amphibians, aquatic invertebrates, bacteria, protozoa and aquatic non-target plants and algae) exposed to glyphosate and different commercial formulations suggest that the formulations are more toxic than glyphosate alone, indicating that the presence of adjuvants may have an additive or synergistic effect on the total toxicity of glyphosate. The surfactant POEA is often named to be the most toxic compound.

In one example, Marc et al., (2002) showed that adjuvants make sea urchin embryo cell membranes more permeable to glyphosate.

In an acute toxicity test with different frog tadpole species, Roundup was the most toxic of the formulations tested. Glyphosate on the other hand was found to be practically non-toxic (Mann & Bidwell, 1999). Perkins et al. (2000) even find Roundup to be 700 times more toxic to frog embryos than a glyphosate-based formulation without surfactants. This was attributed to the toxicity of the surfactant POEA itself, which was even more toxic than Roundup. They argued that the greater toxicity might be due to enhanced uptake of glyphosate by the embryos. Howe et al. (2004) suggest that the POEA surfactant contributes most, if not all, to the acute toxicity of Roundup to frog tadpoles and that the toxicity of glyphosate-based herbicide formulations is correlated with the percentage of POEA in the formulation. Moore et al. (2012) confirm these findings, suggesting that POEA contributes 100% to the toxicity of Roundup. In the acute toxicity study with frog tadpoles, Howe et al. (2004) find POEA by itself to be the most toxic compound, followed by glyphosate-based formulations known to contain POEA. No acute toxicity could be observed with glyphosate alone and the formulations with unknown surfactants. Similarly, in a chronic exposure experiment with frog tadpoles, exposure to POEA or glyphosate-based formulations containing POEA decreased the number of tadpoles that reached metamorphosis, decreased tadpole length at metamorphosis, increased time to metamorphosis and resulted in tail damage, gonadal abnormalities and intersex animals. The authors suggest that disruption of hormone signalling may be a reason for these symptoms (see also Section 5.5.4. Endocrine disruption and reproductive health). They conclude that concentrations of glyphosate-based formulations that include the surfactant POEA found in ponds after field application can be toxic to the tadpole stages of common North American amphibians. This is also relevant because POEA has a longer half-life than glyphosate.

The surfactant POEA is not the only surfactant enhancing the toxicity of glyphosate towards amphibian tadpoles. The surfactants Agri-dex and Competitor were found to increase acute toxicity of glyphosate to tadpoles of the western toad (Vincent & Davidson, 2015).

Acute aquatic toxicity testing with three different fish species also suggests that surfactants increase toxicity (Mitchell et al., 1987). In the same year Servizi et al. (1987) find that glyphosate is less toxic to fish and water fleas than the surfactant POEA. Similarly, Folmar et al. (1979) find POEA to be the primary toxic agent in Roundup in acute toxicity tests with different aquatic invertebrates including water fleas and midge larvae and fish such as the Rainbow trout, the channel catfish and bluegills. Glyphosate contributed only around 30% to the toxicity of Roundup. Brausch et al. (2007) show that POEAs are both acutely toxic to the water flea *D. magna* and cause sub-lethal effects such as reduced growth. Higher toxicity to *D. magna,* of a commercial glyphosate-based formulation compared to its active ingredient alone has also been found by Pereira et al. (2009). POEA formulations were also shown to be extremely toxic to the fairy shrimp, an aquatic macroinvertebrate. The authors suggest that this was due to disruption of oxygen transport in respiratory surfaces (Brausch & Smith, 2007).

Tsui & Chu (2003) examine if the findings from fish, amphibians and aquatic invertebrates also apply to microorganisms such as bacteria, microalgae, protozoa and microscopic crustacea. They generally find POEA to be most toxic, followed by Roundup, with glyphosate the least toxic. POEA accounted for more than 86% of Roundup toxicity in all tested organisms except photosynthetic microalgae where it accounted for almost 50% of Roundup toxicity. In another study on microalgae, the commercial formulation Spasor exhibited higher toxicity to microalga than its active ingredient glyphosate (Pereira et al., 2009). Tsui & Chu (2004) further tested three glyphosate-based formulations on two crustacean species with similar findings. Roundup containing the surfactant POEA was the most toxic, followed by a formulation with unknown surfactants. The formulation without surfactants was the least toxic. Everett & Dickerson (2003) find Roundup to be at least 100-times more lethal than technical grade glyphosate to ciliated protozoa that are common in freshwater ponds. In an experiment with sea urchin embryos, Marc et al. (2002) suggest that glyphosate requires the presence of the formulated products to provoked cell division dysfunction in the embryos and suggest that the formulation products favour penetration of glyphosate in the embryos. Cedergreen & Streibig (2005) find the Roundup formulation to be approximately four times more toxic to non-target freshwater plants and algae than the active ingredient. Aquatic plants and algae are crucial for the function of aquatic ecosystems. The authors suggest that this was because the blank formulation is in itself phytotoxic.

Wagner et al. (2013) review the available data related to potential impacts of glyphosate-based herbicides on amphibians and conduct a qualitative meta-analysis. They state that, because little is known about environmental concentrations of glyphosate in amphibian habitats and virtually nothing is known about environmental concentrations of the substances added to the herbicide formulations that mainly contribute to adverse effects, glyphosate levels can only be seen as approximations for contamination with glyphosate-based herbicides. The impact on amphibians depends on the herbicide formulation, with different sensitivity of taxa and life stages. Effects on development of larvae apparently are the most sensitive endpoints to study. As with other contaminants, costressors mainly increase adverse effects. The authors state that if and how glyphosate-based herbicides and other pesticides contribute to amphibian decline is not answerable yet due to missing data on how natural populations are affected. Amphibian risk assessment can only be conducted case specifically, with consideration of the particular herbicide formulation. The authors recommend better monitoring of both amphibian populations and contamination of habitats with glyphosate-based herbicides, not just glyphosate, and suggest including amphibians in standardized test batteries to study at least dermal administration.

Rissoli et al. (2016) study the effects of glyphosate and Roundup (in two formulations) on bullfrog tadpoles. They find that glyphosate, RoundUp and Roundup Transorb R exert different effects in bullfrog tadpoles. Bullfrog tadpoles' skin is very sensitive to glyphosate and Roundup formulations, causing distinct skin alterations and impairing oxygen uptake across the skin. However, glyphosate and Roundup formulations altered the respiratory function differently, revealing an influence of the other components of each formulation (surfactants and inert compounds) on the metabolism of tadpoles. Exposure to environmentally relevant concentrations of the herbicides over a 96 h period, although not lethal, resulted in sublethal effects that the authors conclude could threaten the development and survival of frog populations in natural environments.

Bach et al. (2016) study the South-American Creole frog, *Leptodactylus latrans*. They find that the commercial formulation Roundup Ultramax is much more toxic than the active ingredient glyphosate on all the endpoints assessed (mortality, swimming activity, growth, development, and the presence of morphologic abnormalities). Both forms of the herbicide induce similar sublethal effects, though at different concentrations, with RoundUp being five orders of magnitude more toxic than glyphosate alone. Growth and development were the most sensitive endpoints, but all could affect the fitness and survival of frogs in agroecosystems. The authors note that the occurrence of oral abnormalities and alterations in swimming activity must necessarily decrease feeding with deleterious consequences on growth and development. Subsequently, Bach et al. (2018) demonstrate adverse effects of glyphosate and RoundUp Ultramax on the liver of *Leptodactylus latrans* tadpoles (another South American frog species) at concentrations frequently found in the environment. These data showed a difference in the toxicity of two orders magnitude between RoundUp and glyphosate alone. The authors note that, although studies of lethal effects indicate an absence of toxicity of glyphosate with respect to commercial formulations, sub-lethal effects indicate more similarities in the responses produced, thus reducing the toxicity gap between the two compounds.

Jassens & Stoks (2017) also find that RoundUp has stonger effects than glyphosate alone in damselfly larvae, confirming the toxicity of the surfactant POEA. Negative effects on food intake and escape swimming speed were present at lower concentrations following RoundUp exposure compared to glyphosate alone and negative effects on survival, sugar and total energy content and muscle mass did not occur with glyphosate alone. However, glyphosate alone was not harmless: a realistic concentration of 2mg/l resulted in reduced growth rate, escape swimming speed and fat content.

Some authors suggest that ingredients other than surfactants are partly to blame for adverse impacts on aquatic organisms. Reddy et al. (2018a) study the effects of the individual active ingredients of the herbicide Roundup (based on testing two active ingredients, glyphosate and diquat dibromide [DD]) on the aquatic snail *Lymnaea palustris*. DD is used to kill pond weed. These authors conclude that, although the toxicity of commercially-available Roundup to aquatic animals may have many contributing factors including its inactive surfactant, the constituent of Roundup associated with the greatest reproductive disturbances and observed developmental abnormalities of offspring in this study is DD.

Oliveira et al. (2019) study the effects of glyphosate, Roundup and aminomethylphosphonic acid (AMPA; the main degradation product of glyphosate) on *Nitella microcarpa var. wrightii*, a green algae found worldwide. Their results indicate that glyphosate has a stronger inhibitory effect on photosynthetic rate when applied in association with a surfactant (i.e. as Roundup, rather than glyphosate alone). They report that these effects are related both to the concentration of the active ingredient and to exposure time (a statistically significant difference was observed only after 7 days of exposure). A significant reduction in photosynthetic rate of this algae was observed (-42.1%) even at the lowest Roundup concentration tested (0.28 mg l^{-1}), which is the maximum concentration of this herbicide allowed by Brazilian law in water used for irrigation and animal consumption. The authors conclude that even legal concentrations of Roundup in water bodies commonly used for these activities (e.g. streams and small lakes) may present significant environmental risks. They note that the reduction in productivity in green algae may have a negative impact on other organisms that live or feed on the algae.

Sabio y García et al. (2022) compare the effect of five different glyphosate-based herbicides (GBH) as well as of monoisopropylamine salt of glyphosate (GIPA) on aquatic microbial communities from natural shallow lakes that were mixed and allowed to evolve in an outdoor pond, using an 8-day long assay. They conclude that the formulations have effects beyond those exerted by the active ingredients alone and there is lack of real knowledge regarding the consequences of the variety of GBH on natural aquatic ecosystems. Significantly different effects were evident on the structure of microbial communities dependent on the GBH, in spite of the herbicides sharing similar active ingredients.

Le Du-Carrée et al. (2022) report that the nature of the co-formulants used with glyphosate in GBHs can modulate the susceptibility of fish to pathogens.

Bednářová et al. (2020) conclude that Roundup® Concentrate Plus (RCP) and the surfactant POEA are more toxic than pure glyphosate to fruit flies (*Drosophila melanogaster*) and also find evidence that they inhibit fecundity in this species.

In studies with zebrafish and rainbow trout, de Brito Rodrigues et al. (2019) assess the acute toxicity and genotoxicity of the glyphosate-based formulation Atanor 48 (ATN) and its major constituents glyphosate (GLY) and the surfactant polyethoxylated tallow amine (POEA), as well as the main metabolite of of glyphosate, AMPA. In zebrafish, GLY and AMPA caused no acute toxic effect, while ATN and POEA induced significant lethal effects (at relatively high doses). GLY, POEA, ATN and AMPA were genotoxic for zebrafish larvae (the Lowest Observed Effect Concentration, LOEC, was 1.7 mg/L for GLY, ATN, AMPA and 0.4 mg/L for POEA) and POEA induced DNA damage in rainbow trout gonad cells. These varied effects highlight the importance of considering the full formulation of the pesticide, not just its active ingredient, as well as considering multiple endpoints.

Conference abstracts have not been peer reviewed and may be revised subsequently. In a conference abstract, Arumuganathan et al. (2016) report an analysis of the effects of Roundup and its components on the pond snail, *Lymnaea palustris*. A significant decrease in fecundity was observed in snails in all treatment groups. Shifts were observed in both hormone and protein levels when comparing the results of the treatment groups to the control group. In another conference abstract, Kish (2017) state they have recorded data suggesting that at very low concentrations of what is recommended for use, RoundUp is toxic to *Daphnia magna*. They state that this contradicts the EPA’s recommendations for the safe use of glyphosate-based herbicides and also implies that surfactants may play a role in their toxicity. In another abstract at the same conference, Sweeney and Testorf (2017) describe experiments involving glyphosate dilutions between 10% and 0.01% from a Roundup solution that contains 50% glyphosate, and applying them to specimens for periods ranging from 0 to 300 minutes. Results for *D. magna* showed a statistically significant effect where specimens placed in higher concentrations of glyphosate died faster than those at lower concentrations. These times ranged from an average of 9 minutes for specimens placed in a 10% glyphosate solution to an average of 71 minutes for specimens placed in a 0.01% glyphosate solution. The authors report that the controls outlived the time during which the specimens were observed.

Concerning the potential toxic effects of pesticides, the EU Directive governing the placing of plant protection products on the European market (Council Directive 91/414/EEC), requires an ecotoxicological assessment of the effects on aquatic organisms, including fish and water fleas. These studies however usually only focus on the active ingredient rather than on the commercial formulations (Pereira et al., 2009). Cox & Surgan (2006) argue that current testing requirements for pesticides are inadequate to fully assess the health and environmental effects of these mixtures. They recommend that all pesticide ingredients should be identified on product labels with per cent composition and that pesticide registration should be based on the commercial formulations that are sold and used. For example, in the EU, considering these omissions in the current ecotoxicological assessment of pesticides, we argue that the European Food Safety Authority (EFSA) cannot exclude potential adverse impacts of commercial glyphosate-based formulations that would be used in conjunction with RR crops on aquatic biodiversity. Indeed, the Renewal Assessment Report (RAR), that the German Federal Institute for Risk Assessment (BfR) conducted for the re-approval of glyphosate in the EU, acknowledges that there is convincing evidence that tallowamines used as surfactants contribute to glyphosate toxicity (Bauer-Panskus, 2014).

4.4. Impact on terrestrial organisms

Studies in rats and mice are considered separately (in Section 5.5. Health effects of Glyphosate and Roundup), since these studies have generally been conducted with a view to assessing human health effects. Studies of the effects of glyphosate on wild mammals are extremely limited (studies in livestock are discussed in Section 5.3.2. Effects on farmed mammals). Martinez-Haro et al. (2022) develop a method to determine glyphosate concentrations in samples of gastric content from the Iberian hare (*Lepus granatensis*) in Spain. They analyse glyphosate residues in hunted animals from pesticide-treated and pesticide-free areas (75 and 28 hares, respectively), as well as from 11 hares found dead in the field. The prevalence of glyphosate in hunted hares from pesticide-treated areas ranged between 9 and 22%, increasing to 45% in animals found dead and the glyphosate concentrations detected in the gastric content of hares ranged from 0.11 to 16 μg/g. No residues were detected in animals from pesticide-free areas. These authors suggest that wild animals may be subjected to chronic environmental levels of glyphosate that, while not lethal, may be exerting some adverse effects. Since RoundUp Ready GM crops are not grown in Spain, concerns will be greater where RR crops are grown, where environmental levels of glyphosate are likely to be higher.

More is known on the adverse effects of glyphosate on other terrestrial organisms including earthworms, nematodes, aphids, lizards, snails and armadillos.

Hart et al. (2009) assessed the persistence of transgenic DNA in a field of RR maize and identified the *cp4 epsps* transgene in bulk in microarthropods, nematodes, macroarthropods and earthworms sampled within the cropping system. Transgenic DNA concentrations in these animals were significantly higher than in the background soil, suggesting the animals were feeding directly on transgenic plant material. The results suggest that the *cp4 epsps* transgene in RR maize does not significantly degrade within the food web. The guts of these animals may provide an opportunity for genetic transformation into native soil bacteria, although this remains to be established. Whether the presence of the transgene presents a risk for soil animals, including earthworms, is unknown.

Earthworms are one of the most important components of the soil biota. By shredding organic material and mineralising it in their guts, earthworms produce cast that contains plant available nutrients. Earthworm burrowing further fosters macropores, enhances water infiltration and increases soil penetrability for roots, which helps to maintain soil structure. Earthworms thus have a relevant importance for soil conservation, soil fertility, soil nutrient cycling, plant growth and productivity and overall ecosystem functioning. Their abundance and distribution are strongly influenced by environmental conditions, as well as the ecological state of the system.

Because of their importance, earthworms have been used as bioindicators for soil health, soil quality and contamination levels. Furthermore, earthworms are used extensively in terrestrial ecotoxicity studies. The earthworm species *Eisenida fetida* and *Eisenida andrei* are internationally validated species for ecotoxicological tests due to their cosmopolitan distribution, convenience in handling and because they are considered to be representative of soil fauna and earthworms in particular. But other earthworm species such as *Lumbricum rubellus* and *Lumbricum terrestris*, have also been used as test organisms (ISO, 2012a; b; Santadino et al., 2014).

Several ecotoxicological studies have found sublethal, chronic effects of glyphosate on *Eisendia* spp., mainly on fertility and juveniles. Santadino et al. (2014), tested sublethal, chronic effects of environmental relevant doses of glyphosate on different demographic parameters of *E. fetida*, emphasising the importance for ecological risk assessment to not only study acute ecotoxicological effects. Since the isolated analysis of glyphosate effects on different demographic parameters may not show the real effects on the dynamics of the population, they also determined the ecological importance of those effects on earthworms' demographic dynamics using a population dynamic matrix model. Santadino et al. (2014), found glyphosate to significantly increase the number of cocoons produced. They suggest that this increase in fecundity of the earthworms is an initial response to stress. The phenomenon known as hormesis, takes place when small quantities of a stressful agent, such as glyphosate, is actually useful for an organism in suboptimal environments. However, glyphosate negatively affected cocoon fertility. The demographic matrix predicted that chronic exposure to glyphosate results in a negative growth rate, which could lead to local extinction after only six weeks. A sensitivity analysis on the parameters of the matrix further indicated that in the controls, a small change in adult survival and fecundity has the most influence on the growth rate of the population. In contrast, survival from juveniles to adults was shown to be the most important parameter in the population dynamics in treatments with glyphosate. The authors fear that glyphosate could drastically deplete local earthworm populations and because of their importance, cause medium- to long-term soil deterioration.

Domínguez et al. (2016), studied acute and chronic effects of field relevant concentrations of AMPA, one of glyphosate's main metabolites, on *E. andrei*. The longer soil persistence of AMPA might result in higher toxicity risks compared to glyphosate. The results differed between the acute and the chronic assays, emphasising again the importance of conducting long-term chronic ecotoxicological studies. Biomass loss in the short-term acute assay was higher in the control than in the AMPA treatments. The authors suggest that the initial lower biomass loss of earthworms treated with AMPA may occur because earthworms in the control invest more energy and mass in reproduction. Indeed, cocoon production was highest in the control in the acute assay. In contrast, in the long-term chronic assay, biomass losses were significantly higher in all AMPA treatments, except for the highest concentration, and the number of cocoons and juveniles increased with increasing AMPA concentration. The authors suggest that a hormesis effect of glyphosate, as observed by Santadino et al. (2014), could be involved in these results. While Santadino et al. (2014) observed lower fertility of those cocoons, Domínguez et al. (2016) found weights of both juveniles and cocoons to decrease with increasing AMPA concentration. They suggest that juveniles may be more sensitive to AMPA than adults. The production of more, but lighter individuals, might result in weaker offspring. Soil contaminated with high doses of AMPA could decrease earthworm growth and reproduction and ultimately impair their ability to perform key ecosystem functions.

García-Pérez et al. (2016) apply a commercial glyphosate-based herbicide to three types of litter mixed with soil, to study the effects on earthworms. They conclude that repeated application of litter contaminated with glyphosate negatively affects earthworm vitality and increases soil acidity and acid phosphatase activity. The increased soil acidity at the end of the experiment suggests the persistence or accumulation of glyphosate or its subproducts in the soil.

Gaupp-Berghausen et al. (2015) study the effect of Roundup on cast activity and reproduction of earthworms in a greenhouse mesocosm experiment, where Roundup was directly applied on the weeds, at a lower than recommended dose. Two earthworm species, the vertically burrowing earthworm *Lumbricus terrestris* and the horizontally burrowing A*porrectodea caliginosa* were used. According to the authors, those species are more frequently found in agroecosystems than

Eisenida species. Treatment with Roundup increased soil moisture and increased plant available nitrate and phosphate, reflecting the lack of physiologically active, transpiring plants. The authors fear that those nutrients may leach into streams, lakes or groundwater aquifers. After an initial peak, surface cast production of. *L. terrestris* significantly decreased upon herbicide application and almost ceased after three weeks. Roundup reduced both the number and mean mass of produced casts. Four weeks after herbicide application, cumulative cast mass was reduced by 46% compared to untreated mesocosms. This result is surprising, because increased soil moisture commonly stimulates casting activity. The authors suggest that the initial stimulation in surface cast production observed may be caused by the increased availability of dead leaf material after herbicide application. The subsequent decrease however clearly demonstrates a direct impact of the herbicide. No significant decrease in surface casting activity could be demonstrated for the soil-dwelling earthworm *A. caliginosa*. As demonstrated for *Eisenida* species, herbicide application furthermore decreased reproductive success of both *L. terrestris* and *A. caliginosa* by decreasing hatching rate.

In a further short-term greenhouse experiment, Zaller et al. (2014), investigate whether Roundup affects the interactions between the two of the most important soil organisms, earthworms (*L. terrestris)* and arbuscular mycorrhizal fungi (*Glomus mosseae*). On the one hand, herbicide application led to slightly heavier but less active earthworms in the presence of the mycorrhizal fungi. On the other hand, Roundup and earthworms distinctly altered performance of *G. mosseae*. In mesocosms amended with the mycorrhizal fungi, herbicide application decreased root mycorrhization rates. The herbicide also generally declined spore biomass of the mycorrhizal fungi. Given the importance of arbuscular mycorrhizal fungi for plant nutrition, a decline in arbuscular mycorrhizal fungi would also require more fertilisation with not only ecological consequences but also economic consequences for farmland management. Third, concentrations of glyphosate in leachate were significantly interactively affected by earthworms and arbuscular mycorrhizal fungi. While earthworms may increase glyphosate leaching by increasing flow of contaminated water through burrows, arbuscular mycorrhizal fungi may lead to stronger absorption of glyphosate by enhancing soil aggregation. In outdoor experimental systems (mesocosms) not amended with arbuscular mycorrhizal fungi, earthworms indeed significantly increased glyphosate leaching, while mesocosms amended with the mycorrhizal fungi tended to decrease glyphosate leaching.

A recent study presents the first evidence that exposure to glyphosate-based herbicides could shift the gut microbiome in earthworms which could lead to a disruption of fundamental physiological processes and thereby affect the ecological roles of earthworms (Owagboriaye et al., 2021).

Pochron et al. (2019) find that environmental (e.g. soil temperature) as well as intrinsic worm characteristics (e.g. initial body mass) influence worm sensitivity to glyphosate and conclude that *"…earthworms might be sensitive to herbicides under specific conditions".* Their findings might help to explain differing or contradictory results reported in scientific literature on the effects of glyphosate on earthworms.

In conclusion, even though the effect of glyphosate on earthworm health is not fully understood yet, glyphosate and one of its primary metabolites AMPA have been shown to exert sublethal effects on different earthworm species at field relevant concentrations under certain circumstances. Moreover, glyphosate may affect interactions between earthworms and other soil organisms.

Wang et al. (2017b) study the soil nematode *Caenorhabditis elegans*, which constitutes a useful bioindicator of environmental disturbances due to its contact with natural environmental toxins and multiple stressors, such as heavy metals, pesticides, and temperature. In laboratory studies, they find a synergistic type of interaction was observed for acute toxicity with mixtures of arsenic and glyphosate. In these experiments, head thrash frequency and reproduction exhibit concentration dependent decreases in both individual and combined exposures to the tested chemical stressors, and show synergistic interactions even at micromolar concentrations. McVey et al. (2016) publish evidence that chronic exposure of *Caenorhabditis elegans* (*C. elegans*) to a high-use glyphosate-containing herbicide, Touchdown, during the egg stage may adversely affect the developing nervous system. In their study, *C. elegans* hatched from eggs exposed to Touchdown have decreased fecundity compared to non-treated worms. General changes in neurodevelopment are not observed until the fourth larval (L4) stage. García-Espiñeira et al. (2018) study the toxicity of atrazine- and glyphosate-based formulations on *C. elegans*. They find that both herbicides inhibit locomotion and fertility, and glyphosate is more toxic than atrazine. They find the higher toxicity of glyphosate remarkable given that the permitted atrazine and glyphosate concentrations in drinking water are 3 ppb (0.014 μM) and 700 ppb (4.14 μM), respectively. RoundUp produced lethality of 20%, 50%, and 100% at 0.01, 10, and 100 μM glyphosate, respectively and exposure to 10 μM inhibited locomotion by 87%. Brood size was decreased by 23% and 93% after exposure to 0.01 and 10 μM Glyphosate, respectively. The effects of herbicide mixtures were additive. The authors note that both pesticides induced some biological changes at concentrations similar to drinking water standards.

A series of conference abstracts also show harm to *C. elegans* caused by exposure to glyphosate or glyphosate-based herbicides (Adner, 2017; Herndon, 2017; Viazmenski, 2017; Adner & Pettee, 2017).

Studies in other terrestrial organisms have been rather limited. Effects on pollinators are discussed in Section 4.2.5. Pollinators.

Muller et al. (2021) exposed fruit flies, *Drosophila melanogaster*, to either Roundup® Ready to Use, containing pelargonic acid and glyphosate, or Roundup® Super Concentrate, that includes glyphosate and the surfactant polyethoxylated tallow amine (POEA), at sublethal concentrations. Both Roundup® formulations affected ovary development at all concentrations tested, causing reduced ovary volume with fewer mature oocytes compared to the organic control. The results suggest a critical period of increased ovarian sensitivity to glyphosate. The authors conclude that their results support multi-species evidence that glyphosate-based herbicides interfere with normal development of the reproductive systems of non-target organisms.

Saska et al. (2016) demonstrate that treatment with glyphosate-based herbicide alters the life history of the rose-grain aphid (*Metopolophium dirhodum*). In their experiments the average longevity significantly decreased with each increase in the herbicide concentration. Individual aphids that survive the treatment suffer a reduced ability to reproduce, which reduces the chance to build up new populations on reaching a refuge. This is the first study that comprehensively documents such a negative effect on the population of an herbivorous insect.

Smith et al. (2021) report that glyphosate inhibits melanization and increases susceptibility to infection in insects. Melanin, a black-brown pigment found throughout all kingdoms of life, has diverse biological functions. In insects, melanin production is triggered upon wounding or infection, to either clot a wound or restrict a pathogen. In their experiments, the authors demonstrate that glyphosate and AMPA have deleterious effects on insect health in two very different species, *Galleria mellonella* (the greater wax moth) and *Anopheles gambiae* (mosquito species which transmit malaria), by increasing their susceptibility to infection with fungi and malaria parasites, respectively. They argue that glyphosate's interference with melanization could have considerable environmental impact, in a wide variety of insect species, given its stability and wide concentration range.

Gao et al. (2021) find that glyphosate exposure disturbs the bacterial endosymbiont community and reduces body weight of the predatory ladybird beetle (*Harmonia axyridis*). In their experiments, feeding on glyphosate significantly effects the relative abundance of dominant bacteria, so that copy numbers of *Staphylococcus* bacteria were significantly lower and *Enterobacter* were significantly higher.

Gómez-Gallego at al. (2020) study Colorado potato beetles (*Leptinotarsa decemlineata*) reared on potato plants grown in pots containing untreated soil or soil treated with glyphosate-based herbicide (GBH). The beetles' microbial composition was affected by the GBH treatment and the differences in microbial composition between the control and insects exposed to GBH were more pronounced in the adults. The GBH treatment increased the relative abundance of *Agrobacterium* in the larvae and the adults but reduced the relative abundances of *Enterobacteriaceae*, *Rhodobacter*, *Rhizobium* and *Acidovorax* in the adult beetles and *Ochrobactrum* in the larvae. The authors conclude that glyphosate can impact microbial communities associated with herbivores feeding on non-target crop plants. The consequences of glyphosate-induced changes in the microbiota and the function of those bacteria in the Colorado potato beetle remain unknown.

Schaumberg et al. (2016) report experiments using the tegu lizard (*Salvator merianae*), in which they exposed the eggs to RoundUp. A significant increase in DNA damage was observed in all concentrations higher than 100 µg/egg. They warn that DNA damage induced during the embryonic period may interfere with the development and survival of embryos as well as hatchlings. They conclude that their study clearly demonstrates that one of the most common glyphosate-based herbicide formulations, RoundUp, can be genotoxic to tegu lizards.

Luaces et al. (2017) study the effects of glyphosate on the big hairy armadillo (*Chaetophractus villosus*), which has a wide distribution that overlaps with agricultural areas where soybean is grown in Argentina. They test the genotoxic effect of glyphosate on the peripheral blood lymphocytes of this species over a range of concentrations (280, 420, 560, 1120 µmol/L). Their results demonstrate genotoxic effects on these cells, which they conclude strongly suggests that exposure to RoundUp could induce DNA damage in this armadillo species in the wild.

Niedobová et al. (2022) find that the toxicity of the glyphosate herbicide for Pardosa spiders' predatory activity depends on the formulation of the glyphosate product (see also Section 4.3.6. Impact of adjuvants on aquatic non-target organisms).

Maderthaner et al. (2020) study the effects of commercial glyphosate-based herbicides (Roundup LB Plus, Touchdown Quattro, Roundup PowerFlex) on the insect-like creatures known as springtails (Collembola), which are important indicators of soil quality and sustainable land use. They conduct a greenhouse experiment growing a weed population of *Amaranthus retroflexus* in arable field soil with either 3.0 or 4.1% soil organic matter (SOM) content and treated these weeds either with the glyphosate-based herbicides (GBHs) or their respective active ingredients (isopropylammonium, diammonium or potassium salts of glyphosate) at recommended dosages. Control pots were mechanically weeded. They assess effects on the surface activity of the springtail species *Sminthurinus niger*. Both GBHs and their active ingredients increased the surface activity of springtails compared to control pots, but springtail activity was higher under GBHs than under corresponding active ingredients. They interpret these findings as an avoidance behaviour by the springtails of plant material and soil surface contaminated with GBHs or their active ingredients. In addition, stimulation of springtail activity was much higher in soil with higher SOM content than with low SOM content (significant treatment x SOM interaction). The authors suggest that environmental risk assessments (ERAs) for pesticides should be performed with the herbicides that are actually applied in agriculture, rather than only with the active ingredients, and should also consider influences of different soil properties.

Wee et al. (2021) study the multigeneration toxicity of a glyphosate-based herbicide (GBH) to *Allonychiurus kimi* (Lee) (a Collembola, or 'springtail'). The GBH was observed to have no negative effects on adult survivals of all generations, but juvenile production was found to decrease in a concentration-dependent manner. The authors conclude that repeated and long-term use of GBH could have significantly higher negative impacts on non-target soil organisms than expected.

Druart et al. (2017) conduct a full life-cycle (240 days) bioassay using the terrestrial snail, *Cantareus aspersus*, to assess the effects of Bypass, a glyphosate-based herbicide (GBH). They compare with a mixture (R-A) made of diquat (Reglone) and nonylphenols (Agral), known for its endocrine disrupting effects in other organisms, as a control. This is the first full life-cycle bioassay on a terrestrial organism. They used a predicted environmental concentration in soil of 3 mg glyphosate kg^{-1} for Bypass. Ten egg clutches were used for the exposure to Bypass and the negative control. From each clutch, 20 eggs were incubated on Bypass-contaminated soil and 20 other eggs were incubated on control soil. The application of this bioassay to Bypass showed that this common herbicide formulation had contrasted effects, with a significant enhancement of growth speed followed by a marked reduction of the fertility of *C. aspersus* snails. The results indicated that early exposure to Bypass led to delayed effects on eggs laid by exposed adults, either on the fertilization or/and the embryogenesis. The authors suggest that future studies will have to elucidate the mechanism of action to know if the effects of this glyphosate-based herbicide occur through an endocrine mechanism.

4.5. Impact on soil microbial communities

Many studies find that glyphosate changes soil microbial community dynamics by enhancement or suppression of the activity of pathogenic or plant growth-promoting bacteria and fungi. Organisms capable of metabolising glyphosate are increased and organisms to which glyphosate is toxic are reduced. Negative impact on some beneficial soil micro-organisms such as *F. Pseudomonas* and a positive impact on certain plant pathogens such as *Fusarium spp.* that cause disease in many crops, are frequently reported. A change in soil microbial community composition could potentially affect soil quality, soil nutrient dynamics, suppression of disease and plant stress tolerance, which may subsequently impact plant health and ultimately productivity of non-target plants. As noted in Section 3.1.3 Impact of fertilisers on glyphosate efficacy, Monsanto enhanced the second generation of RR soy with a proprietary fungicide coating in an attempt to address some of the agronomic issues. The focus of this section is on environmental issues.

In 1995, Dick and Quinn (1995) found quantitative and qualitative differences between the soil microbial communities found in glyphosate treated and untreated soil samples. Comparing soil microbial communities of two taxonomically identical agricultural soils with different cropping histories, one from an organically managed farm without a history of glyphosate application and one from a farm with a history of RR cropping and glyphosate application of over 10 years, Nye et al. (2014) suggest that long-term repeated glyphosate application affects soil microbial communities. Adding RR soybean plant residues treated with glyphosate to the soils further suggested that the soil with a history of long-term glyphosate exposure already had a community primed for glyphosate residues, whereas the soil from the organic farm started to change in response to glyphosate treatments. Furthermore, RR material that had been exposed to glyphosate caused a differential shift in the communities over RR material that had not been exposed to glyphosate. The authors also showed that a soil history of glyphosate exposure significantly affected microbial stress. Stress was greater for the soil with a history of glyphosate treatment.

Kremer (2017) notes that it is only within the last 5 to 10 years that assessment of glyphosate's detrimental effects on soil and environmental health have become the focus of intensive research efforts. He argues that long-term studies on persistence are needed on sites receiving annual application and on those that are no longer under GM cropping systems to determine the extent of any carryover of residual glyphosate and AMPA. Because soils are diverse within landscapes and among geographic regions, glyphosate fates and effects need to be studied over a range of characteristics to validate assumptions that glyphosate and AMPA are highly retained in fine textured soils and are more biologically available in coarse or sandy soils and that it is imperative that long-term studies of glyphosate include agricultural management variations.

Van Bruggen et al (2021) summarise the evidence of indirect effects of the herbicide glyphosate on plant, animal and human health through its effects on microbial communities. They emphasise that such shifts in microbial community composition have been implicated in enhanced susceptibility of plants to *Fusarium* and *Rhizoctonia* (see Section 4.5.2. Impact on pathogenic fungi), of birds and mammals to toxic *Clostridium* and *Salmonella* species, and of bees to *Serratia* and Deformed Wing Virus, with outbreaks of several animal and plant diseases related to glyphosate accumulation in the environment.

4.5.1. Impact on bacterial communities and beneficial fungi

Newman et al. (2016) find subtle shifts in the rhizosphere bacterial community (i.e. bacteria in the region of soil that is directly influenced by root secretions and associated soil microorganisms) following long-term glyphosate application on RR corn and soybean in the greenhouse. Independent of glyphosate treatment, the rhizosphere bacterial communities of soybean and corn were dominated by members of the phyla *Protobacteria*, *Acidobacteria* and *Actinobacteria*. After four growth periods, *Protobacteria* increased in relative abundance for both crops following glyphosate exposure, while *Acidobacteria* and *Actinobacteria* deceased. The authors suggest that a decrease in *Acidobacteria* could lead to significant changes in the nutrient status of the rhizosphere.

Hertel et al. (2021) warn that intensive application of glyphosate in agriculture is a serious environmental issue because it may negatively affect the biodiversity in the soil and in the gut microbiota of insects. They highlight evidence that bacteria can evolve glyphosate resistance by (i) reducing glyphosate sensitivity or elevating production of the EPSP synthase, by (ii) degrading or (iii) detoxifying glyphosate and by (iv) decreasing the uptake or increasing the export of the herbicide.

Glyphosate has further been found to reduce the ratio of manganese (Mn) reducers to Mn oxidisers upon release in the rhizosphere (Kremer and Means, 2009; Johal and Huber, 2009; Zobiole, 2011). Whilst the Mn-reducing bacteria *pseudomonas fluorescens* are reduced by glyphosate, agrobacteria which are known strong Mn oxidisers appear to be preferentially selected for colonisation of the rhizosphere as glyphosate is released through roots of RR crops (Kremer and Means 2009).

One reason why response to glyphosate varies among soil bacteria may be different sensitivity of intracellular EPSPS to the herbicide. The nitrogen-fixing symbiotic bacterium *Bradyrhizobium japonicum* has a glyphosate sensitive EPSPS enzyme. The sensitivity of *B. japonicum* depends on the herbicide concentration and on the bacterial strain, with some strains being very sensitive to glyphosate (Jaworski, 1972; Moorman et al., 1992). Glyphosate applied to soybeans concentrates in metabolic sinks such as root nodules before being released to the rhizosphere (Coupland & Caseley, 1979), where it could potentially impair sensitive *B. japonicum* and thus nitrogen fixation (King et al., 2001). On the other hand, *Agrobacterium tumefaciens* for example has a naturally glyphosate-resistant EPSPS and has been used to produce RR crops for that reason. Furthermore, Schulz et al. (1985) have shown that different pseudomonad species are insensitive to inhibition by glyphosate due to a glyphosate resistant EPSPS. Indeed, some bacteria have been shown to be able to metabolise glyphosate and use it as a sole source of phosphorus. Liu et al. (1991) showed that several strains of *Rhizobium* and *Agrobacterium* species possess the ability to degrade glyphosate. Cleaving of the carbon-phosphorus bond and subsequent conversion of the breakdown product sarcosine to glycine was suggested as pathway for the breakdown of glyphosate. This pathway was already detected in the late 1980s by Shinabarger and Braymer (1986) and Kishore and Jacob (1997), who studied the degradation of glyphosate by *Pseudomonas* sp. In 1995, Dick and Quinn found that 16% of bacterial strains isolated from both glyphosate treated and untreated soils were able to metabolise glyphosate by an initial cleavage of its carbon-phosphorus bond. Isolates able to use glyphosate as sole source of phosphorus were more common in soils treated with glyphosate. The isolates included *Pseudomonas* and *Arthrobacter* species.

Not all *Pseudomonas* bacteria seem to be insensitive to glyphosate. Kremer et al. (2005) found that growth of pseudomonas bacterial strains generally decreased in root exudates of glyphosate treated plants. Moreover, as mentioned above, growth of the ubiquitous environmental bacterium *Pseudomonas fluorescens* (fluorescent pseudomonas) is inhibited by glyphosate. Fluorescent pseudomonas have a glyphosate-sensitive EPSPS (Schulz et al. 1985). A negative impact of glyphosate on fluorescent pseudomonads was confirmed by Kremer and Means (2009). They further found the RR cultivar itself to significantly decrease populations of fluorescent pseudomonas with populations always higher in non-RR soybean rhizospheres compared to RR soybean rhizospheres. In a greenhouse study with RR soybeans, Zobiole (2011) also found that glyphosate application decreased the bacterium fluorescent pseudomonas. The suppressive effect on fluorescent pseudomonads was greater if glyphosate was applied at the early growth stage and became more significant with increased glyphosate rates. Aristilde et al. (2017) investigate the growth and metabolic responses of soil *Pseudomonas* species with glyphosate at different concentrations, reporting disrupted metabolism.

Mendonca et al. (2019) study the effects of polyethoxylated tallow amine (POEA), a common surfactant used in glyphosate-based herbicide formulations, in three strains of plant-beneficial soil *Pseudomonas* species. They find that the addition of POEA resulted in up to 60% reduction in the biomass growth rate. In the presence of both POEA and glyphosate, the biomass growth rate either remained the same as during exposure to only POEA or decreased by only an additional 5–15%. Therefore, these authors conclude that that growth inhibition in these species was primarily caused by POEA (see also Section 4.3.6. Impact of adjuvants on aquatic non-target organisms).

Yang et al. (2020) report that a glyphosate-tolerant (G2-EPSPS and GAT) GM soybean may induce different changes in functional bacterial species in soil, such as *E. fredii* and *B. elkanii*, compared to the non-GM variety. Chávez-Ortiz et al. (2022) provide evidence that glyphosate-based herbicides alter soil carbon and phosphorus dynamics and microbial activity, in experiments in two soil management conditions: a plot with an history of 5 years of glyphosate application, and an abandoned plot with a history of previous agricultural management without glyphosate applications. They find changes in some processes related to soil carbon and phosphorus dynamics when pure glyphosate and a commercial glyphosate formulation were applied, along with changes in microbial activity and community structure. These researchers find herbicide formulations are more harmful to bacteria than glyphosate itself. By sequencing rhizosphere bacteria in soil samples collected from a field study, Lu et al. (2018) find the glyphosate-tolerant soybean N698 negatively affects *Rahnella*, *Janthinobacterium*, *Stenotrophomonas*, *Sphingomonas* and *Luteibacter* while positively affecting *Arthrobacter*, *Bradyrhizobium*, *Ramlibacter* and *Nitrospira*.

Fluorescent pseudomonads are important multifunctional bacteria, ubiquitous bacteria in agricultural rhizospheres. They produce a range of secondary metabolites, including siderophores and various antibiotics that suppress competing microbial groups. The majority of fluorescent pseudomonads are considered plant growth-promoting rhizobacteria as they are able to antagonise root colonisation of fungal pathogens as well as deleterious rhizobacteria by aggressively colonialising the root surface. Thereby, they contribute to plant health and increased plant yield (Schroth and Hancock, 1982). Their potential as biocontrol agents has been extensively studied (Bagnasco et al., 1998 and Weller, 2007).

In studies on on the soil filamentous fungus *Aspergillus nidulans*, Nicholas et al. (2016) find that RoundUp is much more active than glyphosate alone. For the same species, Poirier et al. (2017) report evidence of possible metabolic disturbance in response to treatment with RoundUp at a dose that does not cause any visible effect. These results indicate that glyphosate-based herbicides have toxic effects on soil filamentous fungi, and thus potential impairment of soil ecosystems, at doses far below recommended agricultural application rate. Mesnage et al. (2020) find a total of 1816 distinct genes have their expression altered when a very low a dose corresponding to the no-observed-adverse-effect level (NOAEL) of Roundup GT Plus is applied to *Aspergillus nidulans*. Liu et al. (2018) also find that soil fungi are impaired by glyphosate. They collect loam soil at a depth of 0–20 cm from an agriculturally used site in China that has not received any agrichemicals and apply glyphosate at the recommended rate of 50 mg active ingredient kg^{-1} soil and 10-fold this rate, to simulate multiple glyphosate applications during a growing season. They investigate the effects on the composition of soil microbial community after six months. They find that, under the higher glyphosate application rate, microbial biomass carbon was reduced by 45%, and the numbers of the cultivable bacteria and fungi were decreased by 84 and 63%, respectively. The fungal biomass was reduced by 29% under both application rates. The bacterial community in the soil that had received the high glyphosate application rate was dominated by gram-negative (G-) bacteria (decreasing bacterial diversity and inhibiting G+ bacteria), which increased their catabolic activity in response to environmental stress. The authors conclude that the soil fungal community was impaired by the recommended glyphosate application rate and the high glyphosate application rate also had significant effects on the structure and functional and genetic diversity of the soil microbial community. Vázquez et al. (2021) explore changes in the diversity and structure of soil fungal communities in semiarid grasslands, after different doses of glyphosate were applied under field conditions, and demonstrate an overall negative effect of glyphosate on soil fungal communities.

4.5.2. Impact on pathogenic fungi

The extensive use of glyphosate in agriculture is a significant factor in the re-emergence of diseases once considered efficiently managed. Many soil-born pathogens such as root rot, crown rot, sudden death syndrome in soybeans or take-all disease of cereals amongst others are increased upon glyphosate treatment of weeds and non-GM crops (see Johal and Huber, 2009 and Kremer and Means, 2009 for an overview). Many studies report that pathogens of the genera *Fusarium* and *Pythium* increase due to glyphosate treatment and dominate the fungal community. Glyphosate applied to the winter annual weeds henbit and downy brome, significantly increased rhizosphere population of *Fusarium solani* f. sp. *pisi* and *Pythium ultimum*. Thus, control of those weeds before crop planting may expose subsequently planted crops to higher populations of these pathogens (Kawate et al., 1997). Meriles et al. (2006) find that glyphosate concentration and previous crop residue influence soil born fungi populations. A significant positive correlation between *Fusarium* and *Pythium* populations, respectively and glyphosate concentration was found. *Phytium* species showed a higher and more uniform response. A 180-day exposure to glyphosate led to quantitative and qualitative changes in the fungal community, with *Fusarium ssp*. being the dominating group isolated (Krzysko-Lupicka and Sudol, 2008). Martinez et al. (2018) review the evidence and conclude that glyphosate-based herbicides have the potential to enhance the population and/or virulence of some phytopathogenic microbial species in the crop rhizosphere. Using a a long-term glyphosate greenhouse experiment, Lee (2018) finds that long-term glyphosate application can upset the delicate balance between beneficial and non-beneficial microorganisms in the glyphosate resistant soybean rhizosphere. Carranza et al. (2019) also report that glyphosate has a significant effect on *Fusarium graminearum, F. verticillioides and F. oxysporum* growth parameters, and that the disease severity of *Fusarium* species to maize seedlings significantly increases with increasing glyphosate concentrations. However, in two-year field studies conducted by the US Department of Agriculture (USA), Kepler et al. (2020) report no effect of glyphosate treatment on the relative abundance of organisms such as *Fusarium* species. These authors conclude that tillage and other farming system differences appear to be the main drivers of soil microbiome structure.

On the other hand, *Fusarium* and *Pythium* have also been found to increase the herbicidal activity of glyphosate. Johal & Rahe (1984) found that glyphosate is less effective against bean plants in sterilised soil and vermiculite compared to unsterilised soil. Dead plants were found to be colonised by various fungi, whereas healthy plants never yielded pathogenic fungi. The types of fungi isolated from dead plants varied with the medium in which plants were grown. Plants grown in unsterilized soil, mostly yielded soil-associated root pathogenic fungi such as *Phytium* and *Fusarium*, whereas those grown in sterilised soil or vermiculite yielded predominantly air-borne seed-disseminated saprophytes and facultative parasites. When sterilised soil or vermiculite were infested with *Phytium* and *Fusarium,* most plants died after glyphosate treatment. In contrast, none of the control plants, glyphosate-treated plants in sterilised soil without fungi added, or untreated plants in soil infested with fungi, died. When the fungicide Metalaxyl was added to the sterilised soil and vermiculite reinfested with *Phytium*, the plants were effectively protected from the herbicidal action of glyphosate. Metalaxyl could however not block the herbicidal action of glyphosate in the unsterilised soil.

The increased disease severity caused by soil-borne pathogens after glyphosate treatment is not solely found in susceptible crops. Sanogo et al. showed, that RR soybeans respond to infection by *Fusarium virguliforme* (formerly *Fusarium solani* f. sp. *Glycines*) after glyphosate application in a similar way to conventional cultivars. In growth chamber and greenhouse experiments (Sanogo et al., 2000) as well as under field conditions (Sanogo et al. 2001), there was a significant increase in severity of sudden death syndrome caused by *Fusarium virguliforme* in soybeans treated with glyphosate compared with non-treated plants. Frequency of isolation of *Fusarium virguliforme* from roots of conventional as well as RR soybeans was increased after application of glyphosate compared with the control treatment where no herbicide was applied. Inoculation of soybean plants with *Fusarium virguliforme* decreased shoot dry-weight index compared to noninoculated plants. This decrease was further deepened when inoculated plants were sprayed with glyphosate. Similarly, in a greenhouse study with RR soybeans, Zobiole (2011) found that glyphosate application increased root colonisation by *Fusarium* species. *Fusarium* colonisation of roots increased steadily as soybean growth progressed and as glyphosate rate increased. In a research summary from a 10-year RR crop production and rhizosphere microbial ecology project conducting field trials with soybean and maize cultivars, Kremer and Means (2009) report that glyphosate significantly increases *Fusarium* colonisation of both RR soybean and maize roots. In maize, *Fusarium* root colonisation was higher after glyphosate treatment, compared to a non-glyphsoate herbicide. *Fusarium* colonisation of soybean roots was higher on RR soybeans treated with glyphosate compared to RR soybeans receiving a non-glyphosate herbicide or no herbicide. Conventional soybean cultivars always showed lowest root colonisation. This suggests that RR soybeans might even be more susceptible to root infection by pathogenic fungi than conventional crops. This however contrasts with the findings of Sanogo et al., where the response of RR and conventional soybean cultivars to infection by *Fusarium virguliforme* after glyphosate application was similar.

Increased disease severity upon glyphosate application is also found in RR sugar beet. In a greenhouse study with RR sugar beet inoculated with certain isolates of *Rhizoctonia solania* and *Fusarium oxysporum*, Larson et al. (2006) observed increased disease following glyphosate treatment. They suggest, that the timing of glyphosate application may affect disease severity and that in the presence of certain soil-borne diseases, treatment with glyphosate-based herbicides should be conducted with precaution. They further suggest, that the increase in disease is not fungal mediated but may be a cultivar- or isolate- specific response to glyphosate treatment.

4.5.3. Possible mechanisms of increased disease severity upon glyphosate treatment

Many different mechanisms through which glyphosate might increase disease severity in plants have been suggested in the literature and are discussed in the following sections.

4.5.3.1. Stimulation of fungal growth by altered root exudates

Early research showed, that upon application and foliar absorption, glyphosate is transported (translocated) systemically towards metabolic sinks including plant roots, where appreciable amounts of unmetabolised glyphosate are eventually released into the rhizosphere (Coupland & Caseley, 1979). The leaking of glyphosate (exudation) through RR soybean roots was also demonstrated by Kremer et al. (2005). They further showed that glyphosate application results in increased soluble carbohydrate and amino acid root exudation, compared with plants that received no glyphosate. The RR cultivar receiving no glyphosate appeared to inherently release higher amounts of carbohydrate and amino acids compared with the conventional soybean cultivar that received no glyphosate treatment. This led the authors to suggest that not only glyphosate application but also the genetic modification for glyphosate resistance affected carbohydrate and amino acid translocation and release through roots.

Such described changes in the leaking of root fluids (exudates) can affect soil microorganisms. These effects can either be positive, for example if the microorganisms can use the exudates as nutrient source, or negative, if the exudates are toxic to the microorganisms.

Different studies suggest that some soil-borne pathogens can metabolise glyphosate. Krzysko-Lupicka & Orlik (1997) found that glyphosate decreased the total number of fungal species as well as the strain composition if used either as the sole source of phosphorus or as the sole source of carbon. Some soil-born fungi were however capable of growing on glyphosate as the sole source of phosphorus or carbon with *Mucor*, *Trichoderma* and *Fusarium* even being predominantly found in media containing glyphosate compared to the control medium, although not all the results of this study are consistent. *Fusarium* ssp. could also grow on glyphosate as the sole source of phosphorus in the study of Krzysko-Lupicka and Sudol (2008).

Concerning carbohydrate and amino acid exudates, Griffiths et al (1998) found that microbial community structure changed consistently upon continuous release of a synthetic root exudate, comprising soluble carbohydrates and amino acids, into simulated rhizospheres. With increasing substrate loading, fungi dominated over bacteria, showing that not only composition of exudates but also quantity of available substrates influence microbial community.

By means of *in vitro* bioassays, Kremer et al. (2005) monitored growth response of different fungal (*Fusarium* spp.) and bacterial (*Pseudomonas* spp) strains in soybean root exudates containing both glyphosate and high levels of soluble carbohydrates and/or amino acids. Consistent with Krzysko-Lupicka & Orlik (1997) and Griffiths et al (1998) they found that bacterial growth generally decreased in root exudates of glyphosate-treated plants, whereas different *Fusarium* strains developed significantly higher biomass in root exudates. The authors suggest that glyphosate application stimulated fungal growth by serving as a nutrient source and by the associated high levels of soluble carbohydrates and amino acids.

Glyphosate-induced susceptibility to soil-borne pathogens due to increased nutrient leakage from treated plants was already suggested by Johal and Rahe in 1984.

4.5.3.2. Increase in host susceptibility to soil-borne pathogens

Some studies suggest that an increased susceptibility of host plants to soil-borne pathogens may cause higher disease severity upon glyphosate treatment. In 1984, Johal and Rahe already suggested that this glyphosate-induced susceptibility to soil-borne pathogens might be attributed to suppression of defence meachnisms.

i) Decreased key plant defence compounds to fight fungi

To prevent the growth and spread of a plant pathogen, plants use a mechanism called hypersensitive response that causes rapid cell death in the region surrounding the infection. Johal and Rahe (1988) suggest that whereas the hypersensitive response may be responsible for initial inhibition or at least delay of fungal development, it is however inadequate to contain the pathogen itself. They further indicate that phytoalexins, antifungal host metabolites that accumulate in and around hypersensitive host cells, are needed to contain the pathogen in the dead cell. In an experiment with beans inoculated with the fungus *Colletotrichum lindemuthianum,* Johal and Rahe found that glyphosate interferes with the expression of defence against *C. lindemuthianum* in beans by suppressing their ability to produce phytoalexins.

Inhibition of EPSP synthase and subsequent starvation of treated plants of aromatic amino acids was considered to be the sole mode of action of glyphosate. But the shikimate pathway also gives rise to different plant defence compounds such as phytoalexins, salicyclic acid, pathogenesis-related proteins and lignin-based defence mechanisms (Johal and Rahe 1984, Larson, 2006, Kremer et al. 2005, Johal and Huber, 2009; Johal and Rahe, 1988; Liu et al. 1997). The infection by soil-borne pathogens caused by the inability of pants to synthesise those defence components might thus be a "secondary mode of action" of glyphosate (Kremer and Means, 2009; Johal and Rahe, 1984; Yamada 2009).

But why does this affect RR crops that are genetically modified to have a glyphosate insensitive EPSP synthase? Johal and Huber (2009) argue that RR crops would only be unaffected if the transgene is completely insensitive to glyphosate and operates in exactly the same way upon glyphosate treatment that the native EPSPS does in the absence of glyphosate, both under normal and stressful conditions and independent of the level of glyphosate applied. They consider this unlikely and believe that RR crops are vulnerable to fungal diseases following glyphosate treatment under at least some conditions. Gressel (2002) suggest that the transgenic EPSPS in RR soybeans is considerably less efficient than the wild-type enzyme and might produce insufficient amounts of phytoalexins. According to Larson (2006), a slight inhibition of EPSPS would already be substantial enough to inhibit plant defences but in turn not affect plant growth.

ii) Decreased nutritional status of the plant to defend itself

Micronutrients can activate or inhibit many critical physiological functions and are essential for many metabolic pathways. A change or reduction in availability of micronutrients can greatly affect plant growth and resistance to diseases and pests (Johal & Huber, 2009).

Many diseases such as take-all disease, rice blast, potato scab, or corn stalk rot are inversely related to manganese (Mn) availability and may be the result of reduced resistance from induced Mn deficiency. Since Mn is needed for the plant's resistance mechanisms, some pathogens produce Mn oxidising enzymes at the infection site to compromise the plant's resistance mechanism. But environmental conditions that reduce the availability of Mn for plant uptake also predispose plants to disease. Glyphosate released to the rhizosphere has been shown to reduce Mn-reducing organisms and increase Mn-oxidising organisms and thus limit Mn availability for plant uptake and active defence reactions (Johal and Huber, 2009). Moreover, glyphosate has also been shown to chelate essential micronutrients such as manganese or iron rendering them immobile and unavailable for plant uptake and translocation. Thus, increased crop diseases following glyphosate application may be the result of reduced resistance from induced micronutrient deficiency. However, this view is not universally accepted and other researchers argue that chelating metal cations do not significantly affect plant mineral nutrition (Duke, 2018). In field studies conducted in 2013 and 2014 in two US states, Reddy et al. (2018b) find that neither glyphosate nor the glyphosate-resistant transgene affected yield or mineral content of leaves or seed, except for occasional (<5%) significant effects that were inconsistent across minerals, treatments, and environments. A review by Mertens et al. (2018) concludes that further research should be undertaken to elucidate the role of glyphosate as a chelating agent.

4.5.3.3. Decrease of pathogen antagonists

Kremer et al. (2005) argue that decreasing the growth of soil bacteria that compete for soybean root exudates may further favour fungal growth. Indeed, Kremer and Means (2009) found a negative relationship between population size of fluorescent *pseudomonad*s and *Fusarium* root colonization, with about 85% of fluorescent pseudomonas cultures being antagonistic toward *Fusarium*. They suggest that glyphosate and RR soybean may enhance *Fusarium* root colonization through not only stimulating growth on the fungal pathogen but also by suppressing bacterial antagonists such as *pseudonomads*.

4.6. Can RR crops help to mitigate climate change?

Approximately one-third of global greenhouse gas (GHG) emissions come from agriculture and the trend is rising. These emissions result from the production of fertilisers and pesticides, livestock, fuel use from agricultural machinery and equipment, soil degradation and land-use change amongst others (Liu et al., 2015). Thus, there is a huge potential to reduce GHG emissions and thereby mitigate climate change in agriculture.

Tillage is the preparation of land for growing crops by disturbing the soil, using methods such as digging and ploughing. ‘Conventional tillage’ usually involves ploughing (using tractors) to kill weeds, and to aerate the soil, followed by secondary tillage to control weeds, produce finer soil, and/or incorporate fertiliser. There are many different types of tillage which can vary in intensity. ‘Conservation tillage’ reduces the amount of tillage, with the aim of reducing soil erosion and water loss and keeping more beneficial arthropods in the soil. ‘No-till’ means that the ground is not ploughed at all. No-till can be used in organic farming using agro-ecological farming methods, such as crop rotation and mulching. However, a major expansion in no-till farming occurred in North and South America with the introduction of GM Round Up Ready (RR) crops. This is because weeds could be killed by blanket spraying the crop with glyphosate-based herbicides (such as RoundUp), instead of using ploughing.

GM crops have been reported to reduce the level of greenhouse gas (GHG) emissions. According to PG Economics, GM crops saved about 28 billion kg of carbon dioxide from being emitted to the atmosphere in 2013 (Brookes & Barfoot, 2015). They attribute the carbon dioxide saving mainly to two factors: reduced pesticide use (involving fewer spray runs) and the switch to no-till (NT) or reduced-till (RT) cropping systems. With less pesticide applied by mechanical means, they say less fuel is used and thus less carbon dioxide is emitted. Additionally, they argue that less tractor fuel was used in NT or RT cropping systems. Such conservation tillage systems would also mitigate climate change by sequestration of carbon in soil, thereby preventing carbon dioxide emission to the atmosphere. Moreover, additional carbon dioxide could be assimilated from the atmosphere, because of higher crop production. These authors, funded by Bayer Crop Science, claim 2.456 billion kg of carbon dioxide was saved through reduced fuel use on GM crops in 2018 (of which 2.95 billion kg is from HT crops, whilst the remainder is from insect-resistant Bt crops) and 5.606 billion of extra carbon was sequestered in the soil (all from GM HT crops), compared to conventional (non-GM) crops (Brookes & Barfoot, 2020).

However, we already showed that for RR crops, the overall amount of glyphosate sprayed and the number of applications per year quickly began to rise after a first reduction (See Section 3.1.1 Herbicide use) and that one of the main reasons is the emergence of glyphosate resistant (GR) weeds (see Section 3.1.2. Superweeds). Contrary to the arguments made by PG Economics, this led to higher inputs of herbicides (Benbrook, 2012a; 2016; Schultz et al., 2021), thereby using more fuel for applying it (see also Section 6. Industry response). The argument that RR crops reduce greenhouse gas emissions by reducing herbicide use is thus flawed. But what about the switch to no-till (NT) or reduced-tillage (RT)?

There are two problems with the claim that GM herbicide-tolerant crops reduce carbon emissions by encouraging adoption of no-till farming. Firstly, there is evidence that, whilst the use of no-till increased in the United States from 1998 to 2016, it has subsequently shrunk again – this is likely at least partly due to the increasing presence of glyphosate-resistant weeds (as described in Section 3.1.2. Superweeds). Secondly, the benefits of no-till farming in terms of reducing carbon loss have been exaggerated, as discussed below.

Yu et al. (2020) examine how tillage intensity has changed across the USA. They find an increase of no-till land in corn-soybean rotation by 71.6% from 1998 to its peak year in 2008, as the percentage of herbicide-tolerant GM corn and soybean rose to over 90%. However, they also find the trend toward lower tillage intensity has subsequently reversed, although herbicide-tolerant GM corn and soybeans still dominate the market. Although there are many uncertainties in how soil carbon loss is calculated (discussed further below), these authors calculate that the total soil carbon change from 1998 to 2008 was 10.0 Tg of carbon accumulation, but from 2008 to 2016 was 19.2 Tg of carbon loss. These authors speculate that one possible reason for rising tillage intensity after 2008 is due to increasing resistance of weeds to herbicides, which may have compelled farmers to return to ploughing. In a further modelling study of US corn–soybean cropping systems, Lu et al. (2022) conclude that, "*The GHG* [Greenhouse Gas] *mitigation benefit (−5.5 ± 4.8 TgCO2e yr^{-1}) of decreasing tillage intensity before 2008 has been more than offset by increased GHG emissions (13.8 ± 5.6 TgCO2e yr^{-1}) due to tillage reintensification under growing pressure of weed resistance*". Thus, any benefits of no-till agriculture on carbon loss have now been reversed.

As noted above, there are also significant uncertainties regarding how much carbon loss is actually reduced by using no-till systems. Several publications have referred to the potential of no-till (NT) or reduced till (RT) farming systems to increase soil organic matter and sequester carbon (see for example Corsi et al., 2012; UNEP, 2013). But according to Powlson et al. (2014), the potential for climate change mitigation has been widely overestimated. They state that there is a strongly developed concentration gradient with depth under no-till. The apparent increase in soil organic carbon is not a net increase in soil organic carbon stock but results from redistribution of carbon nearer to the soil surface, with increased soil organic carbon in the 15-20 cm layer top-soil. When comparing soil samples from at least 40 cm depth, no overall increase in soil carbon levels under no-till have been found. In a 41 year experiment in France, no-till led to no increase in soil organic carbon (Powlson et al., 2014). In addition, the soil can only take up a limited amount of carbon and thus, annual rates of accumulation decline as the carbon content saturates. Baker et al. (2007) argue that sampling protocol may have biased the results of studies that found that soil disturbance by tillage was a primary cause of the historical loss of soil organic carbon. They find that, in the few studies where sampling extended deeper than 30 cm, conservation tillage has shown no consistent accrual of soil organic carbon, instead showing a difference in the distribution, with higher concentrations near the surface in conservation tillage and higher concentrations in deeper layers under conventional tillage. They conclude that evidence that conservation tillage promotes carbon sequestration is not compelling. Added to this, the emergence of GR weeds forces famers now to once again go back to mechanical weed management practices such as tillage, reversing any potential advantages from conservation tillage, as noted above. In a modelling study, which also reviews and takes account of some of the criticism of earlier claims about carbon sequestration, Graham et al. (2021) conclude that their "*results indicate that the global potential for SOC* [Soil Organic Carbon] *sequestration from NT* [No-Till] *adoption may be more limited than reported in some studies and promoted by policymaker*s".

Moreover, RR crops do not decrease other GHG emissions associated with agriculture, such as the production of fertiliser or pesticides, but rather increase them. In just one example, replacing chemical fertiliser with organic manure significantly decreased greenhouse gas emissions in an experiment in eastern rural China and has according to Liu et al. (2015) the potential to reverse the agricultural ecosystem from a carbon source to a carbon sink.

Furthermore, what RR crops are produced and used for is also an important consideration, which is mainly for animal feed and biofuels (see Section 5.1. Food production, land use and sustainability). In the U.S. 40% of corn harvest, of which the majority is RR corn, was processed to ethanol in 2014 (Ranum et al., 2014). In 2014, production and use of corn ethanol resulted in 27 billion kg more carbon emissions than if conventional gasoline were used according to calculations by the Environmental Working Group (Cassidy, 2015a). This is because converting rainforests, peatlands, savannas, or grasslands to produce food crop–based biofuels in Brazil, Southeast Asia, and the United States releases 17 to 420 times more carbon dioxide than the annual greenhouse gas (GHG) reductions that these biofuels would provide by displacing fossil fuels (Fargione et al., 2008).

To summarize, RR crops do not have the potential to mitigate climate change. In the short term, farmers newly planting RR crops may indeed be able to switch to conservation tillage. But on the one hand it is not even clear to what extent no-till or reduced tillage can increase net soil organic carbon, and on the other hand, glyphosate resistant weeds will evolve sooner or later, forcing farmers to go back to ploughing and weeding, to apply even more herbicides and correspondingly use more fuel. Other methods, like ending the use of corn for biofuels and reducing intensive meat production, seem more promising in saving greenhouse gas emissions in agriculture.

4.7. Antibiotic resistance

In 2014, the World Health Organisation (WHO) warned that resistance to antibiotics has reached alarming levels in many parts of the world, threatening modern medicine and becoming a growing public health risk. With antibiotics becoming less effective, treatments of patients become more difficult, costly or even impossible. Common infections and minor injuries could become deadly once again. In 2009, it was estimated that in Europe approximately 25,000 people die each year from antibiotic resistance (ECDC/EMEA, 2009). But while common antibiotics become less useful, the development of new antibiotics is lagging behind, with no major new classes of antibiotics having been discovered since 1984 (WEF, 2013). The World Health Organisation (WHO) names major gaps in surveillance on antibiotic resistance and has called for urgent action (WHO, 2014). Increasingly, governments around the world are starting to pay attention to this problem. The WHO continues to argue that antibiotic resistance is one of the biggest threats to global health, food security, and development today (WHO, 2020).

Bacteria resistant to a particular antibiotic have an evolutionary advantage and can thus increase quickly. The more a particular antibiotic is used, the more this process is accelerated. A major role in antibiotic resistance development is the overuse of antibiotics in the meat industry. In the U.S. 80% of the antibiotics sold, are used in meat and dairy production as growth promoters and to treat diseases. Increasing demand for meat around the world is expected to raise antimicrobial consumption in livestock by two thirds from 2010 to 2030 (Boeckel et al., 2015).

Some GM plants used in agriculture include antibiotic resistance genes. Some (but not all) transgenic crops, including RR crops, contain antibiotic resistance marker genes (ISAAA, 2014a; 2014b) that have been transferred to the plant cells together with the gene of interest by means of a plasmid vector. These marker genes help scientists determine if a plant cell has been successfully genetically modified and whether it contains the gene of interest. This is necessary because the GM technique is inefficient, with only 1-2% of cells being successfully transformed. To identify these cells and efficiently use them to grow into plants they can be cultured in a medium containing an antibiotic, for example ampicillin. Transformed cells containing the marker gene will survive in the medium, while other, non-transformed cells will die.

The concern has been raised whether these antibiotic resistance genes could be transferred from GM plants to soil- and plant-related bacteria or to bacteria in the gastrointestinal tracts of humans and animals and lead to an increased level of antibiotic resistance in micro-organisms. In Europe, this concern is reflected in the EU directive on the deliberate release into the environment of genetically modified organisms (2001/18/EC), that demands that antibiotic resistance marker genes are monitored and used with caution: *"Member States and the Commission shall ensure that GMOs which contain genes expressing resistance to antibiotics in use for medical or veterinary treatment are taken into particular consideration when carrying out an environmental risk assessment, with a view to identifying and phasing out antibiotic resistance markers in GMOs which may have adverse effects on human health and the environment."* The EFSA GMO panel further suggests that some antibiotic resistance marker genes ought not to be used at all and others used only on a limited basis.

Chen et al. (2012) found the ampicillin resistance gene, β-lactam antibiotic (blá), originating from synthetic plasmid vectors, in microbes from six Chinese rivers with significant human interaction.

Although the source is unclear, the blá gene is used in some herbicide resistant crops. Although the source of the contamination is not clear, the authors suggest that *"Contamination of environmental microbes with synthetic plasmid vector-sourced antibiotic resistance genes may represent a yet unrecognized source of antibiotic resistance"*.

Another concern is that herbicides could be a possible driver of antibiotic resistance in different microorganisms. Glyphosate for example is not only an herbicide but also an antibiotic. For that reason, Monsanto patented the antibicrobial activity of glyphosate against a wide range of bacteria, parasites and fungi containing the EPSPS enzyme. Some bacteria and fungi are however highly resistant to glyphosate. As described above, the resistance gene in strain CP4 of *Agrobacterium tumefaciens* was used to create glyphosate tolerant crops in the first place. Van Bruggen et al. (2018) point out that the intensification of glyphosate use is correlated to the emergence of many genera of glyphosate resistant bacteria and fungi – and, more alarmingly, that some of the resistance mechanisms found in glyphosate resistant bacteria are the same that confer resistance to clinically important antibiotics. They note that antibiotic resistance is widespread in agricultural soils that were not exposed to high antibiotic concentrations. Their earlier studies found a high percentrage of bacteria isolated from citrus groves, roots and rhizospheres to be resistant to penicillin, although penicillin is not used in citrus orchards. These bacteria however showed significant cross-resistance to Roundup which is applied frequently in citrus groves.

Van Bruggen et al. (2018) develop a hypothesis that "*the selection pressure for glyphosate-resistance and the associated resistance to antibiotics in the soil microbiome result in transfer of antibiotic resistant bacteria from soil to plants, animals and humans through the food web, even in urban and hospital environments*", and warn that this could lead to increases in antibiotic resistance to clinically important antimicrobial agents. Similarly, Raoult et al. (2021) suggest that glyphosate *"…substantially modifies the microbial ecosystem, and that this modification may lead to changes in the susceptibility of the resident bacteria and selection of resistant bacteria in the environment that may further spread into clinical strains"* They recommend evaluating the role of glyphosate in the observed increase in antibiotic resistant bacteria, particularly in countries that use few antibiotics in humans but use glyphosate massively in agriculture. More specific evidence for these concerns comes from Kurenbach et al. (2015), who report that exposures of the bacteria *Escherichia coli* and *Salmonella enterica* serovar *Typhimurium* (bacteria associated with food poisoning) to sublethal concentrations of commercial formulations of dicamba, 2,4-D, and glyphosate - all herbicides used in genetically engineered HT crops - were found to induce a changed response to clinically relevant antibiotics. Exposure to sub-lethal levels of Roundup, for example, significantly increased the concentration of two antibiotics (kanamycin and ciprofloxacin) necessary to kill the gut bacteria *Escherichia coli* and *Salmonella enterica*. Exposure to sublethal levels of 2,4-D and Kamba (dicamba) increased the tolerance of *S. enterica* and *E. coli* to 4 and 3 antibiotics, respectively. Kurenbach et al. (2017) further demonstrate that the active ingredients alone can change the reponse of antibiotics to *S. enterica.* For the majority of combinations, herbicide exposure increased minimum inhibitory antibiotic concentration. The most pronounced effect was that glyphosate increased the kanamycin concentration needed fivefold and dicamba exposure increased the chloramphenicol concentration sevelfold. Kurenbach et al. (2017) also find common co-formulants of these commercial formulations to have an effect on antibiotic response, even at concentrations permitted in food, but these effects were generally weaker than the ones observed for the active ingredients. One possible explanation for this phenomenon is that if bacteria are exposed to concentrations of a toxin, such as Roundup, that doesn't kill them, they activate so-called efflux pumps that move the toxin out of the cell. This increased efflux, possibly combined with a decreased permeability into the cell, could be responsible for the decreased susceptibility to these antibiotics. In pesticides and active ingredients, these effects were observed at levels higher than the residues allowed in food but below what is often used in rural settings. Pesticide-induced antibiotic resistance could thus affect people in rural areas or honeybee hives treated with antibiotics, amongst other possibilities. Antibiotics and herbicides are also detected in waterways that could potentially maintain resistant bacteria. The effect could be increased if different chemicals are combined (Kurenbach et al., 2015; Grossman, 2015a). Van Bruggen et al. (2018)

highlight that the intensification of the use of dicamba and 2,4-D will likely increase tolerance to these herbicides in microbial communities, which could further impact antibiotic resistance in bacteria. In a soil microcosm herbicide exposure experiment, Liao et al. (2021) further show that application of glyphosate, glufosinate, and dicamba, increases the prevalence of antibiotic resistance genes as well as mobile genetic elements, that facilitate horizontal gene transfer in bacteria, in soil microbiomes. They subsequently collected soil samples across China to compare soil microbiomes from fields that have continuously been exposed to glyphosate for at least 10 years with those that had not been exposed to herbicides at all. They confirmed the association of herbicide application with higher abundance of antibiotic resistance genes and mobile genetic elements. Liao et al. conclude: "*The role of herbicides in global antibiotic resistance problem should thus be re-evaluated, to better understand associated risks for the prevalence of ARGs [antibiotic resistance genes] in agricultural environments where soil microbiota is repeatedly exposed to herbicides during weed control*."

Da Costa et al. (2022) report evidence that a glyphosate-based herbicide cross-selects for antibiotic resistance genes in bacterioplankton communities in water from a lake. Daisley et al. (2022) review evidence regarding the unintended effects of pesticides (including glyphosate) on microbial life. Amongst other conclusions, these authors state, "*Antimicrobial resistance is a current global threat to health, and it is imperative that the role of agrochemical use in the development of antimicrobial resistance is fully studied and appreciated*". They also highlight that regulatory oversight of agrochemical usage is inadequate and fails to address potential effects on ecosystem microbiomes which are in turn critical to environmental health.

These studies suggest that herbicide tolerant crops may either directly increase antibiotic resistance in microbes by horizontal gene transfer of antibiotic resistance marker genes, or indirectly via the corresponding herbicides that are increasingly applied to HT crop fields.

4.8. Conclusions

Ecosystems are comprised of countless complex interactions where minor interferences can have major unforeseen effects. The widespread adoption of HT crops and the associated increase of environmental exposure to Roundup and other herbicides can impact ecosystems directly with lethal and sub-lethal effects on non-target organisms and also through more complex indirect effects, as in the case of the Monarch butterfly.

5. Does society benefit from RR crops?

5.1. Food production, land use and sustainability

The industry often states that GM crops are essential to feed an ever-increasing population. But this argument is highly flawed. As discussed above, RR crops have failed to bring about the promised increases in crop yields, and conventional breeding methods have proven more efficient to develop higher yielding crops. Moreover, there is no causal link between a rise in production and a global decline in hunger. Global population in 2019 had reached more than 7.7 billion, and is predicted to grow to approximately 10.9 billion by 2100, when population growth is expected to end, mainly due to falling global fertility rates (Cilluffo & Ruiz, 2019). In 2013, enough food was already produced for 12-14 billion people (UNCTAD, 2013) but according to the World Food Agriculture Organization (FAO) almost 795 million people still suffered from hunger in 2015 (FAO, IFAD & WFP (2015). According to the Food and Agriculture Organization of the United Nations (FAO), total production of primary crops increased by 53 percent between 2000 and 2019, hitting a record high of 9.4 billion tonnes in 2019, but undernourishment increased sharply between 2019 and 2020 (during the COVID-19 pandemic) and nearly 10 percent of the world population suffered from hunger in 2020, compared to 8.4 percent in 2019 (ReliefWeb, 2021). The primary reasons for hunger are poverty and lack of access to affordable food (Tscharntke et al., 2012). Conflict, weather extremes and economic shocks were the main drivers behind food insecurity in 2021, with poverty and inequality as underlying causes (EU/FAO/WFP, 2022).

Adding to this is the fact that crop production is not exclusively and efficiently used as food. Worldwide, only 55% of all crop calories were grown for direct human consumption in 2013 (Cassidy et al., 2013). The rest is grown to produce animal feed, biofuels or for other industrial uses. Crops used for animal feed and biofuels are highly productive crops such as soybeans and maize. Global meat production grew by 44 percent between 2000 and 2019 to reach 337 million tonnes (ReliefWeb, 2021). Most soy (around 75% measured by weight in 2018) is fed to animals in livestock production systems, with around 3.8% going to biofuels and other industrial applications, and only 19.2% to direct human consumption as food (mainly as soybean oil) (Fraanje & Garnett, 2020). Similarly, around 74% of the global maize production is used for animal feed (Cassidy et al., 2013). And in the U.S., 40% of the maize harvest was processed to ethanol in 2014 (Ranum et al., 2014). Soybean and maize are the top two GM crops, the majority of which are Roundup Ready (See Section 1. Introduction) and are largely not grown for direct human consumption. While calories used for biofuels are completely lost from the food system, calories used to feed animals, eventually serve to indirectly feed humans. However, 89% of the produced grain calories are lost in the process due to an inefficient feed-to-edible food conversion (Cassidy et al., 2013). Shifting crop calories used for animal feed and biofuels to direct human consumption could, according to Cassidy et al. (2013), potentially feed an additional 4 billion people and in the U.S. alone an additional 1 billion people.

Further, many crop calories are lost during food production, transport and storage as well as in retail facilities, restaurants and at private households etc., so tackling food waste is an important way to improve food supply. According to FAO (2011) about one third of global food production gets lost or is wasted. However, even with enough calories produced and used for direct human consumption, a lot of people lack access to affordable food. It is highly questionable whether growing GM crops for animal feed, increasing corporate control of the food chain, and the resulting changes in land use, bring any benefits to such people (see Sections 3.1.5. Seed prices, patents and corporate control and 3.5. Impact of RR crops on farmers' choice, land rights and indebtedness.).

It is also questionable whether sparing land for nature needs higher intensity of farming to produce adequate food (Tscharntke et al., 2012). Strategies to increase yields without explicitly considering the actual and potential cost of biodiversity losses can compromise ecosystem functionality and resilience in agriculture. Rather, food security and food sovereignty need to increase in areas where the hungry live, based on robust, eco-efficient approaches. Further, in the case of RR crops, yields have not increased compared to non-GM crops (see Section 3.2. Impact of RR crops on yield) and there has been significant expansion of intensive agricultural monocultures into previously diverse ecosystems (see Section 4.2.2 Land use and biodiversity).

According to the Environmental Working Group (Cassidy, 2015b), crop yields have only increased about 20 percent in the past 20 years. Genetically modified (GM) organisms such as RR crops, have not substantially improved global food security during this time and relying on increased yields from GM crops will fall short of meeting future goals. Alternative approaches such as smarter resource use, improving livelihoods of small-scale farmers, reducing food waste and small changes in diets, such as reducing meat consumption or swapping from grain-fed beef to chicken or grass-fed beef, have, according to the Environmental Working Group, the potential to double calorie availability and are more promising to improve food security.

Oliveira and Hecht (2016) discuss key environmental debates surrounding soy agribusiness in South America, challenging especially the common arguments that agroindustrial intensification ‘spares land’ for conservation while increasing production to ‘feed the world’. They demonstrate that these arguments hinge on limited data from a peculiar portion of the southern Amazon fringe and hide other multiple political and ecological problems associated with the sector. Less than 6% of all soy produced in the world is consumed directly as human food, and virtually all of it in South America is crushed to produce livestock feed and edible oil, as well as biodiesel and other industrial products, with much of the animal feed exported to support increased poultry and pig production in Europe and East Asia, particularly China. Partnerships between major seed and agrochemical input manufacturers with major soybean trading companies (e.g. Monsanto with Cargill, Syngenta with Bunge) enable these agribusinesses up- and down-stream from soy farms to effectively control the inputs and farming practices of most soy farmers across South America, and lock in prices and delivery of portions of their harvests through prearranged provision of fertilizer, pesticides, herbicides and seeds. Hundreds of thousands of farm units are operated by a handful of companies that manage millions of hectares across South America. The trend toward farmland and wealth concentration has accelerated with the introduction of GM technologies and aggravated the already unequal distribution of farmland, credit and capital. Expanding monocultures of RR soy have led to human pesticide exposures via aerial spraying (See Section 5.5.7. Acute and chronic health effects associated with drift of glyphosate and other pesticides and use by farmworkers), negative ecosystem impacts including deforestation, and the loss of more than 50% of the Cerrado. In the Mato Grosso region, there is some evidence that soy production has been able to expand whilst the Amazon has been protected. However, in general, the intensification of profitable land uses tends to enhance its spread rather than to confine it spatially and the conversion of other ecosystems (particularly the Cerrado) to soy is far higher than the Amazon.

Soy is mainly exported from the four countries of South America’s Southern Cone: in Brazil around 25 percent of the harvest is for domestic consumption, mainly as vegetable oil, in Paraguay and Uruguay it is only 5 percent, while in Argentina there is an intermediate percentage (15 percent) (Wesz Jr, 2016). China assumes a great importance in the total value of Uruguayan (67 percent), Brazilian (50 percent) and Argentinian (25 percent) exports; in the Paraguayan case, marketing focuses mainly on Europe (which is also the main recipient of Argentinean meal). The world cereal trade is controlled by four major transnational firms: ADM, Bunge, Cargill and Dreyfus (called ABCD due to their initial letters).

A 2015 study compared the sustainability of the Brazilian GM and non-GM soybean meal chains with regard to all three dimensions of sustainability (environmental, economic and social). The soybean meal chain consisted of the agricultural level, processing, transport to port and transoceanic transportation. The profitability of both chains is measured by the difference of the total aggregated outputs and inputs, adjusted for the negative externalities of production. The latter include global warming potential, eutrophication potential, deforestation, toxicity to the environment, farmers and consumers, loss of employment. The study found production of non-GM soybean meal to be more sustainable than the GM chain (Gaitán-Cremaschi et al., 2015). An earlier study by Ortega et al. (2005) compared agricultural systems classified in two main categories in Brazil: biological (organic and ecological) and industrial (agrochemical and no-tillage with herbicides). Biological models included the family managed ecological farms of the south and the organic enterprises in the central region. As industrial models, farms that adopted green-revolution standards (in the south) and agricultural enterprises that adopted no tillage (with or without the use of transgenic seeds) in the south and central region were considered: these were designated as "chemical" and "herbicide" farms in the analysis, respectively, The authors find that biological models show better environmental, economical, and social performance indicators.

Even advocates of GM crops now accept that HT crops are not the future of agriculture. Former UK Life Sciences Minister, George Freeman MP (Minister for Science, Research and Innovation until July 2022) stated: "*The first generation, if you like 'GM1.0', was very crude, particularly the original Monsanto monoculture model: "Spray everything that dies apart from the thing we have protected." I do not think anyone thinks that is a particularly progressive way of doing 21st century agriculture, but what we are now seeing is really elegant 'GM2.0'—the very subtle use of naturally occurring traits. That is incredibly exciting science, and somehow we have to find a way through Parliaments and commissions to explain that to electorates and win their trust in an appropriate regulatory framework*" (House of Commons Science and Technology Committee, 2016). Former senior scientists at DuPont and Corteva Agriscience conclude a recent book chapter, "*Today, glyphosate-based crop systems are still mainstays of weed management, but they cannot keep up with the capacity of weeds to evolve resistance. Growers desperately need new technologies, but no technology with the impact of glyphosate and GR crops is on the horizon. Although the expansion of GR crop traits is possible into new geographic areas and crops such as wheat and sugarcane and could have high value, the Roundup Ready® revolution is over*" (Green & Siehl, 2021).

However, in reality, HT crops dominate the market for commercial GM crops, and are likely to continue to do so, because selling agrichemicals and herbicide-tolerant GM seeds together can be highly profitable.

5.2. Consumers' reluctance to eat GM crops

RR crops are designed to make farming practices easier for farmers but have no advantages for consumers compared to conventional crops. Consumers worldwide are reluctant to eat GMOs. But often it is not a question of choice. In the US for example more than 90% of all corn and soya is genetically modified (USDA NASS, 2014) and retailers don't have to label products containing GMOs. However, manufacturers will be required to label some products containing GMOs (using a 5% ingredient threshold) by 2022 under a new National Bioengineered Food Disclosure Standard (NBFDS) (Berry, 2021). According to a New York Times Poll in 2013, 93% of Americans were in favour of GMO labelling (Kopicki, 2013) and sales of food labelled as "non-GM" were rising steeply (see Section 3.3.2. Effects of the increasing demand for non-GM seeds and foods on RR crop marketing). In 2014, Vermont became the first US state to adopt a law requiring labels for foods containing GM ingredients. The law should have come into effect in July, 2016. The states of Maine and Connecticut also adopted labelling laws, but they would only come into force once other states also enforce similar legislations (ENS, 2014). In 2016, California narrowly rejected mandatory GMO labelling (47% to 53%). The "California Right to Know Genetically Engineered Food Act" was opposed by a coalition of GMO companies including Monsanto, Dupont, BASF, Bayer, Dow, and Syngenta along with U.S. multinational food companies such as Pepsi, Kraft, Nestle, Coca-Cola, Kellogg, Unilever and others. Monsanto alone invested U.S.$8.1 million in the "No" campaign (Paull, 2018). Much weaker federal legislation has since been passed which will pre-empt such state laws and provide less information for consumers. Although controversial, this federal law will require some form of GM labelling for some GM food products, although consumers will have to scan the bar code and check online to see whether genetically modified products were used (Washington Times, 2016). Surveys in Canada also show that, if given a choice, most consumers would choose to buy a non-GM food item (Briere, 2017). There have also been calls for the mandatory labelling of genetically modified (GM) foods in Canada (NDP, 2016).

In Europe, a 2010 poll found that 84% of European citizens have heard about GM food. Of those polled, only 23% thought the development of GM foods should be encouraged. Europeans that had already heard about GM food before were generally more concerned about it than those that have not (Eurobarometer, 2010). In Switzerland, a 2015 poll found 66% of citizens are against GMO cultivation and only 21 percent are in favour (Univox; 2015). The majority of European consumers support continued compulsory labelling on all genetically modified food, and also want products from animals fed with GM crops to be labelled (which is not currently the case) (Foote, 2021). Although GM HT crops are not grown in Europe, GM maize and soya is imported for use in animal feed: however, import approvals are controversial and take place without approval from a 'qualified majority' of EU member states, and despite opposition from the European Parliament (European Parliament, 2015a,b,c, 2016a,b,c,d).

Due to consumer reluctance to eat GMOs, many major retailers have excluded GMOs from their own brand food products and some manufacturers don't want to purchase agricultural goods from regions with high GM crop production (Devos et al., 2009). In the EU, labelling is required for food or feed containing more than 0.9% of EU-authorised GMO-resources of each ingredient according to Regulation (EC) no. 1829/2003 on genetically modified food and feed and Regulation (EC) no. 1830/2003 concerning the traceability and labelling of genetically modified organisms and the traceability of food and feed products produced from genetically modified organisms. Food and feed products that contain less than 0.9% GMO-resources do not have to be labelled if the presence of the GMO was adventitious or technically unavoidable. However, products such as eggs, milk and meat that were produced using GM-feed don't have to be labelled and are sold in the EU. Research conducted by the Food Standards Agency in 2012 revealed that UK consumers were generally unaware that farmers are using GM feed and the fact that the resulting products don't have to be labelled. Once made aware, two thirds wanted products from animals fed GM feed to be labelled. According to a survey from the Forsa Institute for Social Research and Statistical Analysis conducted in Germany in April 2014, 93% of 1000 interviewed persons thought that animal products containing GMOs should be labelled. Almost 80% wished animals were not fed with GMOs at all and the vast majority would even pay more for GM-free meat and dairy (Forsa, 2014).

Examples of certified GM-free foods are given above (see Section 3.3.2. Effects of the increasing demand for non-GM seeds and foods on RR crop marketing). However, it should be noted that supplying the GM-free foods that consumers want is made more difficult by large-scale GM soy and maize production. In countries where GM crops are grown, the costs of segregation are often borne by non-GM producers (see Section 3.4. Economic and regulatory implications of RR crop cultivation on coexistence with conventional crops).

5.3. Impacts of GM crops and foods on the health of humans and farmed animals

5.3.1. Compositional & qualitative differences between RR and non-RR crops

Despite public scepticism towards foods containing GMOs, the industry repeatedly states that RR crops are as safe and nutritious to eat as any other crop because there are no compositional or qualitative differences between RR and conventional or organic crops. Several studies support this statement (see for example Harrigan et al., 2007; Lundry et al., 2008; McCann et al., 2005; Padgette et al., 1996; Taylor et al., 1999), however other authors disagree (Hilbeck et al., 2011, Mesnage et al., 2016, Vilperte et al., 2016). The focus of this report is on herbicide tolerant GM crops, therefore we focus on the potential health issues associated with the blanket spraying of such crops with weedkillers, particularly the glyphosate-based herbicides associated with RoundUp

Ready GM crops (the effects of other herbicides which are sprayed on newer HT GM crops are considered in Section 7. Environmental and health effects of other herbicides).

Typically, health safety studies focus on potential risks from the GM product and the genetic change itself and do not measure residues of herbicides and their metabolites. They use RR soy that was grown under strictly controlled conditions, either not treated with glyphosate or at doses lower than those applied by farmers. Pesticide residues should however always be integrated in compositional studies as RR crops do not only differ from their conventional counterpart in the inserted gene but also in the applied management practice. Not only glyphosate but commercial herbicides such as Roundup should be used, as they contain adjuvants that can increase overall toxicity (see Section 5.5.1. Adjuvants and Section). Hilbeck et al (2011) point out that RR crops now contain higher residues of glyphosate and its primary metabolite AMPA, than when glyphosate was used on conventional crops. Pesticide residues can contaminate food crops either by direct pesticide application, by pesticide drift, by uptake from contaminated soil or water, or through food processing (Rubio et al., 2014). Adjuvants may increase glyphosate residue levels in crops by enhancing adhesion of glyphosate to plant surfaces and by facilitating translocation of glyphosate into plant tissues, where it can not be dissipated (Myers et al., 2016).

Arregui et al. (2004) find higher concentrations in soybean leaves and grains, when glyphosate is sprayed several times during the crop cycle, which only became possible with glyphosate tolerant crops. Bøhn et al. (2014), measure pesticide residues in RR, conventional and organic soybeans from Iowa and find significantly higher levels of glyphosate and AMPA residues in RR soybeans compared to conventional and organic soy where they find none of those chemicals. This suggests that pesticide residues are an important compositional difference. Bohm et al. (2014) compare conventional and RR soybeans in Brazil and find that glyphosate residues in the seeds are above levels permitted by Brazilian law. Both glyphosate and AMPA were found in soil and RR soybean seed in the two glyphosate treatments used in the experiments. Glyphosate concentrations of 15 and 21 mg kg^{-1} in seeds were detected in the treatments with one and two glyphosate applications, respectively, meaning that residue levels were above the 10 mg kg^{-1} limit permitted by the Brazilian Agency for Sanitary Vigilance (ANVISA). In commercial farms, the concentrations of glyphosate found in seeds were 12 mg kg^{-1} and 21 mg kg^{-1} for the Sananduva and Pelotas locations studied, respectively. AMPA concentration was similar to that of glyphosate, reaching 16.3 and 24.3 mg kg^{-1} in seed for one and two applications of glyphosate, respectively. For the commercial areas, AMPA concentrations were 19 and 25 mg kg^{-1} in Sananduva and Pelotas, respectively.

Xu et al. (2019) review the evidence of glyphosate contamination in grains and foods. They find that, overall, glyphosate residues in grains and foods were below the current maximum residue levels (MRLs) set by regulators, but that more studies are needed to further elucidate any health-related concerns.

Viljoen et al. (2021) investigate the presence of glyphosate and glyphosate-tolerant events in 81 maize and soybean food products purchased from local supermarkets in South Africa. The majority of products contained glyphosate (66.7%) but at a level below the maximum residue limit (MRL). Glyphosate herbicide-tolerant (HT) event(s), from GM crops, were detected in 70.4% of products but were not associated with the presence of glyphosate in all products, suggesting that the production of GM herbicide-tolerant (HT) maize and soybean in South Africa is the main, but not the only, source of glyphosate in these foods. The authors conclude that South African consumers are exposed to low levels of glyphosate reported to cause genotoxic effects at the cellular level.

Human exposure to glyphosate is considered further in Section 5.4. Human exposure to glyphosate and Roundup.

Bøhn et al. (2014), further find that different agricultural practices affect the quality of the soybeans. Organic soybeans have a healthier nutritional profile, with more sugars, protein and zinc and less fiber and omega-6, than both conventional and GM-soy. In Section 3.2.1. Impact of glyphosate on plant health and crop productivity, we considered how glyphosate may reduce nutrient uptake and translocation in RR crops treated with glyphosate. Zobiole et al. (2010b) suggest that a lower nutrient concentration in RR crops does not only impact plant health and productivity but might also affect animal and human health since these essential nutrients are taken up via crops and are often deficient among people. Zobiole et al. (2010c) found glyphosate to alter seed nutrient concentrations and polyunsaturated fatty acid percentages. Whilst glyphosate increased the percentage of monounsaturated fatty acids, which are not essential to the human diet, it decreased the percentages of two important polyunsaturated fatty acids, linoleic acid and α-linolenic acid. This is problematic because humans cannot synthesise those essential fatty acids. Omega-3 and omega-6 fatty acids in seeds were also affected by glyphosate. In a two-year field experiment, Bellaloui et al. (2008) studied the effect of glyphosate application on the seed composition in RR soybeans. They also found glyphosate to result in a decreased linolenic acid percentage compared with the non-treated soybean. However, they used application rates that were higher than recommended, representing a “worst case scenario”. Further effects observed in this study were a higher protein percentage and a higher oleic acid percentage.

5.3.2. Effects on farmed mammals

This section considers adverse effects on mammals consuming GM HT crops as animal feed, with a particular focus on residues of glyphosate in animal diets. Studies in animals (mainly rats) undertaken to assess human health effects are considered in (Section 5.5. Health effects of Glyphosate and Roundup). Studies in birds including poultry are considered in Section 4.2.3. Farmland Birds).

Reviews of the effects of GM crops on farm animals have generally found little evidence of adverse health effects (de Vos & Swanenburg, 2018). However, most of the experimental studies lasted one commercial production round or even shorter. Remarkably, only a few experimental studies in this review mentioned clinical examination of the animals as a health parameter that was studied, and many published studies suffer from serious weaknesses with respect to experimental design, statistical analysis, and the use of non-GM feed for comparison purposes. In addition, studies submitted to regulators do not usually use material (e.g. GM soybeans) that has been sprayed with glyphosate-based herbicides, at least not at the levels used today in farmers fields (Miyazaki et al., 2019). Thus, the potential adverse effects of high residues of glyphosate in animal feed have rarely been examined.

The maximum residue levels (MRLs) of glyphosate plus AMPA allowed by regulators in farm products vary widely, depending on the commodity and regulatory agency, ranging from 0.05 mg/kg for most animal products (except for meat byproducts), 0.1 to 40 mg/kg in many plant products for human consumption, and up to 530 mg/kg in grass and fodder (Van Bruggen et al., 2021).

Sørensen et al. (2021) review potential consequences of feed residues of glyphosate for livestock health and productivity. They focus on the documented antimicrobial and mineral-chelating properties of glyphosate, and discuss potential effects on livestock health and productivity, assuming legal levels of residual glyphosate in feed from Roundup Ready and desiccated crops. These authors find that the literature on the potential effects of glyphosate on livestock is very scarce and mainly consists of *in vitro* studies. They were unable to identify any reports on the levels of glyphosate in the guts of livestock given feed with residues of glyphosate, and state that the potential effects of feed-derived glyphosate on the gut microbiota of livestock are poorly investigated. They conclude that a solid basis of *in vivo* (live animal) studies with livestock in physiological and productive phases, particularly sensitive to disorders in mineral status and in the gut microbiota, is needed. In a laboratory experiment, Ackermann et al. (2015) find that glyphosate has an inhibitory effect on select groups of the ruminal microbiota taken from a 4-year-old non-lactating Holstein–Friesian cow, whilst increasing the population of pathogenic species.

In a long-term pig feeding study, pigs from a commercial piggery were fed with diets containing commercially grown GM and non-GM soy and corn, respectively. The GM diet contained RR soybeans and stacked RR and insect resistant corn. Carman et al. (2013) found that GM-fed pigs showed a significant increase in severe stomach inflammation and had 25% heavier uteri compared non-GM-fed pigs. Although it is difficult to draw firm conclusions from a single study, the authors regret that long-term toxicological feeding studies with GM and non-GM fed to farm animals are scarce. Such long-term feeding studies are needed, given the wide-spread use of GM feed used for livestock.

Only a few subsequent studies have examined the potential effects of glyphosate on the health of livestock.

Larsen et al. (2022) conduct an animal study where pigs were exposed to glyphosate while feeding. Two groups of pigs had 20 ppm and 200 ppm of glyphosate added to the feed, respectively, whilst a control group had no glyphosate added (104 pigs were used in total, and slaughtered 9/10 or 35 days after treatment for analysis). The aim of the study was to determine whether there are any epigenetic effects of glyphosate on pig genes, particularly in terms of DNA methylation and gene expression. No changes were found in the small intestine. However, a significant increase in expression of the enzyme TET3, responsible for demethylation, was observed in the kidneys of pigs exposed to 200 ppm glyphosate. The authors also report that glyphosate induces gene-specific DNA hypomethylation in the IL18 gene promoter in the liver of pigs exposed to glyphosate. Thus, there is evidence that glyphosate can induce gene expression changes and gene-specific epigenetic effects in pigs. The authors note that the control pigs did not have zero glyphosate in their feed because it was hard to obtain such feed (although no additional glyphosate was added), and this could account for the lack of observed differences in other enzymes.

Spinaci et al. (2020) also conduct experiments using pigs. In laboratory experiments, they examine the biological impact of both glyphosate and Roundup on female pig gametes (eggs). They conclude that glyphosate and its formulation Roundup impair pig oocyte (egg) maturation. In these experiments, Roundup at the same glyphosate-equivalent concentrations was found to be more toxic than pure glyphosate (see also Section 5.5.1. Adjuvants).

Perego et al. (2017) study the effects of RoundUp on cells from cattle. They find that glyphosate in formulation may act as an endocrine disruptor chemical in cattle. In their study, RoundUp impairs bovine granulosa cell proliferation and steroid production and has more potent effects than glyphosate alone. They conclude that RoundUp may have the potential to impair reproductive function in cattle. Additional studies are needed, because so little research has been done.

Alarcón et al. (2020) study neonatal (newborn) exposure to glyphosate in Friesian ewe lambs. Twelve lambs were exposed to glyphosate-based herbicides (GBH) (2 mg/kg of body weight/day) through injections, from postnatal day (PND) 1 to PND14; on PND45, the uteri were obtained to evaluate histomorphological and molecular parameters, and compared with ten controls. They find that neonatal exposure to GBH decreased cell proliferation and altered the expression of molecules that control proliferation and development in the uterus. They conclude that all these changes might affect the female reproductive health of sheep and that GBH may act as an endocrine-disrupting chemicals (EDCs) (see also 5.5.4. Endocrine disruption and reproductive health). In an earlier study, Alarcón et al. (2019), the same research group finds that GBH exposure alters the ovarian follicular dynamics and gene expression, and the proliferative activity of the ovaries and uterus of lambs. In a laboratory study, Wróbel et al. (2022) find that glyphosate has the potential to disturb cervical cells in cows.

Jarrell et al. (2020) note that livestock worldwide are the largest consumers of glyphosate-tolerant crops (as animal feed) and argue that risk assessment should consider the reproductive health of breeding lines. They review the literature and identify numerous adverse effects of glyphosate-based herbicides in animal reproduction. They note that very few studies have investigated the effects of these exposures on agriculturally important animals, and the majority of those that have, have not investigated reproductive health and performance. Reproductive health is not a consideration for many livestock, which may only be grown to market weight for meat production, but is relevant to breeding populations. Jarrell et al. (2020) argue that exposure to glyphosate-based herbicides could be one of the reasons for loss of fertility in livestock.

5.3.3 Impacts of GM feed on animal products

Animal products derived from GM fed animals have been approved for human consumption on the basis that no recombinant DNA fragments have been found in any organ or tissue samples of animals fed with genetically modified feed (EFSA, 2007). It is generally considered that meal derived proteins and DNA are degraded into amino acids and nucleic acids during digestion and cannot pass directly to the circulatory system. Spisák et al. (2013) have, however, shown that plant DNA can in fact avoid digestive degradation and end up in human blood. The published evidence that DNA fragments can survive and reach the blood and tissues of human and animal consumers is reviewed by Nawaz et al. (2019). For example, feeding studies with fish (Chainark et al., 2008), pigs (Mazza et al., 2005; Sharma et al. 2006) and sheep (Sharma et al. 2006) fed transgenic soybeans, maize or canola suggest that DNA fragments (endogenous and transgenic) can survive digestive processes and be taken up into the animal's blood, organs and tissues. Nevertheless, potential health effects remain unclear.

In this report, our focus is not on the potential effects of GM crops as such, but on herbicide tolerant (HT) GM crops, including Roundup Ready (RR) crops. As potential adverse health effects of RR crops could stem from agrochemicals, in the next sections we will consider human exposure to Roundup and glyphosate and the health implications of this.

5.4. Human exposure to glyphosate and Roundup

As shown above, environmental exposure to Roundup, glyphosate and AMPA increased with the introduction of RR crops (see Section 3.1.1 Herbicide use and Section 4.1. Increased environmental occurrence of glyphosate and AMPA). Thus, it can be assumed that human exposure to these agrochemicals via air, drinking water and the food chain has also gone up. However, data about human exposure to glyphosate are often scarce. Moreover, what is generally considered a safe level of exposure to glyphosate varies between regions and changes over time. Before the introduction of RR crops, in the early 1980s, the acceptable daily intake (ADI[3]) of glyphosate in the U.S. was 17.5 times lower than it is today (CFS, 2015b). In Europe, where to date no RR crops are cultivated, the ADI is still six times lower (0.3 mg/kg/day) than in the U.S. (1.75 mg/kg/day) (CFS, 2015b; European Commission, 2002; Myers et al., 2016). Antoniou et al. (2012) argue that when German regulators set the ADI for glyphsosate at 0.3 mg/kg/day they did not use the most appropriate species and did not properly consider a relevant study that identified adverse effects at low levels Paganelli et al., 2010). They suggest an ADI of 0.1 mg/kg/day would be more accurate and further argue that the ADI might even be as low as 0.025 mg/day. However, in its 2016 glyphosate renewal assessment report, the German Federal Institute for Risk Assessment (BfR), even called for an increase of the EU ADI from 0.3 mg/kg/day to 0.5 mg/kg/day (Myers et al., 2016). This would still be 3.5-times below the U.S. ADI. Taking into account current uncertainties regarding safety and exposure to glyphosate (as discussed below), Myers et al. (2016) argue that the U.S. EPA should impose a 10-fold safety factor on glyphosate, reducing the ADI to 0.175 mg/kg/day.

Bøhn & Millstone (2019) estimate that glyphosate-tolerant soybeans produced on commercial farms in the USA, Brazil and Argentina accumulate in total an estimated 2,500–10,000 metric

[3] The analogue standard units used in the U.S. are the chronic Reference Dose (cRfD) and the chronic Population Adjusted Dose (cPAD), respectively. To avoid confusion we will always refer to the ADI during this report.

tonnes of glyphosate per year, which enter global food chains. Based on residues found in glyphosate tolerant soybeans in Iowa, the amount of glyphosate entering the food chain would be 9 g/tonne of soy. This would add up to 2430 tonnes of glyphosate residues from the 270 million MT of GT soy produced globally in the 2016/2017 season. However, farm samples from Brazil have shown average residue levels of glyphosate at 38.5 mg/kg, i.e., nearly twice as high as the maximum accepted residue level (MRL) as specified by the international standards body, the Codex Alimentarius Commission, and the EU. In Argentina, average and maximum residue-levels were measured at 31.7 mg/kg and 72.8 mg/kg, respectively. In addition, other chemicals in glyphosate-based herbicides, such as adjuvants (e.g. POEA), are not measured, even though they may be more toxic (see Section 5.5.1. Adjuvants). In contrast, scientists from Bayer Crop Science (which now owns Monsanto) argue that "*exposures to glyphosate from food are well below the amount that can be ingested daily over a lifetime with a reasonable certainty of no harm*" (Vicini et al., 2021).

Louie et al. (2021) conduct a comparative evaluation of dietary exposure to glyphosate resulting from for three eating patterns recommended in the U.S. In this study, the 95th percentile of glyphosate ingestion at 2,000 calories/day for adults for the U.S.-Style, Mediterranean-Style, and Vegetarian eating patterns ranged from 38 to 960, 39 to 1100, and 39 to 880 µg/day, respectively, below the current U.S. EPA chronic oral reference dose (RfD) of 0.1 mg/kg/day. These authors conclude that ingestion of certain high residue foods, particularly grains and legumes, is a driver of total dietary glyphosate body burden regardless of dietary style.

The level of glyphosate allowed in drinking water is 7000 times higher in the U.S. (0.7 mg/L; US EPA, 2009) compared with the EU (0.1 µg/l.; Council Directive 98/83/EC; Monsanto 2005b). For food and feed, the maximum residue level (MRL) of glyphosate has also been increased in countries that produce or import RR crops. In Europe, for example, the MRL for glyphosate in soybeans has increased 200–fold from 0.1 to 20 mg/kg in 1999 (Bøhn et al., 2014). Bøhn et al., (2014) question that adjustment in these levels were due to new evidence indicating that glyphosate was less toxic than previously understood and explain it rather as a response to observed increased levels of glyphosate. Confirming this, the Australian Food Authority requested that the tolerance level for glyphosate in soybean be raised from 0.01 mg/kg to 20 mg/kg in order that RR soybeans could be imported from the U.S. (Buffin & Jewell, 2001). In the U.S., glyphosate maximum residue levels for soybeans are 40 mg/kg for grain and 100 mg/kg for hay and forage. As for soybeans, the MRL has been raised for several other crops as well. Most dramatically in alfalfa dry hay and silage, the MRL increased 2000-fold from 0.2 mg/kg in 1993 to 400 mg/kg in 2015 (Benbrook, 2016).

There is a lack of transparency when it comes to the data that exposure thresholds are based upon. This data is supplied by the manufacturers during the registration process and considered proprietary. Thus the data is usually not available for independent review. Moreover, in the U.S., the risk assessment of glyphosate is mostly based on out-dated studies, since only few studies relevant for assessing risks to human health have been submitted to the EPA since the late 1980s. Similarly, in the EU, the BfR still relied on the same industry-supplied proprietary data for the renewal assessment report, that originally led to setting the EU ADI of glyphosate at 0.3 mg/kg/day. Yet, in 2016, BfR recommended a higher ADI (Myers et al., 2016). Myers et al. (2016) argue that the establishment of appropriate glyphosate threshold levels should be based on "up-to-date science".

Farmers and other operators can be directly exposed to glyphosate-based formulations when they are spraying it onto their fields. People living in the area surrounding glyphosate application can be exposed to glyphosate by herbicide drift from the area where it has been applied. Acquavella et al. (2004) examined the urine of 48 farmers on the day they applied glyphosate to their fields and detected measurable levels of glyphosate in the urine of 60% of them. Farmers who did not use rubber gloves showed five times higher glyphosate in their urine. Similarly, Mesnage et al. (2012) found glyphosate residues in the urine of a farmer 7 hours after spraying. They also detected glyphosate in the urine of one of his children living at a distance from the field. Lozano-Kasten et al. (2021) study urine samples from 95 children between the ages of 6 and 16 in a rural community in western Mexico. In this study, all samples tested positive for glyphosate and glyphosate levels were related to the season and the age of the children, with peak levels of 3.2 ng/ml in May 2018. In a study of 90 urine samples from farmers in Mato Grosso, Brazil, between 2017 and 2018, de Melo et al. (2020) found glyphosate residues in some of the samples, with the highest level at 7.13ng/mL (well below the permited limit).

Gillezeau et al (2020) review the evidence on human exposure to glyphosate, including children. They find that the amount of work published on glyphosate levels in the population continues to be very limited. Only 4299 individuals have been tested worldwide for their urinary glyphosate level and only 520 of them are children. Nevertheless, they identify six data sets from four distinct studies reporting on children. All the studies confirm the presence of glyphosate in urine samples from children, both within and outside of agricultural communities, with values exceeding those measured in adults when the corresponding values were available. The average glyphosate levels reported in children ranged from 0.28 µg/L to 2.5 µg/L. In addition, they describe the average urinary glyphosate level in occupationally exposed adults as "*disconcertingly high*" (4.0 µg/L, ranging from 1.3 to 12.0 µg/L), although lower than found in an earlier review (Gillezeau et al., 2019). These authors conclude that tracking exposure to products such as glyphosate in children is a pressing public health priority.

Subsequently, Ferreira et al. (2021) measure glyphosate in the urine of 41 Portuguese children (2–13 years old), finding detectable levels in 95.1% of the samples (1.77 ± 0.86 µg/L), up to a maximum value of 4.35 µg/L. These authors report that glyphosate concentrations were higher in the urine of children aged 7–9 years, living near agricultural areas (within 1 km), with a higher percentage of consumption of home-produced foods, and whose parents applied herbicides in the backyard. They calculate that the exposure of these children represents 1 to 5.58% of the established Acceptable Daily Intake (ADI) of glyphosate (0.5 mg/kg bw/day). Nevertheless, they conclude that the young age of the participants should be considered, as the ADI was adopted based on adults.

Nomura et al. (2022) study urinary concentrations of glyphosate in Japanese children from 2006 to 2015. Detectable glyphosate concentrations were found in 41% of the 234 children. The 75th percentile and maximum concentrations of urinary Gly were 0.20 and 1.33 µg/L, respectively, and the levels increased over time.

In 2022, a report by the National Health and Nutrition Examination Survey (NHNES), a unit of the Centers for Disease Control and Prevention (CDC), found that out of 2,310 urine samples, taken from a group of Americans intended to be representative of the US population, 1,885 had detectable traces of glyphosate (Gillam, 2022; NHNES, 2022). Almost a third of the participants were children ranging from six to 18.

Rendón-von Osten and Dzul-Caamal (2017) measure glyphosate in groundwater, bottled drinking water, and the urine of subsistence farmers from various localities of the Hopelchén municipality in Campeche, Mexico, where glyphosate-resistant GM crops are grown. They report glyphosate concentrations up to 1.42 µg/L in groundwater and up to 0.47 µg/L in urine samples of subsistence farmers. In contrast, concentrations in urine from the urban reference group (fishermen in Campeche) had the lowest mean concentration (0.22 µg/L). The highest mean levels of glyphosate in bottled drinking water were 0.65 µg/L. Almost all bottled drinking water samples in this study exceeded the acceptable limits of glyphosate for human consumption in the European Union (0.1 µg/L), however they did not exceed legal limits in Mexico. These authors conclude that the measured glyphosate concentrations in groundwater and bottled drinking water indicate an exposure and excessive use of glyphosate in these agricultural communities.

In their study of glyphosate and AMPA in topsoil in Brazil, da Silva et al. (2021) argue that, "*Even considering the uncertainties of the indirect exposure assessment model, the results showed that GLY concentrations in the areas sampled may represent a carcinogenic risk to public health since* *they are higher than the reference risk value of 1 × 10^{-4}*". These authors find glyphosate (GLY) and AMPA at peak concentrations of 66.38 and 26.03 mg/kg soil respectively.

It is not only farmers and their families who are exposed to glyphosate-based herbicides, as they are also widely used at roadsides, pavements or in public parks and school grounds (Sustainable Pulse, 2014). In a survey conducted by civil society groups, glyphosate was detected in 62% of 21 samples of drinking water that were tested across the US. The highest detected level of glyphosate was 0.33 µg/l and thus 3 times higher than the maximum allowed level for glyphosate in drinking water in the EU (0.1 µg/l) but still far below the maximum contaminant level (MCL) in the U.S. of 700 µg/l (Moms Across America and Sustainable Pulse, 2014; US EPA, 2009). The civil society tests should be more thoroughly investigated and replicated by the EPA.

Another route of exposure is via the food chain. As shown above (Section 5.3.1. Compositional & qualitative differences between RR and non-RR crops), glyphosate and AMPA can accumulate in RR crops (Arregui et al., 2004; Bøhn et al.,2014). Studies on glyphosate residues in food are however scarce. In 2011, the USDA demonstrated that 90% of 300 soybean samples tested contained glyphosate residues at concentrations of 1.9 ppm and 2.3 ppm respectively (Myers et al., 2016). The UK Food Standards Agency residue testing conducted in 2012, found glyphosate residue levels of 0.2 mg/kg or more in 25% of bread samples tested, likely due to the use of glyphosate as a dessicant to dry wheat before harvest (Myers et al., 2016).

Rubio et al. (2014) demonstrate that glyphosate residues are frequently found in honey samples and soy sauce. Of all tested honey samples 59% contained glyphosate residues above the limit of quantification. For soy sauce it was 36% of all analysed samples. In general, honey from GM crop adopting countries contained higher levels of glyphosate than honey from countries that limit or prohibit GM crop cultivation. The highest levels of glyphosate in honey were found in the U.S. (Rubio et al., 2014). Berg et al. (2018) analysed honey taken directly from 59 bee hives on the Hawaiian island of Kaua'i for glyphosate residue and found that only agriculture land use showed a strong positive correlation with glyphosate concentration. In addition, high glyphosate concentrations were also detected when extensive golf courses and/or highways were nearby, suggesting herbicide migration from the site of use into other areas by bees. De Souza et al. (2021) determine residues of glyphosate and AMPA in honey samples from five Brazilian States. Six samples showed GLY levels above the EU maximum residue limit (0.05 µg g^{-1}) and one sample showed AMPA at 0.10 µg g^{-1}. The authors note that this study indicates the presence of glyphosate residues in honey from regions that have had high losses of bee colonies and at the same time, frequent use of glyphosate in agriculture. In contrast, no transfer of glyphosate from beeswax to honey was detected in a study of 379 Belgian apiaries, although contaminated bee bread (pollen) may cause sublethal effects on honeybees (as discussed in Section 4.2.5. Pollinators) (El Agrebi et al., 2020).

Rodrigues et al. (2018) evaluate presence of glyphosate and AMPA residues in soy-based infant formulas during the years 2012–2017, undertaking 105 analyses carried out on 10 commercial brands from different batches. Among those samples that contained levels above the limit of quantification, the variation of glyphosate residues was from 0.03 mg kg^{-1} to 1.08 mg kg^{-1} and for AMPA residues was from 0.02 mg kg^{-1} to 0.17 mg kg^{-1}. De Souza et al. (2021) assess exposure to glyphosate residues in soy-based infant formulas, by testing 117 commercial samples from the Brazilian market. The levels of glyphosate and AMPA in the samples ranged from not detected (ND) to 1.08 mg kg^{-1} and ND to 0.17 mg kg^{-1}, respectively. An exposure assessment showed a glyphosate intake of up to 15.42 µg kg^{-1} body weight for 0 to 5 month-old babies and of up to 8.16 µg kg^{-1} body weight for 6 to 11 month-old infants. The authors compared these values with the acceptable daily intake (ADI) and conclude that they are not of concern.

In Argentina, Testbiotech (2013) found that over 60% of RR soybean samples contained more than the maximum residue level of 20 mg/kg for glyphosate, with residue level of up to almost 100 mg/kg. In Mexico, González-Ortega et al. (2017) detected glyphosate in 44.4% of food samples that were positive for the herbicide-tolerant events. At the same time, the herbicides were absent from artisan Tortilla samples assayed.

Rodrigues et al. (2020) take samples from three GM crops in commercial areas in 2012/2013 to 2017/2018 seasons in different Brazilian agricultural regions. They report glyphosate residues levels in genetically modified corn ranging from not detected (ND) to 0.15 mg kg^{-1}, in GM soybean ranging from ND to 2.81 mg kg^{-1}, and in GM cotton ranging from ND to 1.78 mg kg^{-1}. AMPA residues levels indicated a correlation with the glyphosate residues. These glyphosate residues levels are within the Maximum Residue Limits (MRLs) set in Brazil.

In Europe, glyphosate-tolerant GM crops are generally not sold in foods for human consumption, but do enter the food chain as animal feed. In nine of 24 analysed conventional eggs in Denmark, Foldager et al. (2021) find the concentration of glyphosate in yolk was above the detection limit but below the quantification limit, indicating that traces of glyphosate are common in conventional eggs.

In the U.S., the USDA and FDA test for pesticide residues in food to help ensure that pesticide residues are kept within the required maximum residue level (MRL). However, USDA and FDA both currently do not test for glyphosate residues in food, claiming such testing is too expensive and because glyphosate has been considered safe (Gillam, 2014; 2016). Thus there is a huge lack of data about the exposure to glyphosate via food. In 2015, the EPA, who in the past has advised USDA that glyphosate residues do not pose a threat to human health, announced it would consider recommending sampling for glyphosate to U.S. regulators in the future (Gillam, 2015c). While the USDA still does not plan to test for glyphosate residues in food, the FDA is moving forward to test for glyphosate in certain food including soybeans, corn, milk, and eggs, for the first time in the agency's history (Gillam, 2016). As noted above, MRLs of glyphosate in food or feed have increased in countries that produce or import RR crops. This poses the question of whether glyphosate residues are taken up via food and feed in animals and humans. Krüger et al. (2014a) showed that glyphosate that accumulates in feed can be consumed by animals and be detected in their organs and urine. They found that conventional husbandry cows showed a higher glyphosate concentration in their urine, than cows held in a GM free region. Organic food also seems to decrease the risk of glyphosate uptake by humans, as Krüger et al. further found glyphosate residues to be significantly lower in the urine of people consuming predominantly organic food than in urine of people consuming conventional food. In a study conducted by Friends of the Earth Europe (2013b), 44% and 36% of 182 urine samples received from 18 European countries showed traces of glyphosate and AMPA, respectively. Depending on the EU state, detection frequency reached up to 90%. The highest glyphosate concentration, 1.8 µg/l was found in Latvia and the highest AMPA concentration, 2.6 µg/l in Croatia. Moms Across America and Sustainable Pulse (2014) detected generally much higher glyphosate residues in human urine, than the Friends of the Earth Europe survey with the highest detected level being 18.8 µg/l, although these results so far lack independent replication. Despite uncertainties due to the lack of official monitoring data, the higher level of glyphosate found in the US compared to the EU could be due to the large-scale cultivation of RR crops in the US, compared to the EU.

In a study of 6848 participants recruited between 2018 and 2020, Grau et al. (2022) report that they detect quantifiable urine glyphosate levels in 99% of the French population, with higher values in men, in younger people, and in farmers. These authors report a mean of with a mean of 1.19 ng/ml + / − 0.84 after adjustment to body mass index (BMI) and that lower glyphosate levels are associated with dominant organic food intake and filtered water. Lemke et al. (2021) report concentrations of glyphosate and AMPA in the German Environmental Survey for Children and Adolescents 2014–2017. In 52% of the samples (46% for AMPA) the urinary glyphosate concentrations were above the limit of quantification of 0.1 µg/L.

Ingestion of pesticides is not limited to dietary uptake. Research shows that urinary pesticide levels are also associated with pesticide loadings on hands and thus the mere handling of food (Shalat et al., 2003).

Can glyphosate residues also bio-accumulate in human bodies? Monsanto scientists have stated that glyphosate is excreted unchanged in the urine and does not accumulate in the body and undergo metabolism in humans. But there is no official testing of glyphosate in human bodies. Due to concerns about the lack of data of glyphosate in food and people, Moms Across America and Sustainable Pulse (2014) started a small pilot study to test women's breast milk for glyphosate. Their findings suggest that glyphosate can bio-accumulate (i.e. increase in concentration) in human bodies. They found glyphosate levels higher than 75 µg/l in the breast milk of 3 out of 10 tested American women, which is much higher than the European Drinking Water Directive allows (0.1 µg/l, Council Directive 98/83/EC). They did not detect glyphosate in the breast milk of participating mothers that have been eating organic and non-GM food only for several months to two years. The findings of Moms Across America and Sustainable Pulse require further investigation and independent replication by the U.S. Environmental Protection Agency and other government regulators. Testing for glyphosate in breast milk by the Green party in Germany appears to confirm that glyphosate can accumulate in human bodies, although further peer reviewed studies are still needed. They found traces of glyphosate higher than allowed in European drinking water in all 16 breast milk samples tested. The sample stem from women across Germany that mainly eat conventional food (Bündnis 90/Die Grünen, 2015). In response to the Mom's Across America and Sustainable Pulse's test results, Washington State University (WSU) researchers conducted a yet to be peer-reviewed and published study, where they claim that glyphosate does not accumulate in breast milk (WSU, 2015). This study was contested, and conflicts of interest have been pointed out: such as the fact that the test used to measure glyphosate in the breast milk samples was developed and conducted by Monsanto and personal affiliations of the authors with Monsanto (Grossman, 2015b; Sustainable Pulse, 2015a; b). There remain limited peer-reviewed scientific studies published on the topic and it is clear that preliminary findings of glyphosate in breast milk require further replication. For that reason, the Feed the World project and the Organic Consumer Association launched a validated public glyphosate test (OCA, 2015). In Brazil, Camiccia et al. (2022) collected sixty-seven milk samples from lactating women in the city of Francisco Beltrão, Paraná, living in urban (26 women) and rural (41 women) areas, at the peak of glyphosate application in corn and soy crops in the region (April and May 2018). Glyphosate was detected in all breast milk samples analyzed with a mean value of 1.45 µg/L. The estimation of the total amount of glyphosate ingested by breastfeeding babies in a period of 6 months was described by the authors as significant. The authors conclude that their results suggest that the studied lactating population was contaminated with glyphosate, possibly through continued environmental exposure. Glyphosate was also detected in drinking water samples from the urban area and in artesian well water from the rural area of the region where the studied population lived.

Evidence that residues of glyphosate are found in urine and can potentially bio-accumulate in human bodies, is according to the industry no reason for concern, as glyphosate based-formulations are relatively safe for mammals and humans because they lack the shikimate pathway, respectively the EPSPS enzyme (see Section 2. Background). However, in the study of Krüger et al. (2014a), chronically ill humans had significantly higher glyphosate residues in their urine than healthy humans. With the increased exposure of humans to those chemicals it seems crucial to evaluate the associated risks and to take a precautionary approach to potential increases in exposure. In the next section we will consider scientific findings on the impact of glyphosate-based formulations on human health.

5.5. Health effects of Glyphosate and Roundup

When glyphosate was approved for use in 1974 it appeared to be safe because its acute toxicity (i.e., following a single dose of glyphosate) appears to be low. However, subsequently, attention has shifted to the effects of long-term exposure to low doses (Shaw, 2021). Carvalho et al. (2020a) argue that the identification of glyphosate as a toxic compound responsible for causing disease in human beings and damage to other biological species is not surprising news. These authors express concern about how regulatory assessments have tended to give more weight to industrial reports than to independent scientific studies. Related legal actions are discussed in Section 8. Lawsuits).

In vitro, clinical and epidemiological studies have suggested that glyphosate-based formulations may pose serious health hazards, including cell death, endocrine disruption, DNA damage, non-Hodgkin lymphoma and other types of cancer, chronic kidney disease and preterm births. Evidence for these concerns is discussed further below. In some studies, toxic effects are observed at low doses that could be found as residues in food and in drinking water. In 2015, the World Health Organisation's (WHO) cancer agency, the International Agency for Research on Cancer (IARC), classified glyphosate as "probably carcinogenic to humans". Glyphosate may also kill essential microorganisms in the gastro-intestinal tract. One research group has undertaken studies in rats which find some evidence of inter-generational effects (using so-called 'epigenetic' biomarkers of disease) (Ben Maamar et al, 2020).

Van Bruggen et al. (2021) note that, in animals and humans, glyphosate exposure and concentrations in urine have been associated with intestinal diseases and neurological as well as endocrine problems, but cause-effect relationships need to be determined in more detail.

In a review of published studies, Bai and Ogbourne (2016) conclude that it is unlikely but not impossible that human exposure will reach theoretical maximum daily intake levels for glyphosate through consumption of contaminated crops or other food. They also note that maximum residue levels (MRLs) set by regulators may not necessarily suggest a safe level of a pesticide residue in or on food or feed. Food or feed produced from GM glyphosate-resistant crops contain significantly higher residue concentrations than other crops and their cultivation also increases the chance of drift and contamination of other crops. Chronic glyphosate exposure at lower concentrations can potentially result in risks to human health as chronic, sub-chronic and reproductive toxicity can occure at lower concentrations. These authors also report a striking dearth of glyphosate and AMPA food residues analysis in the peer-reviewed literature, including a complete absence of data for any species of fish.

Furthermore, the health risk assessment of pesticides in the European Union and in the United States focuses almost exclusively on the stated active ingredient, despite the fact that adjuvants can also be toxic in their own right with numerous negative health effects having been reported in humans and on the environment (Mesnage & Antoniou, 2018; Nagy et al., 2020; Ghandi et al., 2021).

Torretta et al. (2018) provide a critical review of the effects of glyphosate exposure on humans through the food chain. They highlight widespread global contamination of soil, water, food and other products and conclude that it is the duty of regulators to place the "precautionary principle" before economic interests, namely the protection of citizens and the environment from exposure to a substance whose impacts are not yet fully known.

In a review of relevant findings, Marino et al. (2021) report the following problems with studies of glyphosate-based herbicides (GBHs): *"(i) studies carried out in vivo and in vitro do not give final indications of the acceptable daily intake (ADI); (ii) the existing data about glyphosate genotoxicity and cytotoxicity are still conflicting, as a result of different experimental conditions used in the research thereabout; (iii) there are no data about glyphosate-induced long-term effects on general populations or exposed farmers; (iv) GBHs seem to exhibit higher toxic effects than glyphosate alone, but studies on this matter are still few*". In the view of these authors, it is not possible to have a univocal opinion on the safety of glyphosate and, "*it appears that the human health risk associated with glyphosate could still be underestimated*".

This section considers some of the evidence for adverse health effects from chronic exposure to glyphosate and glyphosate-based herbicides.

5.5.1. Adjuvants

As discussed above, Roundup formulations are a mixture of glyphosate and various adjuvants and surfactants such as polyoxyethylene tallowamine (POEA) that enhance the chemical and physical efficacy of glyphosate and have been shown to increase the toxicity of glyphosate, particularly against aquatic non-target organisms (see Section 4.3.6. Impact of adjuvants on aquatic non-target organisms). Many toxicological studies conducted with human, mouse and rat cells confirm the findings from aquatic non-target organisms and suggest that looking at the effects of glyphosate alone is insufficient for a comprehensive assessment of the possible risks to human health resulting from the cultivation of RR crops (see for example Benachour et al., 2007, Benachour & Séralini, 2009; Clair et al., 2012; Gasnier et al., 2009; Mesnage et al., 2013, 2014; Moore et al., 2012; Richard et al., 2005; Walsh et al., 2000; Young et al., 2015; Vanlaeys et al., 2018; Dedeke et al., 2018; Defarge et al., 2018). Mesnage et al. (2013) tested the toxicity of 9 glyphosate-based formulations, a formulation without glyphosate and the major adjuvant (polyethoxylated tallowamine POE-15) alone on human cells. They find that all formulations were more toxic than glyphosate alone. Thereby the major adjuvant alone was around 10,000 times more toxic than glyphosate alone (Mesnage et al., 2013). Richard et al. (2005), find glyphosate-based formulations to be significantly more toxic to human placenta cell cultures than glyphosate alone. The surfactant POEA was the most potent of all in the study of Benachour & Séralini (2009), thereby also confirming results from aquatic non-target organisms. In fact, differential toxicity between pesticide formulations and their active ingredients appears to be a general feature of pesticide toxicity (Mesnage et al., 2014). The real toxicity of Roundup might thus be underestimated and the acceptable daily intake (ADI) of glyphosate (0.3 ppm), should therefore be adjusted to the fully formulated herbicide. Cox and Surgan (2006) suggest that some adjuvants might increase dermal absorption or penetration of the active ingredient and diminish the efficacy of protective clothing by increasing permeation of the active ingredient through gloves or by impeding laundry removal of the active ingredient. As noted above (Section 4.3.6. Impact of adjuvants on aquatic non-target organisms), newer formulations of glyphosate-based herbicides may use adjuvants with reduced toxicity, however there is no regulatory requirement to disclose surfactants and only the active ingredients are assessed by regulators (Mesnage et al., 2019). GBH formulations containing POAE are progressively being phased out in Europe and replaced by a new generation of surfactants, but this does not appear to be happening in the USA.

Tush & Meyer (2016) measure POEA in agricultural soils from six U.S. states. Adsorption experiments of POEA to selected soils showed that POEA adsorbed much more strongly than glyphosate. POEA was detected on soil samples collected between February and early March from corn and soybean fields from ten different sites in five other states (Iowa, Illinois, Indiana, Missouri, Mississippi) and in a soil sample from an agricultural field in Kansas. They note the potential widespread occurrence of POEA on agricultural soils, and persistence into the following growing season. They conclude that the presence of POEA on all 21 field samples analyzed indicates that the occurrence of POEA on soils is probably pervasive where glyphosate is applied.

Chłopecka et al. (2017) investigate the effect of glyphosate-based herbicide Roundup and its co-formulant, POEA, on the motoric activity of rat intestine. They state that their results indicate very high toxicity of POEA which exceeds the toxicity of the commercial formulations. Besides, they postulate that glyphosate and POEA may display antagonistic interaction towards the motoric activity of gastrointestinal tract. The results indicate that Roundup and POEA significantly affect the motoric activity of gastrointestinal smooth muscle when used in a wide range of doses. The significant reaction induced by Roundup was observed when the herbicide was used in doses which correspond to the highest environmental concentrations of Roundup found in some water sediments.

5.5.2. Cytotoxicity, genotoxicity, neurotoxicity & cancer

The WHO's cancer agency, IARC, has classified glyphosate as probable carcinogen (see Section 5.5.2.1. The WHO's cancer agency classification of glyphosate as probable carcinogen and its consequences). In this section we discuss some of the evidence of toxicity to cells (cytotoxicity), DNA (genotoxicity) and evidence that this may lead to increased risk of cancer or neurological disorders.

Several studies that tested cytotoxicity of Roundup formulations and glyphosate alone in different human cell lines *in vitro* and in animals, found decreased cell viability and cell death through necrosis or apoptosis and loss of mitochondrial transmembrane potential at doses lower than the recommended herbicide agricultural dilutions, lower than the maximal level of residues authorised in GM feed or comparable to levels recommended as acceptable for Australian drinking water (1mg/L) (Benachour et al., 2007; Benachour & Séralini, 2009; Clair et al., 2012; Gasnier et al., 2009; Mesnage et al., 2013, 2014; Richard et al., 2005, Young et al., 2015). Richard et al. (2005) found the effect to be dose and time dependent. Mesnage et al. (2017) also present results which imply that chronic consumption of extremely low levels of Roundup, at admissible glyphosate-equivalent concentrations, are associated with marked alterations of the liver proteome and metabolome. This is consistent with findings by Mills et al. (2019) that patients with non-alcoholic steatohepatitis (NASH) have significantly higher glyphosate excretion (suggesting higher exposures) than patients without NASH.

However, not all findings from cytotoxicity studies have been consistent. Townsend et al. (2017) find that the cytotoxicity of glyphosate appears to be minimal for physiologically relevant concentrations, but the compound has a definitive cytotoxic nature in human cells at high concentrations. Utilizing human Raji cells, DNA damage was quantified using the comet assay, while cytotoxicity was further analyzed using MTT viability assays. Several glyphosate concentrations were assessed, ranging from 15 mM to 0.1 µM. The authors find that glyphosate treatment is lethal to Raji cells at concentrations above 10 mM, yet has no cytotoxic effects at concentrations at or below 100 µM. Treatment concentrations of 1 mM and 5 mM induce statistically significant DNA damage to Raji cells following 30-60 min of treatment, however, cells show a slow recovery from initial damage and cell viability is unaffected after 2 h. At these same concentrations, cells treated with additional compound in this study did not recover and maintained high levels of DNA damage.

The cell cycle is responsible for cell division and the growth and development of all living organisms. Regulation of the cell cycle includes the detection and repair of genetic damage and ensures that the genome is correctly replicated and divided. Replication errors, as well as damaged or incomplete DNA lead to activation of cell cycle checkpoints that can halt the cell cycle process and prevent that erroneous DNA is passed to daughter cells. Failure to activate the checkpoints is associated with genetic disorders and instability or predisposition to cancer. Marc et al. (2002, 2004a, 2004b) have shown that several glyphosate-based formulations provoke cell cycle dysfunction in sea urchin embryos, a recognised model for cell cycle studies. Cell cycle checkpoints were altered, impeding DNA replication and cell division. The results of Marc et al. (2004b), indicate that cell cycle dysfunction is already induced at concentrations much lower than the manufacturers recommended spraying concentrations. This suggests a high risk by inhalation for people in the vicinity of spraying.

Cell cycle dysfunction can be an indication of tumor cells and human cancers. George et al. (2010) showed that glyphosate had tumor promoting activity in mouse skin. In 2012, Séralini et al. published a long-term study comparing rats raised on GM maize (corn) (event NK603) that was treated with or without Roundup and with Roundup alone. The GM-fed rats developed increased tumours and liver and kidney disease compared to the control group for all treatments. The study was meant as a follow up to Monsanto's investigation on the safety of NK603 that did not reveal such effects. The main differences between the two study designs is that the period of observation was extended from 90 days to two years and Roundup instead of Glyphosate was used in the study of Séralini et al. This shows the importance of long-term feeding studies and that it is insufficient to only apply glyphosate, rather than the actual formulations used in the field. Séralini's paper was highly criticized and later withdrawn by the journal in which it was published on the grounds of inconclusiveness of the data. Criticism also came from the European Food Safety Authority (EFSA), which was requested by the European Commission to review the publication. With regard to five evaluation criteria, derived from their 'guidance on repeated-dose 90-day oral toxicity study in rodents on whole food/feed', they concluded that the publication is of "inadequate design, analysis and reporting" and does not question the existing safety evaluation of maize NK603 (EFSA, 2013). However, as a response to the EFSA review, Hilbeck & Meyer (2013) analysed how Monsanto's technical study and the subsequent peer-reviewed publication (Hammond et al., 2004) complied with the EFSA requirements compared to the Séralini publication. They found that a lot of the criticism of the Séralini study would similarly apply to Monsanto's study and publication. They concluded that applying the evaluation criteria to the publication of Séralini et al. only, constitutes a double standard. Extending the comparative analysis to 21 peer-reviewed long-term studies published in the last 20 years that used the same rat strain as Séralini et al. and Monsanto, Hilbeck & Meyer (2013) further found that the EFSA criteria and requirements applied to the Séralini study are hardly fulfilled by any of these publications. In 2014, the findings of Séralini et al. were republished in another peer-reviewed journal (Séralini et al., 2014). In the same year, Monsanto withdrew its NK306 corn from the EU pipeline for cultivation. Arguments continue regarding conflicts-of-interest and the role of industry in GM safety studies (Krimsky and Gillam, 2018; Séralini, 2020).

In a review, Agostini et al. (2020) find that there is clear evidence of glyphosate toxicity in human cells, where detrimental effects are dependent on the cell type, chemical composition, as well as magnitude and time of exposure, among other factors. Adverse effects of glyphosate exposure on human health were observed in epidemiological studies; however, most of these studies have not determined the glyphosate dosage to confirm a direct effect.

Portier (2020) conducts a comprehensive analysis of the animal carcinogenicity data for glyphosate from chronic exposure studies in rats and mice. The author concludes that exposure of rats and mice to glyphosate in 13 separate carcinogenicity studies demonstrates that glyphosate causes a variety of tumors that differ by sex, species, strain and length of exposure.

Kwiatkowska et al. (2017) show that glyphosate (at high concentrations from 0.5 to 10 mM) may induce DNA damage in white blood cells (leucocytes), such as human peripheral blood mononuclear cells (PBMCs), and cause DNA methylation in human cells. They report that glyphosate induced DNA lesions, which were effectively repaired. However, PBMCs were unable to repair DNA damage induced by glyphosate completely. The authors note that changes in DNA methylation pattern may lead to genetic instability and ultimately to cancer: however, further work is needed to confirm this study.

In a study in 177 children aged 10–11 years old in Cyprus, Makris et al. (2022) present the first children's health dataset demonstrating anassociation between AMPA and DNA oxidative damage, globally. They state that these results need to be replicated in a larger study.

Rossetti et al. (2021) review evidence of epigenetic changes associated with exposure to glyphosate, glyphosate-based herbicides and AMPA, in humans and rodents. They find several lines of evidence which indicate that the exposure to these compounds could alter the epigenome, disrupting the mRNA expression and protein levels of key genes involved in normal functions and thus, potentially producing negative consequences.

Lucia et al. (2022) examine the association of glyphosate exposure (measured in urine samples) with blood DNA methylation in a cross-sectional study of 392 postmenopausal women. They conclude that glyphosate and AMPA exposure are associated with DNA methylation differences that could promote the development of cancer and other diseases, although further studies are needed to replicate these results.

Cattani et al. (2017) investigate the effects of subchronic exposure to glyphosate-based herbicide (GBH) on some neurochemical and behavioral parameters in immature and adult rat offspring. Rats were exposed to 1% GBH in drinking water (corresponding to 0.36% of glyphosate) from gestational day 5 until postnatal day 15 or 60. Results showed that GBH exposure during both prenatal and postnatal periods causes oxidative stress, and affects neurotransmission in the brains (hippocampus) of offspring (both immature and adult rats). The effects of GBH exposure were associated with oxidative stress and depressive-like behavior in offspring on day 60, demonstrated by prolonged immobility time and decreased time of climbing observed in a forced swimming test. These authors conclude that subchronic exposure to GBH might result in outcomes ranging from oxidative damage to impairment of brain function, which may account for depressive-like behavior later in life. Ait Bali et al. (2017) find that exposure to GBH from juvenile age through adulthood in mice leads to neurobehavioral changes that stem from the impairment of neuronal developmental processes. They study the neurobehavioral effects of GBH following acute, subchronic (6 weeks) and chronic (12 weeks) exposure (250 or 500 mg/kg/day) in mice treated from juvenile age until adulthood. They find that, unlike acute exposure, both subchronic and chronic exposure to GBH induced a decrease in body weight gain and locomotor activity, and an increase of anxiety and depression-like behaviours, which they describe as neurotoxic effects. Baier et al. (2017) also report behavioural impairments in mice which inhale a glyphosate-based herbicide (GBH). They conclude that repeated inhaled exposure to GBH in mice affects the central nervous system probably altering neurotransmission pathways that participate or regulate locomotor activity, anxiety and memory. The authors conclude that the inhalation route is a possible pathway for GBH access to the nervous system. Gallegos et al. (2018) find that exposure to a GBH during early stages of rat development affects brain oxidative stress markers as well as the activity of enzymes. Their results indicate that chronic exposure to a GBH during pregnancy and lactation produces an imbalance in brain oxidative stress as well as in the activity of several brain enzymes (GOT, GPT, AChE, and AP) in specific brain areas. They conclude that these alterations could contribute to the neurobehavioral variations reported previously by them, and to the impairment in recognition memory described in this paper.

Rueda-Ruzafa et al. (2019) review the impacts of glyphosate on gut microbiota and possible neurological effects. They conclude that more studies are required to determine the implication of glyphosate in behavioural disorders. Costas-Ferreira et al. (2022) review the evidence for toxic effects of glyphosate on the nervous system. They find that that exposure to glyphosate or its commercial formulations induces several neurotoxic effects, citing evidence that exposure during the early stages of life can seriously affect normal neural cell development, exert a significant toxic effect on neurotransmission and induce processes that lead to neuronal death, as well as the appearance of behavioral and motor disorders. They conclude that exposure to glyphosate produces important alterations in the structure and function of the nervous system of humans, rodents, fish, and invertebrates at doses that are lower than the limits set by regulatory agencies. Barnett et al. (2022) weigh the evidence regarding chronic glyphosate exposure on the gut microbiome (see also Section 5.5.5. Impact on the gut bacterial community and link to food-borne diseases), and the potential consequences on the gut-brain axis correlated with increased incidence of neuropsychiatric conditions. They highlight several ways that glyphosate can influence mental health and behavior through changes in the gut-brain-microbiome axis. However, they note that the doses used within the literature are generally much higher than the average person in North America would be exposed to through diet or environmental exposures alone. Thus, although environmental exposure to glyphosate and glyphosate-based herbicides has the potential to negatively influence neurodevelopment and behavior across generations, more research and monitoring is needed.

5.5.2.1. The WHO's cancer agency classification of glyphosate as probable carcinogen and its consequences

In 2015, the World Health Organisation's (WHO's) cancer agency, the International Agency for Research on Cancer (IARC), asked 17 experts to assess the carcinogenicity of 5 organophosphate pesticides, including glyphosate. In the framework of this process, they classified glyphosate as "probably carcinogenic to humans" (Group 2A), citing different studies that reported increased risk for non-Hodgkin lymphoma and other types of cancer such as skin tumours or the rare tumour renal tubule carcinoma (Guyton et al., 2015). This classification is only one step below the risk designation "known carcinogen". The American Cancer Society quickly followed suit, also listing glyphosate as probably carcinogenic to humans (American Cancer Society, 2015). According to Professor Kortenkamp, professor of human toxicology at Brunel University in London, national agricultural bodies take IARC's announcement very seriously: "The important thing is 2A categorisation in the IARC is equivalent to 1B in the European Union, which means it will not receive authorisation" (Turner, 2015b). Monsanto rejected the IARC classification and requested transparency on the process and clarification on the scientific basis of the classification (Monsanto, 2015b). According to EcoWatch, they demanded that the WHO retract the report, claiming that the report was biased (Pantsios, 2015). Others think that IARC has underestimated the threats from glyphosate (PAN International, 2015). The U.S. Environmental Protection Agency (EPA), in 1985 also came to the conclusion that glyphosate might cause cancer based on experiments showing tumours in glyphosate-treated rodents. It was subsequently classified as Class C: "suggestive evidence of carcinogenic potential." Six years later, in 1991, after input from Monsanto led to a reinterpretation of these studies, EPA reversed this decision, re-classifying glyphosate two classes below to Class E: "Not likely to be carcinogenic to humans" (US EPA, 1991; CFS, 2015b). After the IARC report, the EPA said it would take their findings into account in the formal review of the safety of glyphosate (Cressey, 2015a). The California EPA already took action and announced its intention to reclassify glyphosate to "known to cause cancer" (Levin, 2015). Meanwhile the first lawsuits were filed against Monsanto by agricultural and horticultural workers claiming that Roundup caused their cancers and Monsanto misled the public and regulators such as the EPA about the dangers of the herbicide (Gillam, 2015e). These lawsuits are discussed further in Section 8.1 Glyphosate lawsuits.

In the EU, the German Federal Institute for Risk Assessment (BfR) and the EFSA concluded in their re-assessment of glyphosate, that glyphosate was "unlikely to pose a carcinogenic hazard to humans" (EFSA, 2015b). These opposite results concerning the risks of glyphosate led to a conflict between the EFSA and BfR on the one side and the IARC on the other side, about the different assessment methods used (EFSA, 2016a; IARC, 2016; Portier et al., 2015). Contrary to the IARC assessment, studies considered by EFSA and BfR focussed only on the active ingredient and not on the herbicide formulations actually used in the field. Whilst IARC based its assessment on publicly available data and opened their meetings to observers, the German regulator and EFSA also considered industry-supplied, proprietary data. The EU's re-assessment of glyphosate also lacks transparency regarding their experts. Over 80% of the national experts involved refused to disclose their names to the public and fill out a declaration of interest. Not a single name from the rapporteur state, Germany, was disclosed. In contrast, IARC's experts are all known and all excluded conflicts of interest (CEO, 2016; Cressey, 2015b). PAN Germany explains how based on a weight of evidence approach, BfR and EFSA provided five reasons for dismissing the carcinogenic effects of glyphosate, and critically assessed these reasons, challenging BfR and EFSA to rebut their points with concrete arguments or to admit they are correct (PAN Germany, 2017a).

In the USA, a series of internal Monsanto Co. Documents, revealed via a court order, reportedly raised questions about the company's long-standing claims about the safety of Roundup (Gillam, 2017c). The court documents reportedly raised concerns about collusion between the Environmental Protection Agency (EPA) and Monsanto (Durden, 2017; Gilliam, 2017a; Hakim, 2017; Rosenblatt et al., 2017; United States District Court Northern District of California, 2017; US Right to Know, 2017a). Congressman Ted W. Lieu called for consumers to immediately stop using RoundUp and for a Department of Justice investigation to look into any potential misconduct by employees of the EPA (Lieu, 2017). The case also raised concerns about company secrecy

(Gillam, 2017b) and led U.S. Right to Know to sue the EPA for the release of documents on glyphosate (US Right to Know, 2017b). Disagreements within the EPA itself were also reported (GM Watch, 2017a; Davies, 2017). See also Section 8.1 Glyphosate lawsuits.

In Europe, there has also been a debate about the trustworthiness of the science underpinning regulatory decisions (Simon, 2017a,b). In particular, the independence of the The European Chemicals Agency (ECHA) has been questioned (GM Watch, 2017b; Greenpeace, 2017a; Johnston, 2017). In contrast to the IARC, the ECHA's Committee for Risk Assessment (RAC) agreed to maintain the classification of glyphosate as a substance causing serious eye damage and being toxic to aquatic life with long-lasting effects, but concluded that the available scientific evidence did not meet the criteria to classify glyphosate as a carcinogen, as a mutagen or as toxic for reproduction (ECHA, 2017). The ECHA opinion was criticised by environmental organisations (Deutsche Welle, 2017; Greenpeace, 2017b; Health and Environmental Alliance, 2017; PAN Germany, 2017b; PAN UK, 2017) and the French environment minister (Ministère de l'Environnement, de l'Énergie et de la Mer, 2017), but was welcomed by industry groups (Nelsen, 2017).

The IARC classification "probably carcinogenic" urgently calls for more research, to determine to what degree glyphosate is carcinogenic to humans, especially considering its widespread use. There is typically a time-lag between exposure to a carcinogen and observed elevated cancer rates. Thus, the full effect of rising glyphosate use may not have been shown yet (CFS, 2015b).

Feulefack et al. (2021) conduct a review and statistical meta-analysis of the evidence that Childhood Brain Cancer (CBC) may be linked to parental pesticide exposure. They conclude that there is an association between CBC and parental pesticides exposure before childbirth, after birth, and residential exposure. Khan et al. (2022) find that prenatal pesticide exposure is associated with an increased risk of neuroblastoma (a rare type of cancer that mostly affects babies and young children). Both these papers state that their findings are in line with the IARC Monograph evaluating the carcinogenicity of diazinon, glyphosate, malathion, parathion, and tetrachlorvinphos.

Weisenburger (2021) reviews evidence that glyphosate and glyphosate-based formulations (GBFs) are a cause of the cancer of the lymphatic system, Non-Hodgkin Lymphoma (NHL), finding "*coherent and compelling evidence that glyphosate and GBFs are a cause of NHL in humans exposed to these agents*." In statistical studies, exposure to glyphosate is associated with increased risk of non-Hodgkin's lymphoma (NHL). However, the results of meta-analyses of glyphosate exposure and NHL risk depend on assumptions made about both exposure level and latency period before cancer develops, with a higher exposure and longer latency period associated with higher risk (Kabat et al., 2021).

Following the IARCs classification of glyphosate as a probable carcinogen, campaigns to restrict, phase out or ban the use of glyphosate grew immediately around the world (Where is Glyphosate Banned?, 2022). For example:

- In Argentina, 30,000 doctors, scientists and environmentalists called for a ban on glyphosate. The Federation of Health Professionals of Argentina (Fesposa) called on the Ministry of Health to ban the herbicide. Furthermore, the Society of Pediatric Hematology-Oncology (SAHOP) demanded the immediate prohibition of all glyphosate fumigations. María Victoria Dunda, lawyer and member of the Lawyers Network of Fumigated Towns claims rural schools are frequently fumigated and the number of teachers with a medical leave due to cancer has been steeply growing over the past decade. In the light of the IARC findings, Greenpeace Argentina asked the Minister of Agriculture for a nationwide ban of glyphosate (Aranda, 2015; Koop, 2015; Maxwell, 2015). More than 400 towns and cities in Argentina have passed measures restricting glyphosate use (Where is Glyphosate Banned?, 2022).

- In Brazil, the public state prosecutor Anselmo Henrique Cordeiro Lopes asked the National Health Surveillance Agency (ANVISA) to conduct a toxicological re-evaluate of glyphosate, aiming for a national ban on glyphosate-based herbicides. The public prosecutor also launched an investigation into whether regulatory authorisations for RR crops should be revoked (Canal Rural, 2015). In August of 2018, a federal judge in Brasilia ruled that new products containing glyphosate could not be registered in the country. However, this ruling was later overturned (Where is Glyphosate Banned?, 2022).

- In Colombia, coca eradication programmes funded by the U.S. involves aerial spraying of glyphosate. Following the IARC's designation of glyphosate as a probable carcinogen, Colombia's health ministry recommended an immediate suspension of fumigation with glyphosate (Brodzinsky, 2015). The recommendation was backed by the U.N. representative of the High Commissioner for Human Rights Todd Howland (Telesur, 2015). Following this recommendation, Colombian president Juan Manuel Santos announced in May 2015, that glyphosate will be banned from spraying of illegal plantings and that they will find other ways to combat coca production (BBC News, 2015). Farmers in Colombia long complained that the spraying destroys not only coca plants but also legal crops and that glyphosate has led to many health-related problems including skin rashes, respiratory problems, diarrhoea and miscarriages (Brodzinsky, 2015). However, the controversial spraying programme was re-started in 2017 (Telesur, 2017). Idrovo & Rodríguez-Villamizar (2018) regret the reversal, stating: *"This decision is not only going back on a public policy that aimed to protect human health, especially in vulnerable populations, but also seems to ignore the complexities of the problems related to rural territories with difficult access, where these illicit crops are grown…What will be the health consequences of this setback in public health?"*. In March of 2019, the President asked for the judicial ban on aerial glyphosate spraying to be lifted, but in July of 2019, the court maintained the judicial ban on glyphosate (Where is Glyphosate Banned?, 2022).

- In the U.S., movements against glyphosate also began. People who claim exposure to Roundup caused them to develop a rare form of cancer filed lawsuits across the country (Baum Hedlund Aristei & Goldman, 2016). These lawsuits are discussed further in Section 8.1 Glyphosate lawsuits. In California, the decade long debate about the use of glyphosate to control plants in Marin County heated up due to the IARC report (Seidman, 2015). In New York, a bill was announced in May 2015 that would require limiting synthetic pesticides including Roundup in City parks (New York City Council Member Ben Kallos, 2015). In Californa, a Fresno County Superior Court judge ruled against Monsanto in its fight to prevent California regulators from listing the key ingredient in Roundup as a carcinogen (Rodriguez, 2017; Kennedy, 2017). Numerous US cities have restricted or banned glyphosate and, in 2021, Bayer announced it would stop selling it's glyphosate-based herbicides (the RoundUp brand) in garden stores from 2023 (Where is Glyphosate Banned?, 2022).

- In Mexico, the government decided to gradually replace the use, acquisition, distribution, promotion and import of glyphosate and glyphosate-based formulations with sustainable and culturally appropriate alternatives that are safe for human health and biodiversity. The transition phase will end in January 2024. Low toxicity agrochemicals, biological or organic products, agroecological practices and intensive labour are mentioned as potential alterantives to glyphosate (DOF, 2020). In April 2021, a Mexican judge sided with Bayer and provided a temporary reflief from the ban. Shortly thereafter, a Mexican court however reaffirmed the glyphosate ban (Reuters, 2021; Where is Glyphosate Banned?, 2022).

- In Canada, there are now restrictions on glyphosate use in some provinces and cities. In February of 2022, Canada's Federal Court of Appeals issued a ruling that Health Canada did not follow its own protocols for regulating herbicides like Roundup (glyphosate). This ruling could impact glyphosate's status in the country (Where is Glyphosate Banned?, 2022).

- In Costa Rica, the country's National System of Conservation Areas issued a guideline prohibiting the use of glyphosate in Costa Rica's 11 Protected Wild Areas in December 2019 (Where is Glyphosate Banned?, 2022).

- Bermuda suspended approval and importation of all glyphosate-based products with immediate effect (Today in Bermuda, 2015). In Barbados, the Government announced that people would need a licence to purchase glyphosate (Where is Glyphosate Banned?, 2022).

- Bahrain and five other countries in the Gulf Cooperation Council (GCC) have reportedly banned glyphosate (Where is Glyphosate Banned?, 2022).

- Fiji announced in 2020 that glyphosate would be banned from January 2021 (Where is Glyphosate Banned?, 2022).

- In India the states of Punjab and Kerala have reportedly banned glyphosate (Where is Glyphosate Banned?, 2022).

- In the EU, the International Society of Doctors for the Environment (ISDE) sent an appeal to officials at the EU parliament and Commission to immediately, permanently and with no exceptions ban the production, trade and use of glyphosate-based herbicides in the EU (ISDE, 2015). The body representing European agricultural workers, EFFAT, called for an exit strategy that promotes alternative substances in order to do away with glyphosate as quickly as possible (EU Reporter, 2016). Germany's state consumer protection ministers called for an EU-wide ban on private use of glyphosate as well as glyphosate use close to consumers. The legal basis needed for a ban is however missing at the moment. As the approval period for glyphosate in the EU ended on December 31, 2015, the EU Commissions' new approval procedure for glyphosate had to be completed first (Sarmadi, 2015). Several NGOs including Greenpeace and the Alliance for Cancer Prevention, asked the European Commissioner for Health and Food Safety to suspend the EU approval of glyphosate for uses that could lead to exposure of workers and the public (Lynn et al., 2015). In his response, the Commissioner however stated that a precautionary action was not considered necessary and that probably no decision would be taken until the Commission decided whether to extend the approval period for glyphosate (Lewis, 2015). Subsequently, the Commission proposed further restrictions including banning the co-formulant POE-tallowamine from glyphosate-based products (European Commission, 2016b). In June 2016, the European Commission extended its approval for weed-killer glyphosate by 18 months, after EU member states repeatedly failed to take a decision to extend the license approval (Reuters, 2016a). Amid fierce arguments by EU member states, the European Commission granted a five-year extension on the use of glyphosate in the EU in November 2017 (Casassus, 2019; European Commission, 2017). It is argued that a number of shortcomings in the EU pesticide authorisation process have led to the renewal of glyphosate. These include amongst others the selective use and omission of published data, invalid dismissal or exclusion of adverse effects, misue of historical control data, misuse of statistical analytical tools, failure to assess toxicity of mixtures, lack of transparency and conflict of interest, inlcuding the fact that safety testing of pesticides is carried out by the companies that manufacture the products in questions (Robinson et al. 2020). Despite the extention, some businesses and authorities in Europe started to limit glyphosate use or call for it to be banned. Glyphosate is currently authorised for use in the EU until December 2022, and a new review began in 2021 (EFSA, 2021).

- Belgium banned the individual use of glyphosate. In 2017, Belgium voted against relicensing glyphosate in the EU. The country was also one of six EU member states to sign a letter to the EU Commission calling for "*an exit plan for glyphosate*…" The city of Brussels banned the use of glyphosate within its territory as part of its "zero pesticides" policy (Where is Glyphosate Banned?, 2022).

- The Czech Republic's Agriculture Minister Miroslav Toman said the country will limit glyphosate use starting in 2019, banning glyphosate as a weedkiller and drying agent (Where is Glyphosate Banned?, 2022).

- In Denmark, the Danish Working Environment Authority (WEA) went a step further than the IARC and declared glyphosate a carcinogen. The decision is backed by one of the world's leading and highly respected toxicologists, Philippe Grandjean (GMWatch, 2015; Møller, 2015). In July 2018, the Danish Government implemented new rules banning the use of glyphosate on all post-emergent crops to avoid residues on food (Where is Glyphosate Banned?, 2022)

- Germany passed legislation in February of 2021 to ban glyphosate by 2024 (Where is Glyphosate Banned?, 2022). Concerning private use, 350 toom Baumarkt DIY stores that belong to the German retail group REWE, announced they would stop selling glyphosate-containing products as of October, 2015 (REWE Group, 2015).

- In 2015, the then French Environment and Energy Minister Ségolène Royal called on garden shops to stop selling Roundup (Reuters, 2015). In April 2016, France's health and safety agency announced it would ban weedkillers that combine the chemicals glyphosate and tallowamine because of concerns over possible health risks (Reuters, 2016b). After the European Commission extended the approval of glyphosate use in the EU, French President Emmanuel Macron immediately asked the French government to ban the product. Based on the IARC finding, a Lyon court banned the sale of Roundup Pro 360 to professionals in January 2019 (Casassus, 2019). In May of 2019, French Agriculture Minister Didier Guillaume announced that France would eliminate the use of glyphosate by 2021 with limited exceptions (Where is Glyphosate Banned?, 2022). Whilst President Macron still supports the ban, it has been delayed and French farmers have been offered financial aid in return. In the meantime, France's ANCES agency withdrew 36 glyphosate-based products from the market and around 20 mayors have banned the use of glyphosate in their municipalities.

- Italy has placed restrictions on the use of glyphosate (Where is Glyphosate Banned?, 2022).

- Austria passed a total ban on glyphosate in January 2020 (Peng et al. 2020). However, this was not implemented. A partial ban on glyphosate use (on "sensitive" areas and for private use) was adopted in June 2021 (USDA, 2021).

- Luxembourg became the first EU country to ban the use of glyphosate, by the end of 2020 (Where is Glyphosate Banned?, 2022).

- The two biggest retailers in Switzerland, Migros and Coop, announced in May 2015 that they would no longer sell products containing glyphosate (Coop, 2015; Schweizerbauer, 2015).

- The Dutch Parliament avoted in 2014 to ban the sales of all glyphosate-based herbicides to private persons from the end of 2015 due to health and environmental concerns (Sustainable Pulse, 2015d).

- Concerning agricultural use, the UK Soil Association called for a ban on the use of glyphosate by farmers (Soil Association, 2015). The London Borough of Hammersmith & Fulham became the first council in London to halt the use of glyphosate-based herbicide sprays in parks and open spaces (Horticulture Week, 2016). Dozens of boroughs and towns have followed suit (Where is Glyphosate Banned?, 2022).

- Malta began the process of banning glyphosate in 2015 (Times of Malta, 2016). In July 2019, it banned the use of glyphosate in public places (Where is Glyphosate Banned?, 2022).

5.5.3 Chronic Kidney Disease

Chronic Kidney Disease (CKD) is a major cause of death among males in poor regions of Sri Lanka. "Chronic Kidney Disease of unknown etiology" (CKDu) is the term now used for CKD observed in young men in agricultural communities. Sri Lanka is not alone: health workers have reported CKDu in Mexico, Nicaragua, El Salvador, and the state of Andhra Pradesh in India (Gunatilake et al., 2019). CKDu is CKD that does not follow typical patterns of age distribution or have a direct association with diabetes or hypertension. It is believed to be linked to geo-environmental risk factors (variable climate, temperature, air quality, water quality and drought) combined with agro-environmental risk factors (exposure to fertilizers, soil conditioners, herbicides, fungicides and pesticides) (Wilke et al., 2019). Jayasumana et al. (2014) first hypothesized the association of glyphosate use, the most widely used herbicide in the disease endemic area in Sri Lanka, and its unique metal chelating properties, with CKD. Although these authors argue that glyphosate alone did not cause an epidemic of chronic kidney disease, they conclude that it may destroy the renal tissues of thousands of farmers when it forms complexes with a local water hardness and toxic metals. Further research has shown that people in the disease endemic area are exposed to multiple heavy metals as well as glyphosate (Jayasumana et al., 2015). Gunatilake et al. (2019) support the view that glyphosate in particular is working synergistically with most of the other factors involved (exposure to other pollutants and physical labour in high temperatures) to increase toxic effects. In a study of urine pesticide concentrations and biomarkers of kidney damage, Abdul et al. (2021) report evidence that occupational paraquat and glyphosate exposure may cause a decline renal functions among rural farming communities in Sri Lanka. Upamalika et al. (2022) review potential molecular mechanisms and conclude that oxidative stress induced by environmental exposures, including to glyphosate, likely play a role in the initiation and progression of CKDu. Babich et al. (2020) argue that metals in drinking water, even at safe levels, can impede kidney development at an early age, leading to increased susceptibility to other agrochemicals such as glyphosate. An investigation in El Salvador supported the hypothesis that CKDu was caused by systemic toxicity from agrochemicals (e.g., paraquat, glyphosate), which particularly affect the kidneys and to which farmers/farmworkers (who may also become dehydrated in the fields) are most exposed (Herrera-Valdés et al., 2019).

5.5.4. Endocrine disruption and reproductive health

Endocrine disrupting chemicals (EDCs) are chemicals that interfere with the hormonal system of mammals, such as oestrogens and androgens (female and male sex hormones). They are said to cost the European Union more than €150 billion a year in health costs and lost economic potential, with pesticides accounting for the major economic impact (Trasande et al., 2015). Various studies show endocrine disrupting effects of glyphosate and Roundup and other adverse effects on reproductive health, such as damage to reproductive organs, sperm and eggs. Jarrell et al. (2020) review the literature on glyphosate-based herbicide formulations and reproductive toxicity in animals. They highlight that glyphosate-based herbicides have potential to cause adverse effects in animal reproduction, including disruption of key regulatory enzymes in androgen synthesis, alteration of serum levels of estrogen and testosterone, damage to reproductive tissues and impairment of gametogenesis (the production of sperm and eggs).

Muñoz et al. (2021) conduct the first review that consolidates the mechanistic evidence on glyphosate as endocrine-disrupting chemical (EDC). They conclude that glyphosate satisfies at least 8 key characteristics of an EDC. However, they argue that prospective cohort studies are still needed to elucidate the real effects in the human endocrine system. In addition to animal and laboratory studies, they cite evidence from some epidemiological studies which show that women exposed to glyphosate have increased risk of late miscarriages and a decrease in fecundability (the probability of achieving pregnancy and/or live birth wthin a cycle).

Mohammadi et al. (2021) conduct a systematic review and meta-analysis on the studies in which the alteration of at least one sexual hormone including testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol was reported as a measured outcome in rats. Their meta-analysis of eight eligible studies finds a considerable effect of glyphosate exposure on decreasing of testosterone (7 studies), LH (3 studies) and FSH (3 studies). These authors conclude that glyphosate intake could have major effects on the health of reproductive systems.

Serra et al. (2021) review the mechanisms of action of glyphosate and glyphosate-based herbicides in female and male fertility in humans and animal models. They report that glyphosate acts at the hypothalamic, pituitary, gonadal, uterine, placental, and embryonic development levels. Moreover, alterations can be transmitted to the next generation through epigenetic effects. In this review, glyphosate-based herbicides (GBHs) were found to be more harmful than glyphosate alone, likely related to the presence of formulants such as POEA (see Section 5.5.1. Adjuvants).

Kalofiri et al. (2021) highlight how even the EU's relatively complete regulatory framework for Endocrine Disruptor Chemicals (EDCs) does not ensure an effective way of dealing with endocrine disruptors. They use glyphosate as an example to reveal discrepancies in the implementation of EU pesticides regulation, which they argue means the system is inadequate to protect human health.

This Section includes studies in mammals only (mainly rodents). Evidence of adverse effects on the reproductive health of other organisms also exists and is considered in Section 4. Environmental impacts of RR crops and associated glyphosate-based herbicide regime). Potential adverse effects on the reproductive health of farmed mammals are considered in Section 5.3.2. Effects on farmed mammals.

5.5.4.1. Impact on oestrogen synthesis and female reproductive health

In 2005, Richard et al. found evidence that Roundup may act as a potential endocrine disrupting chemical in human placental cells at doses still below the classical agricultural dilutions. Roundup negatively effects aromatase activity, which converts androgens into oestrogens. These results suggest that Roundup may induce reproductive problems. Different experimental studies with animal and human cells seem to confirm the endocrine disrupting effects of glyphosate-based formulations and glyphosate alone. Benachour et al. (2007) found Roundup and glyphosate alone to inhibit oestrogen synthesis, through reduction of aromatase activity at nontoxic levels in human embryonic and placental cells. They suggest that contamination with Roundup may have an impact on human reproduction and fetal development. Gasnier et al. (2009) found inhibition of androgen to oestrogen conversion at sub-agricultural levels of Roundup also in human liver cells. The first endocrine disruption actions were found even at dilutions 800 times lower than the level authorized in some food or feed. Thongprakaisang et al. (2013) found that low and environmentally relevant concentrations of pure glyphosate possessed oestrogenic activity. Glyphosate increased cell proliferation in hormone-dependent breast cancer cells, but not in hormone-independent breast cancer cells.

Guerrero Schimpf et al. (2017), find that neonatal exposure to glyphosate-based herbicide (GBH) disrupts postnatal uterine development at the neonatal and prepubertal period in rats. They note that all these changes may alter the functional differentiation of the uterus, affecting female fertility and/or promoting the development of neoplasias. In further studies in rats, Varayoud et al. (2016) find that GBH modulates the expression of estrogen-sensitive genes, and Ingaramo et al. (2017) conclude that neonatal GBH exposure may lead to embryo losses by disturbing uterine signaling.

Ingaramo et al. (2020) review the endocrine-disrupting effects of exposure to glyphosate and GBHs at low or "environmentally relevant" doses in female reproductive tissues. They find that glyphosate and GBHs may have the properties to be endocrine disrupting chemicals (EDCs). They conclude that these herbicides cause adverse effects on the ovary and the female reproductive tract, impairing embryo implantation and/or development, even when animals are exposed to low doses. In addition, glyphosate and GBHs inhibit aromatase activity and stimulate estrogenic pathways. Therefore, these authors conclude that there may be a link between the endocrine activities of glyphosate/GBHs and adverse effects on female reproduction. Ingaramo et al. (2022) publish further evidence that exposure to low doses of glyphosate-based herbicide (GBH) alters uterine function in rats. In their experiments, they report that neonatal GBH exposure alters the expression of angiogenesis-related molecules at neonatal uterine development. Angiogenesis is a process where new blood vessels are formed from the existing ones.

Milesi et al. (2021) review i) the routes and levels of human exposure to glyphosate-based herbicides (GBHs), ii) the potential estrogenic effects of glyphosate and GBHs in cell culture and animal models, iii) their long-term effects on female fertility and mechanisms of action, and iv) the consequences on health of successive generations. They conclude that there is extensive accumulated experimental evidence about the negative impact of glyphosate and GBHs on pregnancy outcomes, however there are just a few epidemiological studies on reproductive health, making it hard to reach definitive conclusions.

Lorenz et al. (2020) investigate the effects of perinatal exposure to a glyphosate-based herbicide (GBH) or glyphosate alone on female fertility in rats. They find similar results in GBH- and glyphosate-exposed rats, and suggest that the active ingredient (glyphosate) might therefore be responsible for the deleterious effects. Both pure glyphosate and its formulation increased preimplantation losses. The number of implanted embryos in female rats was reduced after *in utero* and lactational exposure. These authors report that a low dose of either glyphosate or GBH exhibits endocrine disrupting effects which may have potential significant health implications for animal and human populations.

Lesseur et al. (2021) measure levels of glyphosate and its degradation product AMPA in 94 pregnant women in the USA, using 2nd trimester maternal urine samples. Glyphosate and AMPA were detected in 95% and 93% of the samples (median 0.22 ng/mL and 0.14 ng/mL, respectively). The mothers were recruited as mother-infant pairs in the Infant Development and the Environment Study (TIDES). The anogenital distance (AGD), which can act as a measure of hormone disruption, was measured in male and female offspring. In female infants, high maternal urinary glyphosate (above the median) was associated with longer anoclitoral distance, but this was no longer significant after covariate adjustment. The authors conclude that glyphosate may act as a sex-specific endocine disruptor, but more research is needed.

Kaboli Kafshgiri et al. (2021) conduct a systematic review of glyphosate's effects on female reproductive systems. They conclude findings to date support an association between GBH exposure and female reproductive system diseases. However, they state that more studies are needed to identify the mechanisms disrupting the effects of GBH and their underlying mechanisms.

5.5.4.2. Impact on testosterone synthesis and male reproductive health

In an *in vivo* study, Wistar rats (a type of laboratory rat often used in studies) were daily exposed to a commercial formulation of glyphosate (Roundup Transorb). This led to reduced testosterone production, alterations in testicular weights and in seminiferous tubule morphology, as well to a significant delay in the pubertal age in a dose-dependant manner (Romano et al., 2010). In 2012, Clair et al. (2012) also found Roundup and glyphosate to decrease testosterone in rat testicular cells by 35% at environmental doses also found in urine of agricultural workers and their families. Residue levels 400 times higher than this are accepted in some feed in the U.S. Similarly, Abarikwu et al. (2015) also found glyphosate to decrease testosterone level in Wistar rats which could explain the further observed decrease in epididymis weight and the impaired sperm quality. Nardi et al. (2017) found a decrease in testosterone in animals receiving a rich soy milk diet during prepubertal development. This change occurs in all groups receiving soy milk, supplemented or not with glyphosate. However, endocrine disruption was more evident in groups supplemented with glyphosate.

In a study in male albino rats, Owagboriaye et al. (2017) found that Roundup may interfere with spermatogenesis and impair fertility in male gonads. They assess the effect of Roundup on the reproductive capacity of 32 adult male albino rats randomized into 4 groups of 8 rats per group orally exposed to Roundup at 3.6 mg/kg body weight (bw), 50.4 mg/kg bw and 248.4 mg/kgbw of glyphosate concentrations for 12 weeks while the control group was given distilled water. Significant alterations in the level of all the reproductive hormones measured (including testosterone) were observed in rats exposed to Roundup, as well as markers of oxidative stress. Significant reductions in sperm count and percentage sperm motility and significant increases in abnormal sperm cells were also observed in the exposed rats, as well as severe degenerative testicular lesions. The authors deduce that the reduction in testosterone level observed in the exposed rats was due to the negative impact of RoundUp on their testes. They conclude that Roundup has the capacity to induce reproductive toxicity in the male reproductive system of the exposed animal and that it is also a potent endocrine disruptor. They regard this as a public health concern considering the increasing use of Roundup and presence of its residues in food and drinking water, which leads to possible routes of exposure in humans.

Cai et al. (2017) conduct a systematic review of epidemiological studies on the association between glyphosate exposure and sperm concentrations of rodents. The results of their meta-analysis support the hypothesis that glyphosate exposure decreases sperm concentration. They conclude that glyphosate is toxic to the male rodent's reproductive system.

Zhao et al. (2021) investigate one mechanism through which glyphosate may impair male fertility in mice. In their experiments, serum testosterone levels were drastically reduced in mice treated with glyphosate over a four-week period, and glyphosate exposure also reduced testosterone production in TM3 cells (a cell line derived from mouse testes). In these glyphosate-exposed cells, the nuclear receptor NR1D1 was upregulated, inhibiting expression of StAR genes involved in testosterone synthesis.

Anifandis et al. (2017) find that a quantity of 1 mg/L of Roundup was found to exert a deleterious effect on the progressive motility of sperm from 66 healthy human volunteers. Subsequently, Anifandis et al. (2018) study the effect of 0.36 mg/L glyphosate on sperm motility and sperm DNA fragmentation (SDF) in thirty healthy men. They find no effect on SDF, but sperm progressive motility of glyphosate-treated samples was significantly reduced one hour after treatment, in comparison to controls. However, they state this is high concentration of glyphosate that greatly exceeds normal environmental exposures.

5.5.4.3. Impact on Progesterone synthesis

Walsh et al. (2000) found Roundup to significantly decrease the steroid hormone progesterone in mouse cells at non-cytotoxic concentrations. Progesterone is essential for the regulation of the human menstrual cycle and for maintaining pregnancy. Roundup disrupted expression of the steroidogenic acute regulator (StAR) protein, which regulates the rate at which cholesterol is transferred from the outer to the inner mitochondiral membrane and ultimately converted to progesterone. In an *in vitro* study with human cells, glyphosate and Roundup were found to decrease progesterone synthesis at levels comparable to the Australian Drinking Water Guidelines (1mg/L). In this study, endocrine disrupting effects were however a consequence of cell death and thus secondary to cytotoxicity (Young et al., 2015). In both studies, glyphosate alone did not affect progesterone synthesis.

5.5.4.4 Impact on thyroid hormones

A study in rats suggests that exposure to glyphosate-based herbicides before birth may disrupt some aspects of thyroid hormone function (de Souza et al., 2017). A study of occupational exposures in Brazil (Bernieri et al., 2018) reports a significant decrease in thyroid-stimulating hormone (TSH) and increase in triiodothyronine (TT3) and thyroxin (FT4) in 46 rural workers (soybean farmers), compared to 27 people not exposed to pesticides. Levels of the enzyme butyrylcholinesterase (BChE) were lower in exposed group than in control group. The authors conclude that their results suggest that farmers are exposed to mixtures of pesticides with endocrine disruptor properties. Romano et al. (2021) review the evidence that glyphosate and glyphosate-based herbicides could be associated with increased thyroid diseases. They conclude that, although there is a correlation between farmers' exposure to glyphosate-based herbicides and altered thyroid hormone levels or incidence of thyroid pathologies, there are very few studies evaluating the potential mechanisms of toxicity and there has been insufficient consideration of the importance of testing the toxicity of commercial formulations in scientific studies.

5.5.5. Impact on the gut bacterial community and link to food-borne diseases

Monsanto claims that the enzyme EPSPS is only found in plants and not in humans or animals, implying that glyphosate in harmless to humans. In a class action lawsuit, filed in April 2015 in California, Monsanto was accused of false advertising. The plaintiffs argued that the enzyme EPSPS is found in the microbiota in the gastro-intestinal tract and therefore does exist in human and animals (Phillips, 2015; Case No: BC 578 942). As noted above, Monsanto even patented glyphosate as an antimicrobial for its use in preventing or treating pathogenic infections caused by parasites of the phylum Apicompexa (Abraham, 2010).

Since gut bacteria do contain the EPSP synthase, incorporation of glyphosate residues into the gastro-intestinal tract could thus potentially affect its microbiota. Glyphosate can induce shifts in gut microbiota, as it does in soils (see Section 4.5. Impact on soil microbial communities). Shehata et al. (2013) studied poultry microbiota in vitro and found that while most of the highly pathogenic bacteria, such as *Salmonella* species, *Clostridium botulinum* and *E. coli* are highly resistant to glyphosate, most beneficial bacteria, such as Bifidobacteria and Enterococcus species are either moderately or highly susceptible to glyphosate. Similarly, Ruuskanen et al. (2020b) find that GBH exposure suppresses potentially beneficial microbes in the guts of Japanese quails (see also Section 4.2.3. Farmland Birds). A reduction of beneficial bacterial species in the gastro-intestinal tract microbiota, could disturb the normal gut bacterial community. Shehata et al. (2013) suggest that by reducing beneficial microorganisms that create unfavourable conditions to the growth of pathogens, glyphosate may also benefit pathogenic bacteria indirectly. Bifidobacter for example, create unfavourable conditions for Salmonella, which cause different illnesses, including food poisoning and are big public health concern worldwide. Other beneficial bacteria that were shown to be susceptible to glyphosate in this study create unfavourable conditions for Campylobacter, which cause the food-borne human disease Campylobacterosis. Similarly, Krüger et al. (2013) found that *Enterococcus* species, isolated from cattle, horse and algae, reduced growth and inhibited neurotoxin production of *C. botulinum*, a ubiquitous Gram-positive bacterium that generates botulinum neurotoxins, which can cause botulism in humans and animals. But while enterococci are susceptible to glyphosate, *C. botulinum* are highly resistant to glyphosate (Krüger et al., 2013; Shehata et al., 2013). During the last 1-2 decades, an increase in chronic botulism in cattle has been observed on dairy farms in Germany. The authors suggest that glyphosate residues in animal feed may induce a loss of enterococci and thereby be a predisposing factor responsible for the observed increase in *C. botulinum* on dairy farms.

In a preprint (not yet peer reviewed), Hu et al. (2020) explore the potential effects of glyphosate-based herbicides (GBHs) on urinary metabolites and their interactions with the gut microbiome in rats. Using a small sample of 61 urine samples, they report that, when pups were stratified by sexes, Roundup and glyphosate exposure resulted in significant and distinctive changes in metabolite profiles. They highlight that further research is needed in this area.

Argou-Cardozo & Zeidán-Chuliá (2018) use a systematic review to demonstrate an association between *Clostridium* bacteria colonization of the intestinal tract and autism spectrum disorders (ASD) in children. They hypothesize that environmental glyphosate levels may deleteriously influence the gut–brain axis by boosting the growth of *Clostridium* bacteria in autistic toddlers. Whilst this link is speculative, there are previously reported associations between autism and pesticide use cited in this paper. Pu et al. (2020) and Pu et al. (2021) report experiments in mice in which glyphosate exposure appears to cause behaviors defined as 'autism-like' (e.g. social interaction deficit) and suggest that this issue requires further study.

In a review of the published literature, Van Bruggen et al. (2018) find that shifts in microbial compositions due to selective pressure by glyphosate may have contributed to the proliferation of plant and animal pathogens. They argue that more research is needed on the potential link between glyphosate and antibiotic resistance, but suggest that the selection pressure for glyphosate-resistance in bacteria could lead to shifts in microbiome composition and increases in antibiotic resistance to clinically important antimicrobial agents (see also Section 4.7. Antibiotic resistance).

5.5.6 Glyphosate and pregnancy

Eaton et al. (2022) study the association between urinary glyphosate and AMPA and biomarkers of oxidative stress among pregnant women in Puerto Rico, in the PROTECT birth cohort study. In this study, glyphosate and AMPA were measured in 347 urine samples collected between 16 and 20 weeks gestation and 24–28 weeks gestation. The authors find that concentrations of AMPA in urine were associated with higher levels of certain oxidative stress biomarkers and associations with glyphosate reflected similar trends, although findings were not as strong. They conclude that additional research is required to better characterize the association between glyphosate exposure and biomarkers of oxidative stress, as well as potential downstream health consequences. In another nested case–control study in the PROTECT Cohort (Puerto Rico), Silver et al. (2021) study prenatal exposure to glyphosate and AMPA, and preterm birth. They report that glyphosate and AMPA levels in urine samples collected near the 26th week of pregnancy are associated with increased odds of preterm birth, and call for further study. In a relatively small birth cohort study in Indiana, Parvez et al. (2018) find glyphosate exposure (measured in urine) in pregnancy correlates significantly with shortened pregnancy lengths. Of the 71 women in this study, 93% of the pregnant women had glyphosate levels above the limit of detection (0.1 ng/mL) and the mean urinary glyphosate level was 3.40 ng/mL (range 0.5–7.20 ng/mL).

Paganelli et al. (2010) found malformations in frog and chicken embryos treated with glyphosate and Roundup at doses far lower than those used in agricultural spraying. These effects were attributed to the disruption of the retinoic acid signalling pathway and the resulting dysregulation of genes crucial to the development of the central nervous system. This study is relevant to human risk assessment as the retinoic acid signalling pathway is also present in humans. Krüger et al. (2014b) detected different concentrations of glyphosate in malformed piglets. It was assumed that the rate of malformation increased if the sow feed contained higher levels of glyphosate in the first 40 days of pregnancy. Myers et al. (2016) argue that glyphosate-based herbicides may thus at least be a contributing factor to similar birth defects observed in human populations living in or close to RR cropping regions. These observational studies are discussed in the next section.

5.5.7. Acute and chronic health effects associated with drift of glyphosate and other pesticides and use by farmworkers

Farmworkers are amongst those most exposed to glyphosate. For example, Rydz et al. (2021) estimate that 37 700 to 55 800 workers (11–13% of agricultural workers) were exposed to glyphosate in Canada, using data from the Canadian Census of Population and the Census of Agriculture. Lawsuits regarding glyphosate exposure of farmworkers are discussed in Section 8.1 Glyphosate lawsuits).

Glyphosate spray drift can affect farm workers, bystanders and people living in the surrounding area. Aerial application increases the risk of accidental exposure of neighbouring habitants.

Epidemiological studies and reports of interviews with local people cannot prove cause and effect, nevertheless there are numerous and widespread reports of poisonings due to aerial spraying of RR soybeans in Latin America or coca crops in Colombia, discussed further below. These reports also include death of livestock and domestic animals as well as crop losses due to herbicide drift. Effects have been reported as far as 10 km away from the supposed spray zone. Reported effects include vomiting, diarrhoea, respiratory problems, skin rashes, cancer, infertility, pregnancy problems, and birth defects (PAN Asia & Pacific, 2008, 2012).

These reports are consistent with the IARC (2015) designation of glyphosate as a probable human carcinogen, and with other studies suggesting that chonic exposure to glyphosate and other pesticides can cause a range of other adverse health effects. For example, in the Ontario Farm Family Health Study, Arbuckle et al. (2001) observe moderate increases in risk of early abortions for preconception exposures to any herbicide, and for late abortions, preconception exposure to glyphosate is associated with elevated risk. In the same study, Savitz et al. (1997) find that combinations of farm activities using a variety of chemicals, including glyphosate, are associated with an increased risk of miscarriage in the wives of exposed farm workers. In the Red River Valley, Minnesota, USA, Garry et al. (2002) find that exposure to glyphosate is associated with an increased risk of neurobehavioral developmental effects. In the Agricultural Health Study in Iowa and North Carolina, Hoppin et al. (2008) find an increased risk of atopic asthma in farm women using glyphosate and a number of other pesticides, and Hoppin et al. (2016) find an increased risk of allergic and non-allergic wheeze in male farm workers using glyphosate and some other pesticides. In the same study, Slager et al. (2009) find an increased risk of rhinitis in farm workers who had used glyphosate in the past year. Parks et al. (2016) find an association between the use of specific agricultural pesticides, including glyphosate, and the risk of rheumatoid arthritis in female spouses of licensed pesticide applicators in the Agricultural Health Study.

Zhang et al. (2022b) investigate the health effects of glyphosate on occupational workers in three chemical factories, by analysing serum metabolic alterations. They report that the levels of 27 metabolites changed significantly in the exposed group compared to the controls and argue that some of these changes may act as biomarkers to identify potential health risks.

5.5.7.1. Health effects related to coca spraying in Colombia

In Colombia, coca eradication programmes involve aerial spraying of glyphosate. Evidence of harm from such spraying is relevant to the question of whether aerial spraying of RR crops might also put people at risk. Whilst concrete evidence is hard to establish, farmers in Colombia long complained that the spraying destroys not only coca plants but also other crops and that glyphosate has led to many health-related problems including skin rashes, respiratory problems, diarrhoea and miscarriages (Brodzinsky, 2015). Since the coca fields are close to the Ecuadorian border, spraying has also become a potential health risk for Ecuadorians living close to the border. In 2005, Ecuador and Colombia signed an agreement to not spray in a 10km corridor along the border. Still, significant amounts of glyphosate spray drifted into Ecuador. Following a subsequent lawsuit before the International Court of Justice brought by Ecuador for human and economic damage caused by coca spraying, Colombia agreed in 2013 to pay 15 million US dollars to Ecuador and adopt additional parameters to prevent drift (Benner et al., 2016; Jaramillo & Kraul, 2013). Following the IARC's designation of glyphosate as a probable carcinogen, Colombian president Juan Manuel Santos announced in May 2015, that glyphosate would be banned from spraying of illegal plantings and that they will find other ways to combat coca production (BBC News, 2015). In May 2016, a former top counter-narcotics official warned that a government decision to return to spraying glyphosate will result in deaths (Colombia Reports, 2016). However, the controversial spraying programme was re-started in 2017 (Telesur, 2017). See also Section 5.5.2.1. The WHO's cancer agency classification of glyphosate as probable carcinogen and its consequences.

5.5.7.2. Reported health effects in Argentina due to spray drift

In Argentina, application of glyphosate is often carried out from the air in monoculture plantations of RR soya, thereby causing herbicide drift. In a special investigation in 2013, the Associated Press reported that spray drifts into schools and homes in Argentina (Warren, 2013). The report states that the first serious health problems were reported in 2002, six years after RR crops were approved for use in Argentina, from residents and doctors in soya producing areas. Claimed adverse effects included high rates of birth defects, infertility, stillbirths, miscarriages and cancers. Farmers also complained about lost crops from herbicide drift. Students in Santa Fe reportedly fainted after pesticides drifted into their classrooms. According to the article, the Doctors of Fumigated Towns, a growing movement demanding enforcement of agricultural safety rules, warned that uncontrolled pesticide applications could be causing the growing health problems in the Argentinian farm belt. Speaking for the organisation in a report in Deutsche Welle, pediatrician Ávila Vázquez highlighted concerns regarding cancer, miscarriage and birth defects (Deutsche Welle, 2016).

Another group, known as the Rural Reflection Group (GRR), has also documented increasing health problems in rural areas, according to an article in IPS News (Valente, 2009). The GRR report notes that soybeans fields reach all the way up to the outer streets in some towns. Farm machinery and containers used in spraying are washed and stored in urban areas, and soybeans covered in toxic substances are stored in silos located in the midst of homes, schools and other buildings. The personal accounts compiled in the report come from people in dozens of towns in the provinces of Buenos Aires, Córdoba, Entre Ríos and Santa Fe, where locals are demanding buffer zones around populated areas, which would be off-limits to fumigation planes. In April 2009, the Argentine Association of Environmental Lawyers, filed suit before the Supreme Court in Argentina seeking a nationwide ban on the sale and use of glyphosate (FT, 2009). See also Section 5.5.2.1. The WHO's cancer agency classification of glyphosate as probable carcinogen and its consequences.

Based on 12 months of fieldwork carried out between 2003 and 2013, Lapegna (2016) examines the effects on peasant communities of the growth of agrochemical use in Argentina due to the expansion of GM soybeans. He focuses on the province of Formosa, in northern Argentina, to better understand how rural populations and peasant social movements interpret the discourses and actions of state authorities and interact with them. With the expansion to northern Argentina, GM soybean production entered areas where peasants and indigenous communities comprise most of the rural population. The expansion of GM soybeans has come hand in hand with a steep increase in agrochemical use: at the end of the 1990s, 42 percent of the agrochemicals used in Argentina were utilized for the production of GM soybeans (see also Section 3.1.1.3. Herbicide use in South America). Peasant populations have been particularly affected by the expansion of transgenic agriculture and the exposure to agrochemicals and, in the early 2000s, peasant movements organized contentious collective actions to address these problems. For example, the Peasant Movement of Formosa (MoCaFor) mobilized in 2003 to complain about the effects of agrochemical drifts in rural communities. Since the mid-2000s, however, peasant organizations have played a limited role in protesting transgenic agriculture and agrochemical exposure. Lapegna argues that peasants are restricted to negotiating with rather than confronting authorities or powerful opponents, and that they are thus constrained to accommodating the negative environmental impacts associated with the expansion of GM soybeans. For example, the authorities collected blood samples in cases of alleged health effects due to agricultural drift, but may not have done the correct analyses and never shared the results with the participants.

Sinero and Berger (2012) study the Mothers of Ituzaingo´ Neighbourhood in the city of Co´rdoba, Argentina (Madres de Barrio Ituizaingo´ Anexo) as a case of citizens' practices in defence of human life, health, and the environment. They describe how, on their own initiative, in 2002 the Mothers surveyed over 200 cases of diverse illnesses among which cancer, lupus, hemolytic anemia, Hodgkin's lymphoma, tumors, and leukemia stood out. In 2003, the Ministry of Health, in connection with two epidemiological surveys that had been carried out by the authorities, reported 96 oncological cases, and, adding the hematological pathologies that were found, a total of 109 cases occurred out of a population of 5,000. In 2006, another epidemiological report by Dr. Schinder done for the municipal authorities confirmed that most of the cases of malignant illnesses detected in the neighbourhood appear especially in the zones that are contiguous to the soy fields and to automotive industry waste. He asserted that the incidence and prevalence of serious illnesses, with their respective death rate, are above the rates recorded in other districts of the country. This investigation highlighted that the rate of death at birth in Ituizango´ Anexo is 19.8 per thousand, whereas in the Instituto Provincial de la Vivienda (IPV) neighbourhood, it is only 8.9. Up to the present date, there are no administrative procedures to implement a plan of intervention in cases of environmental pollution and protocols of medical intervention in cases of malformation or intoxication caused by pesticides. The provincial laws and local norms regulating fumigations and specifically prohibiting them in the neighbourhood are frequently not followed. This is evidenced by more than eight complaints filed in court by those neighbours affected since 2002 up to the date of the paper, which had not been settled yet. In the judicial files there are no reports either from the Health Ministry or from any other public authority with respect to environmental health or related to the cases of diseases and deaths, or reports that assert or deny the connection between the pollution factors and the health of the population. These reports are limited to information on the level of toxicity of the substances. Berger and Ortega (2010) provide a more detailed description in Spanish of the struggles of the Madres de Barrio Ituzaingó Anexo.

Oliva et al. (2008) investigate whether there is any relationship between rural environmental factors and reproductive health in the Pampa Humeda in Argentina. Five rural communities in the Pampa Humeda in Argentina were selected, and the data were compared to the national mean. Malformations showed very significant differences and endocrine related cancers showed higher incidence rates compared to the national mean, particularly in some communities. They conclude that there is a relationship between environmental factors and reproductive health conditions in this region. However, this type of study cannot prove cause and effect.

Journalist Fernanda Sández has written a book about the "sprayed small towns" and the link between aerial spraying and the use of GM crops (Larrea, 2016) and a 2017 report by ecologist Walter Pengue has provided further documentary evidence (Pengue, 2017). Avila-Vazquez et al. (2018) study glyphosate exposure and reproductive disorders in an agricultural town (Monte Maíz) in Argentina. In this study, glyphosate was detected in soil and grain dust and was found to be at an even higher concentration in the village soil than in the rural area. These authors report that 650 tonnes of glyphosate are used annually in the region, creating environmental exposure to glyphosate of 79 kg per person per year. They also report that rates of spontaneous abortion and congenital abnormalities are respectively three and two times higher than the national average (10% vs. 3% and 3% - 4.3% vs 1.4% respectively). They conclude that high environmental exposure to glyphosate is associated with increased frequencies of reproductive disorders (spontaneous abortion and congenital abnormalities): however, they note that cause and effect cannot be established by this type of study and further studies are required.

Longhi & Bianchi et al. (2020) conduct an analysis of causes of death in the Argentine Dry Chaco Region from the year 1990, when GM soy was not yet predominant, until 2012 (during which time the area planted with GM soy increasd by 130%, from 455,000 to 1,044,000 hectares). They found no association with mortality, but did find some evidence for an upward change in the trend of mortality from tumors beginning in 1999, coinciding with increased application of the herbicide.

5.5.7.3. Health effects in Paraguay associated with spraying of RR soya

Paraguay is the third most important soya growing country in South America. In an article in Pesticide News, Williamson (2008) describes the impact of RR soya on local communities. The pesticide use and handling decree demands that warning must be given to public and private institutions and neighbouring residents before aerial spraying of herbicides and that the areas to be treated must be indicated. Protective barriers or no-spray zones, respectively, should be established for fields that run alongside public roads and paths to prevent spray drift. Moreover, filling and washing of application equipment close to water sources is prohibited. However, according to the article, no protective equipment is provided for fumigation workers. Moreover, these regulations are only rarely implemented by farm owners and also barely controlled by regulatory agencies. Herbicides are applied regardless of temperature or wind levels. In many cases, family homes and rural schools are completely surrounded by soya and exposed to glyphosate drift. The article states that many acute poisoning incidents linked with pesticide spraying on large-scale farms have been documented in Paraguay.

Benítez-Leite et al. (2007) study the association between exposure to pesticides and congenital malformations in new born babies born in the Regional Hospital of Encarnacion, in the Department of Itapua, Paraguay, using a prospective case-controlled study carried out from March 2006 to February 2007. A total of 52 cases and 87 controls were analyzed. The average number of births each month was 216. The significantly associated risk factors were: living near treated fields (OR 2.46, CI 95% 1.09-5.57, $p<0.02$), dwelling located less than 1 km (OR 2.66, CI 95%; 1.19-5.97, $p<0.008$), storage of pesticides in the home (OR 15.35, CI 95%, 1.96-701.63), $p<0.03$), direct or accidental contact with pesticides (OR 3.19, CI 95%, 0.97-11.4, $p<0.04$), and family history of malformation (OR 6.81, CI 5%, 1.94-30.56, $p<0.001$). Other known risk factors for malformations did not show statistical significance.

Williamson (2008) reports that Paraguay's Health Ministry has recorded pesticide poisoning incidents since 2003. The health registry records show poisoning incidents are correlated with the departments where soya production is concentrated and are most frequent during the main spraying period. A prospective case study conducted between 2006 and 2007 by Health professionals from the Ministry of Public Health, the National University and the health authority in Itapúa revealed an association between parental exposure to pesticides and congenital malformation.

Williamson (2008) also describes a research case study carried out by the NGO BASE Social Investigations (BASE-IS), in which data was collected during 2007 from families living in eight different farmer communities. 78% of the families interviewed report they had suffered from health problems correlated with herbicide spraying. Health symptoms reported include headaches, respiratory and digestive problems and blurred vision. Miscarriages and birth defects were also reported. Over 50% of families reported that they had lost livestock and 56% reported that food crops had been adversely affected, especially by Roundup. Again, whilst such studies cannot prove cause and effect, they highlight the need for further investigation, and a precautionary approach to spraying.

In a second case study described by Williamson (2008), conducted by the Paraguayan Roundtable for Sustainable Rural Development, testimonial data was collected from farmers and indigenous communities living close to large-scale soya or other export crop farms. Health symptoms reported include skin problems such as blistering, open wounds and skin cancer, but also impotence, respiratory problems, brain cancer, hearing problems, miscarriage and serious birth defects. There were also reports of school children fainting after inhaling pesticide vapour. The study further reported families losing livestock, wild animals and food crops due to herbicide drift which contributes to food insecurity (see also Section 3.5.1 Impacts on smallholders in South America).

5.5.7.4. Reported health effects in Brazil associated with spraying of RR soya

Schiesari and Grillitsch (2011) describe how, in a professionally managed, agroindustrial soybean plantation in Brazil, terrestrial and/or aerial pesticide application is an essential aspect of this form of intensive land management. Pignati et al. (2007) report a case of “pesticide rain” in Lucas do Rio Verde city, which appears to be associated with industrial soy production nearby.

Rigotto et al. (2014) consider the problems for public health caused by pesticide spraying in Brazil. Between 2007 and 2011, according to data from the Information System of Compulsory Notification Conditions (SINAN), there was an increase of 67.4% in new non-fatal labour accidents due to pesticides in Brazil, and the coefficient of intoxications had an overall increase of 126.8%, and was even higher among women (178%). However, underdiagnosis and under-notification are widely acknowledged for acute cases and the limitations of the data are even greater when it comes to the assessment of the chronic effects of pesticides, which may result from the gradual increase in consumption and intensification of use of such substances in Brazil. The results of the Food Pesticide Residues Analysis Program, developed by the Brazilian health authority ANVISA, show that in 2011 only 22% of the 1,628 samples analysed were free from these contaminants.

Oliveira et al. (2014) conduct a case-control study with 219 live births with congenital malformations and 862 live births, in Matto Grosso, Brazil. They find that maternal exposure to pesticides is associated with higher incidence of congenital malformations. Silva et al. (2015) explore correlations among variables relating to agricultural production, the use of health services, food consumption and socio-demographic characteristics and prostate cancer mortality rates in Brazilian states. A positive correlation between tons of soybeans planted and mortality from prostate cancer was identifed, suggesting the possible existence of an association between exposure to pesticides and prostate cancer.

In a report for the Latin American and the Caribbean Economic Association, Dias et al. (2020) look at municipalities in the main soybean-producing regions of Brazil and concentrate on the period between 2000 and 2010, when soybean production expanded rapidly following the introduction of genetically modified seeds. They focus on the effect of glyphosate use in one area on health outcomes in other areas that share the same water resources, minimizing the potential bias from the effect of increased agricultural productivity on local socioeconomic outcomes. They argue that this method allows them to use the direction of water flow inside water basins to isolate the adverse effects through water contamination, so that health outcomes in a given location should be affected only by the use of glyphosate upstream, but not downstream, from it. They report that locations receiving water from areas that expanded the use of glyphosate experienced significant deteriorations in birth outcomes, including significant increases in infant mortality, in the incidence of pre-term births, and in the frequency of low birth weights. In this study, the average increase in glyphosate use in the sample during this period led to an increase in the infant mortality rate of 0.88 per 1,000 births (or 5% of the average). The authors argue that this is likely a lower bound to the effect of glyphosate use on infant health, since they do not look at areas of use and do not consider other potential morbidity effects.

5.6. Conclusions

With the large-scale commercialisation of RR crops, human exposure to glyphosate via air, drinking water and the food chain increased drastically, although systematic data of human exposure to glyphosate are widely lacking. Different studies suggest health effects caused by glyphosate-based formulations, ranging from cell death, endocrine disruption, DNA damage, non-Hodgkin lymphoma and other types of cancer, chronic kidney disease and preterm births. The IARC classification of glyphosate as "probably carcinogenic to humans", and evidence linking glyphosate to other adverse health effects, is consistent with a rise in health problems reported in areas of large-scale RR soya production in South America, and observations of adverse health effects in US farm workers using glyphosate and other pesticides.

6. Industry response

The industry's answer to the development of GR weeds is mainly herbicide-centric and includes a) developing herbicide tolerant (HT) crops with enhanced tolerance to glyphosate, b) increasing the herbicide platform used on RR crops and c) developing new HT crops with tolerance to additional herbicides (Desquilbet et al. 2019).

These industry responses are discussed further below. They all raise significant concerns about the potential for an explosion in herbicide-resistant weeds, with resistance to multiple herbicides. In the USA, the farming press has already noted, "*increasing resistance to dicamba and 2,4-D, cross resistance to the auxin herbicides and some residuals and the potential for metabolic resistance in a few weed species*", and reports that weed scientists questioning if this means the end of an era in herbicides (Laws, 2022). Metabolic resistance refers to a situation in which weeds can develop enzymes that can convert an active ingredient into metabolites that don't kill the plant. In cotton grown in the USA, Nichols (2018) reports that "*great selection pressure has been placed on the remaining effective post-emergence mechanisms of action, the PPOs and glufosinate and now the auxins, 2,4-D and dicamba*" and notes that "*the costs of weed control in tillage, trait costs, increased herbicide use, and hand weeding have greatly increased with respect to those of 10 years ago*".

In addition, Duke et al. (2018) reports that glufosinate-resistant crops, which had little initial market penetration during the earlier years of RR crop production, have been turned to by some farmers as a result of GR weeds, "*resulting in record sales of glufosinate in recent years in the US*". Glufosinate-resistant Palmer Amaranth (pigweed) has been confirmed in the USA, in Arkansas, Missouri and Mississippi (Unglesbee, 2021a; Noguera et al., 2022). Noguera et al. (2022) note that if these resistant plants are not controlled by other means, crop productivity will certainly be reduced and the resistance problem to glufosinate (GFA) will escalate. They conclude that "*resistance to herbicides in general, and A. palmeri resistance to multiple herbicides (including GFA) in particular, is a threat to food security and economic sustainability*".

Another aspect of the industry response is the use of other (supposedly beneficial, but likely ineffective) traits as a 'Trojan Horse' to smuggle herbicide tolerant GM traits into new crops and markets. For example, HB4 GM wheat, developed by Bioceres, is tolerant to glufosinate, but is being promoted for its supposedly drought tolerant properties (Paixão, 2020; Little, 2022), despite the industry's poor record at delivering complex traits such as drought tolerance using genetic engineering (Union of Concerned Scientists, 2012). Camelina (a plant also known as 'false flax') with altered oil content, developed by Yield10 Bioscience as a supposedly "low-carbon feedstock oil" for biofuels, has added herbicide tolerant traits, leading the company to claim "*we will be positioned to introduce herbicide tolerant Camelina to a broad range of growers to enable access to acres on a large scale*" (Yield10 Bioscience, 2022). Similarly, in the UK, a GM camelina touted as a means to produce omega 3 fish oils on land is also tolerant to glufosinate (ACRE, 2019). GM maize varieties being trialled for supposedly drought tolerant properties in Africa, as part of the TELA project supported by the Gates Foundation and Bayer, are also being stacked with glyphosate-tolerance in some cases (African Centre for Biodiversity, 2021). These projects are consistent with the industry's awareness that, although RoundUp Ready crops are failing, there may still be opportunities to profit from expanding into new geographic areas and/or new crops before resistant weeds take hold (Green & Siehl, 2021). This PR strategy acts as a distraction from the negative consequences of growing HT GM crops, and as a means to attempt to dump failing HT traits onto new markets.

The environmental impacts of the relevant herbicides are reviewed in Section 7. Environmental and health effects of other herbicides.

6.1 Increasing herbicide rates on RR crops

Since herbicide resistant weeds can, in cases of moderate resistance, still be killed by higher doses of herbicides, biotech companies have developed crops with enhanced tolerance to glyphosate. In 2006, Monsanto introduced RR Flex cotton, which can tolerate higher rates of glyphosate than the original RR cotton (Villar and Freese, 2008). Dun et al. (2014) and Guo et al. (2015) suggest combining the two basic strategies that have been used in glyphosate tolerant crop development - expression of an insensitive form of EPSPS and insertion of a gene that catalyses the inactivation of glyphosate – in order to enhance tolerance in transgenic crops. Guo et al. (2015) report tolerance up to fourfold the label rate in soybean. Simultaneously, growers are advised to increase the application rate and frequency to control weeds in RR crops. Kumar et al. (2018), for example, recommend growers to proactively apply up to four maximum use rates of glyphosate in sugar beet fields where glyphosate resistant kochia is not yet a problem.

6.2 Increasing the herbicide platform used on RR crops

Biotech companies also recommend increasing the herbicide platform used on RR crops. They suggest using multiple modes of action in rotation, and sequences or mixtures, in order to minimise the risk of weed resistance. An agronomist at the University of Minnesota and North Dakota State University, and former Monsanto program lead, proposes controlling tough weeds in sugar beets, such as waterhemp, with pre-emergence soil-applied herbicides, such as metolachlor, followed by applications with the same or other herbicides after crop emergence (Pates, 2015). In the fight against the notorious Palmer amaranth weed, farmers are now encouraged to use pre-emergence herbicides before or during planting, possibly multiple times. BASF sells Zidua Pro, which contains pyroxasulfone, imazethapyr, saflufenacil and 59% other, undisclosed, ingredients for that purpose (Bomgardner, 2019, BASF, 2017). Furthermore, herbicide tank mixes are suggested. Evans et al. (2016), partially supported by funding from Monsanto, study glyphosate resistance in the weed *Amaranthus tuberculatus* using data on A*. tuberculatus* glyphosate resistance frequency, landscape, soil, as well as farm management and weed data from 105 central Illinois, U.S. grain farms. They conclude that tank-mixing of different herbicide modes of action is the best tool to manage resistance in *A. tuberculatus*. They state that rotation of different herbicide modes of action would be less effective, as the GR trait may be maintained in dormant seedbanks and be enriched the next time glyphosate is applied. Nevertheless, the authors conclude that although measures such as herbicide mixing may delay glyphosate resistance or other herbicide resistant weed traits, they are unlikely to prevent them, and long-term weed management will require truly diversified management practices that minimize selection for herbicide resistant traits.

A survey conducted in 17 states in Brazil, reveals that 97% of respondents use tank mixtures, usually with 2 to 5 products at the highest recommended doses (Gazziero 2015). Nevertheless, Brazil has a huge problem with glyphosate resistant weeds as well as cross- and multiple resistances (see Section 3.1.2. Superweeds). In their RR corn guide, Monsanto suggests that farmers in California and Arizona tank mix glyphosate with atrazine, pendimethalin or s-metolachlor for pre-emergence weed control. Of these, atrazine is not approved for use in the EU. For post-emergence weed control, they suggest using foramsulfuron, diflufenzopyr and dicamba, or 2,4-D and dicamba or just 2,4-D in combination with glyphosate. All of those herbicides are also approved in the EU (European Commission, 2016a; Monsanto, 2012a). Monsanto also suggests using soil-acting herbicides, such as flumioxazin, sulfentrazone, acetochlor and pyroxasulfone as part of the RR crop “platform”, in addition to glyphosate-based herbicides, to fight GR weeds in the U.S. EU approval of acetochlor was withdrawn due to a series of risks to human health and the environment and sulfentrazone is not approved in the EU. Neither is pyraxosulfone, which has no history of safe use (PAN UK & GM Freeze, 2013). Flumioxazin has EU approval until 30th June 2016 (European Commission, 2016b). A weed management technical lead with Monsanto Canada also advises farmers to tank mix herbicides in order to apply two or more modes of action to their fields. In 2014, 21 percent of glyphosate used by Western Canadian farmers was already tank mixed with other herbicides (Pratt, 2016a). In tank-mixes, safety levels are calculated for each active ingredient separately. Possible combinatorial, additive or synergistic effects of the joint application of all herbicide active ingredients, let alone insecticides, fungicides or other components, are not assessed and remain unknown (Myers et al., 2016).

In the soybean sector in Argentina, the reality of resistant weeds means farmers have to include more crop rotations, more herbicides and also mechanical and cultural weed control methods (Vivian et al., 2013). In Brazil, other herbicides — such as imazethapyr and imazapic — are frequently applied to reduce the emergence of weeds during the fallow period and/or associated with the herbicide 2,4-D on burndown, about 15-20 days before the sowing (Vivian et al, 2013). To reduce Conyza species competition, which can cause yield losses above 70% for soybean it is recommended to implement winter management by mixing residual herbicides and glyphosate plus 2,4-D.

In Canada, three-way resistance to imazethapyr, atrazine, and glyphosate was confirmed in 80% of the samples of waterhemp seeds collected from 25 locations across Ontario and Quebec in 2016 and 2017 (Benoit et al., 2020).

Duke et al. (2018) report that, “*as GR* [glyphosate-resistant] *weed challenges emerged in US GR crop fields, growers were forced to add alternative herbicides to control glyphosate-resistant weeds. Grower weed control costs tripled, as evidenced by the rapid resurgence of non-glyposate herbicide use in US soybean crops. For example, acifluorfen use rebounded. Paraquat use in soybeans and maize increased, as did imazethapyr and metribuzin use in soybeans*”.

A major problem remains the inadequate examination by regulators of the effects of mixtures of herbicides on human health and the environment (Sprinkle & Payne-Sturges, 2021). In one example, Niedobová et al. (2019a) find synergistic effects of glyphosate formulation herbicide and tank-mixing adjuvants on Pardosa spiders (ground-dwelling wolf spiders) in a laboratory study. In these experiments, Roundup klasik Pro® did not have any effect on the predatory activity of Pardosa spiders, but pure surfactants as well as herbicide-and-surfactants tank mixes significantly decreased predatory activity.

If the EU were to approve the use of RR crops, it might then come under pressure to authorise more herbicides proposed to use with RR crops or re-approve acetochlor which was withdrawn in 2010 for health and environmental reasons (PAN UK & GM Freeze, 2013). Moreover, mixing herbicides would likely increase the quantity of herbicidal compounds required and might thus increase chemical costs for farmers, as well as exposure for growers and applicators and the overall environmental impact. Low-dose application on the other hand can increase the potential for selecting cross-resistance evolution (Evans et al., 2016). Evans et al. (2016) conclude that herbicide mixes may delay evolution of resistance but not prevent it and thus don’t represent a permanent solution.

6.3 Developing new transgenic crops with resistances to additional herbicides

As a further strategy to address the problem of glyphosate resistant weeds, the industry has developed new GM herbicide tolerant (HT) crops which are resistant to additional weedkillers, such as 2,4-D, dicamba, and isoxaflutole. The return to these older, more toxic herbicides is a result of the lack of new herbicide modes of action being commercialised in more than 30 years (Gould et al. 2018). The US Department of Agriculture (USDA) argue that GM maize and soybeans with resistance to multiple herbicides will become the norm in future (Nandula, 2019). GM soybeans and maize with resistance to dicamba and 2,4-D are already on the market, and these are being stacked with existing GM resistance traits (to glyphosate and/or glufosinate) or other herbicides (such as isoxaflutole).

To advocates, new HT crops are a new tool to manage herbicide resistant weeds (by changing to different herbicides with different modes of action): however, they also note that new resistant weeds are already beginning to develop (Brunharo et al., 2022). Benbrook (2018) notes that in the USA, in crop year 2018, around three quarters of the soybean seed offered to farmers expressed the glyphosate-resistance gene, plus either dicamba or 2,4-D resistance genes. Some cultivars planted in 2018 were resistant to five or more herbicides. Moreover, most farmers in the USA and Canada are pushed into planting these next-generation herbicide tolerant GM crops whether they want to or not, because the seed companies release the most popular seeds (for example, bred to have higher yields) only as GM herbicide-tolerant versions in these countries (Benbrook, 2018; Brunharo et al., 2022). This is the so-called ‘transgenic treadmill’, which locks farmers into escalating costs as they are trapped into buying ever more expensive seeds and multiple herbicides to deal with the failure of RR crops (Binimelis et al., 2009; Mortensen et al., 2012).

Monsanto (now owned by Bayer) has developed the herbicide system called the Roundup Ready Xtend Crop System, in which dicamba-tolerant crops can be sprayed with the new Roundup Xtend herbicide that contains dicamba and glyphosate. Dicamba tolerant soybean and cotton were approved by the USDA APHIS in January 2015 (Monsanto, 2012b; Gillam, 2015a). Monsanto has also developed cotton and maize which are tolerant to both glufosinate and dicamba (Monsanto, 2021c, 2015a). Monsanto’s investments of more than US$ 1 billion in a production facility for dicamba, represents a step away from its reliance on glyphosate (Gillam, 2015b). In November 2016, EPA registered Monsanto’s new dicamba formulation XtendiMax for post-emergence applications on soybean and cotton. After the publication of the 2016 decision, two additional post-emergence dicamba herbicides, Engenia (BASF) and FeXapan (Corteva) were approved by EPA. These formulations were registered for post-emergence use as they showed lower volatility when compared to other dicamba formulations. The soybean and cotton seeds were sold commercially prior to these pesticide product registrations (US EPA, 2018a). In 2016, USDA APHIS further deregulated a dicamba and glufosinate tolerant corn variety (AgriPulse, 2016; USDA APHIS, 2016b). In October 2018, EPA extended the registration of the three dicamba herbicides until December 20, 2020 (US EPA, 2018a). A fourth over the-the-top dicamba herbicide (Tavium from Syngenta) was registered by EPA in April 2019, also until December 20, 2020 (US EPA, 2019b). However, in June 2020, the Ninth Circuit (the largest of the thirteen courts of appeals in the USA) vacated the EPA’s approval of three out of these four post-emergence dicamba-based herbicides. In response, weed scientists in the U.S. recommend either increasing application rates and frequencies of glyphosate; adding other post emergence herbicides to glyphosate tank mixes; or switching to another herbicide-tolerant platform (for example Enlist E3, LibertyLink or LL GT27) that rely on other additional active ingredients, such as 2,4-D, isoxaflutole. Others argue that without dicamba there is no option for post-emergence control, since many important weeds already have resistances to glyphosate, ALS-inhibitors or PPO-inhibitors (Unglesbee, 2020a). In October of the same year, EPA however re-registered two of these herbicides again (Rizzuto & Vasquez, 2020). This followed the EPA admitting to omitting scientific evidence on dicamba’s drift risk during the 2018 re-registration process (US EPA, 2021b). See also Section 8.2.1 Dicamba lawsuits.

Dow Agroscience (today Corteva Agriscience), another U.S. company, has developed the herbicide tolerant system called the Enlist Weed Control System. The Enlist Weed Control System includes genetically modified (GM) crops that are tolerant to the broadleaf herbicide Enlist that contains 2,4-D and glyphosate. Farmers growing the crops must also use Dow's new herbicide Enlist Duo that contains 2,4-D and glyphosate because it is meant to minimise drift and volatilisation (Pollack, 2014). In August 2014, USDA APHIS published its final Environmental Impact Statement (EIS), recommending that the 2,4-D tolerant soybean and corn should be fully deregulated (USDA APHIS, 2014b). In September 2014, USDA approved the 2,4-D resistant crops for cultivation (Pollack, 2014; USDA APHIS, 2014). Just one month later, the EPA also approved the herbicide Enlist Duo for use on genetically engineered corn and soybean in 6 states and later in an additional 9 states (US EPA, 2014). In 2017, the EPA amended the registration to allow the use in an additional 19 states and additionally also on genetically engineered cotton tolerant to 2,4-D and glufosinate (US EPA, 2018b). In November 2015, however, the EPA asked the U.S. Court of Appeals for the Ninth Circuit to revoke the approval because it found a patent application from Dow claiming a synergistic effect between glyphosate and 2,4-D, although information provided to the EPA at the time it made its registration decision did not contain this information. This means that the herbicide is potentially more toxic than the agency initially assumed. This was the first time the EPA has ever asked a court to revoke a decision it has made on a pesticide (Pollack, 2015; No. 14-73359, 2015). In January 2016, the federal appellate court however rejected the request (Callahan, 2016). In addition to soybean and corn, genetically engineered 2,4-D tolerant cotton was deregulated in 2015 (USDA APHIS, 2015). Enlist Duo faces its own legal challenges but remains registered for over-the-top use at the time of writing (see Section 8.2.2 2,4-D lawsuit).

The German company Bayer, in collaboration with M.S. Technologies and Mertec LLC (MS Technologies, 2020a; b), has developed genetically modified soybeans that tolerate glyphosate herbicides as well as certain HPPD/Group27 herbicides. The soybeans were approved for cultivation in the US in 2013 (USDA APHIS, 2013). In 2018, the US Department of Agriculture's Animal and Plant Health Inspection Service (USDA APHIS) further approved HPPD/Group27 and glyphosate tolerant cotton developed by Bayer for cultivation in the US (USDA APHIS, 2018). At the same time, Bayer and MS Technologies commercialised LibertyLink® GT27™ soybeans, a stacked trait that is tolerant to glyphosate, glufosinate and isoxaflutole herbicides (ISAAA, 2018). However, no HPPD/Group27 herbicides were allowed to be used on these soybeans (ISAAA, 2018). When Bayer bought the US company Monsanto, they had to sell agricultural businesses and assets worth about $9 billion in the largest antitrust-related divestiture in American antitrust enforcement history (Mangan, 2018). The divestiture also included selling its HPPD/Group27 tolerant crops and corresponding herbicide (then called Balance GT Soybeans and Balance herbicides) to the German chemical company BASF (Unglesbee, 2018). In Spring 2020, the U.S. EPA approved the use of BASF's Alite 27 herbicide, an isoxaflutole herbicide belonging to the class of HPPD inhibitors, on HT soybeans in certain US counties as a new tool to combat so-called "superweeds" (BASF, 2021; Hines, 2020a; US EPA, 2020). Although the herbicide's registration was opened for public comment, it was not listed in the federal register, where the agency generally provides notice of a significant rule change. As a consequence, comments from the public health community and environmental groups were lacking (Hettinger, 2020). The soybean and herbicide combination was expected to be available starting in Spring 2021 and thus farmers would be able to spray the approved glyphosate and isoxaflutole herbicides simultaneously, with potential combinatorial effects to human health and the environment (Reuter, 2015). Previously, the U.S. EPA has determined that isoxaflutole is a likely human carcinogen and prone to drift (US EPA, 1998), which adds to concerns regarding the probable carcinogenicity of glyphosate (ISAAA, 2015; see also Section 5.5.2.1. The WHO's cancer agency classification of glyphosate as probable carcinogen and its consequences). Further common effects, endpoints or modes of action of isoxaflutole and glyphosate include effects on the liver, tumours in liver and thyroid and teratogenic effects (Reuter, 2015).

There are however some restrictions on the use of isoxaflutole. Isoxaflutole is known to persist in the environment and to leach into and accumulate ground- and surface waters. In the USA, it is not allowed to be used in the two biggest soybean-growing states Iowa and Ilinois because of the groundwater heights and the soil types in these states. It is further only allowed in counties without endangered plants that might be growing near fields that could be treated. A big concern is that farmers may not be able to follow the restrictive use conditions of Alite 27, BASF's isoxaflutole herbicide. Applicators for example have to determine how much organic matter is in the soil and how high the water table is beneath their fields (Bomgardner & Erickson, 2020; US EPA, 1998). Although it is classified as a restricted-use pesticide, this highlights that the strategies proposed by the industry to deal with GR weeds, involve the spraying of ever more herbicides.

Other stacked trait crops that are tolerant to three different herbicides include Monsanto's Bollgard II XtendFlex cotton which is tolerant to dicamba, glyphosate and glufosinate and its SmartStax™ Pro x Enlist™ maize which is tolerant to glyphosate, glufosinate and 2,4-D (ISAAA, 2020a; b). In 2019, Monsanto (now Bayer) filed a petition with the USDA for determination of nonregulated status of a genetically engineered corn variety resistant to five active ingredients: glyphosate, glufosinate, dicamba, 2,4-D and quizalofop (Monsanto, 2019). In its application Monsanto says the maize will provide growers with "*an opportunity to delay selection for further resistance to glyphosate and other herbicides that are important in crop production*," and, "*Additionally, dicamba, glufosinate, and 2,4-D individually or in certain combinations provide control of herbicide-resistant weeds, including glyphosate-resistant biotypes of Palmer amaranth (Amaranthus palmeri), marestail (Conyza canadensis), common ragweed (Ambrosia artemisiifolia), giant ragweed (Ambrosia trifida) and waterhemp (Amaranthus tuberculatus)*." Moreover, some of these traits not only confer tolerance to a single active ingredient but to a whole herbicide group. The gene inserted in isoxaflutole tolerant crops, for example, confers tolerance to certain HPPD inhibitors, a group of herbicides that isoxaflutole herbicides belong to, but which also includes other herbicide families such as mesotrione herbicides. According to available literature, LibertyLink® GT27™ soybeans are indeed also tolerant to mesotrione herbicides. The gene inserted in Dow AgroSciences 2,4-D tolerant soybean variety DAS-44406-6 is also tolerant to other phenoxy herbicides. That means farmers could, in theory, add further active ingredients to their weed management (Miyazaki et al., 2019). Miyazaki et al. (2019) raise the concern that manufactures often do not include the full range of herbicides their crops are tolerant to in field trials and animal feeding studies, leading to an insufficient risk assessment of these herbicide tolerant crops. These crops further exacerbate concerns about adverse environmental impacts, pesticide residues in the food chain, and the future evolution of weeds which will become resistant to multiple herbicides (Mortensen et al. 2012).

These herbicide tolerant crops allow farmers to apply additional herbicides such as 2,4-D, dicamba, isoxaflutole or glufosinate during the whole cropping season at high rates, with the risk of detrimental effects to the environment and human health (see Section 7. Environmental and health effects of other herbicides). The use of herbicide mixtures is expected to be commonplace in Roundup Ready® XtendFlex® and Enlist™ technologies, including combinations of glufosinate, glyphosate, dicamba, and 2,4-D (Meyer et al., 2019). Even though the original justification for developing glyphosate tolerant crops was that we would move away from older, less environmentally benign herbicides like 2,4-D and dicamba, the newer HT crop technologies do not even claim to reduce herbicide input. On the contrary, Agrobiotech companies have been advocating herbicide programs that combine current rates of glyphosate with additional rates of dicamba or 2,4-D, respectively (Mortensen et al., 2012). In 2014, USDA APHIS (USDA APHIS, 2014a; b) estimated post-emergence application on HT crops to increase 2,4-D use 200-600% by 2020 and dicamba use 14.3-fold in cotton and 88 -fold in soybeans, respectively. Recent data by the U.S. Geological Survey indeed confirm, that the use of dicamba on soybean and cotton exploded after EPA's registration of post-emergence dicamba herbicides (see Figure 9). While a yearly average of 231,000 pounds of acid equivalent of dicamba had been applied on cotton in 2012 - 2016, almost 2 million pounds of dicamba were applied to post-emergent cotton in 2017. The increase was even more pronounced in soybeans, with a yearly average of 537,000 pounds of acid equivalent of dicamba applied in 2012 – 2016, and almost 8 million pounds applied in 2017 (*National Family Farm Coalition v. USEPA, 2020).* In Minnesota, dicamba sales grew 3-fold between 2015 and 2016 (Minnesota Department of Agriculture, 2020). Kevin Bradley, plant science professor at the University of Missouri, said "*It's safe to say that we've never applied as much of this one herbicide in our history as what we are* now" (Brown, 2020). In Brazil, the herbicide market share of 2,4-D grew from 7.4% in 2009 to 18.2% in 2017 and has become the second most used herbicide after glyphosate (Alcántara de la Cruz et al. 2020). This increase in herbicide sales and application has to be seen in the context of the increasing area being planted to dicamba and 2,4-D tolerant cotton and soybean. According to Wechsler et al. (2019), the adoption rate of dicamba tolerant seeds following their commercialisation in the U.S. was similar to the rate at which glyphosate tolerant varieties were adopted. Soybean acreage planted with dicamba tolerant seeds increased by 43% from 2016 to 2018. In some states, dicamba tolerant seeds amount to as much as 70 – 80% of the total soybean acreage. For cotton, USDA's 2019 Agricultural Resource Management Survey data suggest that farmers also quickly adopted dicamba tolerant seeds, from 0% of cotton acres being planted with dicamba tolerant seeds in 2016 to 69% in 2019. Some cotton producing states already had over 80 percent of cotton acres planted with dicamba tolerant varieties, the highest percentage being in Missouri (88%). In 2018, half of all soybean and cotton acres in the US, about 56 million acres, were planted with Monsanto's dicamba-tolerant trait, up from 27 million acres the year before (Dodson et al., 2021; Gillam, 2020a).

Increasing application of dicamba and other herbicides across expanding areas, and most likely in the same fields in successive years, creates intense and consistent selection pressure for the evolution of herbicide resistance. Moreover, 2,4-D and dicamba are prone to drift (see Section 7. Environmental and health effects of other herbicides) and it has been shown that repeated herbicide drift exposure can rapidly select for weed resistance (Vieira et al. 2020). It seems evident that the introduction of new GM HT crops with additional modes of action is neither a sustainable nor a permanent solution to combat glyphosate resistant weeds. While stacked trait HT crops may delay the evolution of weed resistance, this will probably not last long (Nature, 2014). Comont et al. (2020) show that using herbicide mixtures to combat the evolution of specialist resistance (such as glyphosate resistance) may promote the evolution of a broader, more generalist cross-resistance mechanism. Thus, this industry-led solution will ultimately result in even more herbicide resistant "superweeds".

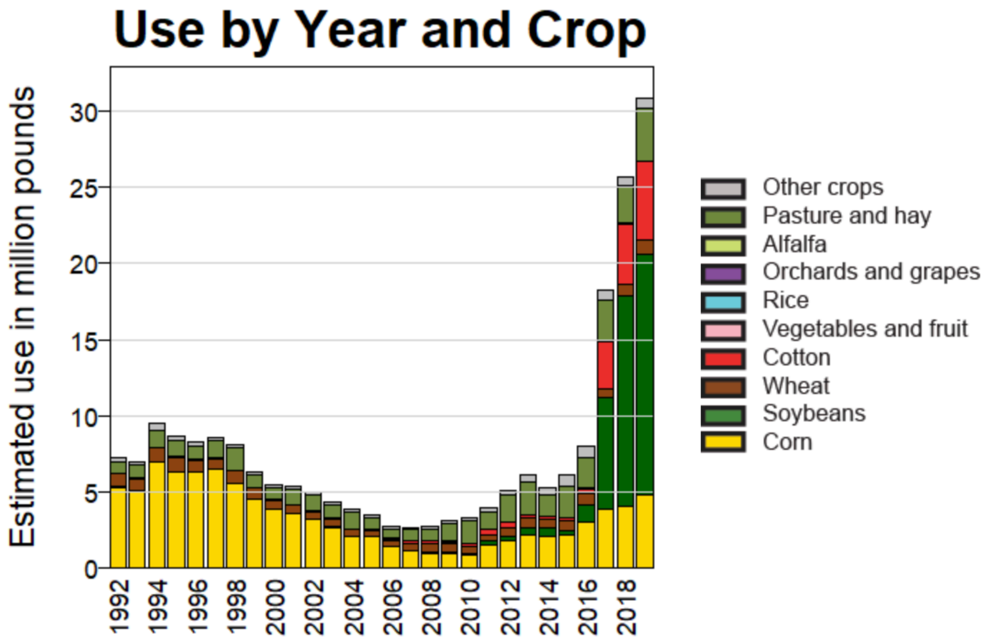

Figure 9. Estimated Agricultural Dicamba use in the U.S. Credit: U.S. Geological Survey Department of the Interior/USGS. This graph is made with low-end estimates and may underestimate actual dicamba use in the U.S. URL: http://water.usgs.gov/nawqa/pnsp/usage/maps/show_map.php?year=2017&map=DICAMBA&hilo=L&disp=Dicamba

The agrochemical companies have argued that resistant weeds will not be a problem because, despite decades of use, only very few weed species have evolved resistance against synthetic auxin herbicides and because multiple independent mutations were necessary to confer resistance. The industry further argues that by planting cultivars with stacked traits, the relevant pesticides would be applied in combination or rotation with glyphosate and thus two distinct herbicide modes of action would need to be overcome by weeds (Mortensen et al., 2012). Weeds with resistances to multiple herbicide modes of action are, however, widely known today (Heap, 2020; Mortensen et al., 2012). Moreover, the new HT crops with resistances against glyphosate and 2,4-D or dicamba, respectively were mainly commercialised to provide farmers that were already struggling with glyphosate resistant weeds with an alternative. At their farms, the probability of selecting for cross-resistance is not the product of two independent mutations but much closer to the probability of finding a resistance mutation to the new mode of action only (Mortensen et al., 2012). In 2019, USDA confirmed that more dicamba tolerant seeds are planted in states with the most glyphosate resistant weeds (Wechsler et al., 2019).

In a field experiment, Mazon et al. (2022) aim to evaluate herbicides to Enlist™ (2,4-D and glyphosate) volunteer corn control and their effects on plant development, crop yield, and physiological seed quality of Enlist™ soybean. They note that the occurrence of volunteer corn tolerant to 2,4-D and FOPs (ryloxyphenoxypropionates) can become a significant weed on soybean cropping systems, affecting the crop yield and reducing seed quality. They test other herbicides that may be used to control resistant volunteers, finding that many options produce insufficient control or damage the soybeans.

As of December 2021, 41 weed species are known to be resistant to synthetic auxin herbicides many of which have cross-resistances to other herbicide groups (Heap, 2021a). Of these, 9 weed species are resistant to dicamba (Heap, 2021b). Recently, the first case of dicamba resistant

Palmer Amaranth, directly resulting from the dicamba tolerant cropping system, was found in Tennessee (Unglesbee, 2020b). Moreover, trials in greenhouses and reports from weed scientists suggest that resistance to dicamba could develop rapidly (Bennett, 2017). Geddes et al (2021) confirm the first cases of kochia (*Bassia scoparia*) in Manitoba with dicamba resistance alone and in combination with glyphosate resistance. In summer 2020, more farmers and scientists noted a decline in the efficacy of dicamba in the USA, particularly against two of the most notorious weeds, Palmer amaranth and tall waterhemp. Palmer amaranth seemingly recovers quicker from dicamba application than ever before, and some samples survive 2.5 times the labelled rate of dicamba herbicides. 14% of waterhemp samples from four U.S. states survived a full rate of dicamba herbicides, and for some of those a second full rate of dicamba also did not provide full control (Unglesbee, 2020b). As of December 2021, 25 weeds resistant to 2,4-D are known, many of which have cross resistances to other herbicides. These also include Palmer amaranth and tall waterhemp (Heap, 2021c). The first 2,4-D resistant tall waterhemp population had already been found in 2009 in Nebraska. According Crespo et al. (2017) this population has at least 30-fold resistance to 2,4-D, compared to susceptible populations and shows cross-resistances to other auxin herbicides, ALS inhibitors, and photosystem II inhibitors. Accelerated 2,4-D metabolism has been reported as a contributing factor for the 2,4-D resistance in this population (Figueiredo et al. 2018). The first 2,4-D resistant Palmer amaranth was reported in 2015 in Kansas. Kumar et al, (2019) confirmed the population to have 3.2-fold resistance to 2,4-D as well as cross-resistance to many other herbicides including 11.8-fold resistance to glyphosate. Mithilda Jugulam, weed physiology professor at Kansas State University reports that a population of Palmer amaranth growing in the university's study fields survived 18 times the labelled rate of 2,4-D (Bomgardner, 2019). Moreover, greenhouse tests show that some waterhemp populations can survive labelled rates of both dicamba and 2,4-D (Unglesbee, 2020c).

For HPPD inhibitors, resistances to two of the most notorious weeds, Palmer amaranth and tall waterhemp, had already been documented in the U.S. in 2009, long before the commercialisation of HPPD tolerant crops. These often have cross-resistances to other herbicide groups. For example, in 2015, a population of Palmer amaranth with resistance to mesotrione in addition to 2,4-D, atrazine, chlorsufuron and glyphosate was reported in Iowa. Another example is a population of tall water hemp detected in 2016 in Illinois, resistant to mesotrione and tembotrione as well as 2,4-D, acifluorfen, atrazine, chlorimuron-ethyl, fomesafen, imazethapyr and lactofen (Heap, 2020).

Cross-resistance to different herbicide modes of action is indeed widespread. A Palmer amaranth biotype from Connecticut was reported to be 10-fold resistant to glyphosate when compared to a susceptible biotype. The biotype was also highly resistant to ALS inhibitors including imazaquin, chlorimuron-ethyl, halosulfuron-methyl and sulfometuron-methyl. The authors recommend growers to *"…use all available weed control tactics, including the use of effective PRE and alternative POST herbicides…"* in order to control this biotype (Aulakh et al. 2021). Italian ryegrass populations from California were shown to be resistant to at least three modes of action, namely glyphosate, ACCase-inhibiting herbicides and paraquat (Tehranchian et al. 2018). In Ontario, Canada, GR horseweed has spread across all 30 counties, the majority of which have multiple-resistant populations. Management of glyphosate and ALS inhibitor-resistant *C. canadensis* requires tank-mixing of three herbicide modes of action (glyphosate, metribuzin and saflufenacil) or the cultivation of newer HT crops (Beckie, 2018). Spaunhorst et al. (2019) showed that Palmer amaranth can survive two- and three-way herbicide mixtures of glyphosate, chlorimuron-ethyl (ALS inhibitor), and fomesafen (PPO inhibitor) that are commonly applied to control Palmer amaranth. In Argentina, an *Amaranthus hybridus* population with multiple resistance to 2,4-D, dicamba, and glyphosate was reported in 2018 (Dellaferrera et al. 2018). In 2020, a population of *Amaranthus hybridus* found in a GR soybean field, exhibited up to 93 and 38-fold higher glyphosate and imazamox resistance, respectively, and showed moderate to high resistance to other ALS-inhibiting herbicides (García et al. 2020). In Brazil, multiple resistance to glyphosate and ALS inhibitors has been identified in *A. palmeri* (Küpper et al. 2017). There is also evidence that some herbicide mixtures can act antagonistically, resulting in less control than would be expected based on the performance of the individual herbicides, which also has implications for weed resistance evolution (Fernández-Escalada et al., 2019; Meyer & Norsworthy, 2019; Meyer et al., 2020; Perkins et al., 2021).

As described above, this circular process of the evolution of resistant weeds and the subsequent development of the next generation of transgenic crops, that allow for an intensified use of herbicides and thus favour the emergence of another round of resistant weeds etc. is called the transgenic-herbicide treadmill (Binimelis et al., 2009; Mortensen et al., 2012). One author describes the introduction of dicamba resistant crops, in response to glyphosate resistant weeds created by the RR GM cropping system, as a "chemical arms race" (Elmore, 2022). Given that the discovery and development of new herbicide active ingredients has slowed dramatically in the last decades (Pratt, 2016a), it seems not only unsustainable but also unwise to risk herbicide resistance to accelerate by allowing new HT crops to be cultivated on a large scale.

6.4 Developing genome edited HT crops

The biotech industry is also investing in R&D on herbicide tolerant crops using newer genetic engineering techniques known as 'gene editing' or 'genome editing' techniques. For example, US company Cibus states "*The approval of gene editing technologies will open up one of the biggest opportunities in agriculture: a new generation of Crop Protection Traits associated with herbicide tolerant that will be able address:*

- *The large number of countries that have not had the benefit of the GMO traits for herbicide tolerance*
- *The large number of crops that have not had the benefit of the GMO traits for herbicide tolerance*
- *Herbicide tolerance traits for the new generation of herbicides*" (Cibus 2022).

Friends of the Earth Europe has highlighted how the business model of many biotech corporations is geared to selling herbicide-tolerant seeds together with the associated herbicides (FoEE, 2022). According to this report, 6 out of 16 gene edited plants listed by the European Joint Research Centre (JRC) as close to commercialisation are herbicide-tolerant (although it remains unclear whether these will be commercialised in practice). At the same time, claims of developing more sustainable crop traits using gene editing have been questioned as lacking credibility (Hüdig et al., 2022).

The genome editing process involves the use of biological molecules (enzymes) which cut the DNA and various mechanisms which then repair it. These techniques include ODM (oligonucleotide directed mutagenesis), CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats), TALENs (Transcription activator-like effector nuclease) or ZNF (zinc-finger nucleases). While these genome editing techniques facilitate the creation of small random insertions or deletions (InDels) at pre-defined sites, it is still difficult to achieve targeted mutagenesis in plants, partly because the lack of control over the DNA repair process. Homology-directed repair coupled with a DNA repair template containing the desired sequence, can lead to targeted mutagenesis. However, there is an intrinsic lower frequency of HDR in plant cells, compared to another type of DNA repair called non-homologous end-joining (NHEJ). Another difficulty is that HDR requires the synchronised delivery of a sufficient amount of the DNA repair template, which remains challenging to achieve and may not work in all species (Ali et al., 2020; Endo et al., 2016; Butt et al., 2017; Li et al. 2020a; Shimatani et al., 2017; Sun et al., 2016; Xu et al., 2020). Therefore, a lot of expectation now lies on novel base-editing and prime-editing techniques, that allow for targeted single nucleotide substitutions and in the case of prime editing also predefined transversions, insertions and deletions, without the need for double strand breaks in the DNA or the use of template DNA: *"…base editing has shown enormous potential for the development of HR in various crop plants*" (Hussain et al., 2021). Editing efficiency of base- and prime editing varies by target site and decreases with increasing length of insertion or deletion (Lin et al., 2020; Xu et al., 2020). Tang et al. (2020) conclude that still "*significant improvements are required to develop efficient plant PEs [prime editors] before prime editing reaches prime time in plants*".

The GM HT crops described so far in this report, which dominate the market, use a method of genetic engineering known as transgenesis, which involves transferring new DNA from another species into plant cells (known as 'transgenes'). Gene editing techniques can also be used to insert DNA from another species. For example, the first application for EU approval of a gene-edited (CRISPR) plant is for a maize that is tolerant to glufosinate herbicide and produces an insecticidal toxin (FoEE, 2022). This GM maize (developed by Pioneer Hi-Bred International, which is owned by Corteva Agriscience) uses a combination of methods, including gene editing, to insert cassettes which express the desired proteins, and is therefore transgenic (Pioneer Hi-Bred International, 2020). Similarly, maize has been edited, using the zinc finger nuclease (ZFN) gene editing technique, to include a modified version of the PAT gene (originally from bacteria) which confers tolerance to glufosinate (Shukla et al., 2009). However, not all gene edited plants are transgenic.

A subset of gene edited plants (not clearly defined, but those which do not use a template to insert new transgenes, and probably from which any transgenes used in the gene editing process have been removed) are sometimes referred to as 'transgene-free', and controversial steps are being taken to deregulate some or all of this subset of gene edited crops in several countries (e.g. in the USA, Japan and Canada, with new proposals in the UK, and options being debated in the EU). There is commercial interest in this approach because environmental risk assessments and food labelling may not be required before some gene edited plants can be marketed. Definitions and proposals for deregulation vary in different countries, but, in essence, this subset of gene editing techniques rely on mutating the crop's own genes and not on introducing foreign genes into the genome of a crop, as is the case with transgenesis, although it should be noted that foreign genes are sometimes introduced in the editing process (and these may or may not be removed later through breeding).

Enzymes originating from bacteria that inactivate or degrade herbicides and that are used in commercialised transgenic crops today, cannot be used in non-transgenic genome editing, as the relevant genes do not exist within the plant. These include, *inter alia*, enzymes such as AAD-1 that confers resistance to 2,4-D, DMO that confers resistance to dicamba and PAT and BAR that confer glufosinate resistance. Instead, to generate so-called 'transgene-free' genome edited herbicide tolerant crops, the strategy is to mutate plant enzymes that are targeted by different herbicides and make them insensitive to the corresponding herbicides (Gosavi et al., 2022). These include EPSPS, the enzyme targeted by glyphosate-based herbicides; ALS (also known as AHAS) that is inhibited by five families of herbicides including sulfonylureas (SU), imidazolinone (IMI), triazolopyrimidine, pyrimidinyl-benzoate and sufonyl-aminocabonyl-triazolinone; ACCase which is responsible for catalyzing the initial step of the biosynthesis of fatty acid; and HPPD that is inhibited by herbicides such as isoxaflutole and mesotrione (Han & Kim, 2019; Hussain et al., 2021; Sherwani, Arif, & Khan, 2015). Newer 'base editing' and 'prime editing' techniques can be used to mutate DNA without the need for donor DNA (Gosavi et al., 2022). Crops that have been gene edited to include herbicide tolerant traits remain at the experimental stage, but include wheat, rice, maize, soybean, potato, rapeseed (canola), flax, cassava, watermelon and tomato (Gosavi et al., 2022).

For HPPD, there is almost no report of plant mutations for herbicide resistance (Han & Kim, 2019). Only the transgenic SYHT0H2 soybean event (isoxaflutole and mesotrione tolerance) is based on a modified oat HPPD enzyme (*Avena sativa* 339 HPPD, missing one amino acid, A111). All other HPPD resistant crop traits are based on a modified bacterial HPPD enzyme (HPPDPF W336). Hawkes et al. (2019) performed targeted mutagenesis of the oat HPPD in tobacco, obtaining a quadruple mutant (VIARIELM) with about 16-fold elevated tolerance to mesotrione compared to the wild-type and without loss of catalytic activity. Maeda et al. (2019) reported a candidate rice gene that could be useful for developing β-triketone tolerant crops.

Research on ACCase inhibitor resistant genome edited plants has been conducted in rice and wheat (Li, C. et al, 2018; 2020; Liu et al., 2020b; Xu et al., 2020; Zhang et al. 2019). All these studies have used base-editing and prime-editing approaches, respectively. This shows, that the focus of new genetic engineering approaches to HT crops primarily lies on point mutations, which may be overcome relatively quickly by weeds (see below). Liu et al. (2020b) further demonstrate that some resistance mutations exhibit fitness costs in crops plants, such as growth retardation and sterility.

There are not many site mutations reported on EPSPS that confer resistance to glyphosate (Han & Kim, 2019). The Donald Danforth Plant Science Center has conducted work on glyphosate resistant cassava by means of CRISPR/Cas9. The work was supported by a grant from the Bill & Melinda Gates Foundation (Hummel et al., 2018). The company Cibus has worked on glyphosate tolerant flax (Sauer et al., 2016) with their Rapid Trait Development System™ (RTDS). In 2010, Cibus and the Flax Council of Canada started to collaborate in developing the glyphosate tolerant variety of flax (Flax Council of Canada, 2016). Cibus had originally announced the HT system would come to the market in 2015 (Pratt, 2014b). In 2014 however, only a few weeks after having received $3 million from the Canadian government to invest in the project, the Flax Council of Canada decided to withdraw its funding agreement because Cibus, "...was unable to meet certain technical thresholds for the project...". The Council, which was to pay $5.5 million to Cibus, had at this point already invested $2.86 million in the project. Don Kerr, then president of the Flax Council, stated "*We didn't see that putting more money towards it at that point was going to be beneficial*." (Government of Canada, 2014; Pratt, 2014b). The Flax Council remained supportive of the project (Pratt 2016b). In 2016, commercialisation was announced for 2019 (U.S.) and 2020 (Canada) (Pratt, 2016c). In 2018, these dates were postponed to 2020 (U.S.) and 2021 (Canada) (Gelinsky, 2018). As of 2021 however, the flax has disappeared from Cibus' development pipeline. At the same time, Cibus still claimed that traits produced with their RTDS System would take fewer than 5 years to reach the market and cost less than $10 million (Cibus, 2021a), which has proven to not be the case.

Research on glyphosate tolerant crops has further been conducted in chilli pepper (Ortega et al., 2018), oilseed rape (Wang et al., 2021) and rice (Li et al., 2016b,c; 2020; Wang, et al., 2015; 2019). According to Hummel et al. (2018), glyphosate concentrations used by Sauer et al. (2016) and Li et al. (2016b) to test glyphosate tolerance at the whole plant level, were too low to determine whether these plants would be tolerant to glyphosate at field rates. Most of these genome editing attempts to render EPSPS less sensitive to glyphosate aim at generating a double site mutation such as TIPS or TIPA, since double mutants have been shown to exhibit a higher glyphosate tolerance than single mutants (Han & Kim, 2019; Moehs et al., 2020; Yu et al. 2015). Li et al. (2020b), aimed to introduce a TIAVPS triple amino acid that has been previously reported in *Amaranthus hybridus* (see Section 3.1.2.2. Causes and Mechanisms for Glyphosate resistant weeds) by means of prime editing and an editing efficiency of 2.2%. Wang et al., 2021, inserted a five amino acid substitution (LFGAAGMCRL) along with the double TIPS mutation. Although glyphosate tolerance was confirmed at the whole plant level, the authors expected the tolerance level to be higher.

By far most research and development on genome edited herbicide resistant crops has been done on ALS inhibitor tolerant crops, as there are many reports of plant mutations that result in resistance to ALS inhibitors, some of which confer cross-resistance to the different families of ALS-inhibiting herbicides (Han & Kim, 2019; Tan et al., 2005). The resistances are mostly due to single amino acid substitutions. Most research on genome edited ALS resistant genome edited crops has been conducted in rice (Ali et al., 2020; Butt et al., 2017; 2020; Endo et al., 2016; Hua et al., 2020; Kuang et al., 2020; Li et al., 2016b; Li et al., 2020c; Okuzaki and Toriyama, 2004; Shimatani et al., 2018; Sun et al., 2016; Wang et al., 2019; Wang et al. 2020; Zhang et al., 2021b). However, there is no commercial outcome from this research to date. Research on ALS tolerance by means of new genetic engineering techniques is also being conducted in wheat (Zhang et al., 2019; Zong et al., 2018), maize (Li et al., 2019), soybean (Kang et al., 2019), oilseed rape (Kang et al,, 2019; Wu et al., 2020), watermelon (Tian et al., 2018) and tomato and potato (Butler et al., 2016; Veillet et al. 2019). No soybeans harbouring ALS resistance mutations have been generated so far (Dong et al., 2021; Kang et al., 2019). Pioneer Hi-Bred International (now Corteva) has for example been working on ALS herbicide tolerant maize using ODM (Zhu et al., 1999; 2000). A single point mutation (S621N) conferred resistance to the imidazolinone herbicide family (Zhu et al., 2000). DuPont Pioneer (now Corteva), on the other hand, made initial attempts to use CRISPR/Cas9 to develop chlorsulfuron resistant maize and soybeans. The resistance is based on a single amino acid change (P165S in the case of maize and P178S in the case of soybean) (Li et al., 2015; Svitashev et al., 2015; 2016). However, the success rate was not high (Han & Kim, 2019).

The company Cibus has developed a sulfonylurea (SU) herbicide tolerant canola supposedly by ODM[4] which they tried to commercialise and market under the trade name Falco™. Cibus originally wanted to launch the canola as early as 2007 (Cookson, 2006). In 2010, founder and former CEO Keith Walker claimed they were going to launch the SU canola in the coming weeks in California and North Dakota (Bigelow, 2010). In 2016 they were however still struggling with yield and quality issues (Cross, 2016). Although the Cibus canola traits were already approved in Canada by 2013, the canola still hadn't received the required varietal registration: this was a problem because, "…*the product's oil content is lower than the minimum threshold of the Canadian canola quality standard*" (Danielson & Watters, 2017). In 2018, Cibus raised $70 million to support the SU canola commercialisation (Einstein-Curtis, 2018). They tried to commercialise and market the canola under the trade name Falco™ with the complementary herbicide Draft® from Rotam North America. The active ingredients of Draft are Thifensulfuron-Methyl and Tribenuron-Methyl (both herbicides from the family of sulfonylureas). Cibus and Rotam recommended using the Falco canola plus Draft herbicide growing system in rotation with glyphosate tolerant crops in order to manage glyphosate resistant volunteer weeds the following year (Cibus, 2019a; Rotam, 2019). However, apart from Common Ragweed, Draft does not control the most widespread and most economically damaging glyphosate resistant weeds, such as Palmer Amaranth, Tall waterhemp and Canadian horseweedo (Rotam, n.d.). Furthermore, Cibus and Rotam do not address the likelihood of cross resistance arising, which is relevant as glyphosate and ALS resistant weeds are both widespread. Taken together, it was very questionable from the start whether the Falco-Draft system will help farmers to better manage their weeds, even in the short term. The new HT cropping system also failed commercially. Despite big plans to introduce the SU canola in China, Europe, and Australia (Bigelow, 2017), as of 2021, Cibus does not mention the Falco brand anymore on their website and the Falco seed website has been made private. Furthermore, the website of Valley Oils Partners LLC, a company funded by Cibus, Rotam and Seleay & Co. which was licensed to sell Cibus' products (Cibus, 2019b), has meanwhile disappeared.

ALS-inhibitor resistant crops are nothing new. Development of conventional imidazolinone tolerant maize began as early as 1982 and commercialisation started in 1992, first as IMI corn, later under the brand name Clearfield. Imidazolinone tolerant canola was first marketed in 1995 as Smart canola and later also under the brand name Clearfield. Imidazolinone tolerant rice and wheat varieties were first marketed in 2001. Clearfield sunflowers were first commercialised in the USA, Argentina and Turkey in 2003 (Tan et al., 2005). Clearfield is marketed by BASF. BASF also markets a transgenic soybean, tolerant to imidazolinones: CV-127-9 soy authorised for food and feed in the EU since 2015 (ISAAA, 2019b). There is, furthermore, a commercial transgenic maize by Pioneer Hi-Bred: 98140, that is tolerant to imidazolinones and cultivated in the US, Canada and Argentina (ISAAA, 2013). Bottero et al. (2022) present the first report on base editing in alfalfa,

[4] It has also been suggested that the tolerance has in fact been achieved spontaneously and not due to the genome editing: "The petitioner hypothesized that the PM2 mutation was the result of a spontaneous somaclonal variation that occurred during the tissue culture process, and not due to the specific oligonucleotide used in the RTDS protocol." http://www.hc-sc.gc.ca/fn-an/gmf-agm/appro/canola-5715-eng.php

creating gene edited alfalfa with tolerance to both sulfonylurea- and imidazolinone-type herbicides. Given that ALS inhibitor resistant crops have been around for more than 20 years, it is questionable whether the investment in R&D of genome edited ALS inhibitor resistant crops makes sense, especially when taking into account current experience with herbicide resistant weed development. In Brazil, where Clearfield rice has been grown, the main problems is the rapid evolution of IMI-resistant weedy rice and the evolution of resistance in grasses (Echinochloa species) and other weeds. Bourdineaud (2020) reviews the toxicity of sulfonylureas and imidazolinones and documents evidence of adverse effects, especially in invertebrates, amphibians and fish.

In the case of glyphosate, a single amino acid substitution in the target gene (EPSPS) (P106S) was enough to confer resistance to glyphosate in different weeds (See for example Baerson et al., 2002; Ng et al., 2003; Perez-Jones et al., 2005; Preston et al., 2009; Wakelin & Preston, 2006; Zhou et al., 2006). As noted above, there are many more single point mutations that confer resistance to ALS inhibitors compared to glyphosate. This does not only make it easier to engineer ALS-tolerant crops by means of genome editing, but also for weeds to evolve resistance. According to Heap & Duke (2018), the initial frequency of glyphosate tolerant weeds is 10 times or more lower than of ALS inhibitor resistant weeds. Having seen how quickly glyphosate resistant weeds became a problem after the introduction of glyphosate resistant GM crops, and the associated increased selection pressure for glyphosate resistance, it is highly questionable whether it is useful to develop ALS resistant crops, when the ALS enzyme is known to be highly prone to spontaneous mutations and weeds are likely to develop resistance even quicker than in the case of glyphosate. Moreover, ALS inhibitor resistant weeds are already common. As of December 2021, the International Survey of Herbicide Resistant Weeds lists 169 weeds with resistances to ALS inhibitors (Heap, 2021d).

More recently Liu et al. (2021b) inserted a point mutation in the rice gene *OSTubA2* (M268T) that confers resistance to at least two dinitroaniline herbicides (pendimethalin and trifluralin). This mutation was first shown by Yamamoto et al. (1998) in resistant goosegrass (*Eleusine indica*). Dinitroaniline herbicides belong to the Microtubule Assembly Inhibitors. Compared to EPSP synthase inhibitors and ALS inhibitors, evolution of weed resistance to this is a mode of action has been relatively slow, although different target-site as well as non-target-site resistances to these herbicides have been reported in at least seven weed species, including *Amaranthus palmeri* (Chen et al., 2021; Liu et al., 2021a). Since the inserted tolerance is based on a single point mutation, it is to be expected, based on past experience, that weeds could overcome the resistance relatively quickly were they to experience more selection pressure due to increased herbicide use. Chen et al. (2021) state: "*However, dinitroaniline herbicide resistance evolution in weeds should not be underestimated, especially in crops-pollination weed species with high levels of genetic diversity."* Moreover, the brief communication of Liu et al. does not make it possible to draw any conclusions on the potential commercial value of the mutation. Almost 30 years ago, a patent for the production of trifluralin-resistant crops, based on a modified tubulin, was filed and no commercial applications have come of it (Dekker & Duke, 1995).

Another issue is that of gene flow to weedy relatives of crop plants. Since its initial commercialisation, Clearfield rice has been cultivated in several countries in North America, Latin America, Asia and Europe with substantial crop acreage. Most countries have incorporated IMI-resistance to their respective local rice varieties. In cultivated rice, weedy rice is one of the most difficult weeds to control. Since cultivated rice and weedy rice belong to the same species, they are also both killed by the same herbicides. It is thus attractive to cultivate IMI tolerant rice in order to selectively control weedy rice with imidazolinone herbicides. However, since they belong to the same species, there is a high danger of gene flow between the cultivated rice and weedy rice (or other wild relatives). This could ultimately lead to the spread of imidazolinone resistant weedy rice and create an even more difficult to control weed. In fact, just a few years after the commercialisation of Clearfield rice (in some cases only one year after planting), gene flow to weedy rice has been reported in the US, Brazil, Colombia, Costa Rica, Italy and Uruguay (Sudianto et al., 2013). Another possibility is that resistant weedy rice could evolve through spontaneous mutations in the field favoured by the selection pressure due to the continuous exposure to IMI herbicides. This may happen within a short period of time since the ALS enzyme is highly prone to spontaneous mutations. This problem is most likely higher in topical areas with no killing frost and with two cropping seasons of rice per year. The evolution of IMI-HR weedy rice has already led to more complications in managing weedy rice in some countries. In Costa Rica, this has even led to the withdrawal of Clearfield rice. Another concern is that IMI herbicide residues could injure the rotational crops (Gressel & Valverde, 2009; Tan et al. 2005; Sudianto et al., 2013).

Apart from the SU tolerant canola and the glyphosate tolerant flax mentioned above, Cibus has worked on herbicide tolerant rice, corn, potato and wheat. As of November 2019, these crops were in the ‘Trait Development’, ‘Trait Validation’ or “Crop Platform Development” phase, respectively (Cibus, 2019c). Three years later, none of these crops have been commercialised yet and potato is not in their development pipeline anymore. Their focus currently lies on soybean, canola and rice. Cibus claims to be working with three different herbicides but does not disclose which ones. Currently they are conducting greenhouse and field trials with these herbicides (Cibus, 2021b). Cibus originally expected to market the herbicide tolerant rice as early as 2008 (Cookson, 2006). By 2018, this date had been postponed to 2020-2023 (Gelinsky, 2018). At the time of writing, Cibus no longer made predictions about when the rice will be ready for commercialisation (Cibus, 2021b). The reasons why the rice is not on the market yet are unclear. In 2022, Cibus’ website stated: “*Our goal is a whole new generation of herbicide traits across the major crop platforms: Soybean, Canola, Rice, Wheat and Corn. Our initial focus is soybean, canola and rice. Currently we are working with three different herbicides. We have had successful greenhouse trials with two of the herbicides and successful field trials with one herbicide. We are expecting several more greenhouse and field trials in 2021 and 2022*” (Cibus, 2022).

Another gene editing company that has been developing herbicide tolerant crops (with TALEN) is Calyxt. Calyxt has had several different herbicide tolerant crops in the product pipeline, including alfalfa, canola, soybean and wheat (Calyxt, 2017a). Since May 2019, these crops have, however, disappeared from the product pipeline without explanation (Calyxt, 2019). In September 2017, Calyxt reported that its herbicide resistant wheat had advanced to phase 1 of their production pipeline, saying: “*Canola and wheat represent major growth opportunities for the Company, and we look forward to continuing along the path of bringing these product candidates to market in a time- and cost-efficient manner.*” (Calyxt, 2017b). The other herbicide tolerant crops had still been at the discovery stage. It is not clear why these crops disappeared from the pipeline, nor what resistances they would have had. However, none of these crops had been submitted to a “Am I Regulated Under 7 CFR part 340?” inquiry at the USDA (USDA APHIS, 2020), suggesting that it was not due to regulatory issues, but rather that they weren’t developed far enough to consider commercialisation yet.

In conclusion, non-transgenic genome editing of herbicide resistant crops relies on mutating essential plant enzymes in order to render them resistant to the corresponding herbicide. This restricts research and development, with most research being conducted on ALS inhibitor and glyphosate herbicide tolerance, both of which are nothing new. The hope is to use ALS inhibitors to effectively combat glyphosate tolerant volunteer crops and weeds. However, conventional ALS tolerant crops have long been commercialised. This shows that novel techniques are used to pursue the same decades-old approach. Given that the inserted mutations are often based on single amino acid substitutions, that the ALS enzyme is highly prone to spontaneous mutations and that there are already almost 170 ALS herbicide tolerant weeds known today, it seems evident that this approach is not solution but will likely increase today’s problem with weed resistance.

The problems associated with existing HT GM crops will not be avoided by using gene editing techniques, since all these experimental crops are genetically engineered to withstand blanket spraying with the associated herbicides.

This chapter illustrates how all strategies proposed by the industry to deal with GR weeds, involve spraying of even more herbicides. Bloomberg Intelligence estimates seed and crop protection products to reach U.S. $2.9 billion by 2020 and U.S. $5.9 billion in 2022 (Allington, 2020). The long-term consequences of such a simple and supposedly cheap short-term solution may indeed become very expensive. Mortensen et al. (2012) argue that instead new policies are needed to promote integrated approaches. Pursuing the industry approach will not only lead to more herbicide resistant weeds and increase risks to the environment and human health, but also to a decline in the science and practice of integrated weed management.

7. Environmental and health effects of other herbicides

This section includes a brief review of the health and environmental effects associated with herbicide tolerant GM crops, other than glyphosate. Glufosinate-tolerant crops were commercialised soon after RoundUp Ready crops, but were never a large part of the market. However, market share has grown due to the spread of glyphosate-resistant weeds (Duke et al., 2018). Newer GM crops, tolerant to multiple herbicdes including dicamba and 2,4-D, have been commercialised as part of the industry's response to glyphosate-resistant weeds (See Section 6. Industry response). Evidence regarding the effects of some of these herbicides on health and the environment is discussed below.

It should be noted that combinations of herbicides can have synergistic effects (i.e. cause greater harm than expected when they are mixed). For example, a recent study has found that the mixture of glyphosate with 2,4-D has a synergistic genotoxic effect on DNA (Congur, 2021). An earlier study found that 2,4-D and glyphosate may also have a small synergistic effect on earthworms (Lazurick et al., 2017). Some additional evidence regarding mixtures of herbicides is discussed in Section 4.3.1.2. Impact of multiple environmental pollutants on amphibians, and in Section 6.2 Increasing the herbicide platform used on RR crops. As noted above, regulators do not take account of the effects of mixtures of herbicides on human health and the environment (Sprinkle & Payne-Sturges, 2021).

7.1 Glufosinate

7.1.1 Health effects

PAN international lists glufosinate as highly hazardous pesticide (PAN International, 2019). In the EU glufosinate is classified as a known or presumed reproductive toxicant according to Regulation 1272/2008/EC and does thus not meet the requirements for authorisation under EU Regulation 1107/2009. In the EU, glufosinate is no longer approved in agricultural production since 31st July 2018 after Bayer withdrew its application for renewal of approval in December 2017 (EFSA, 2017; European Commission, n.d.; Foodwatch, 2018).

Glufosinate targets glutamine synthetase (GS) which is present not only in plants but also in animals (Meister, 1974). GS is ubiquitous in vertebrate brains and plays an important role in the metabolic regulation of glutamate, a well-known excitatory brain neurotransmitter (Calas et al., 2008). It is well documented that acute accidental or suicidal glufosinate poisoning leads to various neurological complications in humans including convulsions and memory loss (Cha et al., 2017; Hirose et al., 1999; Tanaka et al., 1998; Watanabe & Sano, 1998). Glufosinate has also been demonstrated to be embryotoxic in vitro at 10µg/ml, causing neuroepithelial apoptosis, morphological defects, growth retardation and death in mouse embryos (Watanabe & Iwase, 1996; Watanabe, 1997). Moreover, chronic exposure at low doses of glufosinate ammonium has also been demonstrated to lead to various neurotoxic effects in mammals (Calas et al., 2008; Feat-Vetel et al., 2018; Meme et al., 2009). Laugeray et al. (2014) and Herzine et al. (2016) show that low dose perinatal glufosinate exposure (many times below the EPA approved dose) disturbs brain development and leads to behavioural changes in mice reminiscent of autism spectrum disorder-like symptoms. Perinatal exposure to glufosinate may be of particular importance as the blood-brain barrier is not developed sufficiently in embryos and foetuses and the developing brain is more vulnerable to injuries caused by toxins. The authors also highlight that studies using higher doses of glufosinate may not be able to predict the effects at low doses. In that regard, it is important to note that testing early-life exposure to low doses of pesticides is not usually required for regulatory approval of pesticides (Herzine et al., 2016; Laugeray et al., 2014). Laugeray et al. (2014) also suggest that the current no-observed-adverse-effect level (NOAEL) for glufosinate ammonium must be revised. Dong et al. (2020) find that prenatal exposure to glufosinate ammonium leads to neurobehavioral abnormalities in mice. They observed reduced locomotor activity, impaired memory formation and autism-like behaviors in mice at the NOAEL. They suggest that the NOAEL should be reconsidered. The authors further found that the observed negative effects may be linked to a disturbed gut microbiome and metabolism. Similarly, Kim et al. (2020) report perinatal glufosinate exposure to induce behavioural changes in rat offspring, especially abnormal motor coordination. They find glufosinate to disrupt cortical interneuron migration and thereby to affect cortical development in the brain. They suggest the relationship of perinatal glufosinate exposure and developmental disorders including autism should be investigated. Aris & Leblanc (2011) studied whether pregnant woman in Canada are exposed to pesticides associated to genetically modified foods, such as glyphosate, glufosinate and their main metabolites and whether these toxicants cross the placenta and reach the fetus. While glyphosate and glufosinate were only detected in nonpregnant women, the glufosinate metabolite 3-MPPA was also found in the blood of pregnant women and their foetuses (Aris & Leblanc, 2011).

Glufosinate is also a suspected endocrine disruptor. Ferramosca et al. (2021) find glufosinate to negatively affect human sperm mitochondrial respiration efficacy starting from concentration of 1 nM. Ma et al. (2022) study the effects of glufosinate-ammonium on male reproductive health in experiments in mice, finding that glyphosate predominantly impaired the sperm epigenome and transcriptome.

Research suggests that glufosinate might contribute to the development of antibiotic resistant bacteria in the environment, with major implications for human and animal health (Liao et al., 2021). See also Section 4.7. Antibiotic resistance.

7.1.2 Environmental effects

In 1997, Ahn et al. reported that glufosinate-ammonium has potent acaricidal activity (i.e. it kills members of the arachnid subclass Acari, which includes ticks and mites) at a low application rate against the pest spider mite *Tetranychus urticae* and may be a useful tool for *T. urticae* control. GLA is however also toxic to natural enemies of *T. urticae*, including predatory mites and insects (Ahn et al., 2001). Moreover, GLA is toxic to predatory spiders. Niedobová et al., (2019b) demonstrate that the glufosinate herbicide Basta® has a lethal effect on the wolf spider *P. agrestis* at a concentration recommended by manufacturers and commonly used by farmers. The agrochemical was applied to each spider with a pump sprayer to simulate the effect of spiders being sprayed directly in the field during herbicide application. Glufosinate ammonium also affected prey capture efficiency of *P. agrestis*, which is relevant as spiders provide a valuable ecosystem service in agroecosystems as biological control agents. It is possible that the toxicity of Basta® is caused by a surfactant and not primarily by glufosinate ammonium. As in the case of glyphosate, some studies indicate that the herbicide formulations are more toxic than the active ingredient alone (Koyama et al., 1997). These findings are still relevant for environmental risk assessment, as these are the formulations actually applied in the field. Based on their findings, Niedobová et al., (2019b) suggest that the commercially available herbicide formulations and not only the active ingredients should be considered in toxicity assessments and that synergistic effects of the different pesticides and other agrochemicals used in tank mixes should be researched. Kutlesa & Caveney, (2001) further find glufosinate-ammonium (GLA) to be toxic to 5th-instar caterpillars of the Skipper butterfly *Calpodes ethylius* when fed at amounts "*that might realistically be acquired from feeding on GLA-*

treated crops." Caterpillars stopped feeding, had an impaired rectal function and showed symptoms of neurotoxicity before death.

Glufosinate reduces the number of fungi and bacteria in soils and can thus potentially alter the composition of soil ecosystems. Thereby, pathogens such as *Verticillium*, *Fusarium* and *Pythium* seem least affected and beneficial micro-organisms such as *Bacillus subtillus*, *Pseudomonas fluroscens* and *Trichoderma* species, which act as parasites of disease-causing species, seem most affected. This indicates a negative impact of glufosinate on the antagonistic potential of agricultural soils (Ahmad et al., 1995a, b; Ahmad & Malloch, 1995). Glufosinate is also toxic to nitrogen-fixing soil bacteria such as *Rhizobium meliloti*. Low concentrations negatively affected bacterial growth and nodulation, although the latter only under sterile conditions (Kriete & Broer 1996).

Wang et al. (2022b) study the toxicity of glufosinate-ammonium (GLA) in soil to earthworms (*Eisenia fetida*). Although the acute toxicity is low, they find that, at the individual level, exposure to GLA could decrease the earthworms' weight, cocoons, and larvae, even under low-concentrations.

In contrast to glyphosate, limited data are available on the acute toxicity of glufosinate in amphibians. Peltzer et al. (2013) find sublethal concentrations of the glufosinate-based herbicide Liberty® to have neurotoxic symptoms in tadpoles of *Hypsiboas pulchellus*. The herbicide inhibited cholinesterase activity and increased swimming speed and mean distance. Based on LC_{50} values (the concentration expected to kill 50% of the tadpoles), Liberty has further been reported to be five times more toxic to *Scinax squalirostris* tadpoles than the glyphosate-based herbicide Mifos® (Lajmanovich et al., 2022). Babalola et al. (2021) report that the glufosinate-based herbicide Basta is thyroid-active in *Xenopus laevis* tadpoles at environmental relevant concentrations. Thyroid hormones play critical roles in development and reproduction and influence a wide variety of biological functions, including metamorphosis in frogs. Thyroid disuprion could compromise health, fitness, and ultimately survival of aquatic wildlife. Bassó et al. (2022) report experiments on larvae of the toad species *Rhinella arenarum* and *Rhinella dorbignyi* and the frog species *Odontophrynus americanus*. The results of show short-term exposure at environmentally relevant concentrations of glufosinate affects swimming performance and cholinesterase activities (substances that are involved in the nervous system) of amphibian larvae. As noted above (Section 4.3.1.2. Impact of multiple environmental pollutants on amphibians), Lajmanovich et al. (2022) study the combined exposure of microplastics and glyphosate or glufosinate, respectively on tadpoles of the Striped-snouted tree frog, *Scianx squalirostris*, finding polyethylene microplastic particles to increase ecotoxicity of both formulations.

As described above (Section 3.4.2.5. GM contamination threatens biodiversity), a two-year field study in Korea confirmed that pollen-mediated gene flow from glufosinate-ammonium resistant genetically modified soybean to wild soybean could occur under natural field conditions (Yook et al., 2021). Notably, the hybrid progeny had almost 3 times greater seed productivity, 4 times greater pod shattering, and over 18 times greater seed dormancy. In the same section, results from Zhang et al. (2003) and Nam et al. (2019) are described which demonstrate that glufosinate resistance can be transferred from transgenic rice lines to weedy rice; as are findings by Zhang et al. (2018b) who highlight the need to also consider the relevance of gene flow from glufosinate-resistant weeds.

Glufosinate-resistant Palmer Amaranth (pigweed) has been confirmed in the USA, in Arkansas, Missouri and Mississippi (Unglesbee, 2021a; Noguera et al., 2022). Noguera et al. (2022) note that if these resistant plants are not controlled by other means, crop productivity will certainly be reduced and the resistance problem to glufosinate (GFA) will escalate. They conclude that "*resistance to herbicides in general, and A. palmeri resistance to multiple herbicides (including GFA) in particular, is a threat to food security and economic sustainability*".

7.2 Isoxaflutole

7.2.1 Health effects

Isoxaflutole is a 4-hydroxyphenyl-pyruvate-dioxygenase (HPPD) inhibitor which belongs to the Carotenoid Biosynthesis Inhibitors. HPPD catalyses a key step in the biosynthesis of plastoquinone. In plants, its inhibition gives rise to bleaching symptoms (University of California, 2021). Since HPPD genes do not only exist in plants but in most aerobic organisms including animals, HPPD inhibitors may also affect humans (Han & Kim, 2019). The U.S. Environmental Protection Agency has classified isoxaflutole as a probable human carcinogen (US EPA, 1998). PAN international lists isoxaflutole as a highly hazardous pesticide (PAN International, 2019). In the EU, isoxaflutole is classified as "*suspected human carcinogen*" and as reproductive toxicant category 2 (suspected of damaging the unborn child) by EFSA (EFSA, 2016b). In their 2016 peer review of the pesticide risk assessment of isoxaflutole, EFSA considered uses of the active ingredient and the pre-emergence herbicide Merlin Flexx (containing 240 g/L isoxaflutole and 240 g/L cyprosulfamide as a safener, i.e. to reduce isoxaflutole's effect on crop plants) on maize and sweet corn. The main target organ in different species was the liver and liver tumours observed were considered as "potentially relevant to humans". Under "Critical areas of concern" EFSA says "*A high risk to mammals was indicated for all representative uses.*" EFSA also identified risks to operators, workers, residents/bystanders and consumers but was not able to finalise these assessments due to data gaps. Regarding soybeans grown in the U.S., no maximum residue level (MRL) has been set for isoxaflutole, even though this is required in the EU by Regulation (EC) No 396/2005, which covers pesticide residues in food and feed, because of insufficient data provided by the manufacturer. Another critical area of concern in EFSA's assessment was the high potential for groundwater exposure above the drinking water limit of 0.1 µg/L for the herbicidally active and groundwater toxicologically relevant metabolite RPA 202248. RPA 202248 is a metabolite of isoxaflutole that had been found at significant levels in genetically modified crops. EFSA was however unable to evaluate risks to health from this new substance, due to data gaps. Based on these and other EFSA risk assessments, Miyazaki et al. (2019) argue that *"current risk assessment practice for HT GE plants cannot be considered to fulfil EU regulatory standards which require the safety of food and feed to be demonstrated."* It should be noted that independent studies on health effects of isoxaflutole are mostly lacking as nearly all the findings to date are based on industry studies (Reuter, 2015).

7.2.2 Environmental effects

There are some restrictions on the use of isoxaflutole. Isoxaflutole is known to persist in the environment and to leach into and accumulate ground- and surface waters (US EPA, 1998). It is not allowed to be used in the two biggest soybean-growing states Iowa and Ilinois because of the groundwater heights and the soil types in these states. It is further only allowed in counties without endangered plants that might be growing near fields that could be treated. A big concern is that farmers may not be able to follow the restrictive use conditions of Alite 27, BASF's isoxaflutole herbicide. Applicators for example have to determine how much organic matter is in the soil and how high the water table is beneath their fields (Bomgardner & Erickson, 2020; US EPA, 1998).

In the area of ecotoxicology, data gaps have been identified regarding the risk assessments for mammals, aquatic organisms and bees. For wild mammals, a high long-term dietary risk was identified by EFSA (EFSA, 2016b). Based on available endpoints for isoxafutole, aquatic vertebrates were identified as the most sensitive group and a high risk of isoxaflutole to aquatic organisms was identified using exposure estimations. However, with insufficient data on the representative isoxaflutole formulation, the assessment could not be finalised. It should be noted that compared to Merlin Flexx, BASF's Alite 27 soybean herbicide not only contains double the amount of isoxaflutole but can also be sprayed post-emergent on HT soybean in certain U.S. counties. This may increase environmental exposure as well as residue levels of isoxaflutole.

EFSA's risk assessment of isoxaflutole, did however not foresee post-emergence applications on herbicide tolerant crops (EFSA, 2016b). In a study using the isoxaflutole herbicide formulation Fordor (containing 750g isoxaflutole/kg) morphological changes in the digestive system of the stinkbug *Podisus nigrispinus*, a promising biological control agent that effectively contributes to the population balance of phytophagous insects, has been reported (Gonçalves et al., 2016).

7.3 2,4-D

2,4-D belongs to the synthetic auxin herbicides and is used to control broad-leaved weeds. 2,4-D is well-known as a component in the Vietnam War defoliant Agent Orange. Today, more than 600 commercial products containing 2,4-D are available on the market (Laborde et al., 2020). High levels of dioxin (a human carcinogen) can still be found in some 2,4-D mixtures (Neumeister, 2014).

7.3.1 Health effects

Freisthler et al. (2022) note that agricultural application patterns of 2,4-D use over time in the USA are showing major increases, "*particularly since the shift towards weed management through reliance on genetically modified herbicide resistant seeds in the early 2000s triggered the emergence and spread of glyphosate-resistant weeds*". In their study, they examine trends in 2,4-D biomarker concentrations in urine samples from a nationally representative US population from 2001 to 2014, as part of the National Health and Nutrition Examination Survey (NHANES). Of the 14,395 participants included in the study, 4681 (32.5%) had urine 2,4-D levels above the threshold used in the study (which was the highest limit of detection (LOD) across all cycles). The frequency of participants with high 2,4-D levels increased significantly from a low of 17.1% in 2001–2002 to a high of 39.6% in 2011–2012 and high urinary 2,4-D concentrations were associated with 2,4-D agricultural use. Children ages 6–11 years (n = 2288) had 2.1 times higher odds of having high 2,4-D urinary concentrations compared to participants aged 20–59 years and women of childbearing age (age 20–44 years) (n = 2172) had 1.85 times higher odds than men of the same age. These authors regard the the reported association between 2,4-D crop application and human biomonitoring levels as worrisome, particularly for vulnerable populations, and call for monitoring and evaluation to determine the extent to which rising use and exposures cause adverse health outcomes among vulnerable populations (particularly children and women of childbearing age) and highly exposed individuals (farmers, other herbicide applicators, and their families).

Exposure to 2,4-D is known to enhance the production of reactive oxygen species (ROS) in cells (different cell types). Under normal conditions damage caused by ROS is countered by a range of cellular antioxidant defences, such as antioxidant enzymes. An imbalance of ROS and antioxidants, in other words if ROS formation increases to an extent that it overcomes the cellular antioxidant systems, results in oxidative stress. Oxidative stress causes damage to biomolecules including DNA, RNA, proteins and lipids, and can lead to cell damage and ultimately cell death. Oxidative stress may be associated with many human diseases including neurogenerative disease, inflammatory disease, cardiovascular disease, diabetes, and cancer. Antioxidant enzymes and products of lipid peroxidation are considered to be good bioindicators of oxidative stress, induced by xenobiotics such as herbicides (Atamaniuk et al., 2013; Hattab et al., 2015; Lerro et al., 2017; Tayeb et al., 2010). Several studies have shown that 2,4-D induces oxidative stress, in different human and animal cell types *in vitro*, including hepatocytes (Palmeira et al., 1995 rat), red blood cells (Bukowska, 2003; Duchnowicz & Koter, 2002), spermatogonical cells (Mi et al., 2007 chicken) and in several different species, including rats (Pochettino et al., 2013; Tayeb et al., 2010; 2012; 2013), fish (Atamaniuk et al., 2013) amphibians (Lajmanovich et al., 2015) and earthworms (Hattab et al., 2015), *in vivo*. Tayeb et al. (2012) find sub-acute exposure to 2,4-D to induce oxidative renal dysfunction in rats and warn that higher doses of 2,4-D may be implicated in kidney failure. Palmeira et al (1995) find 2,4-D to be hepatotoxic and conclude that it may induce cell death by lipid peroxidation. Similarly, Tayeb et al. (2010) find that 2,4-D induces sub-acute hepatotoxicity and cellular alterations in rats. After four weeks of sub-acute exposure to 2,4-D, body weight significantly decreased. Mi et al. (2007) find 2,4-D to cause cytotoxicity in embryonic chicken spermatogonical cells by increasing lipid peroxidation and suppressing the intracellular antioxidant system. Cell viability and cell number was decreased after 2,4-D exposure. 2,4-D exposure has also been associated with oxidative stress in humans. Lerro et al. (2017) used data from a longitudinal biomarker study of corn farmers and non-farming controls to examine the impact of 2,4-D on different markers of oxidative stress. They conclude: "*Based on these results, as well as supporting evidence from laboratory animals, 2,4-D-induced oxidative stress may be important in the pathogenesis of cancer and other chronic disease outcomes.*" These studies indicate that 2,4-D should be taken seriously as a cytotoxic and potentially genotoxic agent (Tayeb et al., 2010). Studies on the action of 2,4-D in plant bioindicators show that 2,4-D may have cytotoxic, genotoxic and mutagenic effects on plants even at low concentrations (de Castro Marcato et al., 2017). Several studies have also shown cytotoxicity induced by 2,4-D in many different human cell types (IARC, 2018). Genotoxic effects of 2,4-D have been confirmed *in vitro* and *in vivo* in non-mammalian systems, mammalian and human cells, as well as occupationally-exposed humans, as reported by IARC (2018). More recently, Laborde et al. (2020) report cytotoxic and genotoxic effects of 2,4-D and its commercial microformulation, Dedalo Elite, in hamster ovary cells, including enhanced apoptotic occurrence. Ruiz de Arcaute (2016; 2018) further report genotoxicity of 2,4-D in fish (Ruiz de Arcaute et al., 2016; 2018). The determination of the genotoxic profile of a pesticide on is crucial to estimate its carcinogenic and mutagenic potential for non-target organisms (Laborde et al., 2020). In an assessment of glyphosate using mouse cells, 2,4-D and dicamba, Mesnage et al (2021) also highlight that 2,4-D is a potent activator of oxidative stress.

In a study using mice and rats, Mello et al. (2020) report that the data, evaluated by pattern recognition algorithms, showed a robust pattern of distinction between exposed and nonexposed groups to 2,4-D. With chronic exposure, there was an increase in micronuclei and DNA damage in all exposed groups regardless of the exposure route. The authors conclude that both acute inhalation exposure and chronic oral and inhalation exposure to 2,4-D can cause genotoxic effects regardless of concentration.

After the classification of glyphosate as probably carcinogenic to humans, the WHO's International Agency for Research on Cancer (IARC) began to analyse if there is a link between cancer in humans and the herbicide 2,4-D (Gillam, 2015d). 2,4-D is classified as possibly carcinogenic (Group 2B) to humans by IARC (IARC, 2018). Several epidemiological studies suggest a positive association between 2,4-D exposure and different forms of cancer, including non-Hodgkin's lymphoma (NHL), in occupational workers (see for example Band et al., 2011; McDuffie et al., 2001; Mills and Yang, 2007, more references can be found in Guha et al., 2016). Schinasi & Leon (2014) conducted a meta-analysis of NHL and exposure to pesticides in agricultural settings and report a significant elevation of NHL associated with 2,4-D exposure. The meta-analysis by Goodman et al. (2015; 2017), however reported finding no association of 2,4-D exposure and NHL. Smith et al. (2017) criticise Goodman et al., stating that they focused their analyses on comparing groups that had experienced any versus no exposure (ever vs. never) to 2,4-D only and did not specifically look at high-exposure groups: "*When subjects with any 2,4-D exposure are considered as the exposed group, subjects with fairly low exposures can be included in the "exposed" group, and the overall average exposure in the group is likely to be lower than that in groups solely composed of highly exposed workers. Because the average exposures in these "any exposure" groups are lower, RR* [Relative Risk] *increases in these groups are also likely to be low (i.e., closer to 1.0) and thus more susceptible to issues relating to low power, bias, and confounding*". In their meta-analysis on the issue, the associations of 2,4-D exposure and NHL in epidemiologic studies was indeed higher when selecting the highest exposure categories. It was however still significant when selecting for ever vs. never exposed. The association to NHL was highest when analysing a subgroup that only includes occupational exposure to 2,4-D. The fact that the association to NHL increases as the likely average exposure increases, is consistent with a positive dose-response pattern. Smith et al. (2017) further point out that with the strong evidence that 2,4-D induces oxidative stress and moderate evidence that 2,4-D causes immunosuppression, the development of NHL becomes biologically plausible as these are "*key characteristics of human carcinogens*" and "*may contribute mechanistically to the development of NHL*"

2,4-D has been classified as a potential endocrine disruptor by the European Union. Very low concentrations of 2,4-D (0.1 to 10 μg/L) statistically changed the sex ratio in the aquatic insect *Chironomus riparius*, a suggested endpoint for endocrine disruptor chemicals, led to mouthpart deformities and to the upregulation of certain defence proteins (Park et al. 2010). Similarly, a commercial formulation of 2,4-D reduced the proportion of males in an experiment with lady beetles, *Colemegilla maculata* (Freydier & Lundgren, 2016). It has been reported that 2,4-D leads to male reproductive toxicity, including testicular dysfunction and infertility (Amer & Aly, 2001; Galimov & Valneeva, 1999; Harada et al., 2016; Marouani et al., 2017). In rats, chronic injection of 2,4-D was found to affect spermatogenesis and fertility (Galimov & Valneeva, 1999). In mice, Harada et al. (2016) find 2,4-D to decrease serum testosterone levels and reduce pregnancy rates in a dose-dependent manner when treated males were mated to untreated females, suggesting impaired male fertility. Amer & Aly (2001), find 2,4-D to increase chromosome aberrations in spermatocyte cells and sperm-head abnormalities after oral administration of 2,4-D at 3.3 mg/kg, also indicating reduced male fertility as well as potential genotoxicity in mice in vivo under the conditions tested. They conclude: *"… more care should be given to the application of 2,4-D on edible crops since repeated uses may underlie a health hazard*." In West African Dwarf goats, exposure to 2,4-D adversely affected sperm counts in a dose-dependent manner (Obidike et al., 2012). The authors conclude: "*This may imply possible spermatogenic dysfunction for human beings…*" An epidemiological study indeed associates 2,4-D exposure with an increased number of dead, abnormal and immotile spermatozoa in farm sprayers (Lerda & Rizzi, 1991). 2,4-D has also been shown to negatively affect mature human spermatozoa directly *in vitro* (Tan et al., 2016). The results suggest that 2,4-D decreases sperm motility and hampers with different physiological processes necessary for penetrating the egg. In the presence of progesterone, these processes were already affected at a very low dose of 2,4-D (1μM), suggesting that the toxicity of 2,4-D may be more significant in the female reproductive tract. Tan et al. (2016) conclude: "*these results suggest that exposure to 2,4-D and its accumulation in the seminal plasma and follicular fluid might increase the risk of infertility*" (Tan et al., 2016). Other epidemiological studies analyse prevalent and incident thyroid disease within the Agricultural Health Study (AHS), a cohort study of licensed pesticide applicators and their spouses from North Carolina and Iowa. They find an association between increasing level of exposure to 2,4-D and hypothyroidism (Goldner et al., 2013; Shrestha et al., 2018). An analysis of the Ontario Farm Family Health Study, further reports an association between 2,4-D and decreased fecundity in women engaged in pesticide-related activities (Curtis et al. 1999).

Horn et al. (2020) extract soil with rainwater where glyphosate and 2,4-D were sprayed on Bt GM maize and measure the effects on androgen receptor (AR) activity. They find that 2,4-D concentrations in rainwater extracts exceeded the WHO's drinking water guideline and glyphosate, the Bt toxin Cry1Ab, and 2,4-D detected and exceeded the EU drinking water guideline. The cells used in their assay were exposed to: single active ingredients; formulations; environmentally relevant concentrations of the active ingredients and formulations; as well as rainwater extracts. These authors conclude that (i) rainwater run-off from maize sprayed with Roundup and 2,4-D contained androgen active substances and (ii) chronic exposure to this water may cause endocrine disrupting effects in humans and aquatic life.

2,4-D has also been confirmed to cause developmental toxicity in offspring. Blakley et al. (1989 a; b) report developmental toxicity of a 2,4-D and picloram combination in mice either when exposing males prior to mating, or females prior and throughout gestation. When used alone, 2,4-D exposure in pregnant animals increased lethality and decreased fetal weight in rat litters at term (Chernoff et al., 1990). Acute exposure before pregnancy also led to increased embryonal death in mice (Vin et al., 1990). A human ecologic study conducted in the U.S. compared malformations in infants from rural agricultural counties with high and low wheat acreage, respectively, with wheat acreage as a surrogate measure for exposure to chlorophenoxy herbicides such as 2,4-D. The study associates higher use of chlorophenoxy herbicides with different birth malformations. Conception during the months of herbicide application increased the likelihood for different birth malformations compared with conceptions during other months of the year (Schreinemachers, 2003).

Silver et al. (2019) detected 2,4-D in umbilical cord blood from a cohort of infants in Fuyang County, China. Prenatal exposure to 2,4-D was significantly associated with slower auditory signal transmission, possibly via the disruption of myelination or of dopaminergic signaling along the auditory pathway. Although the clinical importance of these small deficits in auditory processing as well as whether they may lead to long-term changes in auditory processing are unclear, the authors point out that "*Perturbation of this early stage of neurodevelopment may have the potential for negative effects on learning later in childhood*." The authors note that all infants included in the study were born at term and heathy and that the effect of 2,4-D on more vulnerable groups, such as pre-term and low birth weight infants, should also be investigated.

Potential neurotoxic effects of 2,4-D have also sbeen shown in mice at subchronic levels. 2,4-D decreased the plasma levels of a series of acylcarnitines, which are associated with neurological diseases including Parkinson's disease and Alzheimer's disease (Tu et al., 2019). The authors also find 2,4-D to cause toxicity and substantially impact the gut microbiome in mice at occupationally relevant subchronic low doses. Metagenomic results revealed a distinct gut microbial community with profound changes in several microbial pathways. Tu et al. argue that just because the targeting pathway of a pesticide may not be found in the human body, does not mean that it is safe to humans as plant hormone-related pathways are commonly present in gut bacteria and perturbations of the gut are associated with a number of human diseases.

7.3.2 Environmental effects

The introduction of 2,4-D tolerant crops has created an urgent need to further explore the effects of continuous low-level exposure on the environment. "*In near future, introduction of 2,4-D resistant crops will increase its use in agriculture, which may cause relatively high and potentially unsafe residue levels in the environment*." (Islam et al., 2018). The highest environmental concentrations of 2,4-D are found in soil, air and surface water surrounded by crop fields.

Murschell & Farmer (2019) show that 2,4-D can also be easily and unintentionally transported to off-target areas via the atmosphere. Hwang et al. (2022) show that drift in the downwind direction can damage neighbouring cotton crops.

2,4-D is not easily biodegradable in aquatic environments and is frequently detected in water bodies which is an important environmental problem as this can lead to prolonged exposure of aquatic organisms throughout critical developmental life stages (Anton et al. 2021; de Castro Marcato et al., 2017; Islam et al., 2018).

A number of papers have reported adverse effects on amphibians. As with glyphosate, 2,4-D has been found to inhibit oocyte maturation in the African clawed frog (*Xenopus laevis)* (Stebbins-Boaz et al., 2004; LaChapelle et al., 2007). LaChapelle et al. (2007) conclude that 2,4-D *"…is thus a potential environmental endocrine disruptor with early reproductive effects"* and "*…induces irreversible dysfunction of the meiotic signaling mechanism.*" In a rare exposure and toxicity study with adult amphibians, Lajmanovich et al., 2015, found dermal, sublethal exposure to 2,4-D to induce oxidative stress, oxidative DNA damage and immunological suppression in the common toad *Rhinella arenarum* (Lajmanovich et al., 2015). Chronic exposure experiments with 2,4-D and commercial formulations containing 2,4-D report mutagenic effects, harmful changes to biochemical, physological, developmental and behavioral aspects, as well as morphological abnormalities in different tadpole species, including *Lithobates catesbeianus* (Mesak et al. 2018, Freitas et al. 2019, Viriato et al. 2021), *Rana arenarum* (Aronzon et al. 2011), *Physalaemus* *albonotatus* (Curi et al. 2019) and *Boana pardalis* (Moutinho et al. 2020). Effects vary between species and developmental stage and depend on the formulation and concentration used. 2,4-D is highly persistent in aquatic environments (US EPA, 2004). However, information about 2,4-D levels in surface waters is scarce or entirely lacking in many countries (Aronzon et al. 2011; Curi et al., 2019; Freitas et al. 2019). Therefore, it is difficult to estimate the environmental relevance of some of these studies. In Brazil, a concentration of 3.4 μg/L has been detected in the Vacacaí-Mirim river in Rio Grande do Sul (Marchesan et al. 2010) and up to 74.5 μg/L in surface waters of the basin of the Itajaí river in Santa Catarina (Pinheiro et al., 2010). In 2004, EPA modeled sixteen different crop scenarios and the estimated 60 Day average 2,4-D concentration in surface waters in areas where 2,4-D is heavily used ranged between 5.5 μg/L (ND Spring Wheat) and 45.4 μg/L (NC Apples). In rice paddies, 2,4-D concentration was estimated at 1431 μg/L. These estimates do not account for 2,4-D HT crop scenarios, where 2,4-D use has been estimated to be substantially higher (USDA APHIS, 2014a). Moreover, concentrations in aquatic environments near agricultural sites, such as temporary ponds with low water volume that are used by amphibians during reproduction and larval development are expected to be particularly high (Freitas et al. 2019). Hence, pesticide measurements in temporary ponds near 2,4-D crop fields are necessary in order to correctly estimate the hazard on aquatic organisms. Mesak et al. (2018) simulated a realistic scenario of aquatic contamination by 2,4-D in tropical regions, assuming a situation where a temporary pond is formed by superficial water run-offs caused by a short (20 min) rainfall event, 24 h after direct 2,4-D application to the soil (4.03 g/L or 200 L/ha). For that scenario, the 2,4-D concentration in the pond was set to 1.97 mg/L. At this concentration, 2,4-D had mutagenic effects on bullfrog tadpoles (*Lithobates catesbeianus*) even when only exposed for a short period of time (3 – 9 days). Chronic exposure to a 2,4-D formulation (DMA 806) at a 15-times lower concentration (125 μg/L) relevant for pre-emergence applications in sugarcane, delayed metamorphosis and inhibited growth in bullfrog tadpoles (Freitas et al. 2019). Delayed metamorphosis can decrease survival because tadpoles are extensively vulnerable to predation, aquatic parasites etc. Additionally, in tropical areas where many species develop in ephemeral bodies of water, these may dry up before metamorphosis is completed (Freitas et al. 2019). Delayed metamorphosis and reduced body size were also observed in *Rana arenarum* (Aronzon et al. 2011). In *Physalaemus albonotatus* however, 2,4-D (Amina Zamba) exposure led to accelerated metamorphosis and no significant change in body size (Curi et al. 2019). The 2,4-D formulation did however affect survival and induced morphological abnormalities and liver damage. Further effects observed in bullfrogs include impared respiration and stimulus response, which can further affect survival of tadpoles (Freitas et al. 2019). If responses to an attack are slower, then tadpoles become more vulnerable to predators. Tadpoles also avoided presence of 2,4-D, although they were not able to distinguigh between different 2,4-D concentrations. Similarly, Viriato et al. (2021) found chronic exposure to 2,4-D (DMA) caused embryonic growth inhibition, malformations, injuries to gills, kidney and skin of frog larvae and physiological stress in bullfrog tadpoles. The authors hypothesise that 2,4-D is a respiratory allergen for *L. catesbeianus* tadpoles. Various teratogenic effects were also observed in *Rana arenarum* tadpoles upon chronic exposure (Aronzon et al. 2011).

A number of studies have been undertaken on the impacts of 2,4-D on fish. Salvo et al. (2015) demonstrate that a low dose of 2,4-D and MCPA (2.75 μg/l) significantly reduces cellular oxygen consumption in primary hepatic cells derived from the subtropical fish *Metynnis roosevelti.* MCPA belongs to the same class of herbicides as 2,4-D. Similarly, in pearl eartheater (*Geophagus brasiliensis*), oxygen consumption decreased with increasing 2,4-D concentration (Barbieri, 2009). Atamaniuk et al. (2013) find short-term exposure to 2,4-D at moderately and highly toxic concentrations to induce oxidative stress and increase activities of different antioxidant enzymes in goldfish gills. Ateeq et al. (2006) conduct a histological analysis of the liver and gonads of the fish species *Clarias batrachus.* They report a genotoxic effect of 2,4-D at a sublethal concentration, with clear indication and signs of apoptosis. Genotoxic effects of a 2,4-D-based herbicide at sublethal concentrations were reported in acute and chronic exposure experiments in the Neotropical fish *Cnesterodon decemmaculatus* (Ruiz de Arcaute et al., 2016; 2018). Mixing the 2,4-D-based formulation with a glyphosate-based formulation has been shown to increase genotoxicity on *C. decemmaculatus* syngergistically (Carvalho et al., 2020b). Recent literature further suggests that exposure to ecologically relevant concentrations of 2,4-D and 2,4-D-based formulations, can decrease embryo and larval survival of freshwater fish, negatively impact early development (tail deformities and pericardial edema), and impair locomotion (decrease in swimming behavior), as well as essential visually guided behaviour (prey capture and predator evasion) and associative learning capability (Anton et al., 2021; Dehnert et al., 2018; 2019; 2021; DeQuattro and Karasov, 2016; da Fonseca et al., 2008; Gaaied et al., 2020). Dehnert et al. (2021) show that ecologically relevant concentrations of a commercial 2,4-D herbicide (0.05, 0.50 and 2.00 pp, or mg/L 2,4-D a. e.) reduce survival in early developmental stages of multiple, phylogenetically distant freshwater fish species. The authors voice ecological concerns regarding the use of genetically modified 2,4-D tolerant crops *"Availability of genetically modified crops resistant to 2,4-D and other active ingredients (…), will likely lead to an increase in the use of products with the active ingredient 2,4-D (…) and as more 2,4-D is used on agricultural crops, a rise in non-target organisms exposure could be expected as 2,4-D is known to enter aquatic ecosystems from runoff, leaching, and spray drift (…). As multiple, phylogenetically distant fish species exposed to environmentally relevant concentrations of 2,4-D show significant reduction in survival, it is possible that 2,4-D entering aquatic ecosystems directly or indirectly could potentially impact larval survival, larval recruitment, species populations, and entire ecosystem dynamics."* Gaaied et al. (2020) find a decrease in cholinesterase activity at the lowest dose tested (0.02 mg/L) and suggest that the observed alteration of the locomotor behavior could be associated with the neurological alterations mediated by cholinersterase inhibition. Similarly, da Fonseca et al. (2008) show that 2,4-D exposure reduces acetylcholinesterase (AChE) in the brain of freshwater fish (*Leporinus obtusidens*). A decrease in AChE enzyme activity has been assoiated with a range of behavioral changes in fish exposed to 2,4-D (Anton et al., 2021). Dehnert et al. (2019) discuss that 2,4-D may disrupt transmission of neural signals coding visual input. They conclude: *"Together, our results suggest that 2,4-D alters the development and function of neural circuits underlying vision of larval fish, and thereby reduces visually guided behaviors required for survival."* Similarly, Anton et al. (2021) suggest that the observed impaired associative learing capability in yellow perch (*Perca flavescens*) might be due to a partially impaired visual system or an imbalance of neurotransmitter and recommend further research. They conclude *"Overall, exposure to ecologically relevant levels of commercial 2,4-D herbicides, like WAM40, could negatively impact fitness of juvenile fish by impairing cognitive function and thereby hindering essential behaviors in the natural environment."* The data of DeQuattro and Karasov (2016) further suggest that 2,4-D acts as an endocrine disruptor in the fathead minnow (*Pimephales promelas*).

In a first study on the sublethal effects of 2,4-D on the crayfish *Orconectes rusticus,* Browne and More (2014) find 2,4-D to cause significant behavioral and potential physiological changes in *O. rusticus*. 2,4-D impaired the forage ability of *O. rusticus*, which could lead to reduced fitness in populations of crayfish exposed to 2,4-D. Impacts were found at levels of exposure already reported in streams and rivers in the U.S.

In their review on potential impacts of 2,4-D, Islam et al. (2018) argue that the commercialisation of 2,4-D resistant crops could lead to adverse health effects in populations living in the immediate vicinity of these crops due to the predicted increase in, and hence exposure to, 2,4-D. They report 2,4-D to be toxic to a variety of organisms, including fish, amphibians, insects, earthworms and rodents. In a further review on the toxicity of 2,4-D on non-target organisms, de Castro Marcato et al., 2017 show that although 2,4-D has its main mode of action in plants, it also induces histological, physiological, and behavioural alterations in animals even at low concentrations.

Da Silva et al. (2022) review evidence that exposure to environmental 2,4-D concentrations increase mortality rate in animals. Overall, the 87 data sets collected indicated a significant increase in the mortality rate recorded for animals exposed to environmental concentrations of 2,4-D compared to the controls in the experiments. Fish and birds had higher mortality rates than other animals, and larval and adult animals were more susceptible than juveniles. Commercial formulations caused higher mortality rates than the active substance alone. The authors suggest that further studies are needed regarding the sublethal effects of 2,4-D on animals.

Bautista (2007) reports that typical application rates of 2,4-D equalled or exceeded doses reported, in laboratory studies, to cause adverse effects in eight of ten acute exposures scenarios involving mammals and birds. Vegetation-eating and insect eating birds and mammals were most at risk.

2,4-D has been reported to negatively affect development and reproduction of the earthworm *Eisenia fetida* (Correia and Moreira, 2010). The results of Correia and Moreira (2010) suggest that 2,4-D is more toxic to *E. fetida* than glyphosate. The results of Lazurick et al. (2017) further indicate a possible, small synergistic effect of glyphosate and 2,4-D on *E. fetida*. Direct contact led to severe ill effects, including death. Ingestion however did not affect worms. Hattab et al. (2015) studied cytotoxic effects of sublethal concentrations of 2,4-D on the earthworm *Eisenia andrei*. They find 2,4-D to increase oxidative stress in *E. Andrei*. On the one hand, 2,4-D stimulated membrane lipid peroxidation in exposed earthworms and, on the other hand, the authors also find the activity of antioxidant enzymes to increase. This seems to confirm that 2,4-D enhances the production of reactive oxygen species (ROS) in cells. 2,4-D also decreased lysosomal membrane stability, a very sensitive cellular marker of general stress, and reduced body weight after 7 days of exposure even at the lowest (3.5 mg/kg) concentration.

Coccinellidae, known as ladybugs, are important biological control agents, found in many crop fields, that feed on insect pests such as aphids. Michaud and Vargas (2010) find 2,4-D applied as a topical spray at the recommended field rate to "*represent a significant hazard*" to two species of Coccinellidae, with 25% mortality in *Coleomegilla maculata* larvae and 57.9% mortality in *Hippodamia convergens* larvae. Surviving *C. maculata* larvae experienced a change in developmental time. They recommend to apply 2,4-D early, before overwintered coccinellids enter the fields to begin oviposition, also to not disrupt biological control of aphids. With Enlist Duo being approved for post-emergence application (see Section 6.3 Developing new transgenic crops with resistances to additional herbicides), 2,4-D is, however, now being applied later in the season, increasing the likelihood of direct contact with insects in the field. In accordance with Michaud and Vargas (2010), Freydier & Lundgren (2016) find field relevant concentrations of a commercial formulation of 2,4-D to be highly lethal to larvae of *C. maculata* (the LC_{90} was approximately 13% of the label rate applied for weed control). The formulation and 2,4-D alone also had sublethal effects on the lady beetles at the recommended field rate. Islam et al. (2018) conclude that 2,4-D could reduce biocontrol services of these predatory beetles, if broadly used.

Martínez et al. (2001) found an association between regular applications of the herbicide Tordon®101M, a mixture of 2,4-D and picloram, and a decline in populations of beneficial dung beetles and hence delayed dung degradation.

The increased toxicity of commercial herbicide formulations, compared to the active ingredient alone, is not only observed for glyphosate and glyphsoate-based formulations. A commercial formulation of 2,4-D was for example shown to be up to 10 times more toxic to embryos of the toad species *Rhinella arenarum* than the active ingredient alone (Aronzon et al. 2011).

Finkler et al. (2022) note that studies assessing the toxicity of glyphosate and 2,4-D as a mixture are rare. They report evidence of some cytotoxic and genotoxic effects induced by associated commercial glyphosate and 2,4-D formulations in onions (*Allium cepa*), with the mixture showing significant differences from the two chemicals alone.

7.4 Dicamba

Dicamba is a selective benzodic acid herbicide and belongs to the synthetic auxin herbicides. It has been used for post-emergent control of broadleaf weeds and woody plants since the 1960s

(Lerro et al., 2020).

7.4.1 Health effects

Although there is no clear consensus in the epidemiologic and experimental literature regarding the carcinogenic potential of dicamba, with some inconclusive and sometimes conflicting data (Lerro et al., 2020), several different studies suggest an association between dicamba and genotoxic and cytotoxic effects, as well as different forms of cancer, including non-Hodgkin's lymphoma (Band et al., 2011; Cantor et al., 1992; Espandiari, 1995; 1999; González et al., 2006; 2007; 2009; 2011; Kim et al., 2021; Leon et al., 2019; McDuffie et al., 2001; Perocco et al., 1990; Ruiz de Arcaute et al., 2018; Samanic et al., 2006). On the basis of their results, González et al. (2006) concluded that dicamba should be considered as a potentially hazardous compound in humans. Lipid peroxidation has been suggested as mechanism of action of the cytotoxic effects of dicamba. As far as it is known, dicamba induces tissue damage and cell death in the weedy plants known as cleavers (*Gallium aparine* L.) by lipid peroxidation (Grossmann et al., 2001). A recent study by the National Institutes of Health (NIH) re-evaluated dicamba use in the Agricultural Health Study (AHS). The AHS evaluated data from 57,000 farmers from Iowa and North Carolina between 1993 and 2005 (Samanic et al., 2006). The NIH study added 12 years and 2702 cancers. The study found that pesticide applicators using dicamba had an elevated risk of numerous cancers, including liver and intrahepatic bile duct cancer, acute and chronic lymphocytic leukaemia and mantle cell lymphoma, compared to pesticide applicators not using dicamba (Lerro et al., 2020).

Dicamba is a suspected endocrine disruptor (Zhu et al. 2015). Analyses of prevalent and incident thyroid disease within the AHS, found an association between exposure to dicamba and hypothyroidism (Goldner et al., 2013; Shrestha et al., 2018). A commercial formulation of dicamba reduced the proportion of males in an experiment with lady beetles (*Colemegilla maculata*) (Freydier & Lundgren, 2016). An analysis of the Ontario Farm Family Health Study, reported an association between dicamba and decreased fecundity in women engaged in pesticide-related activities (Curtis et al. 1999). A secondary analysis of the Ontario Farm Family Health study, more specifically looked at pesticide exposure and birth defects and found an association between pre-conception exposure to dicamba and birth defects in male offspring. The authors suggest a male-mediated reproductive effect, assuming that pre-conception exposure is affecting spermatogenesis. (Weselak et al. 2008). Inhibition of spermatogenesis has been demonstrated in adult male rare minnow (*Gobiocypris rarus*) exposed to environmentally relevant concentrations of dicamba (Zhu et al. 2015). In females, the authors observed ovarian degeneration. They conclude that *"…dicamba should be considered a potential endocrine disruptor in fish"* (Zhu et al. 2015). Weselak et al. 2008 named some of the limitations of the study as its retrospective nature, and that the outcomes were self-reported, as well as the lack of some exposure relevant factors, and the modest sample sizes. They also state that it may potentially have missed birth defects from foetuses that did not survive until birth. A study evaluating the effects of environmentally relevant, low-dose exposures to different agrochemicals and their direct effects on mouse preimplantation embryo development, found increased apoptosis caused by dicamba (Greenlee et al., 2004). Embryos composed of fewer cells could result in embryonic death. The authors conclude: *"Our data demonstrate that pesticide-induced injury can occur at a very early period of embryo development and at pesticide concentrations assumed to be without adverse health consequences for humans."* Similarly, very low and low environmentally relevant doses of an herbicide mixture containing dicamba, 2,4-D and MCPP significantly reduced litter size, associated with a decrease in the number of implantation sites. The authors discuss that a decrease in number of embryos implanted may be due to preimplantation blastocysts being negatively affected (Cavieres et al. 2002). Although it is not possible to say what role dicamba played in decreasing the litter sizes, this study shows that concentrations determined as safe in traditional toxicological testing looking at individual compounds only, may have significant adverse effects in real world situations when applied as commercial herbicide mixtures.

Research suggests that dicamba might contribute to the development of antibiotic resistant bacteria in the environment, with major implications for human and animal health (Liao et al., 2021). See also Section 4.7. Antibiotic resistance.

7.4.2 Environmental effects

Dicamba is water soluble and mobile in the environment. Following application, it can volatilise and, depending on the climatic and weather conditions, drift far from the site of initial application (Lerro et al., 2020). Soltani et al. (2020) conduct six experiments on field sites located in Arkansas, Indiana, Michigan, Nebraska, Ontario, and Wisconsin to evaluate the off-target movement of dicamba under field-scale conditions, finding injury levels of up to 55% in both covered and uncovered areas, with damage occurring as far as 250m in Nebraska and Arkansas. In 26 field-scale drift trials conducted in 2014 and 2015, Jones et al. (2019a) report that dicamba was documented to move as much as 152 m from the application area (distance to 5% injury). Jones et al. (2016b) also find that that soybean damaged from dicamba drift can negatively affect offspring. Crop damage caused by dicamba drift has led to litigation, as discussed in Section 8.2.1 Dicamba lawsuits.

Bautista (2007) estimates that the maximum application rate of dicamba plausibly leads to adverse effects on reproduction in vegetation-eating and insect eating birds and mammals. Very little work has explored potential effects of dicamba on insects (Bohnenblust et al. 2013). Freydier & Lundgren (2016) found dicamba at the field recommended rate to significantly reduce longevity and survival of larvae of the lady beetle *Colemegilla maculata* and to also exert sublethal effects on the lady beetles. Apart from acute or chronic direct effects from herbicide exposure, insect species may be indirectly affected by the herbicides impacts on their food resources. Dicamba drift to non-target plants may for example influence arthropod communities in agroecosystems by delaying, reducing or preventing flowering. Bohnenblust et al. (2016) found that sublethal doses of dicamba approximating drift-level rates (0.1-1% of the field application rate) have sublethal effects on two agroecologically significant plant species, which in turn led to reduced pollinator visitation on plants injured by dicamba. They state: "*Moreover, although many pollinator species are generalists, reductions and delays in plant flowering caused by herbicide injury could perturb pollinator communities*." They also found dicamba to alter growth and development of the herbivore butterfly *Vanessa cardui* when feeding on small thistle plants stressed by sublethal drift-level doses of dicamba, potentially due to herbicide-induced reduced nutritional quality of the plants and/or reduced plant size (Bohnenblust et al. 2013).

Ruiz de Arcaute et al. (2018) report genotoxic effects of dicamba at sublethal concentrations in a chronic exposure experiment with the Neotropical fish *Cnesterodon decemmaculatus*. Dicamba is further a suspected endocrine disruptor in fish. Chronic exposure to environmental relevant concentrations of dicamba caused inhibition of spermatogenesis in male testes and ovarian degeneration in adult Chinese rare minnow (*Gobiocypris rarus*), a species that has been widely used to assess endocrine disrupting chemicals (Zhu et al., 2015). The authors state: *"These results indicate that sex hormone homeostasis and normal reproduction of fish could be affected by dicamba".* The authors further find that dicamba could induce hepatic tissue damage in rare minnow.

8. Lawsuits

There have been numerous lawsuits relevant to the cultivation of GM herbicide-tolerant crops in the United States.

One set of lawsuits relates to claims that exposure to glyphosate causes cancer and harms endangered species (See Section 8.1 Glyphosate lawsuits).

Another set of lawsuits relates to crop damage caused by farmers spraying dicamba or 2,4-D on to GM crops resistant to these herbicides (see Section 8.2 Dicamba and 2,4-D lawsuits). For example, Elmore (2022) describes how, in 2021, thousands of U.S. growers reported to the Environmental Protection Agency (EPA) that dicamba sprayed by other farmers on dicamba-resistant GM crops damaged crops in fields all over the country.

8.1 Glyphosate lawsuits

Following the IARCs classification of glyphosate as a "probable human carcinogen", in March 2015, numerous lawsuits alleging that past use of Monsanto's Roundup herbicide had contributed to the plaintiffs' development of non-Hodgkin lymphoma (NHL) were filed. 12 cases were filed in 2015, 129 cases in 2016 and a few thousand in 2017. As a result of the first jury trial verdicts in 2018 and 2019, this number further increased to over 40,000 by the end of 2019 and subsequently reached as many as 125,000 lawsuits. In 2016, a group of law firms began to coordinate a litigation against Monsanto (now Bayer) on behalf of individuals with NHL. Three lawsuits were heard before a jury and resulted in victories for the plaintiffs. In each of the trials, juries found that the weight of evidence proved that exposure to glyphosate-based herbicides, such as Roundup, caused the plaintiffs to develop non-Hodgkin lymphoma (NHL), and that Monsanto covered up the risks and failed to warn consumers (Benbrook, 2020; Baum, Hedlund, Aristei & Goldman, n.d.a; Gillam, 2020b).

In June 2022, the U.S. Supreme Court rejected Bayer's bid to dismiss these legal claims by customers and left in place the lower court decision that upheld $25 million in damages awarded to California resident Edwin Hardeman, who had regularly used Roundup for 26 years at his home in northern California before being diagnosed with a form of non-Hodgkin's lymphoma (see Section 8.1.2 Second Trial: *Hardeman v. Monsanto*) (Hurley, 2022). In July 2021, Bayer (which bought Monsanto in 2018) took an additional litigation provision of $4.5 billion in case of an unfavorable ruling by the Supreme Court or in case the justices declined to consider its appeal. The provision came on top of $11.6 billion that the company previously set aside for settlements and litigation (Hurley, 2022). As of May 2022, although nearly 80% of pending claims had been settled (around 100,000 lawsuits), there were still about 26,000-30,000 active Roundup lawsuits, including over 4,000 claims in a class action lawsuit pending in California (Miller, 2022).

Krimsky and Gillam (2018) review the court-released discovery documents obtained from litigation against Monsanto over Roundup and through Freedom of Information Act requests. Their findings include evidence of ghostwriting (in which Monsanto employees write papers on behalf of supposedly independent scientists), interference in journal publication, and what they describe as undue influence of a federal regulatory agency (the US Environmental Protection Agency, EPA) by Monsanto.

In addition to the individuals' cases, described below, groups including the Natural Resources Defense Council, the Center for Food Safety and the Rural Coalition, which represents farmworkers, brought a legal case against the U.S. Environmental Protection Agency (EPA), after it reauthorised the use of glyphosate in January 2020. In June 2022, the 9th Circuit Court of Appeals in California determined that the EPA did not adequately consider whether glyphosate causes cancer and threatens endangered species, and ordered it to look again at the risks it poses (Stempel, 2022).

8.1.1 First trial: *Johnson v. Monsanto*

On January 28, 2016 Dewayne "Lee" Johnson, a former California school district groundskeeper, filed a lawsuit alleging Monsanto's Roundup gave him terminal cancer. On August 10, 2018, just after Bayer bought Monsanto, a jury unanimously found that Monsanto's glyphosate-based herbicide products, Roundup Pro or Ranger Pro, were a "*substantial factor in causing harm to Mr.*

Johnson" and awarded Johnson US$39 million in compensatory damages. The jury also found that the potential risks of these products were "*known or knowable in light of the scientific knowledge that was generally accepted in the scientific community at the time of their manufacture, distribution or sale*", that the company consequently knew or should reasonably have known these dangers but failed to "*adequately warn*" of these dangers, which was "*a substantial factor in causing harm to Mr. Johnson*". The jury further found that Monsanto "*acted with malice or oppression*" and awarded Mr. Johnson an additional US$250 million in punitive damages. On October 22, 2018, the court reduced the punitive damages to US$39 million to match the compensatory damages. The court however denied Monsanto's motion for judgment notwithstanding verdict (JNOV) and its motion for a new trial, thereby upholding the jury's verdict. Monsanto appealed the reduced amount. In July 2020, an appeals court rejected Monsanto's efforts to overturn the trial outcome, stating that abundant evidence had been presented that Roundup products are capable of causing NHL and caused Johnson's cancer in particular. The damages were however cut again to US$10.25 million in compensatory damages and another US$10.25 million in punitive damages, based on arguments about Johnson's life expectancy (Benbrook, 2020; Gillam, 2020d; *Johnson v. Monsanto*, 2018; Sustainable Pulse, 2020). Monsanto subsequently filed a petition with the Supreme Court in California, asking them to review the *Johnson v. Monsanto* verdict (*Johnson v. Monsanto*, 2020). In March 2021, Bayer however announced it would not further pursue appeal of the Johnson verdict, stating that they rather wanted the second case (below) to be reviewed by the Supreme Court (Rosenblatt, 2021).

8.1.2 Second Trial: *Hardeman v. Monsanto*

Edwin Hardeman used Roundup on his property from 1986 to 2012 to treat weeds, overgrowth and poison oak. In 2015, Mr Hardeman was diagnosed with B-cell NHL. On February 12, 2016 he filed a lawsuit against Monsanto. His case was the first Roundup-NHL lawsuit to proceed to trial as part of the federal-district court MDL overseen by Judge Vincent Chhabria in San Francisco. Therefore, the trial was a bellwether case for other plaintiffs in the MDL. At Monsanto's request, the trial was split into two phases by Judge Chhabria. The Phase 1 trial began on February 25, 2019 and focused on the plausibility of Roundup-NHL causality, based on scientific evidence only. On March 19, 2019 the jury issued a verdict on causation, finding that exposure to Roundup was a substantial factor in causing Hardeman's non-Hodgkin lymphoma, thereby allowing the case to proceed to the second phase. The Phase 2 trial began on March 20, 2019 and focussed on Monsanto's knowledge, behaviour and damages. On March 27, 2019 the jury ruled that Roundup "*lacked sufficient warnings of the risk of NHL*" and that "*Monsanto was negligent by not using reasonable care to warn about Roundup's NHL risk*", awarding Mr Hardeman US$5.2 million in compensatory damages and US$75 million in punitive damages. The punitive damages were later reduced to US$20 million in a response to a post-verdict motion by Bayer (Baum, Hedlund, Aristei & Goldman, n.d.b; Benbrook, 2020; *Hardeman v. Monsanto*, 2020; Sustainable Pulse, 2020). Bayer went on to appeal the verdict, arguing that federal regulatory backing of the company's herbicides pre-empts state law and a duty to warn and thus the claims made by Hardeman. In May 2021, the U.S. Court of Appeals for the Ninth Circuit however affirmed the district court's ruling and specifically rejected Bayer's pre-emption argument (Gillam, 2021a).

8.1.3 Third Trial: Pilliod v. Monsanto

The third Roundup cancer case proceeding to trial was brought forward by Alva and Alberta Pilliod, who both had been diagnosed with NHL after spraying Roundup several days per year over several decades on their properties, sometimes wearing shorts and flip-flops. Due to their advanced ages and cancer diagnoses, attorneys asked to expedite the trial. This was the first lawsuit from the California Roundup Judicial Council Coordination Proceedings (JCCP), consolidating hundreds of lawsuits, to go to trial before Judge Winifred Smith. On May 13, 2019 the jury awarded Avla and Alberta Pilliod each US$1 billion in punitive damages, ruling that Monsanto "*engaged in conduct with malice, oppression or fraud*". They also received US$55.2 million in compensatory damages for past and future economic and noneconomic losses. The US$2 billion in punitive damages were reduced to US$69 million as a result of post-trial motions (based on a US Supreme Court guidance that limits the ratio of punitive to compensatory damages to 7:1). The judge however denied Monsanto's motion for JNOV and granted its motion for a trial only under the condition that the Pilliods would not consent to the reduced judgement. On July 26, 2019 the Pilliods however accepted the reduced judgement and the verdict was sustained (Baum, Hedlund, Aristei & Goldman, n.d.c; Benbrook, 2020; *Pilliod v. Monsanto*, 2019). Bayer also appealed this verdict but in August 2021, the 1st Appellate District in the Court of Appeal for California sustained the jury's verdicts. Again, Bayer's pre-emption argument was specifically rejected (Gillam, 2021c).

After losing these three trials, Bayer agreed to negotiate settlements in the Roundup-Cancer litigation. On June 24 2020, Bayer announced that it would pay out over U.S.$10 billion to settle around 75 percent of the estimated 125,000 of people claiming that Roundup caused them non-Hodgkin lymphoma. This would leave about 30,000 cancer claims unresolved. For the ones that agreed to settle, U.S.$8.8 billion to U.S. $9.6 billion would be used to resolve the current litigation and U.S.$1.25 billion would be set aside to address potential future litigation. Thereby, Bayer wanted future Roundup claims to be part of a class agreement that, instead of being heard by juries, would have a five-member "Class Science Panel" determine whether there is a causal connection between Roundup and NHL (despite the general causality between Roundup and NHL already being confirmed by three jury trials). Both the plaintiffs in the class action and the company would then be bound by the Class Science Panel's determination, which was expected to take several years. In the meantime, class members would not have been permitted to proceed with Roundup claims nor to seek punitive damages (Gillam, 2020c). After the unusual proposal was criticised by judge Vince Chhabria of the U.S. District Court for the Northern District of California, stating: "*In an area where the science may be evolving, how could it be appropriate to lock in a decision from a panel of scientists for all future cases?"* and that the court is *"tentatively inclined to deny the motion*", Bayer filed a notice of withdrawal of their proposed settlement plan (Gillam, 2020e; f). In February 2021, Bayer filed a new U.S. $2 billion settlement proposal with the U.S. District Court for the Northern District of California, aiming to resolve potential future claims from Roundup users that already have or may develop non-Hodgkin lymphoma. The plan however faced opposition by a coalition representing dozens of U.S. law firms that found the proposed settlement terms laid out to be too low for individual plaintiffs and unfair to farm workers that may yet develop cancer in the future. Other reasons include the proposed four-year stay on all litigation, the science panel and fact that after the four years nobody in the U.S. could sue Monsanto for punitive damages or medical monitoring again, the dangerous precedent it would set for similar future mass tort litigations and the fact that Roundup would continue to be on the market potentially harming more people (Corporate Crime Reporter, 2021; Gillam, 2021b). In May 2021, judge Chhabria rejected Bayer's settlement proposal. He also suggested including a reference to the 2015 IARC finding on the Roundup label (Hals, 2021). Shortly thereafter, Bayer announced it would stop selling glyphosate-based herbicides on the U.S. Lawn & Garden market as of 2023, hoping to eliminate the primary source of future damage claims. The products will still be available for professional and agricultural markets. Bayer also added another U.S. $4.5 billion toward the Roundup litigations (Gillam 2021c; Loh and Feeley, 2021; Sustainable Pulse, 2021). Even though several courts already rejected it (see above), Bayer hoped to get the U.S. Supreme Court to agree with its pre-emption argument in order to limit the ongoing litigation liability (Gillam, 2021d; e). Meanwhile another class action lawsuit, led by plaintiff John Fenton, began in Australia. Fenton was diagnosed with non-Hodgkin lymphoma in 2008 (Gillam 2021b).

In June 2022, the U.S. Supreme Court rejected Bayer's bid to dismiss the legal claims against it and left in place the lower court decision awarding damages to Hardeman (Hurley, 2022).

8.2 Dicamba and 2,4-D lawsuits

Harm to non-target plants and to crops from pesticide drift increases with the use of synthetic auxins, since some formulations are known to have high volatility (Grover et al., 1972; Sciumbato et al., 2004) and may be especially prone to herbicide drift. According to CFS (2014a), 2,4-D has caused more crop injury than any other herbicide. Dicamba traditionally was used sparingly, because of its track record of volatilising and moving far from where it is sprayed, especially in warm weather (Gillam, 2020a). It is reportedly 75 to 400 times more threatening to non-target plants than glyphosate, particularly to soybeans not engineered to withstand it (Dewey, 2017).

The agrochemical companies however promised that their new formulations of synthetic auxin products would minimise herbicide drift. Additionally, good farmer training and other measures such as special nozzles and buffer zones would avoid unintended crop damage (Gillam, 2020a).

8.2.1 Dicamba lawsuits

Monsanto started to commercialise their dicamba tolerant crops before receiving approval from the U.S. Environmental Protection Agency (EPA) for selling the corresponding new post-emergence dicamba herbicide formulation. At the time, academics were worried that this would encourage farmers to spray their new seeds with older, more volatile dicamba formulations, even though this was prohibited (Gillam, 2020a). Scepticism about the practicability of the proposed measures also remained among farmers. They doubted that all growers of dicamba and 2,4- resistant plants would change the nozzles on their spray rings and buy the new more expensive formulations said to be less volatile, when older labels are available and just as effective (Lutz, 2017). Farmers might also not always abide by appropriate herbicide application practices, for example applying them during inappropriate weather conditions. The new HT crops allowed for dicamba and 2,4-D to be applied later in the season, when not only more susceptible plants and crops are growing but when high temperatures may further increase herbicide volatility (Mortensen et al. 2012, Roseboro, 2012). Mortensen et al. (2012) also feared that once an initial number of growers in a region adopt the new resistant traits, the remaining growers may be compelled to follow suit in order to reduce risk of crop injury from herbicide drift. This could also further decrease crop plant diversity in agroecosystems. Some crops might become challenging to grow in landscapes where auxin-tolerant crops are cultivated. Moreover, repeated herbicide drift exposure to weeds could further exacerbate the weed resistance problem (Vieira et al. 2020).

As predicted, dicamba misuse and herbicide drift led to great crop injury at farms not planting dicamba tolerant crops. According to industry numbers, several million crops acres have been damaged due to dicamba since the introduction of dicamba tolerant crops (Gillam, 2020a), including approximately 3.6 million in 2017 alone (*National Family Farm Coalition v. USEPA, 2020)*. Drift damage cannot only be seen on crops but also on forest trees miles away from agricultural fields, as well as in prairies, nature preserves, state parks, backyards, school yards, cemeteries etc. Forest health specialists state that in some areas, tree mortality due to herbicide damage is higher than from the devastating tree pest Emerald Ash Borer. Although tree damage from herbicide drift is nothing new, the scale of damage in recent years in unprecedented. Unlike field crops such as soybeans and cotton, trees are perennials which means they are getting sprayed year after year. The worry concerns not only the trees but also insects that feed on tree leaves and birds that feed on insects, fruit and seeds (Hettinger, 2020a).

In 2016, there were already reports of crops being damaged by dicamba drift, thought to be due to illegal use (The Progressive Farmer, 2016; NPR, 2016; Arkansas Matters, 2016). As a result, several US states began to restrict dicamba herbicide use or ordered emergency bans (Bunge, 2017; Plume, 2017) and several lawsuits were filed against Monsanto, BASF and the U.S. EPA.

In November 2016, a lawsuit on behalf of Bader Farms, Missouri's largest peach farm, was filed against Monsanto. The lawsuit accused Monsanto of knowingly market Xtend cotton and soybean seeds to farmers without a safe herbicide for post-emergence use. Bader Farms experienced the loss of over 30,000 peach trees due to dicamba drift in 2016 and great drops in yield (Justice Pesticide, 2020; Smith, 2016). While in the early 2000s Bader's trees yielded over 150,000 bushels, the yield had dwindled to 12,000 bushels in 2018 (Hettinger, 2020b). In October 2017, BASF was added as defendant to the case by a motion from Bader Farms (*Bader Farms v. Monsanto*, 2017). Bader Farms claimed that Monsanto and BASF knew their products would cause damage to other farms and conspired "*to create an "ecological disaster" where farmers would be forced to buy dicamba-based products*", thereby increasing demand for their products (Hettinger, 2020b).

In February 2017, a class action lawsuit against Monsanto, claiming the company sold seeds without a safe corresponding herbicide, leading farmers to spray illegal chemicals that drifted onto other farms and destroyed crops, was filed by Missouri attorneys. The class action lawsuit had two Missouri farmers as lead plaintiffs and was filed on behalf of farmers in 10 U.S. states. Hundreds of farmers were expected to eventually join the lawsuit (Martin, 2017; Unglesbee, 2017).

In the course of 2017, many more class action lawsuits, representing thousands of farmers whose fields have been damaged by dicamba drift, followed. In February 2018, a motion for a multidistrict litigation (MDL) was approved, centralising nine actions from different states in Missouri. The MDL includes the Bader Farms, Inc., et al. v. Monsanto Company and the Landers, et al. v. Monsanto Company cases, the first two lawsuits filed in the matter (*Dicamba Herbicides Litigation*, 2018; Neeley, 2018; Steed, 2018). By 2020, the MDL involved 30 lawsuits and 170 plaintiffs but the numbers were thought likely to increase (Davies, 2020).

Internal company documents, obtained by the lawyers representing Bader Farms and presented to the jury, show that Monsanto and BASF had been aware for many years, that their new HT crop systems would likely lead to crop damage due to herbicide drift. In 2009, agricultural experts warned Monsanto that the dicamba-HT crops system could have catastrophic consequences. On the one hand, because farmers were likely to apply old, more volatile dicamba formulation to their dicamba tolerant crops and on the other hand because even the new formulations were still likely to cause herbicide drift strong enough to reach crops on other farms (Gillam, 2020a).

Indeed, complaints about dicamba drift did not stop in the 2017 season, when the new herbicide formulations were introduced, on the contrary, the damage further increased. After the U.S. Environmental Protection Agency (EPA) approved Monsanto's new formulation, called XtendiMax with VaporGrip Technology, which contains dicamba, and stated it proposed to register Enlist Duo, the Dow AgroSciences formulation that contains 2,4-D, Texas winegrowers expressed concern that the use of the chemicals may soon expand to include 3.7 million acres of cotton fields in the High Plains, where cotton is being invaded by weeds immune to Roundup (Lutz, 2017). The winegrowers warned that their industry coud be wiped out as a result. They had already reported grapevines withering as a result of spray drift. Missouri and Arkansas responded to developments with legal restrictions on the use of dicamba (AgriMarketing, 2017).

Since 2017, at least 5,000 complaints were filed with state agencies over dicamba drift damage. The numbers are likely higher as not all affected farmers file official complaints (Gillam, 2020a; Hettinger, 2020a). In 2017, weed scientists expressed concern to EPA, that the new dicamba herbicides are more volatile than manufacturers have indicated. Monsanto acknowledged it did not allow field testing of the new formulation by university researchers in order to not delay registration. Scientists that were denied access to test the volatility of the product lamented that the approval process proceeded without adequate data on volatility (Dewey, 2017).

As the internal documents show, Monsanto expected over 10,000 dicamba damage claims from farmers between 2017 and 2020. The documents however also show that Monsanto and BASF saw affected farmers as potential new clients that would have to buy their seeds in order to protect their crops from dicamba drift damage in the future (Gillam, 2020a, Hettinger, 2020b). Indeed, a lot of soybean farmers buy dicamba-tolerant soybeans at least partly to protect their crops from neighbours spraying dicamba (Charles, 2019). While this may work for soybean farmers, it doesn't help farmers that grow crops that are not genetically modified to resist the chemical, such as winegrowers that have also suffered crops losses due to herbicide drift (Lutz, 2017) or peach farmers like Bill Bader from Bader Farms.

In February 2020, Bader Farms won the first lawsuit and was awarded U.S. $15 million in damages, plus U.S. $250 million in punitive damages. The jury found that Monsanto negligently sold dicamba-tolerant seed in 2015 and 2016 before its new low-volatility dicamba herbicide was approved by EPA and failed to provide adequate warnings about the dangers of off-target movement. The jury also found Monsanto and BASF had engaged in a joint venture and conspiracy, knowingly risking widespread crop damage in order to increase their own profits (Davies, 2020; Gillam 2020b). Monsanto and BASF are planning to appeal the $265m verdict. Following the verdict, the number of farmers seeking legal representation to bring charges against Monsanto (now owned by Bayer) and BASF has increased, with thousands of farmers being expected to become plaintiffs. The Bader trial is a good indicator of how other juries might rule in similar cases and may help to inform a settlement in the MDL. More such "bellwether cases" may be selected and heard by juries before it comes to a settlement in the MDL (Davies, 2020; Gillam, 2020a; 2020b; Hettinger, 2020b).

In June 2020, Bayer announced it would pay up to a total of U.S. $ 400 million to settle the U.S. dicamba drift MDL and claims for the 2015-2020 crop years. Bayer expects a contribution from its co-defendant BASF towards this settlement (Gillam, 2020c). In December 2020, the settlement was finalised. US $300 million will be paid to soybean farmers that can document crop yield loss between 2015 and 2020 due to dicamba injury. BASF was not part of this signed agreement (Unglesbee, 2020d).

Nevertheless, the companies still claim that the farmers are at fault for the crop damage by not correctly following the stewardship guidelines and label instructions (Gillam, 2020a). While new formulations are less prone to drift, and stricter regulation for their application and appropriate farmer training may help decrease damage from herbicide drift, it will not solve the problem. The high likelihood of farmers not being able to follow the complex label instructions for applying post-emergent dicamba herbicides, played an important role in the following lawsuit, brought forward by farm and environmental groups.

In January 2017, the National Family Farm Coalition, the Center for Food Safety, the Center for Biological Diversity, and the Pesticide Action Network, filed a lawsuit against EPA's registration of dicamba for use on genetically engineered soybean and cotton, stating that EPA violated its duties under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Endangered Species Act (ESA) (Center for Food Safety, 2017). Following EPA's re-registration of dicamba herbicides in October 2018, the case was re-filed in January 2019 and in addition to Monsanto's XtendiMax also included dicamba herbicides Engenia (BASF) and FeXapan (Corteva), which were part the re-registration (Unglesbee, 2020e).

In June 2020, the Ninth Circuit's three-judge panel unanimously vacated EPAs approval of dicamba based herbicides, confirming that the EPA had violated the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) in multiple ways and that the EPA "… *substantially understated the risks that it acknowledged and failed entirely to acknowledge other risks*." They did not rule whether or not EPA's registration decision also violates the ESA (*National Family Farm Coalition v. USEPA*, 2020; Renda, 2020a).

According to the court ruling, the EPA understated the risk to non-dicamba tolerant (DT) plants by:

- underestimating the dicamba tolerant (DT) seed acreage planted in 2018, and, correspondingly the amount of post-emergence dicamba herbicide sprayed on DT crops;
- failing to acknowledge that dicamba damage was underreported; and
- failing to acknowledge dicamba drift damage and quantifying or estimating the amount of damage (*National Family Farm Coalition v. USEPA*, 2020).

The court also accused the EPA of failing to acknowledge the high likelihood of substantial non-compliance with label restrictions and resulting dicamba damage, despite the knowledge that label restrictions are difficult if not impossible to follow, stating: "*The 2018 label, for use during the 2019 and 2020 growing seasons … is forty pages long, with myriad instructions and restrictions*", adding "*even before the additional restrictions were added to the 2018 label, many industry professionals had been dismayed by the difficulty in complying with the complex and onerous label requirements. By October 2018, there was substantial evidence that even conscientious applicators had not been able consistently to adhere to the label requirements*." Considering all factors like wind speed, time of day, precipitation forecast and time from the planting of neighbouring agricultural operations does not leave much time for spraying, a study conducted by Purdue University researchers found. Furthermore, the court noted that "*The EPA entirely failed to acknowledge risks of economic and social costs"* as required under FIFRA. These include the likely anti-competitive economic effects due to farmers planting DT varieties as a defensive measure against dicamba drift damage. The court also acknowledged that there is "*…extensive evidence that OTT* [over-the-top] *application of dicamba herbicides has torn apart the social fabric of many farming communities*" by turning "*farmer against farmer, and neighbor against neighbor*" (*National Family Farm Coalition v. USEPA*, 2020).

The ruling makes it illegal for farmers to continue to use dicamba herbicides XtendiMax (Bayer), Engenia (BASF) and FeXapan (Corteva). It does not include Syngenta's post-emergence dicamba formulations Tavium (Unglesbee, 2020f).

The order to set aside the EPA's appproval in the middle of the spray season led to a lot of anger, confusion and uncertainty about the legal status of applying the three dicamba products. After the ruling, only two states ordered a halt to all sales and use of the concerned products, while many U.S. states allowed the sale and use of the dicamba products until receiving further guidance from EPA. Meanwhile both Bayer and BASF paused their sales and distribution of their dicamba herbicides (Unglesbee, 2020g).

On June 8, 2020, EPA issued a final cancellation order for the three dicamba products but allowed farmers to use supplies of the concerned dicamba-based herbicides that they had already purchased at the time of the ruling until end of July (Polansek, 2020; Wheeler, 2020).

As a response, the plaintiffs filed an emergency motion, asking the Ninth Circuit court of appeals to halt all dicamba use (Unglesbee, 2020h). The motion was denied by the Ninth Circuit Court, allowing users to continue to spray any stocks of the concerned herbicides until the end of July (Unglesbee, 2020i).

Meanwhile, weed scientists in the U.S. recommended adding either other post emergence herbicides such as Tavium which is not affected by the ruling, ALS herbicides, PPO inhibitors or LCFA inhibitors to glyphosate tank mixes; switching to another herbicide-tolerant platform, such as 2,4-D, isoxaflutole or glufosinate tolerant crops; or increasing application rates and frequencies of glyphosate. Others argue that without dicamba there is not option for post-emergence control, since many important weeds already have resistances to glyphosate, ALS-inhibitors or PPO-inhibitors (Unglesbee, 2020j)

Corteva and BASF filed motions to intervene in the court's decision (Pucci, 2020). The Ninth Circuit however denied BASF's motion on June 25 (Unglesbee, 2020k). In July 2020, Bayer, BASF and Corteva filed separate petitions asking that a broader group of Ninth Circuit judges re-hear the original case, which was also denied by the Ninth Circuit. BASF and Corteva also complained about not having had a chance to defend their products, since they were only included when the case was re-filed in 2019 and were not part of the original 2017 lawsuit (*Appeals Court Rejects Dicamba Rehearing Request*, 2020; Unglesbee, 2020l). For the 2021 season, Bayer and BASF submitted the same formulations of XtendiMax and Engenia for a new registration, along with new volatility-reducing agents (Unglesbee, 2020m). In October 2020, EPA re-registered XtendiMax and Engenia for use on dicamba tolerant cotton and soybeans for five years and extended the registration for Tavium for the same period of time. (Rizzuto & Vasquez, 2020), even though EPA's own data show that the crop injury from dicamba drift was worse than previously known (Hettinger, 2020d). In February 2021, Corteva Agriscience announced it would discontinue sales of FeXapan herbicide in the U.S. and Canada, stating that customers may still buy Corteva brand dicamba-tolerant soybean products and use them with dicamba herbicides offered through other brands (Corteva Agriscience, 2021a). Internal documents show how much influence the registrants, especially Bayer, had over the re-approval of dicamba (Hettinger, 2021). Following the re-registrations, the National Family Farm Coalition, the Center for Food Safety, the Center for Biological Diversity, and the Pesticide Action Network filed a new lawsuit with the Ninth Circuit to review the decision to permit the continued use of these dicamba formulations (Center for Food Safety et al. V. USEPA, 2020). With the re-registrations EPA also issued some restrictions for the use of these herbicides, that should help minimise drift and protect other farmers' crops, such as applying a volatility-reducing chemical, extending the downwind buffer and implementing a nation-wide cut off date after which dicamba application is prohibited (Hettinger, 2020c). In May 2021, only a few months after the 2020 re-registrations, the EPA released a report admitting to high-ranking officials excluding scientific evidence of dicamba's drift risk prior to its 2018 re-registration (US EPA, 2021b):

"We found that the EPA's 2018 decision to extend registrations for three dicamba pesticide products varied from typical operating procedures. Namely, the EPA did not conduct the required internal peer reviews of scientific documents created to support the dicamba decision. While division-level management review is part of the typical operating procedure, interviewees said that senior leaders in the OCSPP's [Office of Chemical Safety and Pollution Prevention's] *immediate office were more involved in the dicamba decision than in other pesticide registration decisions. This led to senior-level changes to or omissions from scientific documents. For instance, these documents excluded some conclusions initially assessed by staff scientists to address stakeholder risks. We also found that staff felt constrained or muted in sharing their concerns on the dicamba registrations. The EPA's actions on the dicamba registrations left the decision legally vulnerable, resulting in the Ninth Circuit Court of Appeals vacating the 2018 registrations for violating FIFRA by substantially understating some risks and failing to acknowledge others entirely."*

In 2022, the federal judge considering the case against the EPA in the U.S. District Court for the District of Arizona ordered that the EPA should file a report on the status of its ongoing evaluation of its options for addressing future dicamba-related incidents (Unglesbee, 2022a). The environmental and farming organisations subsequently asked the court to lift a stay and expedite their lawsuit demanding EPA vacate its 2020 dicamba registrations of Engenia, Tavium and XtendiMax (Unglesbee, 2022b).

Despite the new restrictions on dicamba use that came with the 2020 re-registration, the number of formal complaints of herbicide injury in 2021 kept pace with the 2020 season in some states. In Minnesota it was even higher than in 2020. In Arkansas, where Dicamba was legal to spray for the first time since 2017, the Arkansas Department of Agriculture estimated that between 650,000 to 800,000 acres of crops were damaged just in the eastern Arkansas areas. Most likely, the formal pesticide injury complaints don't fully reflect the extent of crop injury over fears of neighbourly tensions, jeopardising any future crop insurance claims for other problems, or because farmers don't know the source of the crop injury (Campbell, 2021; Unglesbee, 2021b). The Upper Midwest even reported that 2021 may be the worst year yet when it comes to dicamba damage in the Upper Midwest, although some of the crop injury may also be the result of drought (Rook & Pates, 2021).

Despite these developments, the companies involved are not moving away from the dicamba-tolerant crop system. They are working on new dicamba formulations, some of which are already submitted with the U.S. EPA. They also aim to commercialise new dicamba tolerant traits in the near future, some with tolerances against four or five active ingredients (Unglesbee, 2020n).

8.2.2 2,4-D lawsuit

Corteva Agriscience's Enlist Duo herbicide designed for post-emergence use in 2,4-D tolerant Enlist crops also faced legal challenges in the Ninth Circuit appeals court. Many of the same plaintiffs that won the dicamba case in 2017 also filed a lawsuit against the Enlist Weed Control System (2,4-D and glyphosate), claiming the EPA violated the Endangered Species Act (ESA) and the Federal Insecticide Fungicide and Rodenticide ACT (FIFRA) (Allington, 2020; Begemann, 2020; Unglesbee, 2020o). In July 2020, the Ninth Circuit with a two-judge majority denied the petition to vacate Enlist Duo. The judges' majority opinion however agreed that the EPA had failed to consider potential harm to monarch butterflies from increased Enlist Duo use on milkweed in crop fields. The EPA is now requested to address this issue. In a minority opinion, a third judge argued that EPA had indeed violated the Endangered Species Act and that the Enlist Duo registrations should be vacated. The judge agreed with the plaintiffs that EPA failed to use the best scientific data to assess potential risks to threatened or endangered species. The plaintiffs announced they would challenge the ruling, stating that the EPA ignored well-documented evidence that Enlist Duo harms endangered species such as Hine's emerald dragonflies and Fender's blue butterflies (Renda, 2020b; Unglesbee, 2020p). Until today, Enlist Duo remains registered for over the top use, and unlike the dicamba formulations, this has no cut-off date (Corteva Agriscience, 2021b).

9. Alternatives

The growing failure of RoundUp Ready crops, due to the spread of glyphosate resistant (GR) weeds, provides an opportunity to phase out the use of RR crops and adopt new methods and technologies. The priority should be to reduce and replace the use of herbicides: not to replace RR crops with other herbicide-tolerant crops, whether or not these are GM crops or produced by different methods. Harker et al. (2017) note that weed science credibility and progress requires admission that herbicides should be used less frequently: and that this requires the influence of the herbicide industry to be reduced. It is now widely recognised that "*The vision for the future of HR* [herbicide resistant] *weed management globally should center on reduced herbicide dependency, especially glyphosate*" (Beckie et al., 2019).

Viable alternatives include:

- Increased use of agro-ecological methods, for conventional as well as organic farming, including crop rotations;
- Further development and implementation of spot spraying and precision weeding to target and reduce the use of herbicides.

A detailed review of alternatives is outside the scope of this report, however some further resources are highlighted below.

Agro-ecology is defined by the website www.agroecology.org as:

- The application of ecology to the design and management of sustainable agroecosystems.
- A whole-systems approach to agriculture and food systems development based on traditional knowledge, alternative agriculture, and local food system experiences.
- Linking ecology, culture, economics, and society to sustain agricultural production, healthy environments, and viable food and farming communities.

The United Nations Food and Agriculture Organisation (FAO) states on its website[5]:
"*Agroecology is a scientific discipline, a set of practices and a social movement. As a science, it studies how different components of the agroecosystem interact. As a set of practices, it seeks sustainable farming systems that optimize and stabilize yields. As a social movement, it pursues multifunctional roles for agriculture, promotes social justice, nurtures identity and culture, and strengthens the economic viability of rural areas. Family farmers are the people who hold the tools for practising Agroecology. They are the real keepers of the knowledge and wisdom needed for this agenda. Therefore, family farmers around the world are the keys elements for producing food in an agroecological way*".

Numerous examples of current applications and research and development are available on these websites and elsewhere.

In an alternative approach, precision weeding and precision spraying focus more on the use of modern technologies such as robots to target pesticide applications more precisely and thus reduce their use, or on using lasers to burn targeted weeds (Quartz, 2015; Guardian, 2015; Horticulture Week, 2015; Gonzalez-de-Santos et al., 2017; Beckie et al., 2019b; Oliver 2020; Belton 2021; Peters, 2021). Young (2012) argues that, "*By using the latest technologies that can quickly identify weeds and react with precisely targeted applications, conceptually, weed control tools could be integrated for use at anytime and at any point in a field*". The goal is "*the elimination of weeds while minimizing negative impacts to the environment and economics*". Harvest Weed Seed Control (HSWC) is another weed control practice that does not rely on increasing use of herbicides, but instead tries to limit weed seed production during grain harvest (Walsh et al., 2017). These moves towards reducing inputs are the opposite of the blanket spraying of crops with weedkillers associated with RR or other HT crops.

There are significant opportunity costs associated with investing in 'next-generation' HT crops which are tolerant to more herbicides but which will not solve the long-term problem of resistant weeds and will continue to pose risks to human health and the environment. Investing in alternatives such as agroecology and spot spraying means a supporting a paradigm shift towards using less herbicide, not more, to the benefit of farmers, human health and the environment. It is particularly important that RR crops are not pushed into new countries which have so far avoided stepping onto the "transgenic treadmill".

[5] http://www.fao.org/family-farming/themes/agroecology/en/

References

Abarikwu, S. O., Akiri, O. F., Durojaiye, M. A., & Adenike, A. (2015). Combined effects of repeated administration of Bretmont Wipeout (glyphosate) and Ultrazin (atrazine) on testosterone, oxidative stress and sperm quality of Wistar rats. *Toxicology Mechanisms and Methods*, *25*(1), 70–80. http://doi.org/10.3109/15376516.2014.989349

Abdul, K. S. M., De Silva, P. M. C. S., Ekanayake, E. M. D. V., Thakshila, W. A. K. G., Gunarathna, S. D., Gunasekara, T. D. K. S. C., Jayasinghe, S. S., Asanthi, H. B., Chandana, E. P. S., Chaminda, G. G. T., Siribaddana, S. H., & Jayasundara, N. (2021). Occupational Paraquat and Glyphosate Exposure May Decline Renal Functions among Rural Farming Communities in Sri Lanka. International Journal of Environmental Research and Public Health, 18(6), 3278. https://doi.org/10.3390/ijerph18063278

Abraham, W. (2010). Glyphosate Formulations And Their Use For The Inhibition Of 5-enolpyruvylshikimate-3-phosphate Synthase. U.S. Patent 7,771,736 B2. https://www.lens.org/lens/patent/US_7771736_B2

Abraham, J., Benhotons, G. S., Krampah, I., Tagba, J., Amissah, C., & Abraham, J. D. (2018). Commercially formulated glyphosate can kill non-target pollinator bees under laboratory conditions. *Entomologia Experimentalis et Applicata*, *166*(8), 695–702. https://doi.org/10.1111/eea.12694

AC21 (2012). Enhancing Coexistence: A Report of the AC21 to the Secretary of Agriculture. http://www.usda.gov/documents/ac21_report-enhancing-coexistence.pdf

AC21 (2015). Summary of main USDA activities initiated in response to the November, 2012 AC21 report**.** http://www.usda.gov/documents/response-summary-november-2012-ac21-report.pdf

Ackermann, W., Coenen, M., Schrödl, W., Shehata, A. A., & Krüger, M. (2015). The Influence of Glyphosate on the Microbiota and Production of Botulinum Neurotoxin During Ruminal Fermentation. *Current Microbiology*, *70*(3), 374–382. https://doi.org/10.1007/s00284-014-0732-3

ACRE. (2019). Advice on an application for deliberate release of a GMO for research and development purposes. Advisory Committee on Releases to the Environment. Notification reference: 18/R8/01. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/800590/gmo-camelina-acre-advice-18r801.pdf

Acquavella, J. F., Alexander, B. H., Mandel, J. S., Gustin, C., Baker, B., Chapman, P., & Bleeke, M. (2004). Glyphosate biomonitoring for farmers and their families: results from the Farm Family Exposure Study. *Environmental Health Perspectives*, *112*(3), 321–326.

Adner, C. (2017). How Glyphosate and Roundup® Affect the Growth of *C. Elegans*. Presented at the 2017 AAAS Annual Meeting (February 16-20, 2017), aaas. https://aaas.confex.com/aaas/2017/webprogram/Paper20130.html

Adner, E., Pettee, B., 2017. Toxicity of Glyphosate on the *C. Elegans* Worm: Implications for Soil and Human Health. Presented at the 2017 AAAS Annual Meeting (February 16-20, 2017), aaas. https://aaas.confex.com/aaas/2017/webprogram/Paper20137.html

Afidchao, M. M., Musters, C. J. M., Wossink, A., Balderama, O. F., & de Snoo, G. R. (2014). Analysing the farm level economic impact of GM corn in the Philippines. *NJAS - Wageningen Journal of Life Sciences*. http://doi.org/10.1016/j.njas.2014.05.008

African Centre for Biodiversity. (2021). *Bayer Breathing Life Into Gates' Failed GM Drought Tolerant Maize*. https://acbio.org.za/wp-content/uploads/2022/04/bayer-breathing-life-gates-failed-gm-drought-tolerant-maizeagrarian-extractivism-continues-unabated.pdf

Agapito-Tenfen, S., Lopez, F. R., Mallah, N., Abou-Slemayne, G., Trtikova, M., Nodari, R. O., & Wickson, F. (2017). Transgene flow in Mexican maize revisited: Socio-biological analysis across two contrasting farmer communities and seed management systems. *Ecology and Evolution*, *7*(22), 9461–9472. https://doi.org/10.1002/ece3.3415

Agostini, L. P., Dettogni, R. S., dos Reis, R. S., Stur, E., dos Santos, E. V. W., Ventorim, D. P., Garcia, F. M., Cardoso, R. C., Graceli, J. B., & Louro, I. D. (2020). Effects of glyphosate exposure on human health: Insights from epidemiological and in vitro studies. *Science of The Total Environment*, *705*, 135808. https://doi.org/10.1016/j.scitotenv.2019.135808

Agrawal, A. A., & Inamine, H. (2018). Mechanisms behind the monarch's decline. *Science*, *360*(6395), 1294–1296. https://doi.org/10.1126/science.aat5066

AgriMarketing (2017) States begin restricting use of dicamba herbicides. 23rd January 2017. http://www.agrimarketing.com/s/107922

AgriPulse (2016) APHIS backs two new lines of GE corn. 23 March 2016. http://www.agri-pulse.com/APHIS-backs-two-new-lines-of-GE-corn-03232016.asp

AgWeb (2016) Applegate Farms Moves to Make Its Meat GMO-Free. 13 July 2016. http://www.agweb.com/article/applegate-farms-moves-to-make-its-meat-gmo-free-blmg/

AgWeek (2016) What NASS survey says about soybean protection practices. 1 June 2016. http://www.agweek.com/crops/soybeans/4045309-what-nass-survey-says-about-soybean-protection-practices

Ahmad, I., & Malloch, D. (1995). Interaction of soil microflora with the bioherbicide phosphinothricin. *Agriculture, Ecosystems & Environment*, *54*(3), 165–174. https://doi.org/10.1016/0167-8809(95)00603-P

Ahmad, I., Bissett, J., & Malloch, D. (1995a). Effect of Phosphinothricin on Nitrogen Metabolism of Trichoderma Species and Its Implications for Their Control of Phytopathogenic Fungi. *Pesticide Biochemistry and Physiology*, *53*(1), 49–59. https://doi.org/10.1006/pest.1995.1054

Ahmad, I., Malloch, D., & Bissett, J. (1995b). Influence of the bioherbicide phosphinothricin on interactions between phytopathogens and their antagonists. *Canadian Journal of Botany*, *73*(11), 1750–1760. https://doi.org/10.1139/b95-187

Ahn, Y.-J., Cho, J.-R., Kim, Y.-J., Yoo, J.-K., & Lee, J.-O. (1997). Toxicity of the herbicide glufosinate-ammonium to Tetranychus urticae (Acari: Tetranychidae) under laboratory and field conditions. *Pesticide Science*, *51*(4), 455–461. https://doi.org/10.1002/(SICI)1096-9063(199712)51:4<455::AID-PS667>3.0.CO;2-F

Ahn, Y.-J., Kim, Y.-J., & Yoo, J.-K. (2001). Toxicity of the Herbicide Glufosinate-Ammonium to Predatory Insects and Mites of *Tetranychus urticae* (Acari: Tetranychidae) Under Laboratory Conditions. *Journal of Economic Entomology*, *94*(1), 157–161. https://doi.org/10.1603/0022-0493-94.1.157

Ainley, W. M., Sastry-Dent, L., Welter, M. E., Murray, M. G., Zeitler, B., Amora, R., Corbin, D. R., Miles, R. R., Arnold, N. L., Strange, T. L., Simpson, M. A., Cao, Z., Carroll, C., Pawelczak, K. S., Blue, R., West, K., Rowland, L. M., Perkins, D., Samuel, P., … Petolino, J. F. (2013). Trait stacking via targeted genome editing. *Plant Biotechnology Journal*, *11*(9), 1126–1134. https://doi.org/10.1111/pbi.12107

Ait Bali, Y., Ba-Mhamed, S., & Bennis, M. (2017). Behavioral and Immunohistochemical Study of the Effects of Subchronic and Chronic Exposure to Glyphosate in Mice. *Frontiers in Behavioral Neuroscience*, *11*. https://doi.org/10.3389/fnbeh.2017.00146

Akça, A., Kocabaş, M., & Kutluyer, F. (2021). Glyphosate disrupts sperm quality and induced DNA damage of rainbow trout (Oncorhynchus mykiss) sperm. *Journal of Environmental Science and Health, Part C*, *0*(0), 1–10. https://doi.org/10.1080/26896583.2021.1969180

Alarcón, R., Ingaramo, P. I., Rivera, O. E., Dioguardi, G. H., Repetti, M. R., Demonte, L. D., Milesi, M. M., Varayoud, J., Muñoz-de-Toro, M., & Luque, E. H. (2019). Neonatal exposure to a glyphosate-based herbicide alters the histofunctional differentiation of the ovaries and uterus in lambs. *Molecular and Cellular Endocrinology*, *482*, 45–56. https://doi.org/10.1016/j.mce.2018.12.007

Alarcón, R., Rivera, O. E., Ingaramo, P. I., Tschopp, M. V., Dioguardi, G. H., Milesi, M. M., Muñoz-de-Toro, M., & Luque, E. H. (2020). Neonatal exposure to a glyphosate-based herbicide alters the uterine differentiation of prepubertal ewe lambs. *Environmental Pollution*, *265*, 114874. https://doi.org/10.1016/j.envpol.2020.114874

Albisser Vögeli, G., Burose, F., Wolf, D., Lips, M. (2011). Wirtschaftlichkeit gentechnisch-veränderter Ackerkulturen in der Schweiz. Mit detaillierter Berücksichtigung möglicher Koexistenz-Kosten. Forschungsanstalt Agroscope Reckenholz-Tänikon ART.

Albrecht, A., Fausto, D., Albrecht, L., Migliavacca, R., Eckert, C., & Filho, R. (2020). ECONOMIC INFLUENCES OF THE APPLICATION OF DIFFERENT MANAGEMENTS, FORMULATIONS AND DOSES OF GLYPHOSATE ON ROUNDUP READY® SOYBEAN. *Revista Em Agronegócio e Meio Ambiente; Maringá*, *13*(2), 507–523. https://doi.org/DOI:10.17765/2176-9l68.2020v13n2p507-523

Alcántara-de la Cruz, R., Rojano-Delgado, A. M., Giménez, M. J., Cruz-Hipolito, H. E., Domínguez-Valenzuela, J. A., Barro, F., & De Prado, R. (2016). First Resistance Mechanisms Characterization in Glyphosate-Resistant Leptochloa virgata. *Frontiers in Plant Science*, *7*, 1742. https://doi.org/10.3389/fpls.2016.01742

Alcántara de la Cruz, R., Moraes de Oliveira, G., Carvalho, L., & Silva, M. (2020). *Herbicide Resistance in Brazil: Status, Impacts, and Future Challenges* (pp. 1–25). https://doi.org/10.5772/intechopen.91236

Alesci, C., Gillespie, P. (2015). Chipotle is now GMO-free. CNN Money. http://money.cnn.com/2015/04/26/investing/chipotle-gmo-free/index.html?sr=twmoney042615chipotle0930story

Ali, Z., Shami, A., Sedeek, K., Kamel, R., Alhabsi, A., Tehseen, M., Hassan, N., Butt, H., Kababji, A., Hamdan, S. M., & Mahfouz, M. M. (2020). Fusion of the Cas9 endonuclease and the VirD2 relaxase facilitates homology-directed repair for precise genome engineering in rice. *Communications Biology*, *3*(1), 1–13. https://doi.org/10.1038/s42003-020-0768-9

Allington, A. (2020, June 26). *With Dicamba Canceled, Legal Focus Now Shifts to Corteva's Enlist*. https://news.bloomberglaw.com/environment-and-energy/with-dicamba-canceled-legal-focus-now-shifts-to-cortevas-enlist

Allison, R. (2015). How glyphosate-resistant weeds will ingest all US crops by 2020. Farmers Weekly. http://www.fwi.co.uk/arable/glyphosate-resistant-weeds-will-infest-all-us-crops-by-2020.htm?cmpid=SOC%7CTwitter%7CFarmersWeekly%7Csf14292641%7Csf14292641

Almasri, H., Tavares, D. A., Pioz, M., Sené, D., Tchamitchian, S., Cousin, M., Brunet, J.-L., & Belzunces, L. P. (2020). Mixtures of an insecticide, a fungicide and a herbicide induce high toxicities and systemic physiological disturbances in winter Apis mellifera honey bees. *Ecotoxicology and Environmental Safety*, *203*, 111013. https://doi.org/10.1016/j.ecoenv.2020.111013

Almasri, H., Tavares, D. A., Diogon, M., Pioz, M., Alamil, M., Sené, D., Tchamitchian, S., Cousin, M., Brunet, J.-L., & Belzunces, L. P. (2021). Physiological effects of the interaction between Nosema ceranae and sequential and overlapping exposure to glyphosate and difenoconazole in the honey bee Apis mellifera. *Ecotoxicology and Environmental Safety*, *217*, 112258. https://doi.org/10.1016/j.ecoenv.2021.112258

Almasri, H., Liberti, J., Brunet, J.-L., Engel, P., & Belzunces, L. P. (2022). Mild chronic exposure to pesticides alters physiological markers of honey bee health without perturbing the core gut microbiota. *Scientific Reports*, *12*(1), 4281. https://doi.org/10.1038/s41598-022-08009-2

Alonso, L. L., Demetrio, P. M., Agustina Etchegoyen, M., & Marino, D. J. (2018). Glyphosate and atrazine in rainfall and soils in agroproductive areas of the pampas region in Argentina. *Science of The Total Environment*, *645*, 89–96. https://doi.org/10.1016/j.scitotenv.2018.07.134

Amaro-Blanco, I., Fernández-Moreno, P. T., Osuna-Ruiz, M. D., Bastida, F., & Prado, R. D. (2018). Mechanisms of glyphosate resistance and response to alternative herbicide-based management in populations of the three Conyza species introduced in southern Spain. *Pest Management Science*, *74*(8), 1925–1937. https://doi.org/10.1002/ps.4896

Amer, S. M., & Aly, F. A. E. (2001). Genotoxic effect of 2,4-dichlorophenoxy acetic acid and its metabolite 2,4-dichlorophenol in mouse. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *494*(1), 1–12. https://doi.org/10.1016/S1383-5718(01)00146-2

American Cancer Society (2015). Known and Probably Human Carcinogens. http://www.cancer.org/cancer/cancercauses/othercarcinogens/generalinformationaboutcarcinogens/known-and-probable-human-carcinogens

Andrade, V. S., Gutierrez, M. F., Reno, U., Popielarz, A., Gervasio, S., & Gagneten, A. M. (2021). Synergy between glyphosate and cypermethrin formulations on zooplankton: Evidences from a single-specie test and a community mesocosm experiment. *Environmental Science and Pollution Research*, *28*(21), 26885–26894. https://doi.org/10.1007/s11356-021-12619-0

Anifandis, G., Amiridis, G., Dafopoulos, K., Daponte, A., Dovolou, E., Gavriil, E., Gorgogietas, V., Kachpani, E., Mamuris, Z., Messini, C. I., Vassiou, K., & Psarra, A.-M. G. (2017). The In Vitro Impact of the Herbicide Roundup on Human Sperm Motility and Sperm Mitochondria. *Toxics*, *6*(1), 2. https://doi.org/10.3390/toxics6010002

Anifandis, G., Katsanaki, K., Lagodonti, G., Messini, C., Simopoulou, M., Dafopoulos, K., & Daponte, A. (2018). The Effect of Glyphosate on Human Sperm Motility and Sperm DNA Fragmentation. *International Journal of Environmental Research and Public Health*, *15*(6), 1117. https://doi.org/10.3390/ijerph15061117

Anton, B. J., Dehnert, G. K., & Karasov, W. H. (2021). Subchronic impacts of 2,4-D herbicide Weedestroy®AM40 on associative learning in juvenile yellow perch (Perca flavescens). *Aquatic Toxicology*, *237*, 105909. https://doi.org/10.1016/j.aquatox.2021.105909

Antoniou, M., Habib, M. E. M., Howard, C. V., Jennings, R. C., Leifert, C., Nodari, R. O., Robinson, C. J., & Fagan, J. (2012). Teratogenic Effects of Glyphosate-Based Herbicides: Divergence of Regulatory Decisions from Scientific Evidence. *Environmental & Analytical Toxicology*, *0*(0), 1–13. https://doi.org/10.4172/2161-0525.S4-006

Aono, M., Wakiyama, S., Nagatsu, M., Nakajima, N., Tamaoki, M., Kubo, A., & Saji, H. (2006). Detection of feral transgenic oilseed rape with multiple-herbicide resistance in Japan. *Environmental Biosafety Research*, *5*(2), 77–87. http://doi.org/10.1051/ebr:2006017

AP (2014). Syngenta faces dozens of lawsuits over GMO seed. http://www.dailymail.co.uk/wires/ap/article-2838345/Syngenta-faces-dozens-lawsuits-GMO-seed.html

AP (2015). Mexico groups ask UN to list Monarch reserve as in danger. http://m.apnews.com/ap/db_268779/contentdetail.htm?contentguid=IehqtE9P

Aparicio, V.C., De Gerónimo, E., Marino, D., Primost, J., Carriquiriborde, P., Costa, J.L. (2013). Environmental fate of glyphosate and aminomethylphosphonic acid in surface waters and soil of agricultural basins. *Chemosphere* **93**, 1866–1873. doi:10.1016/j.chemosphere.2013.06.041

Aparicio, V. C., Aimar, S., Gerónimo, E. D., Mendez, M. J., & Costa, J. L. (2018). Glyphosate and AMPA concentrations in wind-blown material under field conditions. *Land Degradation & Development*, *29*(5), 1317–1326. https://doi.org/10.1002/ldr.2920

Appeals Court Rejects Dicamba Rehearing Request. (2020, August 19). American Ag Network. https://americanagnetwork.com/2020/08/appeals-court-rejects-dicamba-rehearing-request/

Aranda, D. (2015). Reclamos contra un pesticida. Pagina 12. http://www.pagina12.com.ar/diario/sociedad/3-272409-2015-05-11.html

Arbuckle, T. E., Lin, Z., & Mery, L. S. (2001). An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population. *Environmental Health Perspectives*, 109(8), 851–857.

Areal, F.J., Riesgo, L., Rodriguez-Cerezo, E. (2013). Economic and agronomic impact of commercialized GM crops: A meta-analysis. *Journal of Agricultural Science* **151**:7-33.

Areal, F. J., & Riesgo, L. (2021). EU Inspections of GM Content in Food and Feed: Are They Effective? *Agriculture*, *11*(9), 842. https://doi.org/10.3390/agriculture11090842

Argou-Cardozo, I., & Zeidán-Chuliá, F. (2018). Clostridium Bacteria and Autism Spectrum Conditions: A Systematic Review and Hypothetical Contribution of Environmental Glyphosate Levels. *Medical Sciences (Basel, Switzerland)*, *6*(2), E29. https://doi.org/10.3390/medsci6020029

Aris, A., & Leblanc, S. (2011). Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. *Reproductive Toxicology*, *31*, 528–533. https://doi.org/10.1016/j.reprotox.2011.02.004

Aristilde, L., Reed, M. L., Wilkes, R. A., Youngster, T., Kukurugya, M. A., Katz, V., & Sasaki, C. R. S. (2017). Glyphosate-Induced Specific and Widespread Perturbations in the Metabolome of Soil Pseudomonas Species. *Frontiers in Environmental Science*, *5*. https://doi.org/10.3389/fenvs.2017.00034

Arkansas Matters (2016) Working 4 You: Illegal Chemical Use Damages Soybeans, Threat of Spread Outside Ag. 1 August 2016. http://www.arkansasmatters.com/news/local-news/working-4-you-illegal-chemical-use-damages-soybeans-threat-of-spread-outside-ag

Aronzon, C. M., Sandoval, M. T., Herkovits, J., & Pérez-Coll, C. S. (2011). Stage-dependent toxicity of 2,4-dichlorophenoxyacetic on the embryonic development of a South American toad, Rhinella arenarum. *Environmental Toxicology*, *26*(4), 373–381. https://doi.org/10.1002/tox.20564

Arregui, M. C., Lenardón, A., Sanchez, D., Maitre, M. I., Scotta, R., & Enrique, S. (2004). Monitoring glyphosate residues in transgenic glyphosate-resistant soybean. *Pest Management Science*, *60*(2), 163–166. http://doi.org/10.1002/ps.775

Arumuganathan, P., Phillips, P. S., Nolan, C. J., & Plautz, C. Z. (2016). Assessment of steroidogenic pathway components following exposure of L. palustris to the herbicide roundup or its components. *Proceedings of the West Virginia Academy of Science*, *88*(1), Article 1. http://pwvas.org/index.php/pwvas/article/view/60

Atamaniuk, T. M., Kubrak, O. I., Storey, K. B., & Lushchak, V. I. (2013). Oxidative stress as a mechanism for toxicity of 2,4-dichlorophenoxyacetic acid (2,4-D): Studies with goldfish gills. *Ecotoxicology*, *22*(10), 1498–1508. https://doi.org/10.1007/s10646-013-1136-z

Ateeq, B., Farah, M. A., & Ahmad, W. (2006). Evidence of apoptotic effects of 2,4-D and butachlor on walking catfish, Clarias batrachus, by transmission electron microscopy and DNA degradation studies. *Life Sciences*, *78*(9), 977–986. https://doi.org/10.1016/j.lfs.2005.06.008

Aulakh, J. S., Chahal, P. S., Kumar, V., Price, A. J., & Guillard, K. (2021). Multiple herbicide-resistant Palmer amaranth (Amaranthus palmeri) in Connecticut: Confirmation and response to POST herbicides. *Weed Technology*, *35*(3), 457–463. https://doi.org/10.1017/wet.2021.6

Avigliano, L., Fassiano, A. V., Medesani, D. A., Ríos de Molina, M. C., & Rodríguez, E. M. (2014a). Effects of Glyphosate on Growth Rate, Metabolic Rate and Energy Reserves of Early Juvenile Crayfish, *Cherax quadricarinatus* M. *Bulletin of Environmental Contamination and Toxicology*, *92*(6), 631–635. http://doi.org/10.1007/s00128-014-1240-7

Avigliano, L., Alvarez, N., Loughlin, C. M., & Rodríguez, E. M. (2014b). Effects of glyphosate on egg incubation, larvae hatching, and ovarian rematuration in the estuarine crab *Neohelice granulata*. *Environmental Toxicology and Chemistry / SETAC*, *33*(8), 1879–1884. http://doi.org/10.1002/etc.2635

Avigliano, L., Canosa, I. S., Medesani, D. A., & Rodríguez, E. M. (2018). Effects of Glyphosate on Somatic and Ovarian Growth in the Estuarine Crab Neohelice granulata, During the Pre-Reproductive Period. *Water, Air, & Soil Pollution*, *229*(2), 44. https://doi.org/10.1007/s11270-018-3698-0

Avila, L. A. de, Marchesan, E., Camargo, E. R., Merotto, A., Ulguim, A. da R., Noldin, J. A., Andres, A., Mariot, C. H. P., Agostinetto, D., Dornelles, S. H. B., & Markus, C. (2021). Eighteen years of Clearfield™ rice in Brazil: What have we learned? *Weed Science*, *69*(5), 585–597. https://doi.org/10.1017/wsc.2021.49

Avila-Vazquez, M., Difilippo, F. S., Lean, B. M., Maturano, E., & Etchegoyen, A. (2018). Environmental Exposure to Glyphosate and Reproductive Health Impacts in Agricultural Population of Argentina. *Journal of Environmental Protection*, *9*(3), 720–726. https://doi.org/10.4236/jep.2018.93016

Babalola, O. O., Truter, J. C., Archer, E., & van Wyk, J. H. (2021). Exposure Impacts of Environmentally Relevant Concentrations of a Glufosinate Ammonium Herbicide Formulation on Larval Development and Thyroid Histology of Xenopus laevis. *Archives of Environmental Contamination and Toxicology*, *80*(4), 717–725. https://doi.org/10.1007/s00244-020-00758-3

Babich, R., Ulrich, J. C., Ekanayake, E. M. D. V., Massarsky, A., De Silva, P. M. C. S., Manage, P. M., Jackson, B. P., Ferguson, P. L., Di Giulio, R. T., Drummond, I. A., & Jayasundara, N. (2020). Kidney developmental effects of metal-herbicide mixtures: Implications for chronic kidney disease of unknown etiology. *Environment International*, *144*, 106019. https://doi.org/10.1016/j.envint.2020.106019

Bach, N. C., Natale, G. S., Somoza, G. M., & Ronco, A. E. (2016). Effect on the growth and development and induction of abnormalities by a glyphosate commercial formulation and its active ingredient during two developmental stages of the South-American Creole frog, Leptodactylus latrans. *Environmental Science and Pollution Research International*, *23*(23), 23959–23971. https://doi.org/10.1007/s11356-016-7631-z

Bach, N. C., Marino, D. J. G., Natale, G. S., & Somoza, G. M. (2018). Effects of glyphosate and its commercial formulation, Roundup® Ultramax, on liver histology of tadpoles of the neotropical frog, Leptodactylus latrans (amphibia: Anura). *Chemosphere*, *202*, 289–297. https://doi.org/10.1016/j.chemosphere.2018.03.110

Bader Farms, Inc. et al v. Monsanto Co., 1:16-CV-299-SNLJ (United States District Court Eastern District of Missouri Southeastern Division October 20, 2017). https://cases.justia.com/federal/district-courts/missouri/moedce/1:2016cv00299/150890/76/0.pdf?ts=1508581129

Baerson, S. R., Rodriguez, D. J., Tran, M., Feng, Y., Biest, N. A., & Dill, G. M. (2002). Glyphosate-resistant goosegrass. Identification of a mutation in the target enzyme 5-enolpyruvylshikimate-3-phosphate synthase. *Plant Physiology*, *129*(3), 1265–1275. http://doi.org/10.1104/pp.001560

Bagavathiannan, M. V., & Norsworthy, J. K. (2016). Multiple-Herbicide Resistance Is Widespread in Roadside Palmer Amaranth Populations. *PLoS ONE*, *11*(4). https://doi.org/10.1371/journal.pone.0148748

Bagnasco, P., De La Fuente, L., Gualtieri, G., Noya, F., & Arias, A. (1998). Fluorescent Pseudomonas spp. as biocontrol agents against forage legume root pathogenic fungi. *Soil Biology and Biochemistry*, *30*(10–11), 1317–1322. http://doi.org/10.1016/S0038-0717(98)00003-0

Bai, S. H., & Ogbourne, S. M. (2016). Glyphosate: Environmental contamination, toxicity and potential risks to human health via food contamination. *Environmental Science and Pollution Research*, *23*(19), 18988–19001. https://doi.org/10.1007/s11356-016-7425-3

Baier, C. J., Gallegos, C. E., Raisman-Vozari, R., & Minetti, A. (2017). Behavioral impairments following repeated intranasal glyphosate-based herbicide administration in mice. *Neurotoxicology and Teratology*, *64*, 63–72. https://doi.org/10.1016/j.ntt.2017.10.004

Bailey, W. A., Poston, D. H., Wilson, H. P., & Hines, T. E. (2002). Glyphosate Interactions with Manganese. *Weed Technology*, *16*(4), 792–799. http://doi.org/10.1614/0890-037X(2002)016[0792:GIWM]2.0.CO;2

Baker, J. M., Ochsner, T. E., Venterea, R. T., & Griffis, T. J. (2007). Tillage and soil carbon sequestration—What do we really know? *Agriculture, Ecosystems & Environment*, *118*(1), 1–5. https://doi.org/10.1016/j.agee.2006.05.014

Band, P. R., Abanto, Z., Bert, J., Lang, B., Fang, R., Gallagher, R. P., & Le, N. D. (2011). Prostate cancer risk and exposure to pesticides in British Columbia Farmers. *The Prostate*, *71*(2), 168–183. https://doi.org/10.1002/pros.21232

Barbosa Lima, I., Boechat, I., & Gücker, B. (2021). Glyphosate in Brazil: Use, aquatic contamination, environmental effects, and health hazards. *Caderno de Geografia*, *31*, 90–115. https://doi.org/10.5752/p.2318-2962.2021v31nesp1p90

Barbieri, E. (2009). Effect of 2,4-D herbicide (2,4-dichlorophenoxyacetic acid) on oxygen consumption and ammonium excretion of juveniles of Geophagus brasiliensis (Quoy & Gaimard, 1824) (Osteichthyes, Cichlidae). *Ecotoxicology*, *18*(1), 55–60. https://doi.org/10.1007/s10646-008-0256-3

Barker, D., Freese, B., Kimbrell, G. (2013). Seed giants vs. U.S. farmers: A report by the Center for Food Safety & Save Our Seeds. Washington, DC: Center for Food Safety, 2013. http://www.centerforfoodsafety.org/files/seed-giants_final_04424.pdf

Barnett, J. A., Bandy, M. L., & Gibson, D. L. (2022). Is the Use of Glyphosate in Modern Agriculture Resulting in Increased Neuropsychiatric Conditions Through Modulation of the Gut-brain-microbiome Axis? *Frontiers in Nutrition*, *9*. https://www.frontiersin.org/article/10.3389/fnut.2022.827384

BASF. (2017). *Zidua® PRO*. BASF. http://www.cdms.net/ldat/ldDAU008.pdf

BASF. (2021). *Alite 27™ Pre-Emergent Soybean Herbicide—LibertyLink® G27™*. https://agriculture.basf.us/content/basf/cxm/agriculture/us/en/agriculture/crop-protection/products/herbicides/alite-27-herbicide.html [Accessed: 12/29/2021]

Bassó, A., Devin, S., Peltzer, P. M., Attademo, A. M., & Lajmanovich, R. C. (2022). The integrated biomarker response in three anuran species larvae at sublethal concentrations of cypermethrin, chlorpyrifos, glyphosate, and glufosinate-ammonium. *Journal of Environmental Science and Health, Part B*, *0*(0), 1–10. https://doi.org/10.1080/03601234.2022.2099197

Battaglin, W. A., Kolpin, D. W., Scribner, E. A., Kuivila, K. M., & Sandstrom, M. W. (2005). Glyphosate, Other Herbicides, and Transformation Products in Midwestern Streams, 20021. *JAWRA Journal of the American Water Resources Association*, *41*(2), 323–332. http://doi.org/10.1111/j.1752-1688.2005.tb03738.x

Battaglin, W. A., Meyer, M. T., Kuivila, K. M., & Dietze, J. E. (2014). Glyphosate and Its Degradation Product AMPA Occur Frequently and Widely in U.S. Soils, Surface Water, Groundwater, and Precipitation. *JAWRA Journal of the American Water Resources Association*, *50*(2), 275–290. http://doi.org/10.1111/jawr.12159

Battisti, L., Potrich, M., Sampaio, A. R., de Castilhos Ghisi, N., Costa-Maia, F. M., Abati, R., Dos Reis Martinez, C. B., & Sofia, S. H. (2021). Is glyphosate toxic to bees? A meta-analytical review. *The Science of the Total Environment*, *767*, 145397. https://doi.org/10.1016/j.scitotenv.2021.145397

Baucom, R. S. (2019). Evolutionary and ecological insights from herbicide-resistant weeds: What have we learned about plant adaptation, and what is left to uncover? *New Phytologist*, *223*(1), 68–82. https://doi.org/10.1111/nph.15723

Bauer-Panskus, A. (2014). Testbiotech comment on the German Renewal Assessment Report (RAR) on the active ingredient glyphosate. Testbiotech.

Baum Hedlund Aristei & Goldman (2016) Plaintiffs File Motion to Consolidate Roundup Cancer Lawsuits Against Monsanto. 3 August 2016. https://www.baumhedlundlaw.com/plaintiffs-consolidate-monsanto-roundup-cancer-lawsuits/

Baum, Hedlund, Aristei & Goldman. (n.d.a). Monsanto Roundup Lawsuit | $2 Billion Roundup Cancer Verdict. *Baum Hedlund*. Retrieved July 31, 2020, from https://www.baumhedlundlaw.com/toxic-tort-law/monsanto-roundup-lawsuit/

Baum, Hedlund, Aristei & Goldman. (n.d.b). Edwin Hardeman v. Monsanto Company | Federal MDL Bellwether Trial. *Baum Hedlund*. Retrieved July 31, 2020, from https://www.baumhedlundlaw.com/edwin-hardeman-v-monsanto/

Baum, Hedlund, Aristei & Goldman. (n.d.c). Pilliod v. Monsanto Company. *Baum Hedlund*. Retrieved August 3, 2020, from https://www.baumhedlundlaw.com/pilliod-v-monsanto-trial/

Bautista, S. L. (2007). A summary of acute risk of four common herbicides to birds and mammals. In: Harrington TB, Reichard SH (eds) *Meeting the challenge: invasive plants in Pacific Northwest ecosystems.* U.S. Department of Agriculture, Forest Service, Portland, OR, pp 77–82

BBC News (2015). Colombia to ban coca spraying herbicide glyphosate. http://www.bbc.com/news/world-latin-america-32677411

Beckie, H. J. (2018). Herbicide resistance in Canada: Biggest threats, best management, and lessons learnt. 21st Australasian Weeds Conference, "Weed Biosecurity - Protecting Our Future", Sydney, New South Wales, Australia, 9-13 September 2018, 1–3.

Beckie, H.J., Harker, K.N. (2017). Our top 10 herbicide-resistant weed management practices. *Pest Manag. Sci.* doi:10.1002/ps.4543

Beckie, H. J., Busi, R., Bagavathiannan, M. V., & Martin, S. L. (2019a). Herbicide resistance gene flow in weeds: Under-estimated and under-appreciated. *Agriculture, Ecosystems & Environment*, *283*, 106566. https://doi.org/10.1016/j.agee.2019.06.005

Beckie, H. J., Ashworth, M. B., & Flower, K. C. (2019b). Herbicide Resistance Management: Recent Developments and Trends. *Plants*, *8*(6), 161. https://doi.org/10.3390/plants8060161

Bednářová, A., Kropf, M., & Krishnan, N. (2020). The surfactant polyethoxylated tallowamine (POEA) reduces lifespan and inhibits fecundity in Drosophila melanogaster- In vivo and in vitro study. *Ecotoxicology and Environmental Safety*, *188*, 109883. https://doi.org/10.1016/j.ecoenv.2019.109883

Begemann, S. (2020, June 11). *Dicamba's Future is Shaky—Is Enlist Next on the Chopping Block?* Ag Professional. https://www.agprofessional.com/article/dicambas-future-shaky-enlist-next-chopping-block

Bellaloui, N., Zablotowicz, R. M., Reddy, K. N., & Abel, C. A. (2008). Nitrogen Metabolism and Seed Composition As Influenced by Glyphosate Application in Glyphosate-Resistant Soybean. *Journal of Agricultural and Food Chemistry*, *56*(8), 2765–2772. http://doi.org/10.1021/jf703615m

Belsky, J., & Joshi, N. K. (2018). Assessing Role of Major Drivers in Recent Decline of Monarch Butterfly Population in North America. *Frontiers in Environmental Science*, *0*. https://doi.org/10.3389/fenvs.2018.00086

Belton, P. (2021, August 14). 'Ten years ago this was science fiction': The rise of weedkilling robots. *The Guardian*. https://www.theguardian.com/environment/2021/aug/14/weedkilling-robots-farming-pesticide-use-sustainable

Benachour, N., Sipahutar, H., Moslemi, S., Gasnier, C., Travert, C., & Séralini, G. E. (2007). Time- and Dose-Dependent Effects of Roundup on Human Embryonic and Placental Cells. *Archives of Environmental Contamination and Toxicology*, *53*(1), 126–133. http://doi.org/10.1007/s00244-006-0154-8

Benachour, N., & Séralini, G.-E. (2009). Glyphosate Formulations Induce Apoptosis and Necrosis in Human Umbilical, Embryonic, and Placental Cells. *Chemical Research in Toxicology*, *22*(1), 97–105. http://doi.org/10.1021/tx800218n

Benbrook, C. M. (2005). Rust, Resistance, Run Down Soils, and Rising Costs-Problems Facing Soybean Producers in Argentina. Retrieved from http://www.keine-gentechnik.de/bibliothek/weltpolitik/studien/benbook_argentinen_gensoja_050101.pdf

Benbrook. C. M. (2009). Impacts of Genetically Engineered crops on Pesticide Use in the United States: The First Thirteen Years. The Organic Center.

Benbrook, C. M. (2012a). Impacts of genetically engineered crops on pesticide use in the U.S. -- the first sixteen years. *Environmental Sciences Europe*, *24*(24), 2190-4715. http://doi.org/10.1186/2190-4715-24-24

Benbrook, C. M. (2012b). Glyphosate tolerant crops in the EU. A forecast of impacts on herbicide use. Prepared for Greenpeace International. https://issuu.com/greenpeaceinternational/docs/glyphosate-tolerants-crops-in-the-eu
Benbrook, C. M. (2016). Trends in glyphosate herbicide use in the United States and globally. *Environmental Sciences Europe*, *28*(1). http://doi.org/10.1186/s12302-016-0070-0
Benbrook, C. M. (2018). Why Regulators Lost Track and Control of Pesticide Risks: Lessons From the Case of Glyphosate-Based Herbicides and Genetically Engineered-Crop Technology. *Current Environmental Health Reports*, *5*(3), 387–395. https://doi.org/10.1007/s40572-018-0207-y
Benbrook, C. (2020). Shining a Light on Glyphosate-Based Herbicide Hazard, Exposures and Risk: Role of Non-Hodgkin Lymphoma Litigation in the USA. *European Journal of Risk Regulation*, 1–22. https://doi.org/10.1017/err.2020.16
Benítez-Leite, S., Macchi, M. L., & Acosta, M. (2007). Malformaciones congénitas asociadas a agrotóxicos. Pediatría (Asunción), 34(2), 111–121.
Ben Maamar, M., Beck, D., Nilsson, E. E., Kubsad, D., & Skinner, M. K. (2020). Epigenome-wide association study for glyphosate induced transgenerational sperm DNA methylation and histone retention epigenetic biomarkers for disease. *Epigenetics*, *16*(10), 1150–1167. https://doi.org/10.1080/15592294.2020.1853319
Benner, P., Mena, H., & Schneider, R. (2016). Modeling Glyphosate aerial spray drift at the Ecuador–Colombia border. *Applied Mathematical Modelling*, 40(1), 373–387. http://doi.org/10.1016/j.apm.2015.04.057
Bennett C (2017) Greenhouse and field trials have Arkansas weed scientists looking for answers. AgWeb. 6th March 2017. http://www.agweb.com/article/first-signs-of-dicamba-resistance-naa-chris-bennett/
Benoit, L., Hedges, B., Schryver, M. G., Soltani, N., Hooker, D. C., Robinson, D. E., Laforest, M., Soufiane, B., Tranel, P. J., Giacomini, D., & Sikkema, P. H. (2020). The first record of protoporphyrinogen oxidase and four-way herbicide resistance in eastern Canada. *Canadian Journal of Plant Science*, *100*(3), 327–331. https://doi.org/10.1139/cjps-2018-0326
Bento, C. P. M., Yang, X., Gort, G., Xue, S., van Dam, R., Zomer, P., Mol, H. G. J., Ritsema, C. J., & Geissen, V. (2016). Persistence of glyphosate and aminomethylphosphonic acid in loess soil under different combinations of temperature, soil moisture and light/darkness. *Science of The Total Environment*, *572*, 301–311. https://doi.org/10.1016/j.scitotenv.2016.07.215
Bequet, L. (2020). Biotech Crops, Input Use and Landslides Case Study of Herbicide Tolerant Corn in the Philippine Highlands. *Ecological Economics*, *177*, 106773. https://doi.org/10.1016/j.ecolecon.2020.106773
Beres, Z. T., Ernst, E. E., Ackley, B. A., Loux, M. M., Owen, M. D. K., & Snow, A. A. (2018)a. High Levels of Glyphosate Resistance in Conyza canadensis from Agricultural and Non-Agricultural Sites in Ohio and Iowa. *Scientific Reports*, *8*(1), 10483. https://doi.org/10.1038/s41598-018-28163-w
Beres, Z. T., Yang, X., Jin, L., Zhao, W., Mackey, D. M., & Snow, A. A. (2018b). Overexpression of a Native Gene Encoding 5-Enolpyruvylshikimate-3-Phosphate Synthase (EPSPS) May Enhance Fecundity in Arabidopsis thaliana in the Absence of Glyphosate. International Journal of Plant Sciences, 179(5), 390–401. https://doi.org/10.1086/696701
Beres, Z. T., Owen, M. D. K., & Snow, A. A. (2019). No evidence for early fitness penalty in glyphosate-resistant biotypes of Conyza canadensis: Common garden experiments in the absence of glyphosate. *Ecology and Evolution*, *9*(24), 13678–13689. https://doi.org/10.1002/ece3.5741
Berg, C. J., King, H. P., Delenstarr, G., Kumar, R., Rubio, F., & Glaze, T. (2018). Glyphosate residue concentrations in honey attributed through geospatial analysis to proximity of large-scale agriculture and transfer off-site by bees. *PLoS ONE*, *13*(7), e0198876. https://doi.org/10.1371/journal.pone.0198876
Berger, M., & Ortega, F. (2010). Populations exposed to agrotoxics: citizens' self-organization in the defense of life and health, Córdoba City, Argentina. Physis: Revista de Saúde Coletiva, 20(1), 119–143. http://doi.org/10.1590/S0103-73312010000100008
Berman, M. C., Llames, M. E., Minotti, P., Fermani, P., Quiroga, M. V., Ferraro, M. A., Metz, S., & Zagarese, H. E. (2020). Field evidence supports former experimental claims on the stimulatory effect of glyphosate on picocyanobacteria communities. *Science of The Total Environment*, *701*, 134601. https://doi.org/10.1016/j.scitotenv.2019.134601
Bernards, M. L., Thelen, K. D., Penner, D., Muthukumaran, R. B., & McCracken, J. L. (2005a). Glyphosate interaction with manganese in tank mixtures and its effect on glyphosate absorption and translocation. *Weed Science*, *53*(6), 787–794. http://doi.org/10.1614/WS-05-043R.1
Bernards, M. L., Thelen, K. D., & Penner, D. (2005b). Glyphosate Efficacy is Antagonized by Manganese. *Weed Technology*, *19*(1), 27–34. http://doi.org/10.1614/WT-03-193R2
Bernieri, T., Rodrigues, D., Barbosa, I. R., Ardenghi, P. G., & Basso da Silva, L. (2019). Occupational exposure to pesticides and thyroid function in Brazilian soybean farmers. *Chemosphere*, *218*, 425–429. https://doi.org/10.1016/j.chemosphere.2018.11.124
Berry, D. (2021, January 21). *Preparing for GMO labeling in 2022*. https://www.foodbusinessnews.net/articles/17559-preparing-for-gmo-labeling-in-2022

Bhardwaj, M. (2022, February 10). EXCLUSIVE Bayer revives plan to introduce new GM cotton seeds in India. *Reuters*. https://www.reuters.com/world/india/exclusive-bayer-revives-plan-introduce-new-gm-cotton-seeds-india-2022-02-10/

Bigelow, B. (2010, October 27). *Xconomy: Agricultural Biotech Cibus Expanding as Launch of First Enhanced Crop Nears*. Xconomy. https://xconomy.com/san-diego/2010/10/27/agricultural-biotech-cibus-expanding-as-launch-of-first-enhanced-crop-nears/ [accessed: 7 February 2020]

Bigelow, B. (2017, August 3). *Xconomy: Cibus Readies Enhanced Crops for Push into Canada, and Beyond*. Xconomy. https://xconomy.com/san-diego/2017/08/03/cibus-readies-enhanced-crops-for-push-into-canada-and-beyond/ [accessed: 7 February 2020]

Binimelis, R. (2008). Coexistence of Plants and Coexistence of Farmers: Is an Individual Choice Possible? *Journal of Agricultural and Environmental Ethics*, *21*(5), 437–457. http://doi.org/10.1007/s10806-008-9099-4

Binimelis, R., Pengue, W., & Monterroso, I. (2009). "Transgenic treadmill": responses to the emergence and spread of glyphosate-resistant johnsongrass in Argentina. *Geoforum*, *40*(4), 623–633. http://doi.org/10.1016/j.geoforum.2009.03.009

Bjerga, A. (2015). US Forced to Import Corn as Shoppers Demand Organic Food. Bloomberg. http://www.bloomberg.com/news/articles/2015-04-15/romanian-corn-imports-to-u-s-surge-as-shoppers-demand-organic

Blakley, P. M., Kim, J. S., & Firneisz, G. D. (1989a). Effects of paternal subacute exposure to Tordon 202c on fetal growth and development in CD-1 mice. *Teratology*, *39*(3), 237–241. https://doi.org/10.1002/tera.1420390305

Blakley, P. M., Kim, J. S., & Firneisz, G. D. (1989b). Effects of preconceptional and gestational exposure to Tordon 202c on fetal growth and development in CD-1 mice. *Teratology*, *39*(6), 547–553. https://doi.org/10.1002/tera.1420390605

Blot, N., Veillat, L., Rouzé, R., & Delatte, H. (2019). Glyphosate, but not its metabolite AMPA, alters the honeybee gut microbiota. *PLoS ONE*, *14*(4), e0215466. https://doi.org/10.1371/journal.pone.0215466

Boccioni, A. P., Lajmanovich, R. C., Peltzer, P. M., Attademo, A. M., & Martinuzzi, C. S. (2021a). Toxicity assessment at different experimental scenarios with glyphosate, chlorpyrifos and antibiotics in Rhinella arenarum (Anura: Bufonidae) tadpoles. *Chemosphere*, *273*, 128475. https://doi.org/10.1016/j.chemosphere.2020.128475

Boccioni, A. P. P. C., García-Effron, G., Peltzer, P. M., & Lajmanovich, R. C. (2021). *The Effect of Glyphosate And Ciprofloxacin Eexposure On The Gut Bacterial Microbiota Diversity of Rhinella Arenarum (Anura: Bufonidae) Tadpoles*. https://doi.org/10.21203/rs.3.rs-492368/v1

Boeckel, T. P. V., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. A., Robinson, T. P., Teillant, A., Laxminarayan, R. (2015). Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences*, *112*(18), 5649–5654. http://doi.org/10.1073/pnas.1503141112

Bohm, G.M.B., Rombaldi, C. V., Genovese, M. I., Castilhos, D., Alves, R., … Rumjanek, N. G. (2014). Glyphosate Effects on Yield, Nitrogen Fixation, and Seed Quality in Glyphosate-Resistant Soybean. *Crop Science*, **54**(4), 1737–1743. http://doi.org/10.2135/cropsci2013.07.0470

Bøhn, T., Cuhra, M., Traavik, T., Sanden, M., Fagan, J., & Primicerio, R. (2014). Compositional differences in soybeans on the market: Glyphosate accumulates in Roundup Ready GM soybeans. *Food Chemistry*, *153*, 207–215. http://doi.org/10.1016/j.foodchem.2013.12.054

Bøhn, T., & Lövei, G. L. (2017). Complex Outcomes from Insect and Weed Control with Transgenic Plants: Ecological Surprises? *Frontiers in Environmental Science*, *5*. https://doi.org/10.3389/fenvs.2017.00060

Bøhn, T., & Millstone, E. (2019). The Introduction of Thousands of Tonnes of Glyphosate in the food Chain—An Evaluation of Glyphosate Tolerant Soybeans. *Foods*, *8*(12), 669. https://doi.org/10.3390/foods8120669

Bohnenblust, E., Egan, J., Mortensen, D., & Tooker, J. (2013). Direct and Indirect Effects of the Synthetic-Auxin Herbicide Dicamba on Two Lepidopteran Species. *Environmental Entomology*, *42*, 586–594. https://doi.org/10.1603/EN13021

Bohnenblust, E. W., Vaudo, A. D., Egan, J. F., Mortensen, D. A., & Tooker, J. F. (2016). Effects of the herbicide dicamba on nontarget plants and pollinator visitation. *Environmental Toxicology and Chemistry*, *35*(1), 144–151. https://doi.org/10.1002/etc.3169

Bollani, S., de Cabo, L., Chagas, C., Moretton, J., Weigandt, C., de Iorio, A. F., & Magdaleno, A. (2019). Genotoxicity of water samples from an area of the Pampean region (Argentina) impacted by agricultural and livestock activities. *Environmental Science and Pollution Research*, *26*(27), 27631–27639. https://doi.org/10.1007/s11356-018-3263-9

Bomgardner, M. (2019, August 3). *Palmer amaranth, the king of weeds, cripples new herbicides*. Chemical & Engineering News. https://cen.acs.org/business/specialty-chemicals/Palmer-amaranth-king-weeds-cripples/97/i31

Bomgardner, M., & Erickson, B. (2020). *New weed control tool comes with an asterisk* (Volume 98, Issue 22) [Map]. C&EN. https://cen.acs.org/food/agriculture/New-weed-control-tool-comes/98/i22

Bonansea, R. I., Filippi, I., Wunderlin, D. A., Marino, D. J. G., & Amé, M. V. (2017). The Fate of Glyphosate and AMPA in a Freshwater Endorheic Basin: An Ecotoxicological Risk Assessment. *Toxics*, *6*(1), 3. https://doi.org/10.3390/toxics6010003

Bomfim, N. C., Costa, B., Souza, L., Justino, G., Aguiar, L., & Camargos, L. (2017). Glyphosate Effect on Nitrogen Fixation and Metabolization in RR Soybean. *Journal of Agricultural Science*, *9*(10), p114. https://doi.org/10.5539/jas.v9n10p114

Bonifacio, A. F., Cazenave, J., Bacchetta, C., Ballesteros, M. L., de los Ángeles Bistoni, M., Amé, M. V., Bertrand, L., & Hued, A. C. (2016). Alterations in the general condition, biochemical parameters and locomotor activity in Cnesterodon decemmaculatus exposed to commercial formulations of chlorpyrifos, glyphosate and their mixtures. *Ecological Indicators*, *67*, 88–97. https://doi.org/10.1016/j.ecolind.2016.02.011

Booker, H. M., Lamb, E. G., & Smyth, S. J. (2017). Ex-post assessment of genetically modified, low level presence in Canadian flax. *Transgenic Research*, *26*(3), 399–409. https://doi.org/10.1007/s11248-017-0012-7

Bott, S., Tesfamariam, T., Candan, H., Cakmak, I., Römheld, V., & Neumann, G. (2008). Glyphosate-induced impairment of plant growth and micronutrient status in glyphosate-resistant soybean (Glycine max L.). *Plant and Soil*, *312*(1-2), 185–194. http://doi.org/10.1007/s11104-008-9760-8

Botten, N., Wood, L. J., & Werner, J. R. (2021). Glyphosate remains in forest plant tissues for a decade or more. *Forest Ecology and Management*, *493*, 119259. https://doi.org/10.1016/j.foreco.2021.119259

Bottero, E., Gómez, C., Stritzler, M., Tajima, H., Frare, R., Pascuan, C., Blumwald, E., Ayub, N., & Soto, G. (2022). Generation of a multi-herbicide-tolerant alfalfa by using base editing. *Plant Cell Reports*, *41*(2), 493–495. https://doi.org/10.1007/s00299-021-02827-w

Bourdineaud, J.-P. (2022). Toxicity of the herbicides used on herbicide-tolerant crops, and societal consequences of their use in France. *Drug and Chemical Toxicology*, *45*(2), 698–721. https://doi.org/10.1080/01480545.2020.1770781

Boyle, J. H., Dalgleish, H. J., & Puzey, J. R. (2019a). Monarch butterfly and milkweed declines substantially predate the use of genetically modified crops. *Proceedings of the National Academy of Sciences*, *116*(8), 3006–3011. https://doi.org/10.1073/pnas.1811437116

Boyle, J. H., Dalgleish, H. J., & Puzey, J. R. (2019b). Reply to Wepprich and Ries et al.: Alternative methods do not provide support for the contribution of GM crops to monarch declines. *Proceedings of the National Academy of Sciences*, *116*(28), 13749–13750. https://doi.org/10.1073/pnas.1908593116

Boyle, N. K. (2015). Polliantor-mediated gene flow in and among fields of alfalfa produced for seed. A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Washington State University.

Bradshaw, L. D., Padgette, S. R., Kimball, S. L., & Wells, B. H. (1997). Perspectives on glyphosate resistance. *Weed Technology : A Journal of the Weed Science Society of America (USA)*. Retrieved from http://agris.fao.org/agris-search/search.do?recordID=US9737044

Brausch, J. M., Beall, B., & Smith, P. N. (2007). Acute and Sub-Lethal Toxicity of Three POEA Surfactant Formulations to Daphnia magna. *Bulletin of Environmental Contamination and Toxicology*, *78*(6), 510–514. http://doi.org/10.1007/s00128-007-9091-0

Brausch, J. M., & Smith, P. N. (2007). Toxicity of Three Polyethoxylated Tallowamine Surfactant Formulations to Laboratory and Field Collected Fairy Shrimp, *Thamnocephalus platyurus*. *Archives of Environmental Contamination and Toxicology*, *52*(2), 217–221. http://doi.org/10.1007/s00244-006-0151-y

Breloh, L., Alves, L., Freire, A., Koester, J. (2015). Brazilian Soy Industry: German Retailers fueling the rapid growth of non-GMO soy consumption. Global Grain Events. http://www.globalgrainevents.com/articles/3486591/brazilian-soy-industry-german-retailers-fueling-the-rapid-growth-of-non-gmo-soy-consumption.html

Bridi, D., Altenhofen, S., Gonzalez, J. B., Reolon, G. K., & Bonan, C. D. (2017). Glyphosate and Roundup® alter morphology and behavior in zebrafish. *Toxicology*, *392*, 32–39. https://doi.org/10.1016/j.tox.2017.10.007

Briere K (2017) Consumers still opposed to GM food. The Western Producer. 5th January 2017. http://www.producer.com/2017/01/consumers-still-opposed-to-gm-food/

Brito, I.P., Tropaldi, L., Carbonari, C.A., Velini, E.D. (2017). Hormetic effects of glyphosate on plants. *Pest Manag. Sci.* doi:10.1002/ps.4523

Brodeur, J., Suarez, R., Natale, G., Ronco, A., & Zaccagnini, M. (2011). Reduced body condition and enzymatic alterations in frogs inhabiting intensive crop production areas. *Ecotoxicology and Environmental Safety*, *74*, 1370–1380. https://doi.org/10.1016/j.ecoenv.2011.04.024

Brodzinsky, s. (2015). Last flight looms for US-funded air war on drugs as Colombia counts health cost. The Guardian. http://www.theguardian.com/world/2015/may/06/colombia-air-war-drugs-last-flight-looms-health-cost

Brookes, G., Barfoot, P. (2015). GM crops: global socio-economic and environmental impacts 1996-2013. PG Economics Ltd, UK.

Brookes, G., & Barfoot, P. (2020). Environmental impacts of genetically modified (GM) crop use 1996–2018: Impacts on pesticide use and carbon emissions. GM Crops & Food, 11(4), 215–241. https://doi.org/10.1080/21645698.2020.1773198

Brovini, E. M., de Deus, B. C. T., Vilas-Boas, J. A., Quadra, G. R., Carvalho, L., Mendonça, R. F., Pereira, R. de O., & Cardoso, S. J. (2021a). Three-bestseller pesticides in Brazil: Freshwater concentrations and potential environmental risks. Science of The Total Environment, 771, 144754. https://doi.org/10.1016/j.scitotenv.2020.144754

Brovini, E. M., Cardoso, S. J., Quadra, G. R., Vilas-Boas, J. A., Paranaíba, J. R., Pereira, R. de O., & Mendonça, R. F. (2021b). Glyphosate concentrations in global freshwaters: Are aquatic organisms at risk? *Environmental Science and Pollution Research*, *28*(43), 60635–60648. https://doi.org/10.1007/s11356-021-14609-8

Brower, L. P., Castilleja, G., Peralta, A., Lopez-Garcia, J., Bojorquez-Tapia, L., Diaz, S., Melgarejo, D., Missrie, M. (2002). Quantitative Changes in Forest Quality in a Principal Overwintering Area of the Monarch Butterfly in Mexico, 1971–1999. *Conservation Biology*, *16*(2), 346–359. http://doi.org/10.1046/j.1523-1739.2002.00572.x

Brower, L.P., Kust, D.R., Rendón Salinas, E., García-Serrano, E., Kust, K.R., Miller, J., Fernandez del Rey, C., Pape, K. (2004). Catastrophic winter storm mortality of monarch butterflies in Mexico during January 2002. In Oberhauser, K.S., Solensky, M.J (Eds.). The Monarch Butterfly: Biology and Conservation, Cornell University Press, Ithaca, USA (2004), pp. 151–166.

Brower, L. P., Taylor, O. R., Williams, E. H., Slayback, D. A., Zubieta, R. R., & RamíRez, M. I. (2012). Decline of monarch butterflies overwintering in Mexico: is the migratory phenomenon at risk?: Decline of monarch butterflies in Mexico.

Brown, N. (2020, February 19). *Following lawsuit, questions surround increased Dicamba use*. KRCG. https://krcgtv.com/news/local/following-lawsuit-questions-surround-increased-dicamba-use

Browne, A. M., & Moore, P. A. (2014). The Effects of Sublethal Levels of 2,4-Dichlorophenoxyacetic Acid Herbicide (2,4-D) on Feeding Behaviors of the Crayfish O. rusticus. *Archives of Environmental Contamination and Toxicology*, *67*(2), 234–244. https://doi.org/10.1007/s00244-014-0032-8

Brunet Y, Foueillassar X, Audran A, Garrigou D, Dayau S, Tardieu L (2003). Evidence for long-range transport of viable maize pollen. In Boelt B, ed, 1st European Conference on the Coexistence of Genetically Modified Crops with Conventional and Organic Crops, Research Centre Flakkebjerg, pp 74–76.

Brunharo, C. A., Patterson, E. L., Carrijo, D. R., de Melo, M. S., Nicolai, M., Gaines, T. A., Nissen, S. J., & Christoffoleti, P. J. (2016). Confirmation and mechanism of glyphosate resistance in tall windmill grass (Chloris elata) from Brazil. *Pest Management Science*, *72*(9), 1758–1764. https://doi.org/10.1002/ps.4205

Brunharo, C. A. C. G., Gast, R., Kumar, V., Mallory-Smith, C. A., Tidemann, B. D., & Beckie, H. J. (2022). Western United States and Canada perspective: Are herbicide-resistant crops the solution to herbicide-resistant weeds? *Weed Science*, *70*(3), 272–286. https://doi.org/10.1017/wsc.2022.6

Bruns, H. A. (2014). Stacked-Gene Hybrids Were Not Found to Be Superior to Glyphosate-Resistant or Non-GMO Corn Hybrids. *Crop Management*, *13*(1), 0. http://doi.org/10.2134/CM-2013-0012-RS

Buckelew, L. D., Pedigo, L. P., Mero, H. M., Owen, M. D. K., & Tylka, G. L. (2000). Effects of Weed Management Systems on Canopy Insects in Herbicide-Resistant Soybeans. *Journal of Economic Entomology*, *93*(5), 1437–1443. http://doi.org/10.1603/0022-0493-93.5.1437

Buenos Aires Herald (2016) Monsanto eyes inroads in Brazil after Argentina royalty row. Friday, May 20, 2016. http://www.buenosairesherald.com/article/214638/monsanto-eyes-inroads-in-brazil-after-argentina-royalty-row

Buffin, D. & Jewell, T. (2001). The implications of increased use of glyphosate in association with genetically modified crops. Friends of the Earth.

Bukowska, B. (2003). Effects of 2,4-D and its metabolite 2,4-dichlorophenol on antioxidant enzymes and level of glutathione in human erythrocytes. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *135*(4), 435–441. https://doi.org/10.1016/S1532-0456(03)00151-0

Bündnis 90/Die Grünen (2015). Wahrscheinlich Krebserregendes Pflanzengift Glyphsoat in Muttermilch. http://www.gruene-bundestag.de/themen/agrar/glyphosat-in-muttermilch_ID_4396067.html

Bunge, J. (2015). Fields of Gold: GMO-Free Crops Prove Lucrative for Farmers. The Wall Street Journal. http://www.wsj.com/articles/fields-of-gold-gmo-free-crops-prove-lucrative-for-farmers-1422909700

Bunge, J. (2017, July 11). *Arkansas Bans Herbicide as Farmers Blame Neighbors for Crop Damage*. The Wall Street Journal. https://www.wsj.com/articles/arkansas-bans-herbicide-as-farmers-blame-neighbors-for-crop-damage-1499765401

Burchfield, E. K., Schumacher, B. L., Spangler, K., & Rissing, A. (2022). The State of US Farm Operator Livelihoods. *Frontiers in Sustainable Food Systems*, *5*. https://www.frontiersin.org/article/10.3389/fsufs.2021.795901

Burgeff, C., Huerta, E., Acevedo, F., & Sarukhán, J. (2014). How Much Can GMO and Non-GMO Cultivars Coexist in a Megadiverse Country? Retrieved December 15, 2014, from http://www.agbioforum.org/v17n1/v17n1a10-burgeff.htm

Burke (2003). GM crops. Effects on Farmland Wildlife. Farm Scale Evaluations. http://webarchive.nationalarchives.gov.uk/20080306073937/http://www.defra.gov.uk/environment/gm/fse/results/fse-summary-03.pdf

Burke (2005). Managing GM crops with herbicides. Effects on farmland wildlife. Farm Scale Evaluations. http://webarchive.nationalarchives.gov.uk/20080306073937/http://www.defra.gov.uk/environment/gm/fse/results/fse-summary-05.pdf

Burraco, P., & Gomez-Mestre, I. (2016). Physiological Stress Responses in Amphibian Larvae to Multiple Stressors Reveal Marked Anthropogenic Effects even below Lethal Levels. *Physiological and Biochemical Zoology*, *89*(6), 462–472. https://doi.org/10.1086/688737

Business Wire (2016) Bunge to Unveil Non-GMO Project Verified Milled Corn Ingredients and Oils at IFT16. 15 July 2016. http://www.businesswire.com/news/home/20160715005829/en/Bunge-Unveil-Non-GMO-Project-Verified-Milled-Corn

Butler, N. M., Baltes, N. J., Voytas, D. F., & Douches, D. S. (2016). Geminivirus-Mediated Genome Editing in Potato (Solanum tuberosum L.) Using Sequence-Specific Nucleases. *Frontiers in Plant Science*, *7*. https://doi.org/10.3389/fpls.2016.01045

Butt, H., Eid, A., Ali, Z., Atia, M. A. M., Mokhtar, M. M., Hassan, N., Lee, C. M., Bao, G., & Mahfouz, M. M. (2017). Efficient CRISPR/Cas9-Mediated Genome Editing Using a Chimeric Single-Guide RNA Molecule. *Frontiers in Plant Science*, *8*, 1441. https://doi.org/10.3389/fpls.2017.01441

Butt, H., Rao, G. S., Sedeek, K., Aman, R., Kamel, R., & Mahfouz, M. (2020). Engineering herbicide resistance via prime editing in rice. *Plant Biotechnology Journal*, *18*(12), 2370–2372.

Byrne, J. (2015). Brazilian soy exporters, crushers and farmers should 'keep their eyes on' German GM free trend, says retailer. Feed Navigator. http://www.feednavigator.com/Markets/Brazilian-soy-exporters-crushers-and-farmers-should-keep-their-eyes-on-German-GM-free-trend-says-retailer

CABI (2011). Datasheet. Asclepias syriaca (common milkweed). http://www.cabi.org/isc/datasheet/7249

Cacho, M. M. y T. G. (2016). Soybean agri-food systems dynamics and the diversity of farming styles on the agricultural frontier in Mato Grosso, Brazil. The Journal of Peasant Studies, 43(2), 419–441. http://doi.org/10.1080/03066150.2015.1016917

Cai, W., Ji, Y., Song, X., Guo, H., Han, L., Zhang, F., Liu, X., Zhang, H., Zhu, B., & Xu, M. (2017). Effects of glyphosate exposure on sperm concentration in rodents: A systematic review and meta-analysis. *Environmental Toxicology and Pharmacology*, *55*, 148–155. https://doi.org/10.1016/j.etap.2017.07.015

Calas, A.-G., Richard, O., Même, S., Beloeil, J.-C., Doan, B.-T., Gefflaut, T., Même, W., Crusio, W. E., Pichon, J., & Montécot, C. (2008). Chronic exposure to glufosinate-ammonium induces spatial memory impairments, hippocampal MRI modifications and glutamine synthetase activation in mice. *NeuroToxicology*, *29*(4), 740–747. https://doi.org/10.1016/j.neuro.2008.04.020

Callahan, P. (2016). Court clears way for revival of worrisome weedkiller. Chicago Tribune. http://www.chicagotribune.com/news/watchdog/ct-dow-enlist-duo-court-ruling-20160127-story.html

Calyxt. (2017a). Calyxt-Investor-Presentation_September-2017.pdf. https://calyxt.com/wp-content/uploads/2017/09/Calyxt-Investor-Presentation_September-2017.pdf

Calyxt. (2017b, September 25). Calyxt Advances Herbicide-Tolerant Wheat and Improved Oil Composition Canola Product Candidates to Phase 1. Calyxt, Inc. https://ir.calyxt.com/news-events/press-releases/detail/3/calyxt-advances-herbicide-tolerant-wheat-and-improved-oil

Calyxt. (2019). Calyxt-Investor-Presentation_Q2-2019. https://calyxt.com/wp-content/uploads/2019/05/Calyxt-Investor-Presentation_Q2-2019.pdf

Camiccia, M., Candiotto, L. Z. P., Gaboardi, S. C., Panis, C., & Kottiwitz, L. B. M. (2022). Determination of glyphosate in breast milk of lactating women in a rural area from Paraná state, Brazil. *Brazilian Journal of Medical and Biological Research*, *55*. https://doi.org/10.1590/1414-431X2022e12194

Campbell, H. (2021, July 15). *Eastern Arkansas faces potential 650,000 to 800,000 acres of dicamba damage*. Https://Www.Kait8.Com. https://www.kait8.com/2021/07/15/eastern-arkansas-faces-potential-650000-800000-acres-dicamba-damage/

Canal Rural (2015). Ministério Público quer banir glifosato do Brasil. http://www.canalrural.com.br/noticias/agricultura/ministerio-publico-quer-banir-glifosato-brasil-56002

Canosa, I. S., Silveyra, G. R., Avigliano, L., Medesani, D. A., & Rodríguez, E. M. (2018). Ovarian growth impairment after chronic exposure to Roundup Ultramax® in the estuarine crab *Neohelice granulata*. *Environmental Science and Pollution Research*, *25*(2), 1568–1575. https://doi.org/10.1007/s11356-017-0581-2

Canosa, I. S., Silveyra, G. R., Lonné, M. N., Medesani, D. A., & Rodríguez, E. M. (2021). In vitro Interference of a Glyphosate Commercial Formulation with the Stimulation of Ovarian Maturation by Progesterone, in the Estuarine Crab Neohelice granulata. *Bulletin of Environmental Contamination and Toxicology*, *106*(4), 583–588. https://doi.org/10.1007/s00128-021-03107-9

Cantor, K. P., Blair, A., Everett, G., Gibson, R., Burmeister, L. F., Brown, L. M., Schuman, L., & Dick, F. R. (1992). Pesticides and Other Agricultural Risk Factors for Non-Hodgkin's Lymphoma among Men in Iowa and Minnesota. *Cancer Research*, *52*(9), 2447–2455.
Capital Press (2016) Japan, S. Korea suspend U.S. wheat until new test in place. 1 August 2016. http://www.capitalpress.com/Washington/20160801/japan-defers-western-white-wheat-purchases-until-new-test-in-place#.V6AwX7K0lHQ.twitter
Capps, O., & Babula, R. A. (2019). A Methodology to Empirically Assess National and Farm-Specific Damages from Contamination of Grain Supply by a Genetically Engineered Strain. *Journal of Agricultural and Applied Economics*, *51*(3), 495–510. https://doi.org/10.1017/aae.2019.16
Carignan, S. (2021, March 15). *Bayer, Monsanto Allege Texas Cotton Processor 'Saved Seeds'*. Bloomberg Law. https://news.bloomberglaw.com/litigation/bayer-monsanto-allege-texas-cotton-processor-saved-seeds
Carles, L., Gardon, H., Joseph, L., Sanchís, J., Farré, M., & Artigas, J. (2019). Meta-analysis of glyphosate contamination in surface waters and dissipation by biofilms. Environment International, 124, 284–293. https://doi.org/10.1016/j.envint.2018.12.064
Carman, J. A., Vlieger, H. R., Ver Steeg, L. J., Sneller, V. E., Robinson, G. W., Clinch-Jones, C. A., … Edwards, J. W. (2013). A long-term toxicology study on pigs fed a combined genetically modified (GM) soy and GM maize diet. *Journal of Organic Systems*, *8*(1), 38–54.
Carneiro, F. F., Rigotto, R. M., Da Silva Augusto, L. G., Friedrich, K., Campos Búrigo, A. (2015). Dossiê ABRASCO: um alerta sobre os impactos dos agrotóxicos na saúde. Rio de Janeiro: EPSJV; São Paulo: Expressão Popular, 2015. http://aspta.org.br/wp-content/uploads/2015/05/DossieAbrasco_2015_web.pdf
Carranza, C. S., Aluffi, M. E., Benito, N., Magnoli, K., Barberis, C. L., & Magnoli, C. E. (2019). Effect of in vitro glyphosate on Fusarium spp. Growth and disease severity in maize. *Journal of the Science of Food and Agriculture*, *99*(11), 5064–5072. https://doi.org/10.1002/jsfa.9749
Carretta, L., Masin, R., & Zanin, G. (2022). Review of studies analysing glyphosate and aminomethylphosphonic acid (AMPA) occurrence in groundwater. *Environmental Reviews*, *30*(1), 88–109. https://doi.org/10.1139/er-2020-0106
Carvalho, W. F., Ruiz de Arcaute, C., Pérez-Iglesias, J. M., Laborde, M. R. R., Soloneski, S., & Larramendy, M. L. (2019). DNA damage exerted by mixtures of commercial formulations of glyphosate and imazethapyr herbicides in Rhinella arenarum (Anura, Bufonidae) tadpoles. *Ecotoxicology*, *28*(3), 367–377. https://doi.org/10.1007/s10646-019-02029-x
Carvalho, F. P. (2020a). Glyphosate, the herbicide that become a nightmare and the Precautionary Principle. *International Journal of Environmental Studies*, *77*(6), 1012–1023. https://doi.org/10.1080/00207233.2020.1773682
Carvalho, W. F., Ruiz de Arcaute, C., Torres, L., de Melo e Silva, D., Soloneski, S., & Larramendy, M. L. (2020b). Genotoxicity of mixtures of glyphosate with 2,4-dichlorophenoxyacetic acid chemical forms towards *Cnesterodon decemmaculatus* (Pisces, Poeciliidae). *Environmental Science and Pollution Research*, *27*(6), 6515–6525. https://doi.org/10.1007/s11356-019-07379-x
Casassus, B. (2019). French court bans sale of controversial weedkiller. *Nature*. https://doi.org/10.1038/d41586-019-00259-x
Case No: BC 578 942. Class Action Complaint for Damages Preliminary Injunction and Permanent Injunction; False and Misleading Advertising [B&P Code §17500]. Plaintiffs, vs. Monsanto Company, 2015. http://www.monsantoclassaction.org/wp-content/uploads/2015/04/Monsanto-Glyphosate-Class-Action-4.20.2015.pdf
Case, P. (2014). US farmer interest growing in non-GM maize and soya. Farmers Weekly. http://www.fwi.co.uk/news/us-farmer-interest-growing-in-non-gm-maize-and-soya.htm
CASAFE (2014). Estudio de Mercado 2014 de Productos de Protección de Cultivos. https://www.casafe.org/pdf/2018/ESTADISTICAS/Informe-Mercado-Fitosanitarios-2014.pdf
Cassidy, E. S., West, P. C., Gerber, J. S., & Foley, J. A. (2013). Redefining agricultural yields: from tonnes to people nourished per hectare. *Environmental Research Letters*, *8*(3), 034015. http://doi.org/10.1088/1748-9326/8/3/034015
Cassidy, E. (2015a). How Corn Ethanol Is Worse For Climate Change Than The Keystone Pipeline. Environmental Working Group. http://www.ewg.org/agmag/2015/05/how-corn-ethanol-worse-climate-change-keystone-pipeline
Cassidy, E. (2015b). Feeding the World Without GMOs. Environmental Working Group. http://www.ewg.org/research/feeding-world-without-gmos
Catacora-Vargas G, Galeano P, Agapito SZ, Aranda D, Palau T, Nodari RO (2012) Soybean production in the Southern Cone of the Americas: update on land and pesticide use. http://genok.no/wp-content/uploads/2013/04/SOY-SA-Land_Pesticides-ENG.pdf
Cattani, D., Cesconetto, P. A., Tavares, M. K., Parisotto, E. B., De Oliveira, P. A., Rieg, C. E. H., Leite, M. C., Prediger, R. D. S., Wendt, N. C., Razzera, G., Filho, D. W., & Zamoner, A. (2017). Developmental exposure to

glyphosate-based herbicide and depressive-like behavior in adult offspring: Implication of glutamate excitotoxicity and oxidative stress. *Toxicology*, *387*, 67–80. https://doi.org/10.1016/j.tox.2017.06.001
Caulcutt, C. (2009). 'Superweed' explosion threatens Monsanto heartlands. France 24. Published April 19, 2009. http://www.france24.com/en/20090419-'superweed'-explosion-threatens-monsanto-heartlands-
Cavieres, M. F., Jaeger, J., & Porter, W. (2002). Developmental toxicity of a commercial herbicide mixture in mice: I. Effects on embryo implantation and litter size. *Environmental Health Perspectives*, *110*(11), 1081–1085. https://doi.org/10.1289/ehp.021101081
CBAN (2008). Canola. http://www.cban.ca/Resources/Topics/GE-Crops-and-Foods-On-the-Market/Canola
CBD (2014). Monarch Butterfly Moves Toward Endangered Species Act Protection. Feds Issue Initial Positive Finding on Petition Following 90 Percent Decline. http://www.biologicaldiversity.org/news/press_releases/2014/monarch-butterfly-12-29-2014.html
CBD (2015). Settlement: EPA to Analyze Impacts of World's Two Most Widely Used Pesticides on 1,500 Endangered Species. Historic Settlement Means Harms of Atrazine, Roundup Will Be Assessed. http://www.biologicaldiversity.org/news/press_releases/2015/pesticides-06-23-2015.html
CBD. (2022, May 24). Eastern Monarch Butterfly Population Up Slightly, Still Below Extinction Threshold. Center for Biological Diversity. https://biologicaldiversity.org/w/news/press-releases/eastern-monarch-butterfly-population-up-slightly-still-below-extinction-threshold-2022-05-24/
Cedergreen, N., & Streibig, J. C. (2005). The toxicity of herbicides to non-target aquatic plants and algae: assessment of predictive factors and hazard. *Pest Management Science*, *61*(12), 1152–1160. http://doi.org/10.1002/ps.1117
Cederlund, H. (2017). Effects of spray drift of glyphosate on nontarget terrestrial plants—A critical review. *Environmental Toxicology and Chemistry*, *36*(11), 2879–2886. https://doi.org/10.1002/etc.3925
Center for Food Safety. (2017, January 20). *National Family Farm Coalition vs. USEPA - Petition for Review*. http://www.centerforfoodsafety.org/files/dicamba_petition-for-review_filed_12317_01852.pdf
Center for Food Safety et al. v. USEPA, (United States Court of Appeals for the Ninth Circuit). Retrieved December 28, 2021, from https://www.centerforfoodsafety.org/files/nffc-et-al-petition-for-review-final_94768.pdf
CEO (2016). EU review of weedkiller glyphosate adds secrecy to controversy. http://corporateeurope.org/food-and-agriculture/2016/01/eu-review-weedkiller-glyphosate-adds-secrecy-controversy
Cerdeira, A. L., Gazziero, D. L. P., Duke, S. O., & Matallo, M. B. (2011). Agricultural Impacts of Glyphosate-Resistant Soybean Cultivation in South America. *Journal of Agricultural and Food Chemistry*, 59(11), 5799–5807. http://doi.org/10.1021/jf102652y
CFS (2014a). "Agent Orange" Crops Would Trigger Massive Increase in Use of Toxic Pesticide 2,4-D. http://www.centerforfoodsafety.org/press-releases/2811/agent-orange-crops-would-trigger-massive-increase-in-use-of-toxic-pesticide-24-d#
CFS (2014b). Leading Scientists, Over 200 Groups and Companies Call for Monarch Protection. http://www.centerforfoodsafety.org/press-releases/3605/leading-scientists-over-200-groups-and-companies-call-for-monarch-protection#
CFS (2015a). Monarchs in Peril. Herbicide-Resistant Crops and the Decline of Monarch Butterflies in North America. http://www.centerforfoodsafety.org/files/cfs-monarch-report_2-4-15_design_05341.pdf
CFS (2015b). Glyphosate and Cancer Risk: Frequently Asked Questions. http://www.centerforfoodsafety.org/files/glyphosate-faq_64013.pdf
CFS (2016). Lawsuit Launched for Endangered Spcies Act Protection of Monarch Butterflies. http://www.centerforfoodsafety.org/press-releases/4190/lawsuit-launched-for-endangered-species-act-protection-of-monarch-butterflies#
CFS (2017) Public Interest Groups, Farmers File Lawsuit Challenging Monsanto's Toxic Pesticides. 23rd January 2017. http://www.centerforfoodsafety.org/press-releases/4744/public-interest-groups-farmers-file-lawsuit-challenging-monsantos-toxic-pesticides#
CFS & CBD (2016). Notice of Violation of the Endangered Species Act for Failing to Make a Required Finding on the Petition to Protect the Monarch Butterfly. http://www.centerforfoodsafety.org/files/centers-monarch-butterfly-12-mo-noi_11351.pdf
Cha, Y. S., Kim, H., Lee, Y., Choi, E. H., Kim, H. I., Kim, O. H., Cha, K.-C., Lee, K. H., & Hwang, S. O. (2017). The relationship between serum ammonia level and neurologic complications in patients with acute glufosinate ammonium poisoning: A prospective observational study: *Human & Experimental Toxicology*. https://doi.org/10.1177/0960327117715902
Chainark, P., Satoh, S., Hirono, I., Aoki, T., & Endo, M. (2008). Availability of genetically modified feed ingredient: investigations of ingested foreign DNA in rainbow trout Oncorhynchus mykiss. *Fisheries Science*, *74*(2), 380–390. http://doi.org/10.1111/j.1444-2906.2008.01535.x
Chamberlain, D. e., Fuller, R. j., Bunce, R. g. h., Duckworth, J. c., & Shrubb, M. (2000). Changes in the abundance of farmland birds in relation to the timing of agricultural intensification in England and Wales. *Journal of Applie*

Chang, F., Simcik, M. F., & Capel, P. D. (2011). Occurrence and fate of the herbicide glyphosate and its degradate aminomethylphosphonic acid in the atmosphere. *Environmental Toxicology and Chemistry*, *30*(3), 548–555. http://doi.org/10.1002/etc.431
Charles, D. (2019, February 7). Is Fear Driving Sales of Monsanto's Dicamba-Proof Soybeans? *NPR*. https://www.npr.org/sections/thesalt/2019/02/07/691979417/is-fear-driving-sales-of-dicamba-proof-soybeans
Chatham, L. A., Wu, C., Riggins, C. W., Hager, A. G., Young, B. G., Roskamp, G. K., & Tranel, P. J. (2015). EPSPS Gene Amplification is Present in the Majority of Glyphosate-Resistant Illinois Waterhemp (Amaranthus tuberculatus) Populations. *Weed Technology*, *29*(1), 48–55. http://doi.org/10.1614/WT-D-14-00064.1
Chaves, A., Faita, M. R., Ferreira, B. L., Poltronieri, A. S., & Nodari, R. O. (2021). Effects of glyphosate-based herbicide on royal jelly production of Apis mellifera (Hymenoptera: Apidae) in field conditions. *Journal of Apicultural Research*, *60*(2), 277–279. https://doi.org/10.1080/00218839.2020.1844463
Chávez-Ortiz, P., Tapia-Torres, Y., Larsen, J., & García-Oliva, F. (2022). Glyphosate-based herbicides alter soil carbon and phosphorus dynamics and microbial activity. *Applied Soil Ecology*, *169*, 104256. https://doi.org/10.1016/j.apsoil.2021.104256
Chen, X., Gu, H., Yi, J., Zhang, H., Gao, B., & Srinives, P. (2006). Gene flow from transgenic roundup-ready soybean to wild soybean. *7*, *1*, 8–13.
Chen, J., Jin, M., Qiu, Z.-G., Guo, C., Chen, Z.-L., Shen, Z.-Q., Wang, X.-W., Li, J.-W. (2012). A survey of drug resistance bla genes originating from synthetic plasmid vectors in six Chinese rivers. *Environmental Science & Technology*, *46*(24), 13448–13454. http://doi.org/10.1021/es302760s
Chen, J., Huang, H., Zhang, C., Wei, S., Huang, Z., Chen, J., & Wang, X. (2015). Mutations and amplification of EPSPS gene confer resistance to glyphosate in goosegrass (Eleusine indica). *Planta*, *242*(4), 859–868. https://doi.org/10.1007/s00425-015-2324-2
Chen, J., Yu, Q., Patterson, E., Sayer, C., & Powles, S. (2021). Dinitroaniline Herbicide Resistance and Mechanisms in Weeds. *Frontiers in Plant Science*, *12*, 507. https://doi.org/10.3389/fpls.2021.634018
Chernoff, N., Setzer, R. W., Miller, D. B., Rosen, M. B., & Rogers, J. M. (1990). Effects of chemically induced maternal toxicity on prenatal development in the rat. *Teratology*, *42*(6), 651–658. https://doi.org/10.1002/tera.1420420610
Chipotle (2015). Food with Integrity – G-M-Over it. https://chipotle.com/gmo
Chłopecka, M., Mendel, M., Dziekan, N., Karlik, W. (2017). The effect of glyphosate-based herbicide Roundup and its co-formulant, POEA, on the motoric activity of rat intestine – In vitro study. *Environmental Toxicology and Pharmacology* **49**, 156–162. doi:10.1016/j.etap.2016.12.010
Chovanec, A., Hofer, R., & Schiemer, F. (2003). Chapter 18 Fish as bioindicators. In B. A. Markert, A. M. Breure, & H. G. Zechmeister (Eds.), *Trace Metals and other Contaminants in the Environment* (Vol. 6, pp. 639–676). Elsevier. https://doi.org/10.1016/S0927-5215(03)80148-0
Chow, L. (2016). Australia: Organic Farmer Dealt Final Blow in Landmark Lawsuit over Monsanto's GMO Contamination. EcoWatch. http://ecowatch.com/2016/02/12/monsanto-lawsuit-gmo-contamination/
Chun, Y. J., Kim, D. I., Park, K. W., Kim, H.-J., Jeong, S.-C., An, J. H., Cho, K. H., Back, K., Kim, H. M., & Kim, C.-G. (2011). Gene flow from herbicide-tolerant GM rice and the heterosis of GM rice-weed F2 progeny. *Planta*, *233*(4), 807–815. https://doi.org/10.1007/s00425-010-1339-y
Cibus. (2019a). Sulfonylurea Herbicide Tolerant Canola | Falco™ Canola. *Falco™ USA*. https://www.falcoseed.com/herbicide/ [accessed 27 November 2019]
Cibus. (2019b). *Cibus Licenses Ultra-High-Oleic Canola Oil Trait To Valley Oils Partners*. https://www.cibus.com/press-release.php?date=040119 [accessed: 12 September 2019]
Cibus. (2019c). *Cibus—Value-Enhancing Traits for Globally accepted Crops*. https://www.cibus.com/crops.php [accessed: 29 November 2019]
Cibus. (2021a). *Cibus Technology—Innovating precision plant breeding*. https://www.cibus.com/our-technology.php [accessed: 10 December 2021]
Cibus. (2021b). *Trait Platforms*. Cibus Driving Sustainable Agriculture. https://www.cibus.com/trait-platforms.php [accessed: 30 December 2021]
Cibus. (2022). *Products—Trait Platforms*. https://www.cibus.com/trait-platforms.php
Cillufo, A., & Ruiz, N. (2019, June 17). World population growth is expected to nearly stop by 2100. *Pew Research Center*. https://www.pewresearch.org/fact-tank/2019/06/17/worlds-population-is-projected-to-nearly-stop-growing-by-the-end-of-the-century/
Cipriano, J., Carrasco, J. F., Arbós, M. (2006). La imposible coexistencia: Siete años de transgénicos contaminan el maíz ecológico y el convencional: una aproximación a partir de los casas de Cataluña y Aragón. Assemblea Pagesa de Catalunya, Greenpeace, Plataforma Transgènics Fora.
Clair, É., Mesnage, R., Travert, C., & Séralini, G.-É. (2012). A glyphosate-based herbicide induces necrosis and apoptosis in mature rat testicular cells in vitro, and testosterone decrease at lower levels. *Toxicology in Vitro*, *26*(2), 269–279. http://doi.org/10.1016/j.tiv.2011.12.009

Clapp, J. (2021). The problem with growing corporate concentration and power in the global food system. *Nature Food*, *2*(6), 404–408. https://doi.org/10.1038/s43016-021-00297-7
Clasen, B., Murussi, C., & Storck, T. (2019). Pesticide Contamination in Southern Brazil. In L. M. Gómez-Oliván (Ed.), *Pollution of Water Bodies in Latin America: Impact of Contaminants on Species of Ecological Interest* (pp. 43–54). Springer International Publishing. https://doi.org/10.1007/978-3-030-27296-8_3
Colombia Reports (2016) Manual coca spraying will kill people: former top Colombia narcotics adviser. 4 May 2016. http://colombiareports.com/manual-spraying-coca-will-kill-people-former-counter-narcotics-official/
Comont, D., Lowe, C., Hull, R., Crook, L., Hicks, H. L., Onkokesung, N., Beffa, R., Childs, D. Z., Edwards, R., Freckleton, R. P., & Neve, P. (2020). Evolution of generalist resistance to herbicide mixtures reveals a trade-off in resistance management. *Nature Communications*, *11*, 3086. https://doi.org/10.1038/s41467-020-16896-0
Congur, G. (2021). Monitoring of glyphosate-DNA interaction and synergistic genotoxic effect of glyphosate and 2,4-dichlorophenoxyacetic acid using an electrochemical biosensor. *Environmental Pollution*, *271*, 116360. https://doi.org/10.1016/j.envpol.2020.116360
Cookson, C. (2006, November 15). *GM crop breakthrough threat to Monsanto*. Financial Times. https://www.ft.com/content/a422e032-74cf-11db-bc76-0000779e2340
Coop (2015). Coop nimmt glyphosathaltige Produkte aus dem Sortiment. http://www.coop.ch/pb/site/medien/node/82126566/Lde/index.html?wt.mc_id=1_MM_NL,2_KW2015-21,3_active&mtype=nl
Corporate Crime Reporter. (2021, April 17). *Gerson Smoger on the Growing Opposition to the Bayer Monsanto Roundup Settlement*. Corporate Crime Reporter. https://www.corporatecrimereporter.com/news/200/gerson-smoger-on-the-growing-opposition-to-the-bayer-monsanto-roundup-settlement/ [accessed: 30 December 2021]
Correia, F. V., & Moreira, J. C. (2010). Effects of Glyphosate and 2,4-D on Earthworms (Eisenia foetida) in Laboratory Tests. *Bulletin of Environmental Contamination and Toxicology*, *85*(3), 264–268. https://doi.org/10.1007/s00128-010-0089-7
Corsi, S., Friedrich, T., Kassam, A., Pisante, M., de Moraes Sà, j. (2012). Soil Organic Carbon Accumulation and Greenhouse Gas Emission Reductions from Conservation Agriculture: A Literature Review. FAO.
Corteva Agriscience. (2021a, February 22). FeXapan® herbicide – Crop Protection. https://www.corteva.us/products-and-solutions/crop-protection/fexapan.html
Corteva Agriscience. (2021b). *Enlist Duo® and Enlist One® herbicides*. https://www.enlist.com/en/herbicides.html [accessed: 12/29/2021]
Costas-Ferreira, C., Durán, R., & Faro, L. R. F. (2022). Toxic Effects of Glyphosate on the Nervous System: A Systematic Review. *International Journal of Molecular Sciences*, *23*(9), 4605. https://doi.org/10.3390/ijms23094605
Coupe, R. H., Kalkhoff, S. J., Capel, P. D., & Gregoire, C. (2012). Fate and transport of glyphosate and aminomethylphosphonic acid in surface waters of agricultural basins. *Pest Management Science*, *68*(1), 16–30. http://doi.org/10.1002/ps.2212
Coupland, D., & Caseley, J. C. (1979). Presence of 14c Activity in Root Exudates and Guttation Fluid from Agropyron Repens Treated with 14c-Labelled Glyphosate. *New Phytologist*, *83*(1), 17–22. http://doi.org/10.1111/j.1469-8137.1979.tb00721.x
Cowie, B. W., Venter, N., Witkowski, E. T., & Byrne, M. J. (2020). Implications of elevated carbon dioxide on the susceptibility of the globally invasive weed, Parthenium hysterophorus, to glyphosate herbicide. *Pest Management Science*, *76*(7), 2324–2332. https://doi.org/10.1002/ps.5767
Cox, C., & Surgan, M. (2006). Unidentified Inert Ingredients in Pesticides: Implications for Human and Environmental Health. *Environmental Health Perspectives*, *114*(12), 1803–1806. http://doi.org/10.1289/ehp.9374
Crespo, R. J., Wingeyer, A. B., Kruger, G. R., Riggins, C. W., Tranel, P. J., & Bernards, M. L. (2017). Multiple-Herbicide Resistance in a 2,4-D–Resistant Waterhemp (Amaranthus tuberculatus) Population from Nebraska. *Weed Science*, *65*(6), 743–754. https://doi.org/10.1017/wsc.2017.39
Cressey, D. (2015a). Widely used herbicide linked to cancer. Nature. http://www.nature.com/news/widely-used-herbicide-linked-to-cancer-1.17181
Cressey, D. (2015b). Debate rages over herbicide's cancer risk. Nature. http://www.nature.com/news/debate-rages-over-herbicide-s-cancer-risk-1.18794
Cristofaro, C. da S., Branco, C. W. C., Rocha, M. I. de A., & Portugal, S. da G. M. (2021). Assessing glyphosate concentrations in six reservoirs of Paraíba do Sul and Guandu River Basins in southeast Brazil. *Revista Ambiente & Água*, *16*. https://doi.org/10.4136/ambi-agua.2615
Cross, B. (2016, March 3). Cibus is on track to launch SU Canola into Canada in 2017. *The Western Producer*. https://www.producer.com/2016/03/cibus-is-on-track-to-launch-su-canola-into-canada-in-2017/ [accessed: 7 February 2020]

Cuhra, M., Traavik, T., & Bøhn, T. (2013). Clone- and age-dependent toxicity of a glyphosate commercial formulation and its active ingredient in Daphnia magna. *Ecotoxicology*, *22*(2), 251–262. http://doi.org/10.1007/s10646-012-1021-1

Cuhra, M., Traavik, T., & Bøhn, T. (2014). Life cycle fitness differences in *Daphnia magna* fed Roundup-Ready soybean or conventional soybean or organic soybean. *Aquaculture Nutrition*, 21(5), 702-713. http://doi.org/10.1111/anu.12199

Cuhra, M., Traavik, T., Dando, M., Primicerio, R., Holderbaum, D. F., & Bøhn, T. (2015). Glyphosate-Residues in Roundup-Ready Soybean Impair Daphnia magna Life-Cycle. *Journal of Agricultural Chemistry and Environment*, *04*(01), 24–36. http://doi.org/10.4236/jacen.2015.41003

Culpepper, A. S., Grey, T. L., Vencill, W. K., Kichler, J. M., Webster, T. M., Brown, S. M., York, A. C., Hanna, W. W. (2006). Glyphosate-resistant Palmer amaranth (Amaranthus palmeri) confirmed in Georgia. *Weed Science*, *54*(4), 620–626. http://doi.org/10.1614/WS-06-001R.1

Curi, L. M., Peltzer, P. M., Sandoval, M. T., & Lajmanovich, R. C. (2019). Acute Toxicity and Sublethal Effects Caused by a Commercial Herbicide Formulated with 2,4-D on Physalaemus albonotatus Tadpoles. *Water, Air, & Soil Pollution*, *230*(1), 22. https://doi.org/10.1007/s11270-018-4073-x

Curtis, K. M., Savitz, D. A., Weinberg, C. R., & Arbuckle, T. E. (1999). The effect of pesticide exposure on time to pregnancy. *Epidemiology (Cambridge, Mass.)*, *10*(2), 112–117.

Dabney, B. (2018). *Hormetic effects of glyphosate and glyphosate-based herbicides on growth of Prymnesium parvum, a harmful alga* [Thesis]. https://ttu-ir.tdl.org/handle/2346/74436

Dabney, B. L., & Patiño, R. (2018). Low-dose stimulation of growth of the harmful alga, Prymnesium parvum, by glyphosate and glyphosate-based herbicides. Harmful Algae, 80, 130–139. https://doi.org/10.1016/j.hal.2018.11.004

da Costa Chaulet, F., de Alcantara Barcellos, H. H., Fior, D., Pompermaier, A., Koakoski, G., da Rosa, J. G. S., Fagundes, M., & Barcellos, L. J. G. (2019). Glyphosate- and Fipronil-Based Agrochemicals and Their Mixtures Change Zebrafish Behavior. *Archives of Environmental Contamination and Toxicology*, *77*(3), 443–451. https://doi.org/10.1007/s00244-019-00644-7

da Costa, N. B., Hébert, M.-P., Fugère, V., Terrat, Y., Fussmann, G. F., Gonzalez, A., & Shapiro, B. J. (2021). *A glyphosate-based herbicide cross-selects for antibiotic resistance genes in bacterioplankton communities* (p. 2021.12.13.472531). bioRxiv. https://doi.org/10.1101/2021.12.13.472531

da Fonseca, M. B., Glusczak, L., Moraes, B. S., de Menezes, C. C., Pretto, A., Tierno, M. A., Zanella, R., Gonçalves, F. F., & Loro, V. L. (2008). The 2,4-D herbicide effects on acetylcholinesterase activity and metabolic parameters of piava freshwater fish (Leporinus obtusidens). *Ecotoxicology and Environmental Safety*, *69*(3), 416–420. https://doi.org/10.1016/j.ecoenv.2007.08.006

Dai, P., Yan, Z., Ma, S., Yang, Y., Wang, Q., Hou, C., Wu, Y., Liu, Y., & Diao, Q. (2018). The Herbicide Glyphosate Negatively Affects Midgut Bacterial Communities and Survival of Honey Bee during Larvae Reared in Vitro. *Journal of Agricultural and Food Chemistry*, *66*(29), 7786–7793. https://doi.org/10.1021/acs.jafc.8b02212

Daisley, B. A., Chernyshova, A. M., Thompson, G. J., & Allen-Vercoe, E. (2022). Deteriorating microbiomes in agriculture—The unintended effects of pesticides on microbial life. *Microbiome Research Reports*, *1*(1), 6. https://doi.org/10.20517/mrr.2021.08

Danielson, E., & Watters, A. (2017). *Canada: Agricultural Biotechnology Annual | USDA Foreign Agricultural Service* (No. CA17042; p. 26). https://www.fas.usda.gov/data/canada-agricultural-biotechnology-annual-1 [accessed: 6 February 2020]

da Silva, K. A., Nicola, V. B., Dudas, R. T., Demetrio, W. C., Maia, L. dos S., Cunha, L., Bartz, M. L. C., Brown, G. G., Pasini, A., Kille, P., Ferreira, N. G. C., & de Oliveira, C. M. R. (2021). Pesticides in a case study on no-tillage farming systems and surrounding forest patches in Brazil. *Scientific Reports*, *11*(1), 9839. https://doi.org/10.1038/s41598-021-88779-3

da Silva, A. P., Morais, E. R., Oliveira, E. C., & Ghisi, N. de C. (2022). Does exposure to environmental 2,4-dichlorophenoxyacetic acid concentrations increase mortality rate in animals? A meta-analytic review. Environmental Pollution, 303, 119179. https://doi.org/10.1016/j.envpol.2022.119179

Davico, C. E., Pereira, A. G., Nezzi, L., Jaramillo, M. L., de Melo, M. S., Müller, Y. M. R., & Nazari, E. M. (2021). Reproductive toxicity of Roundup WG® herbicide: Impairments in ovarian follicles of model organism Danio rerio. *Environmental Science and Pollution Research*, *28*(12), 15147–15159. https://doi.org/10.1007/s11356-020-11527-z

Davidson, C. (2004). Declining Downwind: Amphibian Population Declines in California and Historical Pesticide Use. *Ecological Applications*, *14*(6), 1892–1902. https://doi.org/10.1890/03-5224

Davies S (2016) Class action over Syngenta corn moves forward. AgriPulse. 9th December 2016. https://www.agri-pulse.com/articles/8100-class-action-over-syngenta-corn-moves-forward

Davies S (2017) FIFRA science panel divided on EPA glyphosate cancer study. AgriPulse. 16th March 2017. https://www.agri-pulse.com/articles/9056-fifra-science-panel-divided-on-epa-glyphosate-cancer-study

Davies, S. (2020, February 19). *Following $265M peach farm verdict, dicamba litigation may expand*. https://www.agri-pulse.com/articles/13197-following-265m-peach-farm-verdict-dicamba-litigation-may-expand?v=preview

Davis, A. K., & Dyer, L. A. (2015). Long-Term Trends in Eastern North American Monarch Butterflies: A Collection of Studies Focusing on Spring, Summer, and Fall Dynamics. *Annals of the Entomological Society of America*, sav070. http://doi.org/10.1093/aesa/sav070

Davis, N. (2020, March 9). Argentine Farmers To Strike Against Rise In Taxes. *El Hemisferio*. https://elhem.co/2020/03/09/argentine-farmers-to-strike-against-rise-in-taxes/

de Brito Rodrigues, L., Gonçalves Costa, G., Lundgren Thá, E., da Silva, L. R., de Oliveira, R., Morais Leme, D., Cestari, M. M., Koppe Grisolia, C., Campos Valadares, M., & de Oliveira, G. A. R. (2019). Impact of the glyphosate-based commercial herbicide, its components and its metabolite AMPA on non-target aquatic organisms. *Mutation Research/Genetic Toxicology and Environmental Mutagenesis*, *842*, 94–101. https://doi.org/10.1016/j.mrgentox.2019.05.002

de Carvalho, L. B., Alves, P. L. da C. A., González-Torralva, F., Cruz-Hipolito, H. E., Rojano-Delgado, A. M., De Prado, R., Gil-Humanes, J., Barro, F., & de Castro, M. D. L. (2012). Pool of resistance mechanisms to glyphosate in *Digitaria insularis*. *Journal of Agricultural and Food Chemistry*, *60*(2), 615–622. https://doi.org/10.1021/jf204089d

de Castro Marcato, A. C., de Souza, C. P., & Fontanetti, C. S. (2017). Herbicide 2,4-D: A Review of Toxicity on Non-Target Organisms. *Water, Air, & Soil Pollution*, *228*(3), 120. https://doi.org/10.1007/s11270-017-3301-0

Dedeke, G. A., Owagboriaye, F. O., Ademolu, K. O., Olujimi, O. O., & Aladesida, A. A. (2018). Comparative Assessment on Mechanism Underlying Renal Toxicity of Commercial Formulation of Roundup Herbicide and Glyphosate Alone in Male Albino Rat. *International Journal of Toxicology*, *37*(4), 285–295. https://doi.org/10.1177/1091581818779553

Defarge, N., Spiroux de Vendômois, J., & Séralini, G. E. (2018). Toxicity of formulants and heavy metals in glyphosate-based herbicides and other pesticides. *Toxicology Reports*, *5*, 156–163. https://doi.org/10.1016/j.toxrep.2017.12.025

de Groot, G. S., Aizen, M. A., Sáez, A., & Morales, C. L. (2021). Large-scale monoculture reduces honey yield: The case of soybean expansion in Argentina. *Agriculture, Ecosystems & Environment*, *306*, 107203. https://doi.org/10.1016/j.agee.2020.107203

Dehnert, G. K., Freitas, M. B., DeQuattro, Z. A., Barry, T., & Karasov, W. H. (2018). Effects of low, subchronic exposure of 2,4-Dichlorophenoxyacetic acid (2,4-D) and commercial 2,4-D formulations on early life stages of fathead minnows (Pimephales promelas). *Environmental Toxicology and Chemistry*, *37*(10), 2550–2559. https://doi.org/10.1002/etc.4209

Dehnert, G. K., Karasov, W. H., & Wolman, M. A. (2019). 2,4-Dichlorophenoxyacetic acid containing herbicide impairs essential visually guided behaviors of larval fish. *Aquatic Toxicology*, *209*, 1–12. https://doi.org/10.1016/j.aquatox.2019.01.015

Dehnert, G. K., Freitas, M. B., Sharma, P. P., Barry, T. P., & Karasov, W. H. (2021). Impacts of subchronic exposure to a commercial 2,4-D herbicide on developmental stages of multiple freshwater fish species. *Chemosphere*, *263*, 127638. https://doi.org/10.1016/j.chemosphere.2020.127638

Dekker, J., & Duke, S. O. (1995). Herbicide-Resistant Field Crops. In D. L. Sparks (Ed.), *Advances in Agronomy* (Vol. 54, pp. 69–116). Academic Press. https://doi.org/10.1016/S0065-2113(08)60898-6

De la Fuente, E. B., Suárez, S. A., & Ghersa, C. M. (2006). Soybean weed community composition and richness between 1995 and 2003 in the Rolling Pampas (Argentina). *Agriculture, Ecosystems & Environment*, 115(1–4), 229–236. http://doi.org/10.1016/j.agee.2006.01.009

De La Fuente, E. B., Perelman, S., & Ghersa, C. M. (2010). Weed and arthropod communities in soyabean as related to crop productivity and land use in the Rolling Pampa, Argentina. Weed Research, 50(6), 561–571. http://doi.org/10.1111/j.1365-3180.2010.00811.x

Dellaferrera, I., Cortés, E., Panigo, E., De Prado, R., Christoffoleti, P., & Perreta, M. (2018). First Report of Amaranthus hybridus with Multiple Resistance to 2,4-D, Dicamba, and Glyphosate. *Agronomy*, *8*(8), 140. https://doi.org/10.3390/agronomy8080140

Delouche, J. C., Burgos, N. R., Gealy, D. R., San Martín, G. Z., Labrada, R., Larinde, M., & Rosell, C. (2007). *Weedy rices: Origin, biology, ecology and control*. FAO.

Delta Farm Press (2008). Designing the perfect weed – Palmer amaranth. http://deltafarmpress.com/management/designing-perfect-weed-palmer-amaranth

Delta Farm Press (2016). China approval clears path for Roundup Ready 2 Xtend. Monsanto still awaiting EPA approval for new dicamba formulation. http://deltafarmpress.com/soybeans/china-approval-clears-path-roundup-ready-2-xtend-soybeans

de María, M., Silva-Sanchez, C., Kroll, K. J., Walsh, M. T., Nouri, M.-Z., Hunter, M. E., Ross, M., Clauss, T. M., & Denslow, N. D. (2021). Chronic exposure to glyphosate in Florida manatee. *Environment International*, *152*, 106493. https://doi.org/10.1016/j.envint.2021.106493

de Maria, M., Kroll, K. J., Yu, F., Nouri, M.-Z., Silva-Sanchez, C., Perez, J. G., Moraga Amador., D. A., Zhang, Y., Walsh, M. T., & Denslow, N. D. (2022). Endocrine, immune and renal toxicity in male largemouth bass after chronic exposure to glyphosate and Rodeo®. *Aquatic Toxicology*, *246*, 106142. https://doi.org/10.1016/j.aquatox.2022.106142
de Melo, M. S., Nazari, E. M., Joaquim-Justo, C., Muller, Y. M. R., & Gismondi, E. (2019). Effects of low glyphosate-based herbicide concentrations on endocrine-related gene expression in the decapoda Macrobrachium potiuna. *Environmental Science and Pollution Research*, *26*(21), 21535–21545. https://doi.org/10.1007/s11356-019-05496-1
de Melo, K. G., Jacobucci, S. R. F., Garlipp, C. R., Trape, Â. Z., & Rosa, P. C. P. (2020). Determination of Glyphosate in human urine from farmers in Mato Grosso-BR. *InterAmerican Journal of Medicine and Health*, *3*. https://doi.org/10.31005/iajmh.v3i0.124
Demirci, Ö. (2022). Evaluation of toxic effect of insecticide, herbicide and fungicide as single and mixture on *Gammarus lacustris* using biochemical markers. *Chemistry and Ecology*, *38*(3), 195–210. https://doi.org/10.1080/02757540.2022.2045973
Demonte, L. D., Michlig, N., Gaggiotti, M., Adam, C. G., Beldoménico, H. R., & Repetti, M. R. (2018). Determination of glyphosate, AMPA and glufosinate in dairy farm water from Argentina using a simplified UHPLC-MS/MS method. *Science of The Total Environment*, *645*, 34–43. https://doi.org/10.1016/j.scitotenv.2018.06.340
de Moura, F. R., da Silva Lima, R. R., da Cunha, A. P. S., da Costa Marisco, P., Aguiar, D. H., Sugui, M. M., Sinhorin, A. P., & Sinhorin, V. D. G. (2017). Effects of glyphosate-based herbicide on pintado da Amazônia: Hematology, histological aspects, metabolic parameters and genotoxic potential. *Environmental Toxicology and Pharmacology*, *56*, 241–248. https://doi.org/10.1016/j.etap.2017.09.019
DeQuattro, Z. A., & Karasov, W. H. (2016). Impacts of 2,4-dichlorophenoxyacetic acid aquatic herbicide formulations on reproduction and development of the fathead minnow (Pimephales promelas). *Environmental Toxicology and Chemistry*, *35*(6), 1478–1488. https://doi.org/10.1002/etc.3293
de Souza, J.S., Kizys, M.M.L., da Conceição, R.R., Glebocki, G., Romano, R.M., Ortiga-Carvalho, T.M., Giannocco, G., da Silva, I.D.C.G., Dias da Silva, M.R., Romano, M.A., Chiamolera, M.I. (2017). Perinatal exposure to glyphosate-based herbicide alters the thyrotrophic axis and causes thyroid hormone homeostasis imbalance in male rats. *Toxicology* **377**, 25–37. doi:10.1016/j.tox.2016.11.005
de Souza, A. P. F., Rodrigues, N. R., & Reyes, F. G. R. (2021). Glyphosate and aminomethylphosphonic acid (AMPA) residues in Brazilian honey. *Food Additives & Contaminants: Part B*, *14*(1), 40–47. https://doi.org/10.1080/19393210.2020.1855676
de Souza, A. P. F., Ferreira, G. S., Pagliarini, F. S., & Rodrigues, N. R. (2021). Exposure assessment of glyphosate residues in soy-based infant formulas from the Brazilian market. *Journal of Consumer Protection and Food Safety*, *16*(1), 45–50. https://doi.org/10.1007/s00003-021-01320-6
Desquilbet, M., Bullock, D. S., & D'Arcangelo, F. M. (2019). A discussion of the market and policy failures associated with the adoption of herbicide-tolerant crops. *International Journal of Agricultural Sustainability*, *17*(5), 326–337. https://doi.org/10.1080/14735903.2019.1655191
Deutsche Welle (2016) 'Increasing number of deaths due to glyphosate'. 14 April 2016. http://m.dw.com/en/increasing-number-of-deaths-due-to-glyphosate/a-19183357?utm_content=buffer44ab7&utm_medium=social&utm_source=twitter.com&utm_campaign=buffer
Deutsche Welle (2017) Glyphosate 'will destroy the whole ecosystem'. 16th March 2017. http://www.dw.com/en/glyphosate-will-destroy-the-whole-ecosystem/a-37968836
Devine, C. (2015). Why we're tucking into more healthy food & going GM-free. Herald Scotland. http://www.heraldscotland.com/opinion/14158022.display/
de Vos, C. J., & Swanenburg, M. (2018). Health effects of feeding genetically modified (GM) crops to livestock animals: A review. *Food and Chemical Toxicology*, *117*, 3–12. https://doi.org/10.1016/j.fct.2017.08.031
Devos, Y., Demont, M., Dillen, K., Reheul, D., Kaiser, M., & Sanvido, O. (2009). Coexistence of genetically modified (GM) and non-GM crops in the European Union. A review. *Agronomy for Sustainable Development*, *29*(1), 11–30. http://doi.org/10.1051/agro:2008051
Dewey, C. (2017, August 29). This miracle weed killer was supposed to save farms. Instead, it's devastating them. *Washington Post*. https://www.washingtonpost.com/business/economy/this-miracle-weed-killer-was-supposed-to-save-farms-instead-its-devastating-them/2017/08/29/33a21a56-88e3-11e7-961d-2f373b3977ee_story.html
Di, K., Stewart, C. N., Wei, W., Shen, B., Tang, Z.-X., & Ma, K.-P. (2009). Fitness and maternal effects in hybrids formed between transgenic oilseed rape (Brassica napus L.) and wild brown mustard [B. juncea (L.) Czern et Coss.] in the field. *Pest Management Science*, *65*(7), 753–760. https://doi.org/10.1002/ps.1749
Dias, M., Krenchinski, F., Pereira, V., Moreno, G., Albrecht, L., & Albrecht, A. (2018). *Phytosociological survey of weeds in glyphosate resistant and susceptible soybean cultivation areas*. *13*, 1–7. https://doi.org/10.5039/agraria.v13i4a5592

Dias, M., Rocha, R., & Soares, R. R. (2020). *Down the River: Glyphosate Use in Agriculture and Birth Outcomes of Surrounding Populations*. Latin American And The Caribbean Economic Association. http://vox.lacea.org/files/Working_Papers/lacea_wps_0024_dias_rocha_soares.pdf
Dicamba Herbicides Litigation, MDL No. 2820 (United States Judicial Panel on Multidistrict Litigation February 1, 2018). https://www.courthousenews.com/wp-content/uploads/2020/06/Dicamba.pdf
Dick, R. E., & Quinn, J. P. (1995). Glyphosate-degrading isolates from environmental samples: occurrence and pathways of degradation. *Applied Microbiology and Biotechnology*, *43*(3), 545–550. http://doi.org/10.1007/BF00218464
Dillon, A.J., Varanasi, V.K., Danilova, T., Koo, D.-H., Nakka, S., Peterson, D., Tranel, P., Friebe, B., Gill, B.S., Jugulam, M. (2016). Physical Mapping of Amplified 5-enolpyruvylshikimate-3-phosphate Synthase Gene Copies in Glyphosate-Resistant Amaranthus tuberculatus. Plant Physiol. pp.01427.2016. doi:10.1104/pp.16.01427
Dodson, L., Wechsler, S., Williamson, S., McFadden, J., & Smith, D. (2021, July 6). *USDA ERS - Dicamba-Tolerant Cotton*. USDA Economic Research Service. https://www.ers.usda.gov/amber-waves/2021/july/adoption-of-genetically-engineered-dicamba-tolerant-cotton-seeds-is-prevalent-throughout-the-united-states/
Doering, C. (2015). Farmers turn to GMO-free crops to boost income. Press Citizen. http://www.press-citizen.com/story/money/agriculture/2015/04/18/non-gmo-farming/25951693/
DOF – Diario Oficial de la Federacíon. (2020). Decreto del 31 de diciembre de 2020. Available. http://www.dof.gob.mx/nota_detalle.php?codigo=5609365&fecha=31/12/2020 [17 November 2021]
Domínguez, A., Brown, G. G., Sautter, K. D., Ribas de Oliveira, C. M., de Vasconcelos, E. C., Niva, C. C., Bartz, M. L., Bedano, J. C. (2016). Toxicity of AMPA to the earthworm Eisenia andrei Bouché, 1972 in tropical artificial soil. *Scientific Reports*, *6*, 19731. http://doi.org/10.1038/srep19731
Donald, P. F., Green, R. E., & Heath, M. F. (2001). Agricultural intensification and the collapse of Europe's farmland bird populations. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *268*(1462), 25–29. http://doi.org/10.1098/rspb.2000.1325
Donau Soja (2015a). Europäischer Sojaanbau steigt weiter an. http://www.donausoja.org/PublishingImages/Seiten/Presse/Presseaussendungen/PA%202015/Donau%20Soja%20Presseaussendung_Europäischer%20Sojaanbau%20steigt%20weiter%20an_23.04.2015.pdf
Donau Soja (2015b). Ukraine unterzeichnet Donau Soja Erklärung. http://www.donausoja.org/PublishingImages/Seiten/Presse/Presseaussendungen/PA%202015/Presseaussendung%20Ukraine%20unterzeichnet%20Donau%20Soja%20Erklärung.pdf
Dong, T., Guan, Q., Hu, W., Zhang, M., Zhang, Y., Chen, M., Wang, X., & Xia, Y. (2020). Prenatal exposure to glufosinate ammonium disturbs gut microbiome and induces behavioral abnormalities in mice. *Journal of Hazardous Materials*, *389*, 122152. https://doi.org/10.1016/j.jhazmat.2020.122152
Dong, H., Huang, Y., & Wang, K. (2021). The Development of Herbicide Resistance Crop Plants Using CRISPR/Cas9-Mediated Gene Editing. *Genes*, *12*(6), 912. https://doi.org/10.3390/genes12060912
dos Santos, A.P.R., Rocha, T.L., Borges, C.L., Bailão, A.M., de Almeida Soares, C.M., de Sabóia-Morais, S.M.T., 2017. A glyphosate-based herbicide induces histomorphological and protein expression changes in the liver of the female guppy Poecilia reticulata. *Chemosphere* **168**, 933–943. doi:10.1016/j.chemosphere.2016.10.116
Dow AgroScience (2015). EPA approves Enlist Duo™ herbicide for use in additional states. http://newsroom.dowagro.com/press-release/epa-approves-enlist-duo-herbicide-use-additional-states
Dreoni, I., Matthews, Z., & Schaafsma, M. (2022). The impacts of soy production on multi-dimensional well-being and ecosystem services: A systematic review. *Journal of Cleaner Production*, *335*, 130182. https://doi.org/10.1016/j.jclepro.2021.130182
Druart, C., Gimbert, F., Scheifler, R., & de Vaufleury, A. (2017). A full life-cycle bioassay with Cantareus aspersus shows reproductive effects of a glyphosate-based herbicide suggesting potential endocrine disruption. *Environmental Pollution*, *226*, 240–249. https://doi.org/10.1016/j.envpol.2017.03.061
Duchnowicz, P., & Koter, M. (2003). Damage to the erythrocyte membrane caused by chlorophenoxyacetic herbicides. *Cellular & Molecular Biology Letters*, *8*(1), 25–30.
Duke, S. O., Powles, S. B. (2008). Glyphosate: a once-in-a-century herbicide. Pest Management Science 64: 319-325.
Duke, S. O. (2018). The history and current status of glyphosate. *Pest Management Science*, *74*(5), 1027–1034. https://doi.org/10.1002/ps.4652
Duke, S. O., Powles, S. B., & Sammons, R. D. (2018). Glyphosate – How it Became a Once in a Hundred Year Herbicide and Its Future. *Outlooks on Pest Management*, *29*(6), 247–251. https://doi.org/10.1564/v29_dec_03
Dun, B., Wang, X., Lu, W., Chen, M., Zhang, W., Ping, S., Wang, Z., Zhang, B., & Lin, M. (2014). Development of highly glyphosate-tolerant tobacco by coexpression of glyphosate acetyltransferase gat and EPSPS G2-aroA genes. *The Crop Journal*, *2*(2), 164–169. https://doi.org/10.1016/j.cj.2014.03.003

Durden T (2017) Monsanto Colluded with EPA, Was Unable to Prove Roundup Does Not Cause Cancer, Unsealed Court Docs Reveal. 15th March 2017. http://www.zerohedge.com/news/2017-03-14/court-docs-prove-monsanto-collusion-epa-kill-cancer-study-admits-cant-say-roundup-do
Dyer, G. A., Serratos-Hernández, J. A., Perales, H. R., Gepts, P., Piñeyro-Nelson, A., Chávez, A., Salinas-Arreortua, N., Yúnez-Naude, A., Taylor, J. E., & Alvarez-Buylla, E. R. (2009). Dispersal of Transgenes through Maize Seed Systems in Mexico. *PLOS ONE*, *4*(5), e5734. https://doi.org/10.1371/journal.pone.0005734
Eaton, J. L., Cathey, A. L., Fernandez, J. A., Watkins, D. J., Silver, M. K., Milne, G. L., Velez-Vega, C., Rosario, Z., Cordero, J., Alshawabkeh, A., & Meeker, J. D. (2022). The association between urinary glyphosate and aminomethyl phosphonic acid with biomarkers of oxidative stress among pregnant women in the PROTECT birth cohort study. *Ecotoxicology and Environmental Safety*, *233*, 113300. https://doi.org/10.1016/j.ecoenv.2022.113300
EC (n.d. a) ADOPTION OF NATIONAL LEGISLATION IN ACCORDANCE WITH ARTICLE 26a(1a) OF DIRECTIVE 2001/18/EC. https://ec.europa.eu/food/system/files/2018-10/plant_gmo_auth_nat-measures_summary-cross-border-national-measures.pdf
EC (n.d. b) Restrictions of geographical scope of GMO applications/authorisations: EU countries demands and outcomes. https://ec.europa.eu/food/plants/genetically-modified-organisms/gmo-authorisation/gmo-authorisations-cultivation/restrictions-geographical-scope-gmo-applicationsauthorisations-eu-countries-demands-and-outcomes_en
ECDC/EMEA (2009). Joint technical report: the bacterial challenge: time to react. http://ecdc.europa.eu/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf
ECHA (2017) Glyphosate not classified as a carcinogen by ECHA. Press Release. 15th March 2017. https://echa.europa.eu/de/-/glyphosate-not-classified-as-a-carcinogen-by-echa
EcoWatch (2012) Farmers Continue to Fight Monsanto's 'Seed Police'. Jul 06, 2012. http://www.ecowatch.com/farmers-continue-to-fight-monsantos-seed-police-1881631387.html
Edwards, W. M., Triplett, G. B., & Kramer, R. M. (1980). A Watershed Study of Glyphosate Transport in Runoff. *Journal of Environment Quality*, *9*(4), 661. http://doi.org/10.2134/jeq1980.00472425000900040024x
EFSA (2007). EFSA statement on the fate of recombinant DNA or proteins in meat, milk and eggs from animals fed with GM feed. https://www.greenpeace.de/sites/www.greenpeace.de/files/publications/ergebnis_umfrage_gentechnik_04_2014.pdf
EFSA (2011). Scientific Opinion on application (EFSA- GMO-UK-2008-60) for placing on the market of genetically modified herbicide tolerant maize GA21 for food and feed uses, import, processing and cultivation under Regulation (EC) No 1829/2003 from Syngenta Seeds. EFSA Panel on Genetically Modified Organisms (GMO). EFSA Journal 2011, 9(12): 2480. [94 pp.] doi:10.2903/j.efsa.2011.2480. www.efsa.europa.eu/efsajournal
EFSA (2012) Scientific Opinion on an application (EFSA-GMO-NL-2005-24) for the placing on the market of the herbicide tolerant genetically modified soybean 40-3-2 for cultivation under Regulation (EC) No 1829/2003 from Monsanto. http://www.efsa.europa.eu/en/efsajournal/doc/2753.pdf
EFSA (2013). Review of the Séralini et al. (2012) publication on a 2-year rodent feeding study with glyphsoate formulations and GM maize NK603 as published online on 19 September 2012 in Food and Chemical Toxicology. EFSA Journal 2012; 10(10):2910. doi:10.2903/j.efsa.2012.2910. http://www.efsa.europa.eu/en/efsajournal/pub/2910.htm
EFSA (2014). Proposal from the GMO Panel for a self-task activity to supplement its previous risk mitigation measures reducing exposure of non-target Lepidoptera to maize MON810, Bt11 or 1507 pollen. http://www.testbiotech.org/sites/default/files/EFSA_risk%20mitigation%20measures%20for%20MON810_Bt11_1507.pdf
EFSA (2015a). Updating risk management recommendations to limit exposure of non-target Lepidoptera of conservation concern in protected habitats to Bt-maize pollen. EFSA Panel on Genetically Modified Organisms (GMO). http://www.efsa.europa.eu/en/efsajournal/doc/4127.pdf
EFSA (2015b). Conclusion on Pesticide Peer Review. Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/4302.pdf
EFSA (2016a). Subject: Open letter: Review of the Carcinogenicity of Glyphosate by EFSA and BfR. http://www.efsa.europa.eu/sites/default/files/EFSA_response_Prof_Portier.pdf
EFSA. (2016b). Peer review of the pesticide risk assessment of the active substance isoxaflutole. *EFSA Journal*, *14*(2), 4416. https://doi.org/10.2903/j.efsa.2016.4416
EFSA. (2017, December 22). Request for an EFSA peer review (EFSA Conclusion) on the active substance glufosinate according to Article 13 of Regulation (EU) No 844/2012. Register of Questions. http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2016-00408

EFSA. (2021, June 15). *Glyphosate: EU regulators begin review of renewal assessments | EFSA*. https://www.efsa.europa.eu/en/news/glyphosate-eu-regulators-begin-review-renewal-assessments
Einstein-Curtis, A. (2018, November 29). *US biotech company flirts with initial public offering*. Feednavigator.Com. https://www.feednavigator.com/Article/2018/11/29/US-biotech-company-flirts-with-initial-public-offering [accessed: 7 February 2020]
Eker, S., Ozturk, L., Yazici, A., Erenoglu, B., Romheld, V., & Cakmak, I. (2006). Foliar-Applied Glyphosate Substantially Reduced Uptake and Transport of Iron and Manganese in Sunflower (Helianthus annuus L.) Plants. *Journal of Agricultural and Food Chemistry*, *54*(26), 10019–10025. http://doi.org/10.1021/jf0625196
El Agrebi, N., Tosi, S., Wilmart, O., Scippo, M.-L., de Graaf, D. C., & Saegerman, C. (2020). Honeybee and consumer's exposure and risk characterisation to glyphosate-based herbicide (GBH) and its degradation product (AMPA): Residues in beebread, wax, and honey. *Science of The Total Environment*, *704*, 135312. https://doi.org/10.1016/j.scitotenv.2019.135312
Elgert, L. (2016). "More soy on fewer farms" in Paraguay: challenging neoliberal agriculture's claims to sustainability. *The Journal of Peasant Studies*, 43(2), 537–561. http://doi.org/10.1080/03066150.2015.1076395
Elmore, B. (2022, January 26). The herbicide dicamba was supposed to solve farmers' weed problems – instead, it's making farming harder for many of them. *The Conversation*. http://theconversation.com/the-herbicide-dicamba-was-supposed-to-solve-farmers-weed-problems-instead-its-making-farming-harder-for-many-of-them-174181
Eloy, L., Aubertin, C., Toni, F., Lúcio, S. L. B., & Bosgiraud, M. (2016). On the margins of soy farms: Traditional populations and selective environmental policies in the Brazilian Cerrado. *The Journal of Peasant Studies*, *43*(2), 494–516. https://doi.org/10.1080/03066150.2015.1013099
Endo, M., Mikami, M., & Toki, S. (2016). Biallelic Gene Targeting in Rice1[OPEN]. *Plant Physiology*, *170*(2), 667–677. https://doi.org/10.1104/pp.15.01663
ENS (2014). Court Battle Looms Over Vermont's GMO Food Labeling Law. http://ens-newswire.com/2014/05/23/court-battle-looms-over-vermonts-gmo-food-labeling-law/
E.O.S. Intelligence. (2016, July 6). Genetically Modified Crops' Technology Struggles to Keep Promises in Brazil. *EOS Intelligence - Powering Informed Decision-Making*. https://www.eos-intelligence.com/perspectives/consumer-goods-retail/genetically-modified-crops-technology-struggles-to-keep-promises-in-brazil/
Espandiari, P., Glauert, H. P., Lee, E. Y., & Robertson, L. W. (1999). Promoting activity of the herbicide dicamba (2-methoxy-3, 6-dichlorobenzoic acid) in two stage hepatocarcinogenesis. *International Journal of Oncology*, *14*(1), 79–84.
Espandiari, P., Thomas, V. A., Glauert, H. P., O'Brien, M., Noonan, D., & Robertson, L. W. (1995). The Herbicide Dicamba (2-Methoxy-3,6-dichlorobenzoic Acid) Is a Peroxisome Proliferator in Rats. *Fundamental and Applied Toxicology*, *26*(1), 85–90. https://doi.org/10.1006/faat.1995.1077
ETC Group (2013). Putting the Cartel before the Horse ...and Farm, Seeds, Soil, Peasants etc. Who will control Agricultural Inputs, 2013?
EU Reporter (2016) 'We need an exit strategy for #glyphosate' says #EFFAT. 20 June 2016. https://www.eureporter.co/environment/2016/06/20/we-need-an-exit-strategy-for-glyphosate-says-effat/
EU/FAO/WFP. (2022). Global Report on Food Crises: Acute food insecurity hits new highs. https://www.fao.org/newsroom/detail/global-report-on-food-crises-acute-food-insecurity-hits-new-highs/en
Eurekalert (2014). Palmer amaranth threatens Midwest farm economy, researchers report. http://www.eurekalert.org/pub_releases/2014-06/uoia-pat060314.php
Eurobarometer (2010). Special Eurobarometer 341. Biotechnology. European Commission. http://ec.europa.eu/public_opinion/archives/ebs/ebs_341_en.pdf
European Commission (2002). Review report for the active substance glyphosate. EC Health & Consumer Protection Directorate-General. http://ec.europa.eu/food/fs/sfp/ph_ps/pro/eva/existing/list1_glyphosate_en.pdf
European Commission (2003). Commission Recommendation of 23 July 2003 on guidelines for the development of national strategies and best practices to ensure the co-existence of genetically modified crops with conventional and organic farming. http://ecob.jrc.ec.europa.eu/documents/Recommendation_2003_556.pdf
European Commission (2009). Report from the Commission to the Council and the European Parliament on the coexistence of genetically modified crops with conventional and organic farming. http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=COM:2009:0153:FIN:en:PDF
European Commission (2010). Commission Recommendation of 13 July 2010 on guidelines for the development of national co-existence measures to avoid the unintended presence of GMOs in conventional and organic crops. http://ec.europa.eu/food/plant/docs/plant_gmo-agriculture_coexistence-new_recommendation_en.pdf
European Commission (2016a). EU Pesticide database. Search active substances. http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

European Commission (2016b) Glyphosate: Commission proposes the way forward - Statement by Commissioner for Health and Food Safety, Vytenis Andriukaitis. Brussels, 1 June 2016. http://europa.eu/rapid/press-release_STATEMENT-16-2011_en.htm

European Commission (2017) Implementing Regulation (EU) 2017/2324 of 12 December 2017 renewing the approval of the active substance glyphosate in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011 (Text with EEA relevance.), Pub. L. No. 32017R2324, 333 OJ L (2017). http://data.europa.eu/eli/reg_impl/2017/2324/oj/eng

European Commission. (n.d.). *EU Pesticides database—Glufosinate*. European Commission Website. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/active-substances/?event=as.details&as_id=79

European Parliament (2015a). Parliament rejects national GMO bans proposal. http://www.europarl.europa.eu/news/en/news-room/20151022IPR98805/Parliament-rejects-national-GMO-bans-proposal

European Parliament (2015b). Environment MEPs oppose new GM maize authorization. http://www.europarl.europa.eu/news/en/news-room/20151201IPR05562/Environment-MEPs-oppose-new-GM-maize-authorization

European Parliament (2015c). European Parliament resolution of 16 December 2015 on Commission Implementing Decision (EU) 2015/2279 of 4 December 2015 authorising the placing on the market of products containing, consisting of, or produced from genetically modified maize NK603 × T25 (MON-ØØ6Ø3-6 × ACS-ZMØØ3-2) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (2015/3006(RSP). http://www.europarl.europa.eu/sides/getDoc.do?type=TA&reference=P8-TA-2015-0456&language=EN&ring=B8-2015-1365

European Parliament (2016a). MEPs object to three GM soybean authroisations. http://www.europarl.europa.eu/news/en/news-room/20160129IPR11955/MEPs-object-to-three-GM-soybean-authorisations

European Parliament (2016b). European Parliament resolution on the draft Commission implementing decision authorising the placing on the market of products containing, consisting of, or produced from genetically modified soybean FG72 (MST-FGØ72-2) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (D042684 – 2015/2547(RSP). http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-%2f%2fEP%2f%2fTEXT%2bMOTION%2bB8-2016-0133%2b0%2bDOC%2bXML%2bV0%2f%2fEN&language=EN

European Parliament (2016c). European Parliament resolution on the draft Commission implementing decision authorising the placing on the market of products containing, consisting of, or produced from genetically modified soybean MON 87708 × MON 89788 (MON-877Ø8-9 × MON-89788-1) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (D042682 – 2015/2548(RSP). http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-%2f%2fEP%2f%2fTEXT%2bMOTION%2bB8-2016-0134%2b0%2bDOC%2bXML%2bV0%2f%2fEN&language=EN

European Parliament (2016d). European Parliament resolution on the draft Commission implementing decision authorising the placing on the market of products containing, consisting of, or produced from genetically modified soybean MON 87705 × MON 89788 (MON-877Ø5-6 × MON-89788-1) pursuant to Regulation (EC) No 1829/2003 of the European Parliament and of the Council (D042681 – 2015/2549(RSP). http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-%2f%2fEP%2f%2fTEXT%2bMOTION%2bB8-2016-0135%2b0%2bDOC%2bXML%2bV0%2f%2fEN&language=EN

Evans, J. A., Tranel, P. J., Hager, A. G., Schutte, B., Wu, C., Chatham, L. A., & Davis, A. S. (2016). Managing the evolution of herbicide resistance. *Pest Management Science*, *72*(1), 74–80. http://doi.org/10.1002/ps.4009

Everett, K. D. E., & Dickerson, H. W. (2003). Ichthyophthirius multifiliis and tetrahymena thermophila tolerate glyphosate but not a commercial herbicidal formulation. *Bulletin of Environmental Contamination and Toxicology*, *70*(4), 0731–0738. http://doi.org/10.1007/s00128-003-0044-y

Faghani, M., & Rahimian, Y. (2018). Effect of glyphosate on honey bee (*Apis Mellifera*) performance. *Arthropods*, *7*(3), 77–81.

Faita, M. R., Oliveira, E. de M., Alves, V. V., Orth, A. I., & Nodari, R. O. (2018). Changes in hypopharyngeal glands of nurse bees (Apis mellifera) induced by pollen-containing sublethal doses of the herbicide Roundup®. *Chemosphere*, *211*, 566–572. https://doi.org/10.1016/j.chemosphere.2018.07.189

Faita, M. R., Chaves, A., Corrêa, C. C. G., Silveira, V., & Nodari, R. O. (2022). Proteomic profiling of royal jelly produced by Apis mellifera L. exposed to food containing herbicide-based glyphosate. *Chemosphere*, *292*, 133334. https://doi.org/10.1016/j.chemosphere.2021.133334

Fallon, S. (2014). Monarch butterfly population hits a new low. Switchboard. Natural Resource Defense Council Staff Blog. https://www.nrdc.org/experts/sylvia-fallon/monarch-butterfly-population-hits-new-low

Fallon, S. (2015). Monarch butterflies can't wait another year – EPA needs to act now. Switchboard. Natural Resources Defense Council Staff Blog. https://www.nrdc.org/experts/sylvia-fallon/monarch-butterflies-cant-wait-another-year-epa-needs-act-now

Fan, L., Feng, Y., Weaver, D. B., Delaney, D. P., Wehtje, G. R., & Wang, G. (2017). Glyphosate effects on symbiotic nitrogen fixation in glyphosate-resistant soybean. *Applied Soil Ecology*, *121*, 11–19. https://doi.org/10.1016/j.apsoil.2017.09.015

Fang, J., Nan, P., Gu, Z., Ge, X., Feng, Y.-Q., & Lu, B.-R. (2018). Overexpressing Exogenous 5-Enolpyruvylshikimate-3-Phosphate Synthase (EPSPS) Genes Increases Fecundity and Auxin Content of Transgenic Arabidopsis Plants. *Frontiers in Plant Science*, *9*, 233. https://doi.org/10.3389/fpls.2018.00233

FAO (2011). Global food losses and food waste – Extent, causes and prevention. Rome. https://knowledge4policy.ec.europa.eu/publication/global-food-losses-food-waste-extent-causes-prevention_en

FAO, IFAD & WFP (2015). The State of Food Insecurity in the World 2015. Meeting the 2015 international hunger targets: taking stock of uneven progress. Rome, FAO.

FAO (2016) Statistics by Country (Brazil). http://faostat3.fao.org/browse/R/RP/E

Faria, M., Bedrossiantz, J., Ramírez, J. R. R., Mayol, M., García, G. H., Bellot, M., Prats, E., Garcia-Reyero, N., Gómez-Canela, C., Gómez-Oliván, L. M., & Raldúa, D. (2021). Glyphosate targets fish monoaminergic systems leading to oxidative stress and anxiety. *Environment International*, *146*, 106253. https://doi.org/10.1016/j.envint.2020.106253

Fargione, J., Hill, J., Tilman, D., Polasky, S., & Hawthorne, P. (2008). Land Clearing and the Biofuel Carbon Debt. *Science*, 319(5867), 1235–1238. http://doi.org/10.1126/science.1152747

Fathi, M. A., Han, G., Kang, R., Shen, D., Shen, J., & Li, C. (2020). Disruption of cytochrome P450 enzymes in the liver and small intestine in chicken embryos in ovo exposed to glyphosate. *Environmental Science and Pollution Research*, *27*(14), 16865–16875. https://doi.org/10.1007/s11356-020-08269-3

Feat-Vetel, J., Larrigaldie, V., Meyer-Dilhet, G., Herzine, A., Mougin, C., Laugeray, A., Gefflaut, T., Richard, O., Quesniaux, V., Montécot-Dubourg, C., & Mortaud, S. (2018). Multiple effects of the herbicide glufosinate-ammonium and its main metabolite on neural stem cells from the subventricular zone of newborn mice. *NeuroToxicology*, *69*, 152–163. https://doi.org/10.1016/j.neuro.2018.10.001

Feng, P. C. C., Tran, M., Chiu, T., Douglas Sammons, R., Heck, G. R., & CaJacob, C. A. (2004). Investigations into glyphosate-resistant horseweed (Conyza canadensis): retention, uptake, translocation, and metabolism. *Weed Science*, *52*(4), 498–505. http://doi.org/10.1614/WS-03-137R

Fernandes, G., Aparicio, V. C., Bastos, M. C., De Gerónimo, E., Labanowski, J., Prestes, O. D., Zanella, R., & dos Santos, D. R. (2019). Indiscriminate use of glyphosate impregnates river epilithic biofilms in southern Brazil. *Science of The Total Environment*, *651*, 1377–1387. https://doi.org/10.1016/j.scitotenv.2018.09.292

Fernandes, G. B., Silva, A. C. de L., Maronhas, M. E. S., Santos, A. da S. dos, & Lima, P. H. C. (2022). Transgene Flow: Challenges to the On-Farm Conservation of Maize Landraces in the Brazilian Semi-Arid Region. *Plants*, *11*(5), 603. https://doi.org/10.3390/plants11050603

Fernández, P., Alcántara, R., Osuna, M. D., Vila-Aiub, M. M., & Prado, R. D. (2017). Forward selection for multiple resistance across the non-selective glyphosate, glufosinate and oxyfluorfen herbicides in Lolium weed species. *Pest Management Science*, *73*(5), 936–944. https://doi.org/10.1002/ps.4368

Fernandez-Cornejo et al. (2006). The first Decade of Genetically Engineered Crops in the United States. USDA Economic Research Service.

Fernandez-Cornejo, J., Wechsler, S., Livingston, M., Mitchel, L. (2014). Genetically Engineered Crops in the United States. ERR-162 USDA, Economic Research Service

Fernandez-Cornejo, J., Wechsler, S., & Milkove, D. (2016). The Adoption of Genetically Engineered Alfalfa, Canola, and Sugarbeets in the United States. https://www.ers.usda.gov/webdocs/publications/eib163/eib-163.pdf

Fernández-Escalada, M., Zulet-González, A., Gil-Monreal, M., Royuela, M., & Zabalza, A. (2019). Physiological performance of glyphosate and imazamox mixtures on Amaranthus palmeri sensitive and resistant to glyphosate. *Scientific Reports*, *9*(1), 18225. https://doi.org/10.1038/s41598-019-54642-9

Ferramosca, A., Lorenzetti, S., Di Giacomo, M., Murrieri, F., Coppola, L., & Zara, V. (2021). Herbicides glyphosate and glufosinate ammonium negatively affect human sperm mitochondria respiration efficiency. *Reproductive Toxicology*, *99*, 48–55. https://doi.org/10.1016/j.reprotox.2020.11.011

Ferrante, L., & Fearnside, P. M. (2020). Evidence of mutagenic and lethal effects of herbicides on Amazonian frogs. *Acta Amazonica*, *50*, 363–366. https://doi.org/10.1590/1809-4392202000562

Ferraro, D. O., & Ghersa, C. M. (2013). Fuzzy assessment of herbicide resistance risk: Glyphosate-resistant johnsongrass, Sorghum halepense (L.) Pers., in Argentina's croplands. *Crop Protection*, *51*, 32–39. https://doi.org/10.1016/j.cropro.2013.04.004

Ferreira, C., Duarte, S. C., Costa, E., Pereira, A. M. P. T., Silva, L. J. G., Almeida, A., Lino, C., & Pena, A. (2021). Urine biomonitoring of glyphosate in children: Exposure and risk assessment. *Environmental Research*, *198*, 111294. https://doi.org/10.1016/j.envres.2021.111294

Ferreira-Junior, D. F., Sarmento, R. A., Saraiva, A. de S., Pereira, R. R., Picanço, M. C., Pestana, J. L. T., & Soares, A. M. V. M. (2017). Low Concentrations of Glyphosate-Based Herbicide Affects the Development of Chironomus xanthus. *Water, Air, & Soil Pollution*, *228*(10), 390. https://doi.org/10.1007/s11270-017-3536-9

Feulefack, J., Khan, A., Forastiere, F., & Sergi, C. M. (2021). Parental Pesticide Exposure and Childhood Brain Cancer: A Systematic Review and Meta-Analysis Confirming the IARC/WHO Monographs on Some Organophosphate Insecticides and Herbicides. Children, 8(12), 1096. https://doi.org/10.3390/children8121096

Figueiredo, M. R., Leibhart, L. J., Reicher, Z. J., Tranel, P. J., Nissen, S. J., Westra, P., Bernards, M. L., Kruger, G. R., Gaines, T. A., & Jugulam, M. (2018). Metabolism of 2,4-dichlorophenoxyacetic acid contributes to resistance in a common waterhemp (Amaranthus tuberculatus) population. *Pest Management Science*, *74*(10), 2356–2362. https://doi.org/10.1002/ps.4811

Filomeno, F. (2013). How Argentine Farmers Overpowered Monsanto: The Mobilization of Knowledge-users and Intellectual Property Regimes. *Journal of Politics in Latin America*, 5(3), 35–71.

Fiorino, E., Sehonova, P., Plhalova, L., Blahova, J., Svobodova, Z., & Faggio, C. (2018). Effects of glyphosate on early life stages: Comparison between Cyprinus carpio and Danio rerio. *Environmental Science and Pollution Research*, *25*(9), 8542–8549. https://doi.org/10.1007/s11356-017-1141-5

Finkler, M., Rodrigues, G. Z. P., Kayser, J. M., Ziulkoski, A. L., & Gehlen, G. (2022). Cytotoxic and genotoxic effects induced by associated commercial glyphosate and 2,4-D formulations using the Allium cepa bioassay. *Journal of Environmental Science and Health, Part B*, *57*(2), 133–141. https://doi.org/10.1080/03601234.2022.2034432

Firbank, L. G., Heard, M. S., Woiwod, I. P., Hawes, C., Haughton, A. J., Champion, G. T., Scott, R. J., Hill, M. O., Dewar, A. M., Squire, G. R., May, M. J., Brooks, D. R., Bohan, D. A., Daniels, R. E., Osborne, J. L., Roy, D. B., Black, H. I. J., Rothery, P., Perry, J. N. (2003). An introduction to the Farm-Scale Evaluations of genetically modified herbicide-tolerant crops. *Journal of Applied Ecology*, *40*(1), 2–16. http://doi.org/10.1046/j.1365-2664.2003.00787.x

Flax Council of Canada. (2016). *Questions & Answers | Flax Gene Editing*. https://flaxcouncil.ca/wp-content/uploads/2016/07/2016-QA_FLAX-GENE-EDITING-07.18.16.pdf

Flockhart, D. T. T., Pichancourt, J.-B., Norris, D. R., & Martin, T. G. (2014). Unravelling the annual cycle in a migratory animal: breeding-season habitat loss drives population declines of monarch butterflies. *Journal of Animal Ecology*, n/a–n/a. http://doi.org/10.1111/1365-2656.12253

Foldager, L., Winters, J. F. M., Nørskov, N. P., & Sørensen, M. T. (2021). Impact of feed glyphosate residues on broiler breeder egg production and egg hatchability. *Scientific Reports*, *11*(1), 19290. https://doi.org/10.1038/s41598-021-98962-1

FoEE. (2022). *New GMOs and pesticides: Fast-track to failure*. https://friendsoftheearth.eu/publication/new-gmos-and-pesticides-reduction-fast-track-to-failure/

Folmar, L. C., Sanders, H. O., & Julin, A. M. (1979). Toxicity of the herbicide glyphosate and several of its formulations to fish and aquatic invertebrates. *Archives of Environmental Contamination and Toxicology*, *8*(3), 269–278. http://doi.org/10.1007/BF01056243

Food Standards Agency (2012). GM Labelling – Exploring public responses to the labelling of Gm food and the use of GM-free labelling. Qualitative and guantitative findings.

Foodwatch. (2018, April 19). *Riskantes Pestizid: Zulassung für Glufosinat läuft aus*. Foodwatch DE. https://www.foodwatch.org/de/aktuelle-nachrichten/2018/riskantes-pestizid-zulassung-fuer-glufosinat-laeuft-aus/

Foote, N. (2021, April 7). *Report: Majority of consumers want compulsory labelling on all genetically modified food*. Www.Euractiv.Com. https://www.euractiv.com/section/agriculture-food/news/report-majority-of-consumers-want-compulsory-labelling-on-all-genetically-modified-food/

Forner-Piquer, I., Faucherre, A., Byram, J., Blaquiere, M., de Bock, F., Gamet-Payrastre, L., Ellero-Simatos, S., Audinat, E., Jopling, C., & Marchi, N. (2021). Differential impact of dose-range glyphosate on locomotor behavior, neuronal activity, glio-cerebrovascular structures, and transcript regulations in zebrafish larvae. *Chemosphere*, *267*, 128986. https://doi.org/10.1016/j.chemosphere.2020.128986

Forsa (2014). Meinungen zum Thema Gentechnik in Lebensmitteln. https://www.greenpeace.de/sites/www.greenpeace.de/files/publications/ergebnis_umfrage_gentechnik_04_2014.pdf

Fortune Business Insights. (2022, February). Non-GMO Food Market Size, Trends & Growth | Forecast [2028]. https://www.fortunebusinessinsights.com/non-gmo-food-market-106359

Fraanje, W., & Garnett, T. (2020). *Soy: Food, feed, and land use change*. Food Climate Research Network. https://www.tabledebates.org/building-blocks/soy-food-feed-and-land-use-change

Fraser K (2013). Glyphosate resistant weeds – intensifying. Guelph, Ontario, Canada: Stratus Ag Research. Available at: http://stratusresearch.com/blog/glyphosate-resistant-weeds-intensifying/

Freisthler, M. S., Robbins, C. R., Benbrook, C. M., Young, H. A., Haas, D. M., Winchester, P. D., & Perry, M. J. (2022). Association between increasing agricultural use of 2,4-D and population biomarkers of exposure: Findings from the National Health and Nutrition Examination Survey, 2001–2014. Environmental Health, 21(1), 23. https://doi.org/10.1186/s12940-021-00815-x

Freitas, J. S., Girotto, L., Goulart, B. V., Alho, L. de O. G., Gebara, R. C., Montagner, C. C., Schiesari, L., & Espíndola, E. L. G. (2019). Effects of 2,4-D-based herbicide (DMA® 806) on sensitivity, respiration rates, energy reserves and behavior of tadpoles. *Ecotoxicology and Environmental Safety*, *182*, 109446. https://doi.org/10.1016/j.ecoenv.2019.109446

Freitas-Silva, L. de, Araújo, H. H., Meireles, C. S., & Silva, L. C. da. (2021). Plant exposure to glyphosate-based herbicides and how this might alter plant physiological and structural processes. *Botany*, 1–8. https://doi.org/10.1139/cjb-2021-0033

Freydier, L., & Lundgren, J. G. (2016). Unintended effects of the herbicides 2,4-D and dicamba on lady beetles. *Ecotoxicology*, *25*(6), 1270–1277. https://doi.org/10.1007/s10646-016-1680-4

Fried, G., Petit, S., Dessaint, F., & Reboud, X. (2009). Arable weed decline in Northern France: Crop edges as refugia for weed conservation? *Biological Conservation*, *142*(1), 238–243. http://doi.org/10.1016/j.biocon.2008.09.029

Friends of the Earth Europe (2013a). Problems with glyphosate overuse and alternatives for farmers. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwi1qMT0pJT5AhVGdcAKHaRyDZ8QFnoECAcQAQ&url=https%3A%2F%2Fwww.foeeurope.org%2Fsites%2Fdefault%2Ffiles%2Fpress_releases%2Ffoee_6_problems_with_glyphosate_overuse.pdf&usg=AOvVaw2VkUOcp8vAStrDgLJxAc6o

Friends of the Earth Europe (2013b). Human contamination by glyphosate. http://www.foeeurope.org/sites/default/files/publications/foee_4_human_contamination_glyphosate.pdf

Fries, M., Cabello, A. L., & Sánchez, S. (2019). Monsanto's Legal Strategy in Argentina from a Human Rights Perspective. *Business and Human Rights Journal*, *4*(2), 357–363. https://doi.org/10.1017/bhj.2019.11

FT(2009) Argentina pressed to ban crop chemical. *Financial Times*. 29th May 2009.

Fuchs, B., Saikkonen, K., & Helander, M. (2021). Glyphosate-Modulated Biosynthesis Driving Plant Defense and Species Interactions. Trends in Plant Science, 26(4), 312–323. https://doi.org/10.1016/j.tplants.2020.11.004

Fuchs, B., Laihonen, M., Muola, A., Saikkonen, K., Dobrev, P. I., Vankova, R., & Helander, M. (2022). A Glyphosate-Based Herbicide in Soil Differentially Affects Hormonal Homeostasis and Performance of Non-target Crop Plants. Frontiers in Plant Science, 12. https://www.frontiersin.org/article/10.3389/fpls.2021.787958

Fuglie, K. O., Heisey, P. W., King, J. L., Pray, C. E. (2011). Research Investments and Market Structure in the Food Processing, Agricultural Input , and Biofuel Insustries Worldwide. p13. USDA

Fuller, R. J., Gregory, R. D., Gibbons, D. w., Marchant, J. H., Wilson, J. D., Baillie, S. R., & Carter, N. (1995). Population Declines and Range Contractions among Lowland Farmland Birds in Britain. *Conservation Biology*, *9*(6), 1425–1441. http://doi.org/10.1046/j.1523-1739.1995.09061425.x

Funke, T., Han, H., Healy-Fried, M. L., Fischer, M., & Schonbrunn, E. (2006). Molecular basis for the herbicide resistance of Roundup Ready crops. *Proceedings of the National Academy of Sciences*, *103*(35), 13010–13015. http://doi.org/10.1073/pnas.0603638103

Furst, I. (1999). Swiss Soiled Seed Prompts Tolerance Question. Nature Biotechnology. 17, 629.

FWW & OFARM (2014). Organic Farmers Pay the Price for GMO Contamination. Issue Brief. http://www.foodandwaterwatch.org/sites/default/files/GMO%20Contamination%20Farmers%20IB%20March%202014_0.pdf

Gaaied, S., Oliveira, M., Domingues, I., & Banni, M. (2020). 2,4-Dichlorophenoxyacetic acid herbicide effects on zebrafish larvae: Development, neurotransmission and behavior as sensitive endpoints. *Environmental Science and Pollution Research*, *27*(4), 3686–3696. https://doi.org/10.1007/s11356-019-04488-5

Gabor, C. R., Perkins, H. R., Heitmann, A. T., Forsburg, Z. R., & Aspbury, A. S. (2019). Roundup™ With Corticosterone Functions as an Infodisruptor to Antipredator Response in Tadpoles. *Frontiers in Ecology and Evolution*, *7*. https://www.frontiersin.org/articles/10.3389/fevo.2019.00114

Gabriel, A. & Menrad, K. (2015). Cost of Coexistence of GM and Non-GM Products in the Food Supply Chains of Rapeseed Oil and Maize Starch in Germany. *Agribusiness, 31*(4), 472-490. DOI: 10.1002/agr.21415

Gaines, T. A., Zhang, W., Wang, D., Bukun, B., Chisholm, S. T., Shaner, D. L., Nissen, S. J., Patzoldt, W. L., Tranel. P. J., Culpepper, A. S., Grey, T. L., Webster, T. M., Vencill, W. K., Sammons, R. D., Jiang, J., Preston, C., Leach, J. E., Westra, P. (2010). Gene amplification confers glyphosate resistance in Amaranthus palmeri. *Proceedings of the National Academy of Sciences*, *107*(3), 1029–1034. http://doi.org/10.1073/pnas.0906649107

Gaines, T.A., Barker, A.L., Patterson, E.L., Westra, P., Westra, E.P., Wilson, R.G., Jha, P., Kumar, V., Kniss, A.R. (2016). EPSPS Gene Copy Number and Whole-Plant Glyphosate Resistance Level in *Kochia scoparia*. *PLOS ONE* **11**, e0168295. doi:10.1371/journal.pone.0168295

Gaines, T. A., Patterson, E. L., & Neve, P. (2019). Molecular mechanisms of adaptive evolution revealed by global selection for glyphosate resistance. *New Phytologist*, *223*(4), 1770–1775. https://doi.org/10.1111/nph.15858
Gaitán-Cremaschi, D., Kamali, F. P., van Evert, F. K., Meuwissen, M. P. M., & Oude Lansink, A. G. J. M. (2015). Benchmarking the sustainability performance of the Brazilian non-GM and GM soybean meal chains: An indicator-based approach. *Food Policy*, *55*, 22–32. http://doi.org/10.1016/j.foodpol.2015.05.006
Galimov, S. N., & Valeeva, G. R. (1999). [Effect of 2,4-D ecotoxicants on spermatogenesis and fertility of albino rats]. *Aviakosmicheskaia I Ekologicheskaia Meditsina = Aerospace and Environmental Medicine*, *33*(1), 32–34.
Gallegos, C. E., Baier, C. J., Bartos, M., Bras, C., Domínguez, S., Mónaco, N., Gumilar, F., Giménez, M. S., & Minetti, A. (2018). Perinatal Glyphosate-Based Herbicide Exposure in Rats Alters Brain Antioxidant Status, Glutamate and Acetylcholine Metabolism and Affects Recognition Memory. *Neurotoxicity Research*, *34*(3), 363–374. https://doi.org/10.1007/s12640-018-9894-2
Ganie, Z. A., & Jhala, A. J. (2017). Modeling pollen-mediated gene flow from glyphosate-resistant to -susceptible giant ragweed (Ambrosia trifida L.) under field conditions. *Scientific Reports*, *7*(1), 17067. https://doi.org/10.1038/s41598-017-16737-z
Gao, X., Hu, F., Zhang, S., Luo, J., Zhu, X., Wang, L., Zhang, K., Li, D., Ji, J., Niu, L., Wu, C., & Cui, J. (2021). Glyphosate exposure disturbs the bacterial endosymbiont community and reduces body weight of the predatory ladybird beetle Harmonia axyridis (Coleoptera: Coccinellidae). *The Science of the Total Environment*, *790*, 147847. https://doi.org/10.1016/j.scitotenv.2021.147847
García, M. J., Palma-Bautista, C., Rojano-Delgado, A. M., Bracamonte, E., Portugal, J., Alcántara-de la Cruz, R., & De Prado, R. (2019). The Triple Amino Acid Substitution TAP-IVS in the EPSPS Gene Confers High Glyphosate Resistance to the Superweed Amaranthus hybridus. *International Journal of Molecular Sciences*, *20*(10), E2396. https://doi.org/10.3390/ijms20102396
García, M. J., Palma-Bautista, C., Vazquez-Garcia, J. G., Rojano-Delgado, A. M., Osuna, M. D., Torra, J., & De Prado, R. (2020). Multiple mutations in the EPSPS and ALS genes of Amaranthus hybridus underlie resistance to glyphosate and ALS inhibitors. *Scientific Reports*, *10*(1), 17681. https://doi.org/10.1038/s41598-020-74430-0
García-Espiñeira, M., Tejeda-Benitez, L., & Olivero-Verbel, J. (2018). Toxicity of atrazine- and glyphosate-based formulations on Caenorhabditis elegans. *Ecotoxicology and Environmental Safety*, *156*, 216–222. https://doi.org/10.1016/j.ecoenv.2018.02.075
García-Pérez, J. A., Alarcón, E., Hernández, Y., & Hernández, C. (2016). Impact of litter contaminated with glyphosate-based herbicide on the performance of Pontoscolex corethrurus, soil phosphatase activities and soil pH. *Applied Soil Ecology*, *104*, 31–41. https://doi.org/10.1016/j.apsoil.2016.03.007
Garrett, R. D., Rueda, X., & Lambin, E. F. (2013). Globalization's unexpected impact on soybean production in South America: linkages between preferences for non-genetically modified crops, eco-certifications, and land use. *Environmental Research Letters*, 8(4), 44055. http://doi.org/10.1088/1748-9326/8/4/044055
Garrett, R. D., & Rausch, L. L. (2016). Green for gold: social and ecological tradeoffs influencing the sustainability of the Brazilian soy industry. The Journal of Peasant Studies, 43(2), 461–493. http://doi.org/10.1080/03066150.2015.1010077
Garry, V. F., Harkins, M. E., Erickson, L. L., Long-Simpson, L. K., Holland, S. E., & Burroughs, B. L. (2002). Birth defects, season of conception, and sex of children born to pesticide applicators living in the Red River Valley of Minnesota, USA. Environmental Health Perspectives, 110(Suppl 3), 441–449.
Gasnier, C., Dumont, C., Benachour, N., Clair, E., Chagnon, M.-C., & Séralini, G.-E. (2009). Glyphosate-based herbicides are toxic and endocrine disruptors in human cell lines. *Toxicology*, *262*(3), 184–191. http://doi.org/10.1016/j.tox.2009.06.006
Gasparro, A. (2016). USA; Campbell Soup Backs GMO Labeling Rule. The Wall Street Journal. http://www.wsj.com/articles/campbell-soup-backs-gmo-labeling-rule-1452283288
Gattás, F., De Stefano, L. G., Vinocur, A., Bordet, F., Espinosa, M. S., Pizarro, H., & Cataldo, D. (2018). Impact of interaction between Limnoperna fortunei and Roundup Max® on freshwater phytoplankton: An in situ approach in Salto Grande reservoir (Argentina). *Chemosphere*, *209*, 748–757. https://doi.org/10.1016/j.chemosphere.2018.06.129
Gaupp-Berghausen, M., Hofer, M., Rewald, B., & Zaller, J. G. (2015). Glyphosate-based herbicides reduce the activity and reproduction of earthworms and lead to increased soil nutrient concentrations. *Scientific Reports*, *5*, 12886. http://doi.org/10.1038/srep12886
Gazziero, D. L. P. (2015). Mixtures of pesticides in tank, in Brazilian farms. *Planta Daninha*, *33*(1), 83–92. https://doi.org/10.1590/S0100-83582015000100010
Geddes, C. M., Pittman, M. M., Gulden, R. H., Jones, T., Leeson, J. Y., Sharpe, S. M., Shirriff, S. W., & Beckie, H. J. (2021). Rapid increase in glyphosate resistance and confirmation of dicamba-resistant kochia (Bassia scoparia) in Manitoba. *Canadian Journal of Plant Science*, 1–6. https://doi.org/10.1139/cjps-2021-0169
Gelinsky, E. (2018). *Endbericht_semnar_Gelinsky_November_2018-1*. https://www.bafu.admin.ch/dam/bafu/de/dokumente/biotechnologie/externe-studien-

berichte/Endbericht_semnar_Gelinsky_November_2018.pdf.download.pdf/Endbericht_semnar_Gelinsky_November_2018.pdf [accessed: 1/28/2020]
Gelski, J. (2015). Non-GMO product use rising across all age groups. Food Business News. http://www.foodbusinessnews.net/articles/news_home/Consumer_Trends/2015/07/NonGMO_product_use_rising_acro.aspx?ID={758FD5B6-486B-4F0A-9C56-20188F539F43}&cck=1
George, J., Prasad, S., Mahmood, Z., & Shukla, Y. (2010). Studies on glyphosate-induced carcinogenicity in mouse skin: a proteomic approach. *Journal of Proteomics*, *73*(5), 951–964. http://doi.org/10.1016/j.jprot.2009.12.008
Gandhi, K., Khan, S., Patrikar, M., Markad, A., Kumar, N., Choudhari, A., Sagar, P., & Indurkar, S. (2021). Exposure risk and environmental impacts of glyphosate: Highlights on the toxicity of herbicide co-formulants. *Environmental Challenges*, *4*, 100149. https://doi.org/10.1016/j.envc.2021.100149
Giaquinto, P.C., de Sá, M.B., Sugihara, V.S., Gonçalves, B.B., Delício, H.C., Barki, A., 2017. Effects of Glyphosate-Based Herbicide Sub-Lethal Concentrations on Fish Feeding Behavior. *Bull Environ Contam Toxicol* **98**, 460–464. doi:10.1007/s00128-017-2037-2
Gibbons, D. W., Bohan, D. A., Rothery, P., Stuart, R. C., Haughton, A. J., Scott, R. J., Wilson, J. D., Perry, J. N., Clark, S. J., Dawson, R. J. G., Firbank, L. G. (2006). Weed seed resources for birds in fields with contrasting conventional and genetically modified herbicide-tolerant crops. *Proceedings of the Royal Society B: Biological Sciences*, *273*(1596), 1921–1928. http://doi.org/10.1098/rspb.2006.3522
Gill, J. P. K., Sethi, N., Mohan, A., Datta, S., & Girdhar, M. (2018). Glyphosate toxicity for animals. *Environmental Chemistry Letters*, *16*(2), 401–426. https://doi.org/10.1007/s10311-017-0689-0
Gillam, C. (2014). USDA report says pesticide residues in food nothing to fear. Reuters. http://www.reuters.com/article/2014/12/19/usda-pesticides-report-idUSL1N0U325I20141219
Gillam, C. (2015a). USDA approves Monsanto's new GMO soybeans, cotton. Reuters: http://www.reuters.com/article/2015/01/15/monsanto-xtend-idUSL1N0UU2A120150115
Gillam, C. (2015b). Monsanto to invest more than $1 bln in dicamba herbicide production. Reuters. http://www.reuters.com/article/2015/06/24/monsanto-dicamba-idUSL1N0ZA1XN20150624
Gillam, C. (2015c). U.S. regulators may recommend testing food for glyphsoate residues. Reuters. http://mobile.reuters.com/article/idUSKBN0N82K020150417?irpc=932
Gillam, C. (2015d). U.S. workers sue Monsanto claiming herbicide caused cancer. Reuters. http://mobile.reuters.com/article/idUSL1N11Z20Y20150929?rpc=401&
Gillam, C. (2015e). Agribusiness nervous as WHO cancer unit analyses popular pesticide. Reuters. http://mobile.reuters.com/article/idUSL1N0YK1KK20150529?irpc=932
Gillam, C. (2016). FDA to Start Testing for Glyphosate in Food. Civil Eats. http://civileats.com/2016/02/17/fda-to-start-testing-for-glyphosate-in-food/
Gillam C (2017a) Questions about EPA-Monsanto collusion raised in cancer lawsuits. The Huffington Post. 13th February 2017. http://www.huffingtonpost.com/carey-gillam/questions-about-epa-monsa_b_14727648.html
Gillam C (2017b) Judge Threatens to Sanction Monsanto for Secrecy in Roundup Cancer Litigation. Huffington Post. 10th March 2017. http://www.huffingtonpost.com/entry/judge-threatens-to-sanction-monsanto-for-secrecy-in_us_58c2de66e4b0c3276fb78433?
Gillam C (2017c) Monsanto Weed Killer Deserves Deeper Scrutiny As Scientific Manipulation Revealed.17th March 2017. http://www.huffingtonpost.com/entry/58cc5541e4b0e0d348b34348
Gillam, C. (2020a, March 30). Revealed: Monsanto predicted crop system would damage US farms. *The Guardian*. https://www.theguardian.com/us-news/2020/mar/30/monsanto-crop-system-damage-us-farms-documents
Gillam, C. (2020b, February 26). *Dicamba litigation against Bayer, BASF poised to explode, lawyers say*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tacker/dicamba-litigation-against-bayer-basf-poised-to-explode-lawyers-say/
Gillam, C. (2020c, June 24). *Bayer settles U.S. Roundup, dicamba and PCB litigation for more than $10 billion*. U.S. Right to Know. https://usrtk.org/uncategorized/bayer-settles-u-s-roundup-dicamba-and-pcb-litigation-for-more-than-10-billion/
Gillam, C. (2020d, July 20). *Appeals court upholds groundskeeper's Roundup cancer trial win over Monsanto*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tracker/appeals-court-upholds-groundskeepers-roundup-cancer-trial-win-over-monsanto/
Gillam, C. (2020e, July 7). *Court frowns on Bayer's proposed Roundup class-action settlement*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tracker/court-frowns-on-bayers-proposed-roundup-class-action-settlement/
Gillam, C. (2020f, July 8). *Bayer backs away from plan to contain future Roundup cancer claims*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tracker/bayer-backs-away-from-plan-to-contain-future-roundup-cancer-claims/

Gillam, C. (2021a, May 14). *Another loss for Bayer over Roundup cancer claims as appeals court shoots down preemption argument*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tracker/another-loss-for-bayer-over-roundup-cancer-claims-as-appellate-court-shoots-down-preemption-argument/

Gillam, C. (2021b, February 26). *Bayer's plan for settling future Roundup cancer claims faces broad opposition*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tracker/bayers-plan-for-settling-litigation-faces-opposition/ [accessed: 30 December 2021]

Gillam, C. (2021c, August 10). *Court upholds Roundup trial loss*. Environmental Health News. https://www.ehn.org/roundup-rejected-2654606549.html [accessed: 31 December 2021]

Gillam, C. (2021d, July 20). *Bayer gets lift in pre-trial ruling ahead of Roundup cancer trial*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tracker/bayer-gets-lift-in-pre-trial-ruling-ahead-of-roundup-cancer-trial/ [accessed: 31 December 2021]

Gillam, C. (2021e, August 16). *Bayer seeks U.S. Supreme Court review of Roundup trial loss*. U.S. Right to Know. https://usrtk.org/monsanto-roundup-trial-tracker/bayer-seeks-u-s-supreme-court-review-of-roundup-trial-loss/

Gillam, C. (2022, July 9). 'Disturbing': Weedkiller ingredient tied to cancer found in 80% of US urine samples. The Guardian. https://www.theguardian.com/us-news/2022/jul/09/weedkiller-glyphosate-cdc-study-urine-samples

Gillezeau, C., van Gerwen, M., Shaffer, R. M., Rana, I., Zhang, L., Sheppard, L., & Taioli, E. (2019). The evidence of human exposure to glyphosate: A review. *Environmental Health*, *18*(1), 2. https://doi.org/10.1186/s12940-018-0435-5

Gillezeau, C., Lieberman-Cribbin, W., & Taioli, E. (2020). Update on human exposure to glyphosate, with a complete review of exposure in children. *Environmental Health*, *19*(1), 115. https://doi.org/10.1186/s12940-020-00673-z

Glyphosate Market Outlook 2031. (n.d.). Transparency Market Research. Retrieved 23 May 2022, from https://www.transparencymarketresearch.com/glyphosate-market.html

GMWatch (2015). Danish authority declares glyphosate a carcinogen. http://www.gmwatch.org/news/latest-news/16206-danish-authority-declares-glyphosate-a-carcinogen

GM Watch (2017a) Glyphosate: Discord at the US Environmental Protection Agency. 15th March 2017. http://gmwatch.org/news/latest-news/17505

GM Watch (2017b) ECHA may decide on glyphosate link with cancer this week. 6th March 2017. http://gmwatch.org/news/latest-news/17493

Goldfarb, L., & van der Haar, G. (2016). The moving frontiers of genetically modified soy production: shifts in land control in the Argentinian Chaco. *The Journal of Peasant Studies*, 43(2), 562–582. http://doi.org/10.1080/03066150.2015.1041107

Goldner, W. S., Sandler, D. P., Yu, F., Shostrom, V., Hoppin, J. A., Kamel, F., & LeVan, T. D. (2013). Hypothyroidism and Pesiticide use Among Male Private Pesticide Applications in the Agricultural Health Study. *Journal of Occupational and Environmental Medicine / American College of Occupational and Environmental Medicine*, *55*(10), 1171–1178. https://doi.org/10.1097/JOM.0b013e31829b290b

Golt, A. R., & Wood, L. J. (2021). Glyphosate-Based Herbicides Alter the Reproductive Morphology of *Rosa acicularis* (Prickly Rose). *Frontiers in Plant Science*, *12*. https://www.frontiersin.org/article/10.3389/fpls.2021.698202

Gómez-Gallego, C., Rainio, M. J., Collado, M. C., Mantziari, A., Salminen, S., Saikkonen, K., & Helander, M. (2020). Glyphosate-based herbicide affects the composition of microbes associated with Colorado potato beetle (Leptinotarsa decemlineata). *FEMS Microbiology Letters*, *367*(6). https://doi.org/10.1093/femsle/fnaa050

Goñalons, C. M., & Farina, W. M. (2018). Impaired associative learning after chronic exposure to pesticides in young adult honey bees. *Journal of Experimental Biology*, *221*(7). https://doi.org/10.1242/jeb.176644

Gonçalves, T. S., Soares, M. A., Santos, C. A., Santos, D. A., Santos, J. B., Barroso, G. A., Gonçalves, T. S., Soares, M. A., Santos, C. A., Santos, D. A., Santos, J. B., & Barroso, G. A. (2016). Does the Ingestion of Isoxaflutole Herbicide Affect the Midgut and Salivary Glands of Pentatomidae Predators? *Planta Daninha*, *34*(1), 125–132. https://doi.org/10.1590/S0100-83582016340100013

Gonçalves, B. B., Nascimento, N. F., Santos, M. P., Bertolini, R. M., Yasui, G. S., & Giaquinto, P. C. (2018). Low concentrations of glyphosate-based herbicide cause complete loss of sperm motility of yellowtail tetra fish Astyanax lacustris. *Journal of Fish Biology*, *92*(4), 1218–1224. https://doi.org/10.1111/jfb.13571

Gonçalves, B. B., Giaquinto, P. C., Silva, D. dos S., Neto, C. de M. e S., Lima, A. A. de, Darosci, A. A. B., Portinho, J. L., Carvalho, W. F., & Rocha, T. L. (2019). Ecotoxicology of Glyphosate-Based Herbicides on Aquatic Environment. In *Biochemical Toxicology—Heavy Metals and Nanomaterials*. IntechOpen. https://doi.org/10.5772/intechopen.85157

González, N. V., Soloneski, S., & Larramendy, M. L. (2006). Genotoxicity analysis of the phenoxy herbicide dicamba in mammalian cells in vitro. *Toxicology in Vitro*, *20*(8), 1481–1487. https://doi.org/10.1016/j.tiv.2006.05.001

González, N. V., Soloneski, S., & Larramendy, M. L. (2007). The chlorophenoxy herbicide dicamba and its commercial formulation banvel® induce genotoxicity and cytotoxicity in Chinese hamster ovary (CHO) cells. *Mutation*

Research/Genetic Toxicology and Environmental Mutagenesis, *634*(1–2), 60–68. http://doi.org/10.1016/j.mrgentox.2007.06.001
González, N. V., Soloneski, S., & Larramendy, M. L. (2009). Dicamba-induced genotoxicity in Chinese hamster ovary (CHO) cells is prevented by vitamin E. *Journal of Hazardous Materials*, *163*(1), 337–343. https://doi.org/10.1016/j.jhazmat.2008.06.097
González, N. V., Nikoloff, N., Soloneski, S., & Larramendy, M. L. (2011). A combination of the cytokinesis-block micronucleus cytome assay and centromeric identification for evaluation of the genotoxicity of dicamba. *Toxicology Letters*, *207*(3), 204–212. https://doi.org/10.1016/j.toxlet.2011.09.013
Gonzalez-de-Santos, P., Ribeiro, A., Fernandez-Quintanilla, C., Lopez-Granados, F., Brandstoetter, M., Tomic, S., Pedrazzi, S., Peruzzi, A., Pajares, G., Kaplanis, G., Perez-Ruiz, M., Valero, C., del Cerro, J., Vieri, M., Rabatel, G., & Debilde, B. (2017). Fleets of robots for environmentally-safe pest control in agriculture. *Precision Agriculture*, *18*(4), 574–614. https://doi.org/10.1007/s11119-016-9476-3
González-Ortega, E., Piñeyro-Nelson, A., Gómez-Hernández, E., Monterrubio-Vázquez, E., Arleo, M., Dávila-Velderrain, J., Martínez-Debat, C., & Álvarez-Buylla, E. R. (2017). Pervasive presence of transgenes and glyphosate in maize-derived food in Mexico. *Agroecology and Sustainable Food Systems*, *41*(9–10), 1146–1161. https://doi.org/10.1080/21683565.2017.1372841
Goodman, M.M. (2002). New sources of germplasm: Lines, transgenes, and breeders. In Martinez, J.M., Rincon, F., Marinez, G., eds. (2002). Memoria Congresso Nacional de Fitogenetica. UAAAN, Saltillo, Coah., Mexico.
Goodman, J. E., Loftus, C. T., & Zu, K. (2015). 2,4-Dichlorophenoxyacetic acid and non-Hodgkin's lymphoma, gastric cancer, and prostate cancer: Meta-analyses of the published literature. *Annals of Epidemiology*, *25*(8), 626-636.e4. https://doi.org/10.1016/j.annepidem.2015.04.002
Goodman, J. E., Loftus, C. T., & Zu, K. (2017). 2,4-Dichlorophenoxyacetic acid and non-Hodgkin's lymphoma: Results from the Agricultural Health Study and an updated meta-analysis. *Annals of Epidemiology*, *27*(4), 290-292.e5. https://doi.org/10.1016/j.annepidem.2017.01.008
Gosavi, G., Ren, B., Li, X., Zhou, X., Spetz, C., & Zhou, H. (2022). A New Era in Herbicide-Tolerant Crops Development by Targeted Genome Editing. *ACS Agricultural Science & Technology*. https://doi.org/10.1021/acsagscitech.1c00254
Gould, F., Brown, Z. S., & Kuzma, J. (2018). Wicked evolution: Can we address the sociobiological dilemma of pesticide resistance? *Science*. https://www.science.org/doi/abs/10.1126/science.aar3780
Government of Canada. (2014, October 16). *Harper Government Invests to Improve the Competitiveness of Canadian Flaxseed* [News releases]. Gcnws. https://www.canada.ca/en/news/archive/2014/10/harper-government-invests-improve-competitiveness-canadian-flaxseed.html [6 February 2020]
Graffigna, S., Marrero, H. J., & Torretta, J. P. (2021). Glyphosate commercial formulation negatively affects the reproductive success of solitary wild bees in a Pampean agroecosystem. *Apidologie*, *52*(1), 272–281. https://doi.org/10.1007/s13592-020-00816-8
Graham, K. (2015). No GMO crop trialsin Philippines says Supreme Court. Digital Journal. http://www.digitaljournal.com/news/environment/historic-ruling-by-philippine-supreme-court-bans-gmo-crop-trials/article/452166
Graham, M. W., Thomas, R. Q., Lombardozzi, D. L., & O'Rourke, M. E. (2021). Modest capacity of no-till farming to offset emissions over 21st century. *Environmental Research Letters*, *16*(5), 054055. https://doi.org/10.1088/1748-9326/abe6c6
Grand View Research. (2019, July). Non-GMO Food Market Size Worth $2.76 Billion By 2025 | CAGR 16.5%. https://www.grandviewresearch.com/press-release/global-non-gmo-food-market
Grant, R. (2014). Iowa lawsuits accuse Syngenta over GMO seeds. The Des Moines Register. http://www.desmoinesregister.com/story/money/agriculture/2014/12/30/lawsuits-filed-sygenta-iowa/21051903/
Grau, D., Grau, N., Gascuel, Q., Paroissin, C., Stratonovitch, C., Lairon, D., Devault, D. A., & Di Cristofaro, J. (2022). Quantifiable urine glyphosate levels detected in 99% of the French population, with higher values in men, in younger people, and in farmers. *Environmental Science and Pollution Research*, *29*(22), 32882–32893. https://doi.org/10.1007/s11356-021-18110-0
Grazina, L., Plácido, A., Costa, J., Fernandes, T. J. R., Oliveira, M. B. P. P., & Mafra, I. (2017). Tracing two Roundup Ready^{TM} soybean lines (GTS 40-3-2 and MON89788) in foods commercialised in Portugal. *Food Control*, *73*, 1053–1060. https://doi.org/10.1016/j.foodcont.2016.10.020
Green, J. M., & Siehl, D. L. (2021). History and Outlook for Glyphosate-Resistant Crops. In J. B. Knaak (Ed.), *Reviews of Environmental Contamination and Toxicology Volume 255: Glyphosate* (pp. 67–91). Springer International Publishing. https://doi.org/10.1007/398_2020_54
Greene, S. L., Kesoju, S. R., Martin, R. C., & Kramer, M. (2015). Occurrence of Transgenic Feral Alfalfa (Medicago sativa subsp. sativa L.) in Alfalfa Seed Production Areas in the United States. *PloS One*, *10*(12), e0143296. http://doi.org/10.1371/journal.pone.0143296

Greenlee, A. R., Ellis, T. M., & Berg, R. L. (2004). Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos. *Environmental Health Perspectives*, *112*(6), 703. https://doi.org/10.1289/ehp.6774

Greenpeace International (2006). The Failure of GE Papaya in Hawaii. http://www.greenpeace.org/international/Global/international/planet-2/report/2006/5/FailureGEPapayainHawaii.pdf

Greenpeace (2013). Commission set to recommend approval of controversial new GM maize. http://www.greenpeace.org/eu-unit/en/News/2013/Commission-set-to-recommend-approval-of-controversial-new-GM-maize/

Greenpeace (2017a) ECHA response heightens rather than alleviates conflict of interest concerns. 9th March 2017. http://www.greenpeace.org/eu-unit/en/Publications/2017/ECHA-response-heightens-concerns/

Greenpeace (2017b) EU chemicals agency sweeps glyphosate cancer evidence under the carpet. 15th March 2017. http://www.greenpeace.org/eu-unit/en/News/2017/EU-chemicals-agency-sweeps-glyphosate-cancer-evidence-under-the-carpet/

Gregory, R. D., G. Noble, D., & Custance, J. (2004). The state of play of farmland birds: population trends and conservation status of lowland farmland birds in the United Kingdom. *Ibis*, *146*, 1–13. http://doi.org/10.1111/j.1474-919X.2004.00358.x

Gressel, J. (2002). *Molecular Biology of Weed Control*. CRC Press.

Gressel, J., & Valverde, B. E. (2009). A strategy to provide long-term control of weedy rice while mitigating herbicide resistance transgene flow, and its potential use for other crops with related weeds. *Pest Management Science*, *65*(7), 723–731. https://doi.org/10.1002/ps.1754

Gribbin, C. (2013). Europe demanding more Australian non-GM canola. ABC. http://www.abc.net.au/news/2013-05-21/euro-canola-demand/4702890

Griffiths, B. S., Ritz, K., Ebblewhite, N., & Dobson, G. (1998). Soil microbial community structure: Effects of substrate loading rates. *Soil Biology and Biochemistry*, *31*(1), 145–153. http://doi.org/10.1016/S0038-0717(98)00117-5

Grossmann, K., Kwiatkowski, J., & Tresch, S. (2001). Auxin herbicides induce H2O2 overproduction and tissue damage in cleavers (Galium aparine L.). *Journal of Experimental Botany*, *52*(362), 1811–1816. https://doi.org/10.1093/jexbot/52.362.1811

Grossman, E. (2015a). Study Links Widely Used Pesticides to Antibiotic Resistance. Civil Eats. http://civileats.com/2015/03/24/study-links-widely-used-pesticides-to-antibiotic-resistance/

Grossman, E. (2015b). Is There Herbicide in Breast Milk? Civil Eats. http://civileats.com/2015/07/30/is-there-glyphosate-in-breast-milk/

Grover, R., Maybank, J., Yoshida, K. (1972). Droplet and Vapor Drift from Butyl Ester and Dimethylamine Salt of 2,4-D. *Weed Science*, *20*(4), 320-324.

Grube, A., Donaldson, D., Kiely, T., Wu, L. (2011). Pesticide Industry Sales and Usage. US EPA. http://news.agropages.com/UserFiles/Report/Pdf/20120708204254971d.pdf

Grupo de los Cien & Make way for Monarchs (2014). Decline of the Monarch Butterfly Migration in Eastern North America. http://makewayformonarchs.org/i/archives/525

Guan, Z.-J., Zhang, P.-F., Wei, W., Mi, X.-C., Kang, D.-M., & Liu, B. (2015). Performance of hybrid progeny formed between genetically modified herbicide-tolerant soybean and its wild ancestor. *AoB Plants*, *7*, plv121. https://doi.org/10.1093/aobpla/plv121

Guardian (2015) Hi-tech agriculture is freeing the farmer from his fields. 20th October 2015. https://www.theguardian.com/environment/2015/oct/20/hi-tech-agriculture-is-freeing-farmer-from-his-fields

Guerrero Schimpf, M., Milesi, M. M., Ingaramo, P. I., Luque, E. H., & Varayoud, J. (2017). Neonatal exposure to a glyphosate based herbicide alters the development of the rat uterus. *Toxicology*, *376*, 2–14. https://doi.org/10.1016/j.tox.2016.06.004

Guha, N., Roos, A. D., Kogevinas, M., Loomis, D., & Rushton, L. (2016). O04-3 IARC working group meta-analysis of 2,4-d exposure and the risk of NHL. *Occupational and Environmental Medicine*, *73*(Suppl 1), A8–A8. https://doi.org/10.1136/oemed-2016-103951.20

Gunatilake, S., Seneff, S., & Orlando, L. (2019). Glyphosate's Synergistic Toxicity in Combination with Other Factors as a Cause of Chronic Kidney Disease of Unknown Origin. *International Journal of Environmental Research and Public Health*, *16*(15), 2734. https://doi.org/10.3390/ijerph16152734

Guo, B., Guo, Y., Hong, H., Jin, L., Zhang, L., Chang, R.-Z., Lu, W., Lin, M., & Qiu, L.-J. (2015). Co-expression of G2-EPSPS and glyphosate acetyltransferase GAT genes conferring high tolerance to glyphosate in soybean. *Frontiers in Plant Science*, *6*, 847. https://doi.org/10.3389/fpls.2015.00847

Gurian-Sherman, D. (2009). Failure to Yield - Evaluating the Performance of Genetically Engineered Crops. Cambridge, MA: Union of Concerned Scientiests.

Gurian-Sherman, D. (2013). Genetic Engineering and the Big Challenges for Agriculture – Lessons from the United States. Third World Network Biosafety Briefing.

Gutierrez, M.F., Battauz, Y., Caisso, B., 2017. Disruption of the hatching dynamics of zooplankton egg banks due to glyphosate application. *Chemosphere* **171**, 644–653. doi:10.1016/j.chemosphere.2016.12.110
Guyton, K. Z., Loomis, D., Grosse, Y., El Ghissassi, F., Benbrahim-Tallaa, L., Guha, N., Scoccianti, C., Mattock, H., Straif, K. (2015). Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. International Agency for Research on Cancer. https://www.iarc.who.int/featured-news/media-centre-iarc-news-glyphosate/
Hails, R. S. (2000). Genetically modified plants – the debate continues. *Trends in Ecology & Evolution*, *15*(1), 14–18. http://doi.org/10.1016/S0169-5347(99)01751-6
Haire, B. (2010). Pigweed threatens Georgia cotton industry. Southeast Farm Press. http://southeastfarmpress.com/pigweed-threatens-georgia-cotton-industry
Hakim D (2017) Monsanto Weed Killer Roundup Faces New Doubts on Safety in Unsealed Documents. New York Times. 14th March 2017. https://www.nytimes.com/2017/03/14/business/monsanto-roundup-safety-lawsuit.html?emc=edit_th_20170315&nl=todaysheadlines&nlid=69512715&_r=2
Hall, G. J., Hart, C. A., & Jones, C. A. (2000). Plants as sources of cations antagonistic to glyphosate activity. *Pest Management Science*, *56*(4), 351–358. http://doi.org/10.1002/(SICI)1526-4998(200004)56:4<351::AID-PS151>3.0.CO;2-A
Hals, T. (2021, May 27). Bayer to rethink Roundup in U.S. residential market after judge nixes $2 bln settlement. *Reuters*. https://www.reuters.com/business/healthcare-pharmaceuticals/us-judge-rejects-bayers-2-bln-deal-resolve-future-roundup-lawsuits-2021-05-26/
Hammond, B., Dudek, R., Lemen, J., Nemeth, M. (2004). Results of a 13 week safety assurance study with rats fed grain from glyphosate tolerant corn. *Food Chem Toxicol,* 42:1003-1014.
Han, S. M., Kim, D. Y., Uddin, M. R., Hwang, K. S., Lee, B., Kim, C.-G., & Park, K. W. (2014). Appearance / Instance of Genetically Modified Maize at Grain Receiving Harbors and Along Transportation Routes in Korea. *Weed&Turfgrass Science*, *3*(3), 221–224.
Han, X., & Garcia, P. (2016). GMO Contamination Price Effects in the U.S. Corn Market: StarLink and MIR162. In *2016 Annual Meeting, July 31-August 2, Boston, Massachusetts* (No. 236004; 2016 Annual Meeting, July 31-August 2, Boston, Massachusetts). Agricultural and Applied Economics Association. https://ideas.repec.org/p/ags/aaea16/236004.html
Han, Y.-J., & Kim, J.-I. (2019). Application of CRISPR/Cas9-mediated gene editing for the development of herbicide-resistant plants. *Plant Biotechnology Reports*, *13*(5), 447–457. https://doi.org/10.1007/s11816-019-00575-8
Hansen, L. R., & Roslev, P. (2016). Behavioral responses of juvenile Daphnia magna after exposure to glyphosate and glyphosate-copper complexes. *Aquatic Toxicology*, *179*, 36–43. https://doi.org/10.1016/j.aquatox.2016.08.010
Harada, Y., Tanaka, N., Ichikawa, M., Kamijo, Y., Sugiyama, E., Gonzalez, F. J., & Aoyama, T. (2016). PPARα-dependent cholesterol/testosterone disruption in Leydig cells mediates 2,4-dichlorophenoxyacetic acid-induced testicular toxicity in mice. *Archives of Toxicology*, *90*(12), 3061–3071. https://doi.org/10.1007/s00204-016-1669-z
Hardeman v. Monsanto (2020) United States Court of Appeals for The Ninth Circuit. Nos. 19-16636, 19-16708; D.C. Nos. 3:16-cv-00525-VC, 3:16-md-02741-VC. https://cdn.ca9.uscourts.gov/datastore/opinions/2021/05/14/19-16636.pdf
Harker, K. N., Mallory-Smith, C., Maxwell, B. D., Mortensen, D. A., & Smith, R. G. (2017). Another view. *Weed Science*, *65*(2), 203–205. https://doi.org/10.1017/wsc.2016.30
Harre, N. T., Nie, H., Robertson, R. R., Johnson, W. G., Weller, S. C., & Young, B. G. (2017). Distribution of Herbicide-Resistant Giant Ragweed (Ambrosia trifida) in Indiana and Characterization of Distinct Glyphosate-Resistant Biotypes. *Weed Science*, *65*(6), 699–709. https://doi.org/10.1017/wsc.2017.56
Harrigan, G. G., Ridley, W. P., Riordan, S. G., Nemeth, M. A., Sorbet, R., Trujillo, W. A., Breeze, M. L., Schneider, R. W. (2007). Chemical Composition of Glyphosate-Tolerant Soybean 40-3-2 Grown in Europe Remains Equivalent with That of Conventional Soybean (Glycine max L.). *Journal of Agricultural and Food Chemistry*, *55*(15), 6160–6168. http://doi.org/10.1021/jf0704920
Hart, M. M., Powell, J. R., Gulden, R. H., Levy-Booth, D. J., Dunfield, K. E., Pauls, K. P., … Trevors, J. T. (2009). Detection of transgenic *cp4 epsps* genes in the soil food web. *Agronomy for Sustainable Development*, 29(4), 497–501. http://doi.org/10.1051/agro/2009020
Hartzler B (2003) What, Me Worry? Iowa State Weed Science. 1st May 2003. http://www.weeds.iastate.edu/mgmt/2003/monad.shtml
Harzler B (2004) [Untitled] Iowa State Weed Science. 17th Decmber 2004. http://www.weeds.iastate.edu/mgmt/2004/twoforone.shtml
Hartzler, R. G. (2010). Reduction in common milkweed (Asclepias syriaca) occurrence in Iowa cropland from 1999 to 2009. *Crop Protection*, *29*(12), 1542–1544. http://doi.org/10.1016/j.cropro.2010.07.018
Hattab, S., Boughattas, I., Boussetta, H., Viarengo, A., Banni, M., & Sforzini, S. (2015). Transcriptional expression levels and biochemical markers of oxidative stress in the earthworm Eisenia andrei after exposure to 2,4-

dichlorophenoxyacetic acid (2,4-D). *Ecotoxicology and Environmental Safety*, *122*, 76–82. https://doi.org/10.1016/j.ecoenv.2015.07.014
Hawkes, T. R., Langford, M. P., Viner, R., Blain, R. E., Callaghan, F. M., Mackay, E. A., Hogg, B. V., Singh, S., & Dale, R. P. (2019). Characterization of 4-hydroxyphenylpyruvate dioxygenases, inhibition by herbicides and engineering for herbicide tolerance in crops. *Pesticide Biochemistry and Physiology*, *156*, 9–28. https://doi.org/10.1016/j.pestbp.2019.01.006
Hayhoe, S. J., Neill, C., Porder, S., Mchorney, R., Lefebvre, P., Coe, M. T., … Krusche, A. V. (2011). Conversion to soy on the Amazonian agricultural frontier increases streamflow without affecting stormflow dynamics. Global Change Biology, 17(5), 1821–1833. http://doi.org/10.1111/j.1365-2486.2011.02392.x
Health and Environmental Alliance (2017) ECHA's opinion on glyphosate greeted with concern. 15th March 2017. http://www.env-health.org/resources/press-releases/article/echa-s-opinion-on-glyphosate
Heap, I. M. (1997). The occurrence of herbicide-resistant weeds worldwide. *Pesticide Science*, *51*(3), 235–243. http://doi.org/10.1002/(SICI)1096-9063(199711)51:3<235::AID-PS649>3.0.CO;2-N
Heap, I. (2016). The International Survey of Herbicide Resistant Weeds. Online. Internet. Tuesday, September 6, 2016. Available www.weedscience.com
Heap, I. (2020). *List of Herbicide Resistant Weeds by Herbicide Mode of Action*. Internatonal Herbicide-Resistant Weed Database. http://www.weedscience.org/Pages/MOA.aspx?MOAID=3
Heap, I. (2021). The International Herbicide-Resistant Weed Database. Online. Internet. Friday, August 27, 2021 . Available www.weedscience.org
Heap, I. (2021a, December 10). *Weeds Resistant to Auxin Mimics HRAC Group 4 (Legacy O)*. http://www.weedscience.org/Pages/MOA.aspx?MOAID=24
Heap, I. (2021b, December 10). *Weeds Resistant to the Herbicide Dicamba*. http://www.weedscience.org/Summary/ResistbyActive.aspx
Heap, I. (2021c, December 10). *Weeds Resistant to the Herbicide 2,4-D*. http://www.weedscience.org/Summary/ResistbyActive.aspx
Heap, I. (2021d, December 10). *Weeds Resistant to Inhibiton of Acetolactate Synthase HRAC Group 2 (Legacy B)*. International Herbicide-Resistant Weed Database. http://www.weedscience.org/Pages/MOA.aspx?MOAID=3
Heap, I., & Duke, S. O. (2018). Overview of glyphosate-resistant weeds worldwide. *Pest Management Science*, *74*(5), 1040–1049. https://doi.org/10.1002/ps.4760
Hecht, M., Oehen, B., Schulze, J., Brodmann, P., & Bagutti, C. (2014). Detection of feral GT73 transgenic oilseed rape (Brassica napus) along railway lines on entry routes to oilseed factories in Switzerland. *Environmental Science and Pollution Research International*, *21*(2), 1455–1465. http://doi.org/10.1007/s11356-013-1881-9
Heinemann, J. A., Massaro, M., Coray, D. S., Agapito-Tenfen, S. Z., & Wen, J. D. (2014a). Sustainability and innovation in staple crop production in the US Midwest. *International Journal of Agricultural Sustainability*, *12*(1), 71–88. http://doi.org/10.1080/14735903.2013.806408
Heinemann, J. A., Massaro, M., Coray, D. S., Agapito-Tenfen, S. Z. (2014b). Reply to comment on sustainability and innovation in staple crop production in the US Midwest. *International Journal of Agricultural Sustainability*, *12*(4), 387-390. doi: 10.1080/14735903.2014.939843
Helander, M., Pauna, A., Saikkonen, K., & Saloniemi, I. (2019). Glyphosate residues in soil affect crop plant germination and growth. *Scientific Reports*, *9*(1), 19653. https://doi.org/10.1038/s41598-019-56195-3
Helmer, S. H., Kerbaol, A., Aras, P., Jumarie, C., & Boily, M. (2014). Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (Apis mellifera). *Environmental Science and Pollution Research International*. http://doi.org/10.1007/s11356-014-2879-7
Hendlin, Y. H., Arcuri, A., Lepenies, R., & Hüesker, F. (2020). Like Oil and Water: The Politics of (Not) Assessing Glyphosate Concentrations in Aquatic Ecosystems. *European Journal of Risk Regulation*, *11*(3), 539–564. https://doi.org/10.1017/err.2020.65
Heneghan, C. (2015). The non-GMO industry is growing fast. Where does it go from here? Food Dive. http://www.fooddive.com/news/the-non-gmo-industry-is-growing-fast-where-does-it-go-from-here/404409/
Herbert, L. T., Vázquez, D. E., Arenas, A., & Farina, W. M. (2014). Effects of field-realistic doses of glyphosate on honeybee appetitive behaviour. *The Journal of Experimental Biology*, *217*(19), 3457–3464. http://doi.org/10.1242/jeb.109520
Herek, J. S., Vargas, L., Rinas Trindade, S. A., Rutkoski, C. F., Macagnan, N., Hartmann, P. A., & Hartmann, M. T. (2021). Genotoxic effects of glyphosate on Physalaemus tadpoles. *Environmental Toxicology and Pharmacology*, *81*, 103516. https://doi.org/10.1016/j.etap.2020.103516
Herndon, E., 2017. Effects of Compost From Roundup Ready Corn Stover on the *Caenorhabditis Elegans*. Presented at the 2017 AAAS Annual Meeting (February 16-20, 2017), aaas. https://aaas.confex.com/aaas/2017/webprogram/Paper20134.html
Herrera-Valdés, R., Almaguer-López, M. A., Orantes-Navarro, C. M., López-Marín, L., Brizuela-Díaz, E. G., Bayarre-Vea, H., Silva-Ayçaguer, L. C., Orellana de Figueroa, P., Smith-González, M., Chávez-Muñoz, Y., &

Bacallao-Méndez, R. (2019). Epidemic of Chronic Kidney Disease of Nontraditional Etiology in El Salvador: Integrated Health Sector Action and South-South Cooperation. *MEDICC Review*, *21*(4), 46–52. https://doi.org/10.37757/MR2019.V21.N4.8

Hertel, R., Gibhardt, J., Martienssen, M., Kuhn, R., & Commichau, F. M. (2021). Molecular mechanisms underlying glyphosate resistance in bacteria. *Environmental Microbiology*, *23*(6), 2891–2905. https://doi.org/10.1111/1462-2920.15534

Herzine, A., Laugeray, A., Feat, J., Menuet, A., Quesniaux, V., Richard, O., Pichon, J., Montécot-Dubourg, C., Perche, O., & Mortaud, S. (2016). Perinatal Exposure to Glufosinate Ammonium Herbicide Impairs Neurogenesis and Neuroblast Migration through Cytoskeleton Destabilization. *Frontiers in Cellular Neuroscience*, *10*. https://doi.org/10.3389/fncel.2016.00191

Hettinger, J. (2020, April 3). *EPA sidesteps normal public process to approve BASF's cancer-linked pesticide*. Investigate Midwest. https://investigatemidwest.org/2020/04/03/epa-sidesteps-normal-public-process-to-approve-basfs-cancer-linked-pesticide/

Hettinger, J. (2020a, June 16). *'We've got it everywhere': Dicamba damaging trees across Midwest and South*. Investigate Midwest. https://investigatemidwest.org/2020/06/16/weve-got-it-everywhere-dicamba-damaging-trees-across-midwest-and-south/

Hettinger, J. (2020b, February 14). *Jury awards $265 million to Bader Farms in lawsuit against Bayer, BASF*. Investigate Midwest. https://investigatemidwest.org/2020/02/14/jury-deliberating-in-bader-farms-case-against-bayer-basf-over-dicamba/

Hettinger, J. (2020c, October 28). *EPA allows use of dicamba through 2025, with new restrictions*. Investigate Midwest. https://investigatemidwest.org/2020/10/27/epa-allows-use-of-dicamba-through-2025-with-new-restrictions/

Hettinger, J. (2020d, October 29). *EPA documents show dicamba damage worse than previously thought*. Investigate Midwest. https://investigatemidwest.org/2020/10/29/epa-documents-show-dicamba-damage-worse-than-previously-thought/

Hettinger, J. (2021, September 1). *EPA and Bayer had close contact in 2020 reinstatement of dicamba*. Investigate Midwest. https://investigatemidwest.org/2021/09/01/epa-and-bayer-had-close-contact-in-2020-reinstatement-of-dicamba/

Hewlett, K. L., Azeez, G. S. E. (2008). The Economic Impacts of GM Contamination Incidents on the Organic Sector. IFOAM

Hightower, M. (2015). Division of Ag expands research on non-GMO soybean varieties. High Plains Journal. http://www.hpj.com/crops/division-of-ag-expands-research-on-non-gmo-soybean-varieties/article_d7af3405-48b8-5a89-b409-439294a6eabc.html

Hilbeck, A., Meier, M., & Benzler, A. (2008). Identifying indicator species for post-release monitoring of genetically modified, herbicide resistant crops. *Euphytica*, *164*(3), 903–912. http://doi.org/10.1007/s10681-008-9666-9

Hilbeck, A., Meier, M., Römbke, J., Jänsch, S., Teichmann, H., & Tappeser, B. (2011). Environmental risk assessment of genetically modified plants - concepts and controversies. *Environmental Sciences Europe*, *23*(1), 13. http://doi.org/10.1186/2190-4715-23-13

Hilbeck, A., Lebrecht, T., Vogel, R., Heinemann, J. A., & Binimelis, R. (2013). Farmer's choice of seeds in four EU countries under different levels of GM crop adoption. *Environmental Sciences Europe*, *25*(1), 12. http://doi.org/10.1186/2190-4715-25-12

Hilbeck, A. & Meyer, H. (2013). Rat feeding studies with genetically modified maize - a comparative evaluation of applied methods and tisk assessment standards.

Hines, O. (2020, March 31). *BASF's Alite 27 herbicide receives EPA registration*. https://www.basf.com/us/en/media/news-releases/2020/03/basf-s-alite-27-herbicide-receives-epa-registration-.html

Hirose, Y., Kobayashi, M., Koyama, K., Kohda, Y., Tanaka, T., Honda, H., Hori, Y., Yoshida, K., & Kikuchi, M. (1999). A toxicokinetic analysis in a patient with acute glufosinate poisoning. *Human & Experimental Toxicology*, *18*(5), 305–308. https://doi.org/10.1191/096032799678840110

Hofmann, F., Otto, M., & Wosniok, W. (2014). Maize pollen deposition in relation to distance from the nearest pollen source under common cultivation - results of 10 years of monitoring (2001 to 2010). *Environmental Sciences Europe*, *26*(1), 24. http://doi.org/10.1186/s12302-014-0024-3

Holmes, K. (2002). Organic farmers in Saskatchewan sue over modified seed; Class action alleges crop damage from gene-altered plants. The Toronto Star. http://oapf.saskorganic.com/ts-11jan02.html

Hoppin, J. A., Umbach, D. M., London, S. J., Henneberger, P. K., Kullman, G. J., Alavanja, M. C. R., & Sandler, D. P. (2008). Pesticides and atopic and nonatopic asthma among farm women in the Agricultural Health Study. *American Journal of Respiratory and Critical Care Medicine*, 177(1), 11–18. http://doi.org/10.1164/rccm.200706-821OC

Hoppin, J. A., Umbach, D. M., Long, S., London, S. J., Henneberger, P. K., Blair, A., … Sandler, D. P. (2016). Pesticides Are Associated with Allergic and Non-Allergic Wheeze among Male Farmers. Environmental Health Perspectives. http://doi.org/10.1289/EHP315

Horn, S., Pieters, R., & Bøhn, T. (2020). May agricultural water sources containing mixtures of agrochemicals cause hormonal disturbances? *Science of The Total Environment*, *711*, 134862. https://doi.org/10.1016/j.scitotenv.2019.134862
Horticulture Week (2015) Ladybird Targeted spot sprayer offers reduced herbicide usage. 18th September 2015. http://www.hortweek.com/ladybird-targeted-spot-sprayer-offers-reduced-herbicide-usage/products-kit/article/1364028
Horticulture Week (2016) London council bans contractor use of glyphosate in parks. http://www.hortweek.com/london-council-bans-contractor-use-glyphosate-parks/parks-and-gardens/article/1398373
House of Commons Science and Technology Committee (2016) EU regulation of the life sciences. First Report of Session 2016–17. http://www.publications.parliament.uk/pa/cm201617/cmselect/cmsctech/158/158.pdf
Howard, P. H. (2009). Visualizing Consolidation in the Global Seed Industry: 1996–2008. *Sustainability*, *1*(4), 1266–1287. http://doi.org/10.3390/su1041266
Howe, C. M., Berrill, M., Pauli, B. D., Helbing, C. C., Werry, K., & Veldhoen, N. (2004). Toxicity of glyphosate-based pesticides to four North American frog species. *Environmental Toxicology and Chemistry*, *23*(8), 1928–1938. http://doi.org/10.1897/03-71
Hoyle, B. (1999). Canadian farmers seek compensation for "genetic pollution". *Nature Biotechnology*, 17 (8), 747-748
Hu, J., Lesseur, C., Yu, M., Manservisi, F., Panzacchi, S., Mandrioli, D., Belpoggi, F., Chen, J., & Petrick, L. (2020). Disruption of urine metabolome and its interaction with gut microbiome by low-dose exposure of glyphosate-based herbicide in a rodent model. *Preprint*. https://doi.org/10.21203/rs.3.rs-16601/v1
Hua, K., Jiang, Y., Tao, X., & Zhu, J.-K. (2020). Precision genome engineering in rice using prime editing system. *Plant Biotechnology Journal*, *18*(11), 2167–2169. https://doi.org/10.1111/pbi.13395
Hubbard, K. (2009). Out of Hand: Farmers Face the Consequences of a Consolidated Seed Industry. Farmer to Farmer Campaign on Genetic Engineering, National Family Farm Coalition
Hüdig, M., Laibach, N., & Hein, A.-C. (2022). Genome Editing in Crop Plant Research; Alignment of Expectations and Current Developments. *Plants*, *11*(2), 212. https://doi.org/10.3390/plants11020212
Hummel, A. W., Chauhan, R. D., Cermak, T., Mutka, A. M., Vijayaraghavan, A., Boyher, A., Starker, C. G., Bart, R., Voytas, D. F., & Taylor, N. J. (2018). Allele exchange at the EPSPS locus confers glyphosate tolerance in cassava. *Plant Biotechnology Journal*, *16*(7), 1275–1282. https://doi.org/10.1111/pbi.12868
Hungary Today (2015). Hungary's Farm Ministry to Promote GMO-Free Soya Production. http://hungarytoday.hu/news/hungarys-farm-ministry-promote-gmo-free-soya-production-92842
Hungria, M., I. Carvalho Mendes, A. Shigueyoshi Nakatani, F. Bueno dos Reis-Junior, J.Z. Morais, M.C. Neves de Oliveria, M. Ferreira Fernandes. 2014. Effects of the glyphosate-resistance gene and herbicides on soybean: Field trials monitoring biological nitrogen fixation and yield. *Field Crops Research* 158:43-54.
Hurley, L. (2022, June 21). U.S. Supreme Court rejects Bayer bid to nix Roundup weedkiller suits. *Reuters*. https://www.reuters.com/legal/government/us-supreme-court-rejects-bayer-bid-nix-roundup-weedkiller-suits-2022-06-21/
Hussain, A., Ding, X., Alariqi, M., Manghwar, H., Hui, F., Li, Y., Cheng, J., Wu, C., Cao, J., & Jin, S. (2021). Herbicide Resistance: Another Hot Agronomic Trait for Plant Genome Editing. *Plants*, *10*(4), 621. https://doi.org/10.3390/plants10040621
Hwang, J.-I., Norsworthy, J. K., Houston, M. M., Piveta, L. B., Priess, G. L., Zaccaro-Gruener, M. L., Barber, L. T., & Butts, T. R. (2022). Large-scale evaluation of physical drift and volatility of 2,4-D choline in cotton: A four-year field study. *Pest Management Science*. https://doi.org/10.1002/ps.6960
IARC (2015). Agents Classified by the IARC Monographs, Volumes 1–108. International Agency for Research on Cancer (IARC), World Health Organization (WHO). Last update: 7 April 2015. http://monographs.iarc.fr/ENG/Classification/ClassificationsAlphaOrder.pdf
IARC (2016). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. http://www.efsa.europa.eu/sites/default/files/Letter_from_Dr_Wild_to_Bernhard_Url_160212.pdf
IARC. (2018). *DDT, Lindane, and 2,4-D*. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Lyon. Retrieved January 12, 2022, from https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/DDT-Lindane-And-2-4-D-2016
Idrovo, A. J., & Rodríguez-Villamizar, L. A. (2018). Moving back in policy banning glyphosate use in Colombia. *The Lancet*, *392*(10154), 1194. https://doi.org/10.1016/S0140-6736(18)31883-X
IEA (2016) Defensivos: preços em alta e mercado em baixa pós-desvalorização cambia. http://www.iea.sp.gov.br/out/LerTexto.php?codTexto=14033
IFOAM (2002). Position on genetic engineering and genetically modified organisms. http://www.ifoam.org/sites/default/files/page/files/ifoam-ge-position.pdf. Accessed 3 December 2014.
Inamine, H., Ellner, S. P., Springer, J. P., & Agrawal, A. A. (2016). Linking the continental migratory cycle of the monarch butterfly to understand its population decline. *Oikos*, *125*(8), 1081–1091. https://doi.org/10.1111/oik.03196

INCA (2015). Posicionamento do Instituto Nacional de Câncer José Alencar Gomes da Silva Acerca Dos Agrotóxicos. Ministério da Saúde. http://www1.inca.gov.br/inca/Arquivos/comunicacao/posicionamento_do_inca_sobre_os_agrotoxicos_06_abr_15.pdf

Ingaramo, P. I., Varayoud, J., Milesi, M. M., Guerrero Schimpf, M., Alarcón, R., Muñoz-de-Toro, M., & Luque, E. H. (2017). Neonatal exposure to a glyphosate-based herbicide alters uterine decidualization in rats. Reproductive Toxicology, 73, 87–95. https://doi.org/10.1016/j.reprotox.2017.07.022

Ingaramo, P., Alarcón, R., Muñoz-de-Toro, M., & Luque, E. H. (2020). Are glyphosate and glyphosate-based herbicides endocrine disruptors that alter female fertility? Molecular and Cellular Endocrinology, 110934. https://doi.org/10.1016/j.mce.2020.110934

Ingaramo, P. I., Alarcón, R., Caglieris, M. L., Varayoud, J., Muñoz-de-Toro, M., & Luque, E. H. (2022). Altered uterine angiogenesis in rats treated with a glyphosate-based herbicide. Environmental Pollution, 296, 118729. https://doi.org/10.1016/j.envpol.2021.118729

Iori, S., Rovere, G. D., Ezzat, L., Smits, M., Ferraresso, S. S., Babbucci, M., Marin, M. G., Masiero, L., Fabrello, J., Garro, E., Carraro, L., Cardazzo, B., Patarnello, T., Matozzo, V., Bargelloni, L., & Milan, M. (2020). The effects of glyphosate and AMPA on the mediterranean mussel *Mytilus galloprovincialis* and its microbiota. *Environmental Research*, *182*, 108984. https://doi.org/10.1016/j.envres.2019.108984

ISAAA. (2013). *98140 | GM Approval Database- ISAAA.org*. https://www.isaaa.org/gmapprovaldatabase/event/default.asp?EventID=126 [Accessed: December 9 2019]

ISAAA (2014a): Gene: nptII. Events with Gene nptII. http://www.isaaa.org/gmapprovaldatabase/gene/default.asp?GeneID=18&Gene=nptII

ISAAA (2014b). Gene: bla. Events with gene bla. http://www.isaaa.org/gmapprovaldatabase/gene/default.asp?GeneID=34&Gene=bla

ISAAA (2015). Event Name: MON87708. Authorizations. https://www.isaaa.org/gmapprovaldatabase/event/default.asp?EventID=253

ISAAA. (2018, July 11). *LibertyLink® GT27™ Soybeans Commercialized in the U.S.* http://www.isaaa.org/kc/cropbiotechupdate/article/default.asp?ID=16592

ISAAA (2019a) ISAAA Brief 55-2019: Executive Summary | ISAAA.org. (2019). https://www.isaaa.org/resources/publications/briefs/55/executivesummary/default.asp

ISAAA. (2019b, April 22). *CV127 | GM Approval Database- ISAAA.org*. https://www.isaaa.org/gmapprovaldatabase/event/default.asp?EventID=158 [accessed: 10 December 2021]

ISAAA. (2020a). *MON87427 x MON89034 x TC1507 x MON87411 x 59122 x DAS40278 | GM Approval Database- ISAAA.org*. http://www.isaaa.org/gmapprovaldatabase/event/default.asp?EventID=521

ISAAA. (2020b). *FG72 x A5547-127 | GM Approval Database- ISAAA.org*. https://www.isaaa.org/gmapprovaldatabase/event/default.asp?EventID=412&Event={recEvents.EventName}

ISDE (2015). Appeal to the EU Parliament, to the EU Commission, to the DG Health and Food Safety, DG Environment, DG Agriculture and Rural Development, DG Internal Market. International Society of Doctors for the Environment. http://www.isde.org/Appeal_glyphosate_IARC.pdf

Islam, F., Wang, J., Farooq, M. A., Khan, M. S. S., Xu, L., Zhu, J., Zhao, M., Muños, S., Li, Q. X., & Zhou, W. (2018). Potential impact of the herbicide 2,4-dichlorophenoxyacetic acid on human and ecosystems. *Environment International*, *111*, 332–351. https://doi.org/10.1016/j.envint.2017.10.020

ISO (2012a). Soil quality – Effects of pollutants on earthworms – Part 1: Determination of acute toxicity to Eisenia fetida/Eisenia andrei. ISO 11268-1:2012

ISO (2012b). Soil quality – Effects of pollutants on earthworms – Part 2: Determination of effects on reproduction of Eisenida fetida/Eisenia andrei. ISO 11268-2:2012

Iturburu, F. G., Calderon, G., Amé, M. V., & Menone, M. L. (2019). Ecological Risk Assessment (ERA) of pesticides from freshwater ecosystems in the Pampas region of Argentina: Legacy and current use chemicals contribution. *Science of The Total Environment*, *691*, 476–482. https://doi.org/10.1016/j.scitotenv.2019.07.044

Iversen, M., Grønsberg, I. M., van den Berg, J., Fischer, K., Aheto, D. W., & Bøhn, T. (2014). Detection of Transgenes in Local Maize Varieties of Small-Scale Farmers in Eastern Cape, South Africa. *PLoS ONE*, *9*(12), e116147. http://doi.org/10.1371/journal.pone.0116147

Iwasaki, J. M., & Hogendoorn, K. (2021). Non-insecticide pesticide impacts on bees: A review of methods and reported outcomes. *Agriculture, Ecosystems & Environment*, *314*, 107423. https://doi.org/10.1016/j.agee.2021.107423

Jacobs, A., Kingwell, R. (2016). The Harrington Seed Destructor: Its role and value in farming systems facing the challenge of herbicide-resistant weeds. *Agricultural Systems* **142**, 33–40. doi:10.1016/j.agsy.2015.11.003

James, Clive. 2013. Global Status of Commercialized Biotech/GM Crops: 2013. ISAAA Brief No. 46. ISAAA: Ithaca, NY.

Janssens, L., & Stoks, R. (2017). Stronger effects of Roundup than its active ingredient glyphosate in damselfly larvae. *Aquatic Toxicology (Amsterdam, Netherlands)*, *193*, 210–216. https://doi.org/10.1016/j.aquatox.2017.10.028

Jaramillo, P. & Kraul V. (2013). Colombia to pay Ecuador $15 million to settle coca herbicide suit. http://articles.latimes.com/2013/sep/16/world/la-fg-wn-ecuador-colombia-coca-herbicide-lawsuit-20130916

Jarrell, Z. R., Ahammad, M. U., & Benson, A. P. (2020). Glyphosate-based herbicide formulations and reproductive toxicity in animals. *Veterinary and Animal Science*, *10*, 100126. https://doi.org/10.1016/j.vas.2020.100126

Jarrell, Z. R., Ahammad, M. U., & Benson, A. P. (2021). Reproductive toxicity of roundup®-treated feed on broiler breeder roosters and the amelioration of these deleterious effects with inclusion of humic acids in feed. *Veterinary and Animal Science*, *14*, 100215. https://doi.org/10.1016/j.vas.2021.100215

Jaworski, E. G. (1972). Mode of action of N-phosphonomethylglycine. Inhibition of aromatic amino acid biosynthesis. *Journal of Agricultural and Food Chemistry*, *20*(6), 1195–1198. http://doi.org/10.1021/jf60184a057

Jayasumana C, Gunatilake S, Senanayake P (2014). Glyphosate, Hard Water and Nephrotoxic Metals: Are They the Culprits Behind the Epidemic of Chronic Kidney Disease of Unknown Etiology in Sri Lanka? *International Journal of Environmental Research and Public Health*, 11(2), 2125–2147. http://doi.org/10.3390/ijerph110202125

Jayasumana C, Gunatilake S, Siribaddana S (2015) Simultaneous exposure to multiple heavy metals and glyphosate may contribute to Sri Lankan agricultural nephropathy. *BMC Nephrology*, 16, 103. http://doi.org/10.1186/s12882-015-0109-2

Jia, R., Hou, Y., Feng, W., Li, B., & Zhu, J. (2022). Alterations at biochemical, proteomic and transcriptomic levels in liver of tilapia (Oreochromis niloticus) under chronic exposure to environmentally relevant level of glyphosate. *Chemosphere*, *294*, 133818. https://doi.org/10.1016/j.chemosphere.2022.133818

Johal, G. S. & Rahe, J. E. (1984). Effect of Soilborne Plant-Pathogenic Fungi on the Herbicidal Action of Glyphosate on Bean Seedlings. *Phytopathology*, *74*(8), 950. http://doi.org/10.1094/Phyto-74-950

Johal, G. S., & Rahe, J. E. (1988). Glyphosate, hypersensitivity and phytoalexin accumulation in the incompatible bean anthracnose host-parasite interaction. *Physiological and Molecular Plant Pathology*, *32*(2), 267–281. http://doi.org/10.1016/S0885-5765(88)80022-5

Johal, G. S., & Huber, D. M. (2009). Glyphosate effects on diseases of plants. *European Journal of Agronomy*, *31*(3), 144–152. http://doi.org/10.1016/j.eja.2009.04.004

Johnson v. Monsanto, CGC-16-550128 (Superior Court of the State of California for the County of San Francisco August 10, 2018). http://www.baumhedlundlaw.com/pdf/monsanto-documents/johnson-trial/Johnson-vs-Monsanto-Verdict-Form.pdf

Johnson v. Monsanto, Case No. S264158 (CA Supreme Court, August 31, 2020). Retrieved September 2, 2020, from http://www.glyphosatelitigationfacts.com/main/wp-content/uploads/2020/09/Monsanto-Petition-For-Review-Filed-083120.pdf

Johnston I (2017) EU experts accused of conflict of interest over herbicide linked to cancer. The Independent. 7th March 2017. http://www.independent.co.uk/environment/glyphosate-roundup-weedkiller-cancer-bees-farming-greenpeace-echa-european-chemicals-agency-a7614736.html

Jones, D.K., Hammond, J.I., Relyea, R.A. (2011). Competitive stress can make the herbicide Roundup® more deadly to larval amphibians. *Environ. Toxicol. Chem.* **30**, 446–454. doi:10.1002/etc.384

Jones, G. T., Norsworthy, J. K., & Barber, T. (2019a). Off-Target Movement of Diglycolamine Dicamba to Non-dicamba Soybean Using Practices to Minimize Primary Drift. *Weed Technology*, *33*(1), 24–40. https://doi.org/10.1017/wet.2018.90

Jones, G. T., Norsworthy, J. K., & Barber, T. (2019b). Response of Soybean Offspring to a Dicamba Drift Event the Previous Year. *Weed Technology*, *33*(1), 41–50. https://doi.org/10.1017/wet.2019.2

Jones, F. (2020, May 17). *How (and why) Chipotle Mexican Grill went fully GMO-free*. Food Digital. https://fooddigital.com/retail/how-and-why-chipotle-mexican-grill-went-fully-gmo-free

Justice Pesticide. (2020). *Bader Farms et al v. Monsanto and BASF – Justice Pesticides*. https://justicepesticides.org/en/juridic_case/bader-farms-et-al-v-monsanto-and-basf/

Kabat, G. C., Price, W. J., & Tarone, R. E. (2021). On recent meta-analyses of exposure to glyphosate and risk of non-Hodgkin's lymphoma in humans. *Cancer Causes & Control*, *32*(4), 409–414. https://doi.org/10.1007/s10552-020-01387-w

Kaboli Kafshgiri, S., Farkhondeh, T., & Miri-Moghaddam, E. (2021). Glyphosate effects on the female reproductive systems: A systematic review. *Reviews on Environmental Health*. https://doi.org/10.1515/reveh-2021-0029

Kalofiri, P., Balias, G., & Tekos, F. (2021). The EU endocrine disruptors' regulation and the glyphosate controversy. *Toxicology Reports*, *8*, 1193–1199. https://doi.org/10.1016/j.toxrep.2021.05.013

Kan, G., Tong, Z., Hu, Z., Ma, D., Zhang, G., & Ya, D. (2015). Fitness of hybrids between wild soybeans (Glycine soja) and the glyphosate-resistant transgenic soybean (Glycine max). *Soybean Science*, *34*(2), 177–184.

Kang, B.-C., Woo, J. W., Kim, S.-T., Bae, S.-J., Choi, M., Kim, J.-S., & Kim, S.-G. (2019). Guidelines for C to T base editing in plants: Base-editing window, guide RNA length, and efficient promoter. *Plant Biotechnology Reports*, *13*(5), 533–541. https://doi.org/10.1007/s11816-019-00572-x

Kaskey, K. (2016). Monsanto, Scotts Seek Approval for Golf Grass Gone Wild. Bloomberg. http://www.bloomberg.com/news/articles/2016-01-06/monsanto-scotts-seek-approval-for-golf-grass-they-won-t-sell

Kaspary, T. E., Lamego, F. P., Cutti, L., Aguiar, A. C. de M., Rigon, C. A. G., & Basso, C. J. (2017). Growth, phenology, and seed viability between glyphosate-resistant and glyphosate-susceptible hairy fleabane. *Bragantia*, *76*, 92–101. https://doi.org/10.1590/1678-4499.542

Kawata, M., Murakami, K., & Ishikawa, T. (2009). Dispersal and persistence of genetically modified oilseed rape around Japanese harbors. *Environmental Science and Pollution Research International*, *16*(2), 120–126. http://doi.org/10.1007/s11356-008-0074-4

Kawate, M. K., Colwell, S. G., Alex G. Ogg, J., & Kraft, J. M. (1997). Effect of Glyphosate-Treated Henbit (Lamium amplexicaule) and Downy Brome (Bromus tectorum) on Fusarium solani f. sp. pisi and Pythium ultimum. *Weed Science*, *45*(5), 739–743.

Kelly, D.W., Poulin, R., Tompkins, D.M., Townsend, C.R. (2010). Synergistic effects of glyphosate formulation and parasite infection on fish malformations and survival. *Journal of Applied Ecology* **47**, 498–504. doi:10.1111/j.1365-2664.2010.01791.x

Kennedy RF (2017) California Judge Rules Against Monsanto, Allows Cancer Warning on Roundup. EcoWatch. 11th March 2017. http://www.ecowatch.com/monsanto-california-ruling-roundup-2310904321.html

Kepler, R. M., Epp Schmidt, D. J., Yarwood, S. A., Cavigelli, M. A., Reddy, K. N., Duke, S. O., Bradley, C. A., Williams, M. M., Buyer, J. S., & Maul, J. E. (2020). Soil Microbial Communities in Diverse Agroecosystems Exposed to the Herbicide Glyphosate. *Applied and Environmental Microbiology*, *86*(5), e01744-19. https://doi.org/10.1128/AEM.01744-19

Kesoju, S. R., Kramer, M., Brunet, J., Greene, S. L., Jordan, A., & Martin, R. C. (2021). Gene flow in commercial alfalfa (Medicago sativa subsp. sativa L.) seed production fields: Distance is the primary but not the sole influence on adventitious presence. *PLOS ONE*, *16*(3), e0248746. https://doi.org/10.1371/journal.pone.0248746

Khan, A., Feulefack, J., & Sergi, C. M. (2022). Pre-conceptional and prenatal exposure to pesticides and pediatric neuroblastoma. A meta-analysis of nine studies. *Environmental Toxicology and Pharmacology*, *90*, 103790. https://doi.org/10.1016/j.etap.2021.103790

Kim, K.-T., Kwak, Y.-J., Han, S.-C., & Hwang, J. H. (2020). Impairment of motor coordination and interneuron migration in perinatal exposure to glufosinate-ammonium. *Scientific Reports*, *10*(1), 20647. https://doi.org/10.1038/s41598-020-76869-7

Kim, J., Leon, M. E., Schinasi, L., Baldi, I., Lebailly, P., Freeman, L. B., Nordby, K.-C., Kjaerheim, K., Ferro, G., Monnereau, A., Brouwer, M., Hofmann, J., Straif, K., Kromhout, H., Schuz, J., & Tog, K. (2021). RF-210 Exposure to pesticides and risk of Hodgkin lymphoma in an international consortium of agricultural cohorts (AGRICOH). *Occupational and Environmental Medicine*, *78*(Suppl 1), A129–A130. https://doi.org/10.1136/OEM-2021-EPI.354

Kimbrell A (2016) The Big Lie: Monsanto and the New York Times. 15th December 2016. http://www.huffingtonpost.com/andrew-kimbrell/the-big-lie-monsanto-and-_b_13654204.html?

Kimbrough, L. (2022, January 27). Western monarchs make a spectacular comeback in California. Mongabay Environmental News. https://news.mongabay.com/2022/01/western-monarchs-make-a-spectacular-comeback-in-california/

King, C. A., Purcell, L. C., & Vories, E. D. (2001). Plant Growth and Nitrogenase Activity of Glyphosate-Tolerant Soybean in Response to Foliar Glyphosate Applications. *Agronomy Journal*, *93*(1), 179. http://doi.org/10.2134/agronj2001.931179x

Kish, A., 2017. The Impact Of Roundup® on *Daphnia Magna*. Presented at the 2017 AAAS Annual Meeting (February 16-20, 2017), aaas. https://aaas.confex.com/aaas/2017/webprogram/Paper20104.html

Kishore, G. M., & Jacob, G. S. (1987). Degradation of glyphosate by Pseudomonas sp. PG2982 via a sarcosine intermediate. *The Journal of Biological Chemistry*, *262*(25), 12164–12168.

Kissane, Z., & Shephard, J. M. (2017). The rise of glyphosate and new opportunities for biosentinel early-warning studies. *Conservation Biology*, *31*(6), 1293–1300. https://doi.org/10.1111/cobi.12955

Klein, A.-M., Vaissiere, B. E., Cane, J. H., Steffan-Dewenter, I., Cunningham, S. A., Kremen, C., & Tscharntke, T. (2007). Importance of pollinators in changing landscapes for world crops. *Proceedings of the Royal Society B: Biological Sciences*, *274*(1608), 303–313. http://doi.org/10.1098/rspb.2006.3721

Koch, B. A. (2007). Liability and Compensation Schemes for Damage Resulting from the Presence of Genetically Modified Organisms in Non-GM Crops. European Centre of Tort and Insurance Law. Research Unit for European Tort Law Austrian Academy of Sciences.

Koger, C. H., & Reddy, K. N. (2005). Role of absorption and translocation in the mechanism of glyphosate resistance in horseweed (Conyza canadensis). *Weed Science*. Retrieved from http://agris.fao.org/agris-search/search.do?recordID=US201300983347

Koh, I., Lonsdorf, E. V., Williams, N. M., Brittain, C., Isaacs, R., Gibbs, J., & Ricketts, T. H. (2016). Modeling the status, trends, and impacts of wild bee abundance in the United States. *Proceedings of the National Academy of Sciences*, *113*(1), 140–145. http://doi.org/10.1073/pnas.1517685113

Koop, F. (2015). Campaign against pesticides grows. Buenos Aires Herald. http://www.buenosairesherald.com/article/189440/campaign-against-pesticides-grows

Kopicki, A. (2013). Strong Support for Labeling Modified Foods. The New York Times. http://www.nytimes.com/2013/07/28/science/strong-support-for-labeling-modified-foods.html?_r=0

Koyama, K., Koyama, K., & Goto, K. (1997). Cardiovascular Effects of a Herbicide Containing Glufosinate and a Surfactant:In Vitroandin VivoAnalyses in Rats. *Toxicology and Applied Pharmacology*, *145*(2), 409–414. https://doi.org/10.1006/taap.1997.8196

Krebs, J. R., Wilson, J. D., Bradbury, R. B., & Siriwardena, G. M. (1999). The second Silent Spring? *Nature*, *400*(6745), 611–612. http://doi.org/10.1038/23127

Kremen, C., Williams, N. M., & Thorp, R. W. (2002). Crop pollination from native bees at risk from agricultural intensification. *Proceedings of the National Academy of Sciences*, 99(26), 16812–16816. http://doi.org/10.1073/pnas.262413599

Kremer, R., Means, N., & Kim, S. (2005). Glyphosate affects soybean root exudation and rhizosphere micro-organisms. *International Journal of Environmental Analytical Chemistry*, *85*(15), 1165–1174. http://doi.org/10.1080/03067310500273146

Kremer, R. J., & Means, N. E. (2009). Glyphosate and glyphosate-resistant crop interactions with rhizosphere microorganisms. *European Journal of Agronomy*, *31*(3), 153–161. http://doi.org/10.1016/j.eja.2009.06.004

Kremer, R.J. (2017). Soil and Environmental Health After Twenty Years of Intensive Use of Glyphosate (PDF Download Available). Advances in Plants & Agriculture Research 6, 00224. doi:10.15406/apar.2017.06.00224

Krenchinski, F.H., Albrecht, L.P., Albrecht, A.J.P., Cesco, V.J.S., Rodrigues, D.M., Portz, R.L., Zobiole, L.H.S. (2017). Glyphosate affects chlorophyll, photosynthesis and water use of four Intacta RR2 soybean cultivars. *Acta Physiol Plant* **39**, 63. doi:10.1007/s11738-017-2358-0

Kriete, G., & Broer, I. (1996). Influence of the herbicide phosphinothricin on growth and nodulation capacity of Rhizobium meliloti. *Applied Microbiology and Biotechnology*, *46*(5), 580–586. https://doi.org/10.1007/s002530050864

Krimsky, S., & Gillam, C. (2018). Roundup litigation discovery documents: Implications for public health and journal ethics. *Journal of Public Health Policy*, *39*(3), 318–326. https://doi.org/10.1057/s41271-018-0134-z

Krüger, M., Shehata, A. A., Schrödl, W., & Rodloff, A. (2013). Glyphosate suppresses the antagonistic effect of Enterococcus spp. on Clostridium botulinum. *Anaerobe*, *20*, 74–78. http://doi.org/10.1016/j.anaerobe.2013.01.005

Krüger, M., Philipp Schlendorn, Wieland Schrödl, Hans-Wolfgang Hoppe, Walburga Lutz, & Shehata, A. A. (2014a). Detection of Glyphosate Residues in Animals and Humans. *Journal of Environmental & Analytical Toxicology*, *04*(02). http://doi.org/10.4172/2161-0525.1000210

Krüger, M., Schrödl, W., & Pedersen Ib, S. A. (2014b). Detection of Glyphosate in Malformed Piglets. *J Environ Anal Toxicol*, *4*(230), 2161–0525.

Kruse-Plass, M., Hofmann, F., Kuhn, U., Otto, M., Schlechtriemen, U., Schröder, B., Vögel, R., & Wosniok, W. (2017). Reply to the EFSA (2016) on the relevance of recent publications (Hofmann et al. 2014, 2016) on environmental risk assessment and management of Bt-maize events (MON810, Bt11 and 1507). *Environmental Sciences Europe*, *29*(1), 12. https://doi.org/10.1186/s12302-017-0106-0

Krynak, K. L., Burke, D. J., & Benard, M. F. (2017). Rodeo™ Herbicide Negatively Affects Blanchard's Cricket Frogs (Acris blanchardi) Survival and Alters the Skin-Associated Bacterial Community. *Journal of Herpetology*, *51*(3), 402–410. https://doi.org/10.1670/16-092

Krzysko-Lupicka, T. & Orlik, A. (1997). The use of glyphosate as the sole source of phosphorus or carbon for the selection of soil-borne fungal strains capable to degrade this herbicide. *Chemosphere, 34*(12), 2601-2605.

Krzysko-Lupicka, T., & Sudol, T. (2008). Interactions between glyphosate and autochthonous soil fungi surviving in aqueous solution of glyphosate. *Chemosphere*, *71*(7), 1386–1391. http://doi.org/10.1016/j.chemosphere.2007.11.006

Kuang, Y., Li, S., Ren, B., Yan, F., Spetz, C., Li, X., Zhou, X., & Zhou, H. (2020). Base-Editing-Mediated Artificial Evolution of OsALS1 In Planta to Develop Novel Herbicide-Tolerant Rice Germplasms. *Molecular Plant*, *13*(4), 565–572. https://doi.org/10.1016/j.molp.2020.01.010

Kuester, A., Fall, E., Chang, S.-M., Baucom, R.S. (2017). Shifts in outcrossing rates and changes to floral traits are associated with the evolution of herbicide resistance in the common morning glory. *Ecol Lett* **20**, 41–49. doi:10.1111/ele.12703

Kumar, V., & Jha, P. (2015). Growth and Reproduction of Glyphosate-Resistant and Susceptible Populations of Kochia scoparia. *PLOS ONE*, *10*(11), e0142675. https://doi.org/10.1371/journal.pone.0142675

Kumar, V., Felix, J., Morishita, D., & Jha, P. (2018). Confirmation of Glyphosate-Resistant Kochia (Kochia scoparia) from Sugar Beet Fields in Idaho and Oregon. *Weed Technology*, *32*(1), 27–33. https://doi.org/10.1017/wet.2017.80

Kumar, V., Liu, R., Boyer, G., & Stahlman, P. W. (2019). Confirmation of 2,4-D resistance and identification of multiple resistance in a Kansas Palmer amaranth (Amaranthus palmeri) population. *Pest Management Science*, *75*(11), 2925–2933. https://doi.org/10.1002/ps.5400

Kuphal K (2017) A shift away from GMO. Lakefield Standard. 20th February 2017. http://www.lakefieldstandard.com/Stories/Story.cfm?SID=64527

Küpper, A., Borgato, E. A., Patterson, E. L., Netto, A. G., Nicolai, M., Carvalho, S. J. P. de, Nissen, S. J., Gaines, T. A., & Christoffoleti, P. J. (2017). Multiple Resistance to Glyphosate and Acetolactate Synthase Inhibitors in Palmer Amaranth (Amaranthus palmeri) Identified in Brazil. *Weed Science*, *65*(3), 317–326. https://doi.org/10.1017/wsc.2017.1

Kurenbach, B., Marjoshi, D., Amábile-Cuevas, C. F., Ferguson, G. C., Godsoe, W., Gibson, P., & Heinemann, J. A. (2015). Sublethal Exposure to Commercial Formulations of the Herbicides Dicamba, 2,4-Dichlorophenoxyacetic Acid, and Glyphosate Cause Changes in Antibiotic Susceptibility in Escherichia coli and Salmonella enterica serovar Typhimurium. *mBio*, *6*(2), e00009–15. http://doi.org/10.1128/mBio.00009-15

Kurenbach, B., Gibson, P. S., Hill, A. M., Bitzer, A. S., Silby, M. W., Godsoe, W., & Heinemann, J. A. (2017). Herbicide ingredients change Salmonella enterica sv. Typhimurium and Escherichia coli antibiotic responses. *Microbiology*, *163*(12), 1791–1801. https://doi.org/10.1099/mic.0.000573

Kutlesa, N. J., & Caveney, S. (2001). Insecticidal activity of glufosinate through glutamine depletion in a caterpillar. *Pest Management Science*, *57*(1), 25–32. https://doi.org/10.1002/1526-4998(200101)57:1<25::AID-PS272>3.0.CO;2-I

Kwiatkowska, M., Reszka, E., Woźniak, K., Jabłońska, E., Michałowicz, J., & Bukowska, B. (2017). DNA damage and methylation induced by glyphosate in human peripheral blood mononuclear cells (in vitro study). *Food and Chemical Toxicology*, *105*, 93–98. https://doi.org/10.1016/j.fct.2017.03.051

Laborde, M. R. R., Larramendy, M. L., & Soloneski, S. (2020). Cytotoxic and genotoxic assessments of 2,4-dichlorophenoxyacetic acid (2,4-D) in in vitro mammalian cells. *Toxicology in Vitro*, *65*, 104783. https://doi.org/10.1016/j.tiv.2020.104783

LaChapelle, A. M., Ruygrok, M. L., Toomer, M., Oost, J. J., Monnie, M. L., Swenson, J. A., Compton, A. A., & Stebbins-Boaz, B. (2007). The hormonal herbicide, 2,4-dichlorophenoxyacetic acid, inhibits Xenopus oocyte maturation by targeting translational and post-translational mechanisms. *Reproductive Toxicology*, *23*(1), 20–31. https://doi.org/10.1016/j.reprotox.2006.08.013

Lajmanovich, R. C., Attademo, A. M., Simoniello, M. F., Poletta, G. L., Junges, C. M., Peltzer, P. M., Grenón, P., & Cabagna-Zenklusen, M. C. (2015). Harmful Effects of the Dermal Intake of Commercial Formulations Containing Chlorpyrifos, 2,4-D, and Glyphosate on the Common Toad Rhinella arenarum (Anura: Bufonidae). *Water, Air, & Soil Pollution*, *226*(12), 427. https://doi.org/10.1007/s11270-015-2695-9

Lajmanovich, R. C., Attademo, A. M., Lener, G., Cuzziol Boccioni, A. P., Peltzer, P. M., Martinuzzi, C. S., Demonte, L. D., & Repetti, M. R. (2022). Glyphosate and glufosinate ammonium, herbicides commonly used on genetically modified crops, and their interaction with microplastics: Ecotoxicity in anuran tadpoles. *Science of The Total Environment*, *804*, 150177. https://doi.org/10.1016/j.scitotenv.2021.150177

Lambert, D.M., Larson, J.A., Roberts, R.K., English, B.C., Zhou, X. “Vivian,” Falconer, L.L., Hogan, R.J., Johnson, J.L., Reeves, J.M. (2017). “Resistance is futile”: estimating the costs of managing herbicide resistance as a first-order Markov process and the case of U.S. upland cotton producers. *Agricultural Economics*, **48**, 1-10. doi:10.1111/agec.12341

Lapegna, P. (2013). The Expansion of Transgenic Soybeans and the Killing of Indigenous Peasants in Argentina. ResearchGate, 8(2), 291–308.

Lapegna, P. (2016). Genetically modified soybeans, agrochemical exposure, and everyday forms of peasant collaboration in Argentina. *The Journal of Peasant Studies*, **43**(2), 517–536. http://doi.org/10.1080/03066150.2015.1041519

Larrea A (2016) ‘Experts call Latin America ‘the world’s scrapyard for pesticides’. Buenos Aires Herald. 30th December 2016. http://www.buenosairesherald.com/article/224205/%E2%80%98experts-call-latin-america-%E2%80%98the-world%E2%80%99s-scrapyard-for-pesticides%E2%80%99%E2%80%99

Larsen, K., Christensen, T. B., Højberg, O., & Sørensen, M. T. (2022). Exposure of pigs to glyphosate affects gene-specific DNA methylation and gene expression. *Toxicology Reports*, *9*, 298–310. https://doi.org/10.1016/j.toxrep.2022.02.007

Larson, R. L., Hill, A. L., Fenwick, A., Kniss, A. R., Hanson, L. E., & Miller, S. D. (2006). Influence of glyphosate on Rhizoctonia and Fusarium root rot in sugar beet. *Pest Management Science*, *62*(12), 1182–1192. http://doi.org/10.1002/ps.1297

Larson, C. (2022, July 21). *Beloved monarch butterflies now listed as endangered*. https://phys.org/news/2022-07-beloved-monarch-butterflies-endangered.html

Laugeray, A., Herzine, A., Perche, O., Hébert, B., Aguillon-Naury, M., Richard, O., Menuet, A., Mazaud-Guittot, S., Lesné, L., Briault, S., Jegou, B., Pichon, J., Montécot-Dubourg, C., & Mortaud, S. (2014). Pre- and Postnatal Exposure to Low Dose Glufosinate Ammonium Induces Autism-Like Phenotypes in Mice. *Frontiers in Behavioral Neuroscience*, *8*. https://doi.org/10.3389/fnbeh.2014.00390

Laws, F. (2022, June 22). *Are farmers nearing the end of an era with herbicides?* Farm Progress. https://www.farmprogress.com/weeds/are-farmers-nearing-end-era-herbicides

Lazurick, C., Lidzbarski, N., Owings, R., Brotherton, J., & Steele, E. (2017). Investigating the Toxicity and Accumulation of 2,4-Dichlorophenoxyacetic Acid (2,4-D) and Glyphosate in Eisenia fetida. *Journal of the South Carolina Academy of Science*, *15*(2). https://scholarcommons.sc.edu/jscas/vol15/iss2/6

Le Du-Carrée, J., Boukhari, R., Cachot, J., Cabon, J., Louboutin, L., Morin, T., & Danion, M. (2021). Generational effects of a chronic exposure to a low environmentally relevant concentration of glyphosate on rainbow trout, Oncorhynchus mykiss. *Science of The Total Environment*, *801*, 149462. https://doi.org/10.1016/j.scitotenv.2021.149462

Le Du-Carrée, J., Cabon, J., Louboutin, L., Morin, T., & Danion, M. (2022). Changes in defense capacity to infectious hematopoietic necrosis virus (IHNv) in rainbow trout intergenerationally exposed to glyphosate. *Fish & Shellfish Immunology*, *122*, 67–70. https://doi.org/10.1016/j.fsi.2021.12.021

Lee, N. R. W. (2018). *Long Term Glyphosate Effects on Roundup Ready Soybean Rhizosphere Microorganisms* [The Ohio State University]. https://etd.ohiolink.edu/apexprod/rws_olink/r/1501/10?clear=10&p10_accession_num=osu1525689141453883

Leeb, C., Kolbenschlag, S., Laubscher, A., Adams, E., Brühl, C. A., & Theissinger, K. (2020). Avoidance behavior of juvenile common toads (Bufo bufo) in response to surface contamination by different pesticides. *PLOS ONE*, *15*(11), e0242720. https://doi.org/10.1371/journal.pone.0242720

Leguizamón, A. (2016). Disappearing nature? Agribusiness, biotechnology and distance in Argentine soybean production. *The Journal of Peasant Studies*, *43*(2), 313–330. https://doi.org/10.1080/03066150.2016.1140647

Lehel, J., Szabó, R., Major, L., Grúz, A., & Budai, P. (2021). Model study on chicken embryos to investigate potential teratogenic risk of wild birds due to pesticide and environmental contaminant. Research Square. https://doi.org/10.21203/rs.3.rs-517851/v1

Lemke, N., Murawski, A., Schmied-Tobies, M. I. H., Rucic, E., Hoppe, H.-W., Conrad, A., & Kolossa-Gehring, M. (2021). Glyphosate and aminomethylphosphonic acid (AMPA) in urine of children and adolescents in Germany – Human biomonitoring results of the German Environmental Survey 2014–2017 (GerES V). Environment International, 156, 106769. https://doi.org/10.1016/j.envint.2021.106769

Leon, M. E., Schinasi, L. H., Lebailly, P., Beane Freeman, L. E., Nordby, K.-C., Ferro, G., Monnereau, A., Brouwer, M., Tual, S., Baldi, I., Kjaerheim, K., Hofmann, J. N., Kristensen, P., Koutros, S., Straif, K., Kromhout, H., & Schüz, J. (2019). Pesticide use and risk of non-Hodgkin lymphoid malignancies in agricultural cohorts from France, Norway and the USA: A pooled analysis from the AGRICOH consortium. International Journal of Epidemiology, 48(5), 1519–1535. https://doi.org/10.1093/ije/dyz017

Lerda, D., & Rizzi, R. (1991). Study of reproductive function in persons occupationally exposed to 2,4-dichlorophenoxyacetic acid (2,4-D). *Mutation Research Letters*, *262*(1), 47–50. https://doi.org/10.1016/0165-7992(91)90105-D

Lerro, C. C., Beane Freeman, L. E., Portengen, L., Kang, D., Lee, K., Blair, A., Lynch, C. F., Bakke, B., De Roos, A. J., & Vermeulen, R. C. H. (2017). A longitudinal study of atrazine and 2,4-D exposure and oxidative stress markers among iowa corn farmers. *Environmental and Molecular Mutagenesis*, *58*(1), 30–38. https://doi.org/10.1002/em.22069

Lerro, C. C., Hofmann, J. N., Andreotti, G., Koutros, S., Parks, C. G., Blair, A., Albert, P. S., Lubin, J. H., Sandler, D. P., & Beane Freeman, L. E. (2020). Dicamba use and cancer incidence in the agricultural health study: An updated analysis. *International Journal of Epidemiology*. https://doi.org/10.1093/ije/dyaa066

Lesseur, C., Pirrotte, P., Pathak, K. V., Manservisi, F., Mandrioli, D., Belpoggi, F., Panzacchi, S., Li, Q., Barrett, E. S., Nguyen, R. H. N., Sathyanarayana, S., Swan, S. H., & Chen, J. (2021). Maternal urinary levels of glyphosate during pregnancy and anogenital distance in newborns in a US multicenter pregnancy cohort. *Environmental Pollution*, *280*, 117002. https://doi.org/10.1016/j.envpol.2021.117002

Levin, S. (2015). California EPA moves to label Monsanto's Roundup as 'carcinogenic'. East Bay Express. http://www.eastbayexpress.com/SevenDays/archives/2015/09/05/california-epa-moves-to-label-monsantos-roundup-carcinogenic

Lewis, B. (2015). WHO findings on weed killer will not speed up EU safety review. Reuters. http://www.reuters.com/article/2015/05/12/eu-pesticides-idUSL5N0Y34Y320150512 http://farmertofarmercampaign.com/Out%20of%20Hand.FullReport.pdf

Li, Z., Liu, Z.-B., Xing, A., Moon, B. P., Koellhoffer, J. P., Huang, L., Ward, R. T., Clifton, E., Falco, S. C., & Cigan, A. M. (2015). Cas9-Guide RNA Directed Genome Editing in Soybean. *Plant Physiology*, *169*(2), 960–970. https://doi.org/10.1104/pp.15.00783

Li, M.-H., Xu, H.-D., Liu, Y., Chen, T., Jiang, L., Fu, Y.-H., & Wang, J.-S. (2016a). Multi-tissue metabolic responses of goldfish (Carassius auratus) exposed to glyphosate-based herbicide †Electronic supplementary information (ESI) available. See DOI: 10.1039/c6tx00011h. *Toxicology Research*, *5*(4), 1039–1052. https://doi.org/10.1039/c6tx00011h

Li, J., Meng, X., Zong, Y., Chen, K., Zhang, H., Liu, J., Li, J., & Gao, C. (2016b). Gene replacements and insertions in rice by intron targeting using CRISPR-Cas9. *Nature Plants*, *2*, 16139. https://doi.org/10.1038/nplants.2016.139

Li, T., Liu, B., Chen, C. Y., & Yang, B. (2016c). TALEN-Mediated Homologous Recombination Produces Site-Directed DNA Base Change and Herbicide-Resistant Rice. *Journal of Genetics and Genomics = Yi Chuan Xue Bao*, *43*(5), 297–305. https://doi.org/10.1016/j.jgg.2016.03.005

Li, C., Zong, Y., Wang, Y., Jin, S., Zhang, D., Song, Q., Zhang, R., & Gao, C. (2018). Expanded base editing in rice and wheat using a Cas9-adenosine deaminase fusion. *Genome Biology*, *19*(1), 59. https://doi.org/10.1186/s13059-018-1443-z

Li, Y., Zhu, J., Wu, H., Liu, C., Huang, C., Lan, J., Zhao, Y., & Xie, C. (2019). Precise base editing of non-allelic acetolactate synthase genes confers sulfonylurea herbicide resistance in maize. *The Crop Journal*, *8*(3), 449–456. https://doi.org/10.1016/j.cj.2019.10.001

Li, C., Zhang, R., Meng, X., Chen, S., Zong, Y., Lu, C., Qiu, J.-L., Chen, Y.-H., Li, J., & Gao, C. (2020a). Targeted, random mutagenesis of plant genes with dual cytosine and adenine base editors. *Nature Biotechnology*, *38*(7), 875–882. https://doi.org/10.1038/s41587-019-0393-7

Li, H., Li, J., Chen, J., Yan, L., & Xia, L. (2020b). Precise Modifications of Both Exogenous and Endogenous Genes in Rice by Prime Editing. *Molecular Plant*, *13*(5), 671–674. https://doi.org/10.1016/j.molp.2020.03.011

Li, S., Zhang, Y., Xia, L., & Qi, Y. (2020c). CRISPR-Cas12a enables efficient biallelic gene targeting in rice. *Plant Biotechnology Journal*, *18*(6), 1351–1353. https://doi.org/10.1111/pbi.13295

Liao, H., Li, X., Yang, Q., Bai, Y., Cui, P., Wen, C., Liu, C., Chen, Z., Tang, J., Che, J., Yu, Z., Geisen, S., Zhou, S., Friman, V.-P., & Zhu, Y.-G. (2021). Herbicide Selection Promotes Antibiotic Resistance in Soil Microbiomes. *Molecular Biology and Evolution*, *38*(6), 2337–2350. https://doi.org/10.1093/molbev/msab029

Lieu TW (2017) Rep. Lieu Statement on New Glyphosate Safety Concerns. Press Release. 15th March 2017. https://lieu.house.gov/media-center/press-releases/rep-lieu-statement-new-glyphosate-safety-concerns

Lin, Q., Zong, Y., Xue, C., Wang, S., Jin, S., Zhu, Z., Wang, Y., Anzalone, A. V., Raguram, A., Doman, J. L., Liu, D. R., & Gao, C. (2020). Prime genome editing in rice and wheat. *Nature Biotechnology*, *38*(5), 582–585. https://doi.org/10.1038/s41587-020-0455-x

Lindholm, J. (2014). Some Food Companies Are Quietly Dumping GMO Ingredients. http://www.npr.org/sections/thesalt/2014/07/22/333725880/some-food-producers-are-quietly-dumping-gmo-ingredients?ft=1&f=1006

Little, A. (2022, July 13). Analysis | We Must Learn to Love Genetically Modified Crops. *Washington Post*. https://www.washingtonpost.com/business/energy/we-must-learn-to-love-genetically-modified-crops/2022/07/12/be6f947a-01eb-11ed-8beb-2b4e481b1500_story.html

Liu, C.-M., McLean, P. A., Sookdeo, C. C., & Cannon, F. C. (1991). Degradation of the Herbicide Glyphosate by Members of the Family Rhizobiaceae. *Applied and Environmental Microbiology*, *57*(6), 1799–1804.

Liu, L., Punja, Z. K., & Rahe, J. E. (1997). Altered root exudation and suppression of induced lignification as mechanisms of predisposition by glyphosate of bean roots (Phaseolus vulgarisL.) to colonization byPythiumspp. *Physiological and Molecular Plant Pathology*, *51*(2), 111–127. http://doi.org/10.1006/pmpp.1997.0113

Liu, Q., Li, X. C., Liu, Z. J., Li, T., & Lei, B. J. (2008). Study on Round up Ready gene move to soybean by Anemophily. *Heilongjiang Agricultural Sciences*, *1*, 14–16.

Liu, J., Zhou, B., Yang, C., Li, Y., Jiang, L., Zhang, M., Tao, B., & Qiu, L. (2012). *Gene flowing of genetically modified glyphosate-resistant soybean with EPSPS*. *31*(4), 517–521.

Liu, H., Li, J., Li, X., Zheng, Y., Feng, S., & Jiang, G. (2015). Mitigating greenhouse gas emissions through replacement of chemical fertilizer with organic manure in a temperate farmland. *Science Bulletin*, *60*(6), 598–606. http://doi.org/10.1007/s11434-014-0679-6

Liu, S., Song, X., Hu, Y., Dai, W., & Qiang, S. (2016). Fitness of Hybrids between Two Types of Transgenic Rice and Six Japonica and Indica Weed Rice Accessions. *Crop Science*, *56*(5), 2751–2765. https://doi.org/10.2135/cropsci2015.11.0719

Liu, Y., Li, Y., Hua, X., Müller, K., Wang, H., Yang, T., Wang, Q., Peng, X., Wang, M., Pang, Y., Qi, J., & Yang, Y. (2018). Glyphosate application increased catabolic activity of gram-negative bacteria but impaired soil fungal community. *Environmental Science and Pollution Research*, *25*(15), 14762–14772. https://doi.org/10.1007/s11356-018-1676-0

Liu, B., Xue, K., Liu, L., Shen, W., & Guo, H. (2020a). Research on the gene flow from transgenic EPSPS+PAT soybean S4003 14 to non-transgenic soybeans. 生态与农村环境学报, *36*(3), 367–373. https://doi.org/10.19741/j.issn.1673-4831.2019.0384
Liu, X., Qin, R., Li, J., Liao, S., Shan, T., Xu, R., Wu, D., & Wei, P. (2020b). A CRISPR-Cas9-mediated domain-specific base-editing screen enables functional assessment of ACCase variants in rice. *Plant Biotechnology Journal*, *18*(9), 1845–1847. https://doi.org/10.1111/pbi.13348$
Liu, J. Y., Sheng, Z. W., Hu, Y. Q., Liu, Q., Qiang, S., Song, X. L., & Liu, B. (2021a). Fitness of F1 hybrids between 10 maternal wild soybean populations and transgenic soybean. *Transgenic Research*, *30*(1), 105–119. https://doi.org/10.1007/s11248-020-00230-x
Liu, L., Kuang, Y., Yan, F., Li, S., Ren, B., Gosavi, G., Spetz, C., Li, X., Wang, X., Zhou, X., & Zhou, H. (2021b). Developing a novel artificial rice germplasm for dinitroaniline herbicide resistance by base editing of OsTubA2. *Plant Biotechnology Journal*, *19*(1), 5–7. https://doi.org/10.1111/pbi.13430
Liu, L., Zhang, L., Fu, J., Shen, W., Fang, Z., Dai, Y., Jia, R., Liu, B., & Liang, J. (2022a). Fitness and Ecological Risk of Hybrid Progenies of Wild and Herbicide-Tolerant Soybeans With EPSPS Gene. Frontiers in Plant Science, 13, 922215. https://doi.org/10.3389/fpls.2022.922215
Liu, Z., Shangguan, Y., Zhu, P., Sultan, Y., Feng, Y., Li, X., & Ma, J. (2022b). Developmental toxicity of glyphosate on embryo-larval zebrafish (Danio rerio). *Ecotoxicology and Environmental Safety*, *236*, 113493. https://doi.org/10.1016/j.ecoenv.2022.113493
Livingston, M., Fernandez-Cornejo, J., Unger, J., Osteen, C., Schimmelpfennig, D., Park, T., & Lambert, D. (2015). The economics of glyphosate resistance management in corn and soybean production (Economic Research Report No.184). April 2015. Washington, DC: USDA, ERS. https://www.ers.usda.gov/webdocs/publications/err184/52761_err184.pdf
Loh, T., & Feeley, J. (2021, July 29). Bayer's Roundup Costs Could Top $16 Billion as Provisions Mount. *Bloomberg.Com*. https://www.bloomberg.com/news/articles/2021-07-29/bayer-to-set-aside-4-5-billion-for-potential-roundup-claims
Longhi, F., & Bianchi, S. (2020). Soy, glyphosate and human health. Some evidence in the Argentinian Dry Chaco Region (1990-2012). *Revista Geográfica de América Central*, *65*, 145–174. https://doi.org/10.15359/rgac.65-2.6
Lopes, F. M., Varela Junior, A. S., Corcini, C. D., da Silva, A. C., Guazzelli, V. G., Tavares, G., & da Rosa, C. E. (2014). Effect of glyphosate on the sperm quality of zebrafish Danio rerio. *Aquatic Toxicology (Amsterdam, Netherlands)*, *155*, 322–326. https://doi.org/10.1016/j.aquatox.2014.07.006
Lopes, F.M., Caldas, S.S., Primel, E.G., da Rosa, C.E., 2016. Glyphosate Adversely Affects *Danio rerio* Males: Acetylcholinesterase Modulation and Oxidative Stress. *Zebrafish*. doi:10.1089/zeb.2016.1341
López González, E. C., Siroski, P. A., & Poletta, G. L. (2019). Genotoxicity induced by widely used pesticide binary mixtures on Caiman latirostris (broad-snouted caiman). Chemosphere, 232, 337–344. https://doi.org/10.1016/j.chemosphere.2019.05.218
López González, E. C., Romito, M. L., Latorre, M. A., Siroski, P. A., & Poletta, G. L. (2021). Biomarkers of genotoxicity, immunotoxicity and oxidative stress on Caiman latirostris (Broad-snouted caiman) hatchlings exposed to pesticide formulations and mixtures widely used in agriculture. *Environmental Advances*, *5*, 100114. https://doi.org/10.1016/j.envadv.2021.100114
Lorentz, L., Gaines, T. A., Nissen, S. J., Westra, P., Strek, H. J., Dehne, H. W., … Beffa, R. (2014). Characterization of Glyphosate Resistance in Amaranthus tuberculatus Populations. *Journal of Agricultural and Food Chemistry*, *62*(32), 8134–8142. http://doi.org/10.1021/jf501040x
Lorenz, V., Pacini, G., Luque, E. H., Varayoud, J., & Milesi, M. M. (2020). Perinatal exposure to glyphosate or a glyphosate-based formulation disrupts hormonal and uterine milieu during the receptive state in rats. *Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association*, *143*, 111560. https://doi.org/10.1016/j.fct.2020.111560
Lorraine-Colwill, D. F., Powles, S. B., Hawkes, T. R., Hollinshead, P. H., Warner, S. A. J., & Preston, C. (2002). Investigations into the mechanism of glyphosate resistance in Lolium rigidum. *Pesticide Biochemistry and Physiology*, *74*(2), 62–72. http://doi.org/10.1016/S0048-3575(03)00007-5
Louie, F., Jacobs, N. F. B., Yang, L. G. L., Park, C., Monnot, A. D., & Bandara, S. B. (2021). A comparative evaluation of dietary exposure to glyphosate resulting from recommended U.S. diets. *Food and Chemical Toxicology*, *158*, 112670. https://doi.org/10.1016/j.fct.2021.112670
Lozano-Kasten, F., Sierra-Diaz, E., Chavez, H. G., Peregrina Lucano, A. A., Cremades, R., & Pinto, E. S. (2021). Seasonal Urinary Levels of Glyphosate in Children From Agricultural Communities. *Dose-Response*, *19*(4), 15593258211053184. https://doi.org/10.1177/15593258211053184
Lu, G.-H., Hua, X.-M., Liang, L., Wen, Z.-L., Du, M.-H., Meng, F.-F., Pang, Y.-J., Qi, J.-L., Tang, C.-Y., & Yang, Y.-H. (2018). Identification of Major Rhizobacterial Taxa Affected by a Glyphosate-Tolerant Soybean Line via Shotgun Metagenomic Approach. *Genes*, *9*(4), 214. https://doi.org/10.3390/genes9040214

Lu, H., Lu, J., & He, L. (2019). Modeling and estimation of pollen-mediated gene flow at the landscape scale. *Ecological Indicators*, *106*, 105500. https://doi.org/10.1016/j.ecolind.2019.105500
Lu, T., Xu, N., Zhang, Q., Zhang, Z., Debognies, A., Zhou, Z., Sun, L., & Qian, H. (2020). Understanding the influence of glyphosate on the structure and function of freshwater microbial community in a microcosm. *Environmental Pollution*, *260*, 114012. https://doi.org/10.1016/j.envpol.2020.114012
Lu, C., Yu, Z., Hennessy, D. A., Feng, H., Tian, H., & Hui, D. (2022). Emerging weed resistance increases tillage intensity and greenhouse gas emissions in the US corn–soybean cropping system. *Nature Food*, *3*(4), 266–274. https://doi.org/10.1038/s43016-022-00488-w
Luaces, J. P., Rossi, L. F., Chirino, M. G., Browne, M., Merani, M. S., & Mudry, M. D. (2017). Genotoxic effects of Roundup Full II® on lymphocytes of Chaetophractus villosus (Xenarthra, Mammalia): In vitro studies. *PLOS ONE*, *12*(8), e0182911. https://doi.org/10.1371/journal.pone.0182911
Lucht, G. (2014). Farmers interest in non-GMO beans, corn grows. Iowa Farmer Today. http://www.iowafarmertoday.com/news/crop/farmer-interest-in-non-gmo-beans-corn-grows/article_3f9ceace-8090-11e4-be38-5747c072ef34.html
Lucia, R. M., Huang, W.-L., Pathak, K. V., McGilvrey, M., David, -Dirgo Victoria, Alvarez, A., Goodman, D., Masunaka, I., Odegaard, A. O., Ziogas, A., Pirrotte, P., Norden, -Krichmar Trina M., & Park, H. L. (2022). Association of Glyphosate Exposure with Blood DNA Methylation in a Cross-Sectional Study of Postmenopausal Women. *Environmental Health Perspectives*, *130*(4), 047001. https://doi.org/10.1289/EHP10174
Lucio, F. R., Kalsing, A., Adegas, F. S., Rossi, C. V. S., Correia, N. M., Gazziero, D. L. P., & Silva, A. F. da. (2019). Dispersal and Frequency of Glyphosate-Resistant and Glyphosate-Tolerant Weeds in Soybean-producing Edaphoclimatic Microregions in Brazil. *Weed Technology*, *33*(1), 217–231. https://doi.org/10.1017/wet.2018.97
Lugowska, K. (2018). The effects of Roundup on gametes and early development of common carp (Cyprinus carpio L). *Fish Physiology and Biochemistry*, *44*(4), 1109–1117. https://doi.org/10.1007/s10695-018-0498-9
Lundry, D. R., Ridley, W. P., Meyer, J. J., Riordan, S. G., Nemeth, M. A., Trujillo, W. A., Breeze, M., L., Sorbet, R. (2008). Composition of Grain, Forage, and Processed Fractions from Second-Generation Glyphosate-Tolerant Soybean, MON 89788, Is Equivalent to That of Conventional Soybean (Glycine max L.). *Journal of Agricultural and Food Chemistry*, *56*(12), 4611–4622. http://doi.org/10.1021/jf073087h
Luo, Q.-H., Gao, J., Guo, Y., Liu, C., Ma, Y.-Z., Zhou, Z.-Y., Dai, P.-L., Hou, C.-S., Wu, Y.-Y., & Diao, Q.-Y. (2021). Effects of a commercially formulated glyphosate solutions at recommended concentrations on honeybee (Apis mellifera L.) behaviours. *Scientific Reports*, *11*(1), 2115. https://doi.org/10.1038/s41598-020-80445-4
Lupi, L., Bedmar, F., Puricelli, M., Marino, D., Aparicio, V. C., Wunderlin, D., & Miglioranza, K. S. B. (2019). Glyphosate runoff and its occurrence in rainwater and subsurface soil in the nearby area of agricultural fields in Argentina. *Chemosphere*, *225*, 906–914. https://doi.org/10.1016/j.chemosphere.2019.03.090
Lutri, V. F., Matteoda, E., Blarasin, M., Aparicio, V., Giacobone, D., Maldonado, L., Becher Quinodoz, F., Cabrera, A., & Giuliano Albo, J. (2020). Hydrogeological features affecting spatial distribution of glyphosate and AMPA in groundwater and surface water in an agroecosystem. Córdoba, Argentina. *Science of The Total Environment*, *711*, 134557. https://doi.org/10.1016/j.scitotenv.2019.134557
Lutz EM (2017) Texas winegrowers fear new herbicides will wipe out industry. The Texas Tribune. 2nd January 2017. https://www.texastribune.org/2017/01/02/texas-winegrowers-brace-another-wave-new-herbicide/
Lynn, H., Stoczkiewicz, M., Jensen, G. K., Riss, J., Veillerette, F. (2015). EU response to WHO cancer determination of glyphosate. Alliance for Cancer Prevention, Friends of the Earth Europe, Health & Environments Alliance, Greenpeace European Unit and PAN Europe. http://env-health.org/IMG/pdf/letter_commissioner_andriukaitis_20150407_2_.pdf
Ma, X., Wang, B., Li, Z., Ding, X., Wen, Y., Shan, W., Hu, W., Wang, X., & Xia, Y. (2022). Effects of glufosinate-ammonium on male reproductive health: Focus on epigenome and transcriptome in mouse sperm. *Chemosphere*, *287*(Pt 4), 132395. https://doi.org/10.1016/j.chemosphere.2021.132395
Macedo, M. N., Coe, M. T., DeFries, R., Uriarte, M., Brando, P. M., Neill, C., & Walker, W. S. (2013). Land-use-driven stream warming in southeastern Amazonia. Phil. Trans. R. Soc. B, 368(1619), 20120153. http://doi.org/10.1098/rstb.2012.0153
Maderthaner, M., Weber, M., Takács, E., Mörtl, M., Leisch, F., Römbke, J., Querner, P., Walcher, R., Gruber, E., Székács, A., & Zaller, J. G. (2020). Commercial glyphosate-based herbicides effects on springtails (Collembola) differ from those of their respective active ingredients and vary with soil organic matter content. *Environmental Science and Pollution Research*, *27*(14), 17280–17289. https://doi.org/10.1007/s11356-020-08213-5
Maeda, H., Murata, K., Sakuma, N., Takei, S., Yamazaki, A., Karim, M. R., Kawata, M., Hirose, S., Kawagishi-Kobayashi, M., Taniguchi, Y., Suzuki, S., Sekino, K., Ohshima, M., Kato, H., Yoshida, H., & Tozawa, Y. (2019). A rice gene that confers broad-spectrum resistance to β-triketone herbicides. *Science*. https://doi.org/10.1126/science.aax0379

Maggi, F., la Cecilia, D., Tang, F. H. M., & McBratney, A. (2020). The global environmental hazard of glyphosate use. *Science of The Total Environment*, *717*, 137167. https://doi.org/10.1016/j.scitotenv.2020.137167
Majewski, M. S., Coupe, R. H., Foreman, W. T., & Capel, P. D. (2014). Pesticides in Mississippi air and rain: a comparison between 1995 and 2007. *Environmental Toxicology and Chemistry / SETAC*, *33*(6), 1283–1293. http://doi.org/10.1002/etc.2550
Makris, K. C., Efthymiou, N., Konstantinou, C., Anastasi, E., Schoeters, G., Kolossa-Gehring, M., & Katsonouri, A. (2022). Oxidative stress of glyphosate, AMPA and metabolites of pyrethroids and chlorpyrifos pesticides among primary school children in Cyprus. *Environmental Research*, *212*, 113316. https://doi.org/10.1016/j.envres.2022.113316
Malcolm, S. B. (2018). Anthropogenic Impacts on Mortality and Population Viability of the Monarch Butterfly. *Annual Review of Entomology*, *63*(1), 277–302. https://doi.org/10.1146/annurev-ento-020117-043241
Malone, J. M., Morran, S., Shirley, N., Boutsalis, P., & Preston, C. (2015). EPSPS gene amplification in glyphosate-resistant Bromus diandrus. *Pest Management Science*, n/a–n/a. http://doi.org/10.1002/ps.4019
Mamy, L., Barriuso, E., & Gabrielle, B. (2016). Glyphosate fate in soils when arriving in plant residues. *Chemosphere*, *154*, 425–433. https://doi.org/10.1016/j.chemosphere.2016.03.104
Manalil, S., Werth, J., Jackson, R., Chauhan, B. S., & Preston, C. (2017). An assessment of weed flora 14 years after the introduction of glyphosate-tolerant cotton in Australia. *Crop and Pasture Science*, *68*(8), 773–780.
Mangan, D. (2018, May 29). *US forces Germany's Bayer to shed $9 billion in ag business in biggest ever antitrust sell-off*. CNBC. https://www.cnbc.com/2018/05/29/bayer-will-sell-basf-9-billion-in-assets-to-allow-monsanto-purchase.html
Mann, R. M., Hyne, R. V., Choung, C. B., & Wilson, S. P. (2009). Amphibians and agricultural chemicals: Review of the risks in a complex environment. *Environmental Pollution (Barking, Essex: 1987)*, *157*(11), 2903–2927. https://doi.org/10.1016/j.envpol.2009.05.015
Mann, R. M., & Bidwell, J. R. (1999). The Toxicity of Glyphosate and Several Glyphosate Formulations to Four Species of Southwestern Australian Frogs. *Archives of Environmental Contamination and Toxicology*, *36*(2), 193–199. http://doi.org/10.1007/s002449900460
Marc, J., Mulner-Lorillon, O., Boulben, S., Hureau, D., Durand, G., & Bellé, R. (2002). Pesticide Roundup provokes cell division dysfunction at the level of CDK1/cyclin B activation. *Chemical Research in Toxicology*, *15*(3), 326–331.
Marc, J., Bellé, R., Morales, J., Cormier, P., & Mulner-Lorillon, O. (2004a). Formulated Glyphosate Activates the DNA-Response Checkpoint of the Cell Cycle Leading to the Prevention of G2/M Transition. *Toxicological Sciences*, *82*(2), 436–442. http://doi.org/10.1093/toxsci/kfh281
Marc, J., Mulner-Lorillon, O., & Bellé, R. (2004b). Glyphosate-based pesticides affect cell cycle regulation. *Biology of the Cell*, *96*(3), 245–249. http://doi.org/10.1016/j.biolcel.2003.11.010
Marchesan, E., Sartori, G. M. S., Avila, L. A. de, Machado, S. L. de O., Zanella, R., Primel, E. G., Macedo, V. R. M., & Marchezan, M. G. (2010). *Residues of pesticides in the water of the depression central rivers in the state of rio grande do sul, brazil* (No. 5). *40*(5), Article 5. https://periodicos.ufsm.br/cr/article/view/57735
Marino, M., Mele, E., Viggiano, A., Nori, S. L., Meccariello, R., & Santoro, A. (2021). Pleiotropic Outcomes of Glyphosate Exposure: From Organ Damage to Effects on Inflammation, Cancer, Reproduction and Development. *International Journal of Molecular Sciences*, *22*(22), 12606. https://doi.org/10.3390/ijms222212606
Marouani, N., Tebourbi, O., Cherif, D., Hallegue, D., Yacoubi, M. T., Sakly, M., Benkhalifa, M., & Ben Rhouma, K. (2017). Effects of oral administration of 2,4-dichlorophenoxyacetic acid (2,4-D) on reproductive parameters in male Wistar rats. *Environmental Science and Pollution Research*, *24*(1), 519–526. https://doi.org/10.1007/s11356-016-7656-3
Marques, J. G. de C., Veríssimo, K. J. da S., Fernandes, B. S., Ferreira, S. R. de M., Montenegro, S. M. G. L., & Motteran, F. (2021). Glyphosate: A Review on the Current Environmental Impacts from a Brazilian Perspective. *Bulletin of Environmental Contamination and Toxicology*, *107*(3), 385–397. https://doi.org/10.1007/s00128-021-03295-4
Marshall E. J. P., Brown V. K., Boatman N. D., Lutman P. J. W., Squire G. R., 2001. The impact of herbicides on weed abundance and biodiversity. Defra PN0940. A report for the UK Pesticides Safety Directorate. Bristol: IACR Long Ashton Research Station. http://www.pesticides.gov.uk/Resources/CRD/Migrated-Resources/Documents/R/Research_PN0940.pdf
Martin C (2017) Monsanto facing class action suit over dicamba spraying. Missouri Lawyers Weekly. 16th February 2017. http://molawyersmedia.com/2017/02/16/monsanto-facing-class-action-suit-over-dicamba-spraying/
Martinelli, L. A., Naylor, R., Vitousek, P. M., & Moutinho, P. (2010). Agriculture in Brazil: impacts, costs, and opportunities for a sustainable future. Current Opinion in Environmental Sustainability, 2(5–6), 431–438. http://doi.org/10.1016/j.cosust.2010.09.008

Martínez, I. M., Lumaret, J.-P., & Cruz, M. R. (2001). Suspected side effects of a herbicide on dung beetle populations (Coleoptera: Scarabaeidae). *Comptes Rendus de l'Académie Des Sciences - Series III - Sciences de La Vie*, *324*(11), 989–994. https://doi.org/10.1016/S0764-4469(01)01384-1

Martinez, D. A., Loening, U. E., & Graham, M. C. (2018). Impacts of glyphosate-based herbicides on disease resistance and health of crops: A review. *Environmental Sciences Europe*, *30*(1), 2. https://doi.org/10.1186/s12302-018-0131-7

Martinez-Haro, M., Chinchilla, J. M., Camarero, P. R., Viñuelas, J. A., Crespo, M. J., & Mateo, R. (2022). Determination of glyphosate exposure in the Iberian hare: A potential focal species associated to agrosystems. *Science of The Total Environment*, *823*, 153677. https://doi.org/10.1016/j.scitotenv.2022.153677

Martins-Gomes, C., Silva, T. L., Andreani, T., & Silva, A. M. (2022). Glyphosate vs. Glyphosate-Based Herbicides Exposure: A Review on Their Toxicity. *Journal of Xenobiotics*, *12*(1), 21–40. https://doi.org/10.3390/jox12010003

Mascarenhas, M., & Busch, L. (2006). Seeds of Change: Intellectual Property Rights, Genetically Modified Soybeans and Seed Saving in the United States. *Sociologia Ruralis*, *46*(2), 122–138. http://doi.org/10.1111/j.1467-9523.2006.00406.x

MASIPAG (2013). Socio-economic Impacts of Genetically Modified Corn In the Philippines. http://masipag.org/wp-content/uploads/2013/05/MASIPAG-Book-low-res.pdf

Matozzo, V., Fabrello, J., Masiero, L., Ferraccioli, F., Finos, L., Pastore, P., Di Gangi, I. M., & Bogialli, S. (2018). Ecotoxicological risk assessment for the herbicide glyphosate to non-target aquatic species: A case study with the mussel Mytilus galloprovincialis. *Environmental Pollution (Barking, Essex: 1987)*, *233*, 623–632. https://doi.org/10.1016/j.envpol.2017.10.100

Matozzo, V., Fabrello, J., & Marin, M. G. (2020). The Effects of Glyphosate and Its Commercial Formulations to Marine Invertebrates: A Review. *Journal of Marine Science and Engineering*, *8*(6), 399. https://doi.org/10.3390/jmse8060399

Maxwell, M. (2015). Colombia mulls Roundup ban. Americafruit. http://www.fruitnet.com/americafruit/article/165191/colombia-mulls-roundup-ban

Mazon, A. S., Cechin, J., Piasecki, C., Gazola, J., Henckes, J. R., Meneghello, G., & Agostinetto, D. (2022). Enlist volunteer corn affects the crop development and seed quality of Enlist soybean. *Bragantia*, *81*. https://doi.org/10.1590/1678-4499.20210207

Mazza, R., Soave, M., Morlacchini, M., Piva, G., & Marocco, A. (2005). Assessing the transfer of genetically modified DNA from feed to animal tissues. *Transgenic Research*, *14*(5), 775–784. http://doi.org/10.1007/s11248-005-0009-5

McCann, M. C., Liu, K., Trujillo, W. A., & Dobert, R. C. (2005). Glyphosate-Tolerant Soybeans Remain Compositionally Equivalent to Conventional Soybeans (Glycine max L.) during Three Years of Field Testing. *Journal of Agricultural and Food Chemistry*, *53*(13), 5331–5335. http://doi.org/10.1021/jf0504317

McDuffie, H. H., Pahwa, P., McLaughlin, J. R., Spinelli, J. J., Fincham, S., Dosman, J. A., Robson, D., Skinnider, L. F., & Choi, N. W. (2001). Non-Hodgkin's lymphoma and specific pesticide exposures in men: Cross-Canada study of pesticides and health. *Cancer Epidemiology, Biomarkers & Prevention: A Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, *10*(11), 1155–1163.

McGrath (2015). US wild bee numbers decline as land is converted for biofuel. BBC News. http://www.bbc.com/news/science-environment-35153196

McKay, B., & Colque, G. (2016). Bolivia's soy complex: the development of "productive exclusion." *The Journal of Peasant Studies*, 43(2), 583–610. http://doi.org/10.1080/03066150.2015.1053875

McVey, K. A., Snapp, I. B., Johnson, M. B., Negga, R., Pressley, A. S., & Fitsanakis, V. A. (2016). Exposure of C. elegans eggs to a glyphosate-containing herbicide leads to abnormal neuronal morphology. *Neurotoxicology and Teratology*, *55*, 23–31. https://doi.org/10.1016/j.ntt.2016.03.002

Medalie, L., Baker, N. T., Shoda, M. E., Stone, W. W., Meyer, M. T., Stets, E. G., & Wilson, M. (2020). Influence of land use and region on glyphosate and aminomethylphosphonic acid in streams in the USA. *Science of The Total Environment*, *707*, 136008. https://doi.org/10.1016/j.scitotenv.2019.136008

Meister, A. (1974). 23. Glutamine Synthetase of Mammals. In P. D. Boyer (Ed.), *The Enzymes* (Vol. 10, pp. 699–754). Academic Press. https://doi.org/10.1016/S1874-6047(08)60155-9

Meme, S., Calas, A.-G., Montécot, C., Richard, O., Gautier, H., Gefflaut, T., Doan, B. T., Même, W., Pichon, J., & Beloeil, J.-C. (2009). MRI Characterization of Structural Mouse Brain Changes in Response to Chronic Exposure to the Glufosinate Ammonium Herbicide. *Toxicological Sciences*, *111*(2), 321–330. https://doi.org/10.1093/toxsci/kfp174

Mello, F. de A., Silva, B. B. M., Barreiro, E. B. V., Franco, I. B., Nogueira, I. M., Chagas, P. H. N., Parizi, J. L. S., Pereira, D. R., Rossi, R. C., & Nai, G. A. (2020). Evaluation of genotoxicity after acute and chronic exposure to 2,4-dichlorophenoxyacetic acid herbicide (2,4-D) in rodents using machine learning algorithms. *The Journal of Toxicological Sciences*, *45*(12), 737–750. https://doi.org/10.2131/jts.45.737

Mendez, M. J., Aimar, S. B., Aparicio, V. C., Ramirez Haberkon, N. B., Buschiazzo, D. E., De Gerónimo, E., & Costa, J. L. (2017). Glyphosate and Aminomethylphosphonic acid (AMPA) contents in the respirable dust emitted by an agricultural soil of the central semiarid region of Argentina. *Aeolian Research*, *29*, 23–29. https://doi.org/10.1016/j.aeolia.2017.09.004

Mendonca, C. M., Reed, M. L., Kukurugya, M. A., & Aristilde, L. (2019). Adverse Metabolic Outcomes in Soil Pseudomonas Species Exposed to Polyethoxylated Tallow Amine and Glyphosate. *Environmental Science & Technology Letters*, *6*(8), 448–455. https://doi.org/10.1021/acs.estlett.9b00363

Menéndez-Helman, R. J., Miranda, L. A., Salibián, A., & dos Santos Afonso, M. (2020). Effects on Ultrastructure, Composition and Specific Surface Area of the Gills of Odontesthes bonariensis Under Subchronic Glyphosate-Based Herbicide Exposure. *Bulletin of Environmental Contamination and Toxicology*, *105*(6), 835–840. https://doi.org/10.1007/s00128-020-03031-4

Meriles, J. M., Vargas Gil, S., Haro, R. J., March, G. J., & Guzmán, C. A. (2006). Glyphosate and Previous Crop Residue Effect on Deleterious and Beneficial Soil-borne Fungi from a Peanut–Corn–Soybean Rotations. *Journal of Phytopathology*, *154*(5), 309–316. http://doi.org/10.1111/j.1439-0434.2006.01098.x

Mertens, M., Höss, S., Neumann, G., Afzal, J., & Reichenbecher, W. (2018). Glyphosate, a chelating agent—Relevant for ecological risk assessment? *Environmental Science and Pollution Research International*, *25*(6), 5298–5317. https://doi.org/10.1007/s11356-017-1080-1

Mesak, C., de Oliveira Mendes, B., de Oliveira Ferreira, R., & Malafaia, G. (2018). Mutagenic assessment of Lithobates catesbeianus tadpoles exposed to the 2,4-D herbicide in a simulated realistic scenario. *Environmental Science and Pollution Research International*, *25*(15), 15235–15244. https://doi.org/10.1007/s11356-018-1979-1

Mesnage, R., & Antoniou, M. N. (2018). Ignoring Adjuvant Toxicity Falsifies the Safety Profile of Commercial Pesticides. *Frontiers in Public Health*, *5*. https://www.frontiersin.org/article/10.3389/fpubh.2017.00361

Mesnage, R., Christian Moesch, Le Grand, R., Guillaume, L., Vendomois, J. S., Gress, S., & Séralini, G.-E. (2012). Glyphosate Exposure in a Farmer's Family. *Journal of Environmental Protection*, *03*(09), 1001–1003. http://doi.org/10.4236/jep.2012.39115

Mesnage, R., Bernay, B., & Séralini, G.-E. (2013). Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity. *Toxicology*, *313*(2–3), 122–128. http://doi.org/10.1016/j.tox.2012.09.006

Mesnage, R., Defarge, N., Vendomois, J. S., Séralini, G.-E. (2014). Major Pesticides Are More Toxic to Human Cells Than Their Declared Active Principles. *BioMed Research International*, *2014*, e179691. http://doi.org/10.1155/2014/179691

Mesnage, R., Agapito-Tenfen, S.Z., Vilperte, V., Renney, G., Ward, M., Séralini, G.-E., Nodari, R.O., Antoniou, M.N. (2016). An integrated multi-omics analysis of the NK603 Roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process. *Scientific Reports* **6**, 37855. doi:10.1038/srep37855

Mesnage, R., Renney, G., Séralini, G.-E., Ward, M., Antoniou, M.N. (2017). Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide. *Scientific Reports* **7**, 39328. doi:10.1038/srep39328

Mesnage, R., Benbrook, C., & Antoniou, M. N. (2019). Insight into the confusion over surfactant co-formulants in glyphosate-based herbicides. *Food and Chemical Toxicology*, *128*, 137–145. https://doi.org/10.1016/j.fct.2019.03.053

Mesnage, R., Oestreicher, N., Poirier, F., Nicolas, V., Boursier, C., & Vélot, C. (2020). Transcriptome profiling of the fungus *Aspergillus nidulans* exposed to a commercial glyphosate-based herbicide under conditions of apparent herbicide tolerance. *Environmental Research*, *182*, 109116. https://doi.org/10.1016/j.envres.2020.109116

Mesnage, R., Brandsma, I., Moelijker, N., Zhang, G., & Antoniou, M. N. (2021). Genotoxicity evaluation of 2,4-D, dicamba and glyphosate alone or in combination with cell reporter assays for DNA damage, oxidative stress and unfolded protein response. *Food and Chemical Toxicology*, *157*, 112601. https://doi.org/10.1016/j.fct.2021.112601

Meyer, C. J., & Norsworthy, J. K. (2019). Influence of weed size on herbicide interactions for Enlist™ and Roundup Ready® Xtend® technologies. Weed Technology, 33(4), 569–577. https://doi.org/10.1017/wet.2019.27

Meyer, C. J., Norsworthy, J. K., & Kruger, G. R. (2020). What antagonistic interactions mean for Enlist and Roundup Ready Xtend technologies. *Crop, Forage & Turfgrass Management*, *6*(1), e20044. https://doi.org/10.1002/cft2.20044

Mi, Y., Zhang, C., & Taya, K. (2007). Quercetin Protects Spermatogonial Cells from 2,4-D-Induced Oxidative Damage in Embryonic Chickens. *Journal of Reproduction and Development*, *53*(4), 749–754. https://doi.org/10.1262/jrd.19001

Michail, N. (2015). Non-GMO labels are on the rise in Europe – but why? Foodnavigator. http://www.foodnavigator.com/Market-Trends/Non-GMO-labels-are-on-the-rise-in-Europe-but-why

Michaud, J. P., & Vargas, G. (2010). Relative toxicity of three wheat herbicides to two species of Coccinellidae. *Insect Science*, *17*, 434–438. https://doi.org/10.1111/j.1744-7917.2009.01308.x

Milan, M., Dalla Rovere, G., Smits, M., Ferraresso, S., Pastore, P., Marin, M. G., Bogialli, S., Patarnello, T., Bargelloni, L., & Matozzo, V. (2018). Ecotoxicological effects of the herbicide glyphosate in non-target aquatic species: Transcriptional responses in the mussel Mytilus galloprovincialis. *Environmental Pollution (Barking, Essex: 1987)*, *237*, 442–451. https://doi.org/10.1016/j.envpol.2018.02.049

Milesi, M. M., Lorenz, V., Durando, M., Rossetti, M. F., & Varayoud, J. (2021). Glyphosate Herbicide: Reproductive Outcomes and Multigenerational Effects. *Frontiers in Endocrinology*, *12*. https://www.frontiersin.org/article/10.3389/fendo.2021.672532

Miller, R. V. & Jr. (2022, August 17). Monsanto Roundup Lawsuit Update. Lawsuit Information Center. https://www.lawsuit-information-center.com/roundup-mdl-judge-question-10-billion-settlement-proposal.html

Mills, P. K., & Yang, R. C. (2007). Agricultural exposures and gastric cancer risk in Hispanic farm workers in California. *Environmental Research*, *104*(2), 282–289. https://doi.org/10.1016/j.envres.2006.11.008

Mills, P. J., Caussy, C., & Loomba, R. (2019). Glyphosate Excretion is Associated With Steatohepatitis and Advanced Liver Fibrosis in Patients With Fatty Liver Disease. Clinical Gastroenterology and Hepatology : The Official Clinical Practice Journal of the American Gastroenterological Association, S1542-3565(19)30361-1. https://doi.org/10.1016/j.cgh.2019.03.045

Ministère de l'Environnement, de l'Énergie et de la Mer (2017) Ségolène Royal condamne la décision de l'ECHA de ne pas classer cancérogène probable le glyphosate et appelle les Ministres européens de l'Environnement à continuer à s'opposer à la réapprobation de la substance.16th March 2017. http://www.developpement-durable.gouv.fr/segolene-royal-condamne-decision-lecha-ne-pas-classer-cancerogene-probable-glyphosate-et-appelle

Minnesota Department of Agriculture. (2020). Pesticide Sales Database Search—Results. http://www2.mda.state.mn.us/webapp/lis/chemsold_results.jsp

Mitchell, D. G., Chapman, P. M., & Long, T. J. (1987). Acute toxicity of Roundup® and Rodeo® herbicides to rainbow trout, chinook, and coho salmon. Bulletin of Environmental Contamination and Toxicology, 39(6), 1028–1035. http://doi.org/10.1007/BF01689594

Miyazaki, J., Bauer-Panskus, A., Bøhn, T., Reichenbecher, W., & Then, C. (2019). Insufficient risk assessment of herbicide-tolerant genetically engineered soybeans intended for import into the EU. Environmental Sciences Europe, 31(1), 92. https://doi.org/10.1186/s12302-019-0274-1

Mizuguti, A., Yoshimura, Y., & Matsuo, K. (2009). Flowering phenologies and natural hybridization of genetically modified and wild soybeans under field conditions. *Weed Biology and Management*, *9*(1), 93–96. https://doi.org/10.1111/j.1445-6664.2008.00324.x

Mizuguti, A., Ohigashi, K., Yoshimura, Y., Kaga, A., Kuroda, Y., & Matsuo, K. (2010). Hybridization between GM soybean (Glycine max (L.) Merr.) and wild soybean (Glycine soja Sieb. Et Zucc.) under field conditions in Japan. *Environmental Biosafety Research*, *9*(1), 13–23. https://doi.org/10.1051/ebr/2010004

Mobli, A., Matloob, A., & Chauhan, B. S. (2020). Glyphosate-induced hormesis: Impact on seedling growth and reproductive potential of common sowthistle (*Sonchus oleraceus*). *Weed Science*, *68*(6), 605–611. https://doi.org/10.1017/wsc.2020.77

Moehs, C. P., Austill, W. J., Facciotti, D., Holm, A., Loeffler, D., Lu, Z., Mullenberg, J. C., Slade, A. J., Steine, M. N., Boxtel, J. van, & McGuire, C. (2020). *Development of non-transgenic glyphosate tolerant wheat by TILLING* (p. 2020.07.23.218883). https://doi.org/10.1101/2020.07.23.218883

Mohammadi, K., Sani, M. A., Safaei, P., Rahmani, J., Molaee-Aghaee, E., & Jafari, S. M. (2021). A systematic review and meta-analysis of the impacts of glyphosate on the reproductive hormones. *Environmental Science and Pollution Research*. https://doi.org/10.1007/s11356-021-16145-x

Mohapatra, S., Kumar, R., Sundaray, J. K., Patnaik, S. T., Mishra, C. S. K., & Rather, M. A. (2021). Structural damage in liver, gonads, and reduction in spawning performance and alteration in the haematological parameter of Anabas testudineus by glyphosate- a herbicide. *Aquaculture Research*, *52*(3), 1150–1159. https://doi.org/10.1111/are.14973

Molin, W. T. (2019). How Amaranthus Palmeri Evolved from an Obscure North American Plant to Become the Biggest Weed Problem in the US Corn and Soybean Belt. *Outlooks on Pest Management*, *30*(4), 176–179. https://doi.org/10.1564/v30_aug_08

Mollaee, M., Mobli, A., & Chauhan, B. S. (2020). The response of glyphosate-resistant and glyphosate-susceptible biotypes of Echinochloa colona to carbon dioxide, soil moisture and glyphosate. *Scientific Reports*, *10*(1), 329. https://doi.org/10.1038/s41598-019-57307-9

Møller, P. (2015). Roundup kommer på Arbejdstilsynets kræftliste. http://nyhederne.tv2.dk/2015-05-28-roundup-kommer-paa-arbejdstilsynets-kraeftliste

Moms Across America and Sustainable Pulse (2014). Glyphosate Testing Report: Findings in American Mothers' Breast Milk, Urine and Water. http://www.momsacrossamerica.com/glyphosate_testing_results

Monarch ESA petition (2014). Petition to Protect the Monarch Butterfly (Danaus Plexippus plexippus) Under the Endangered Species Act. http://www.centerforfoodsafety.org/files/monarch-esa-petition-final_61585.pdf (23.09.14).

MonarchLab (2014). Global Distribution. http://monarchlab.org/biology-and-research/biology-and-natural-history/global-distribution

Monastersky, R. (2014). Biodiversity: Life – a status report. *Nature News*, *516*(7530), 158. https://doi.org/10.1038/516158a

Monsanto (1993). Petition for Determination of Nonregulated Status: Soybeans with a Roundup Ready™ Gene Monsanto# 93-089U http://www.aphis.usda.gov/brs/aphisdocs/93_25801p.pdf

Monsanto (2005a). Backgrounder – History of Monsantos's glyphosate Herbicides. www.monsanto.com/products/documents/glyphosate-background-materials/back_history.pdf

Monsanto (2005b). Backgrounder – No Restricion of Autumn Use of glyphosate in Denmark. http://www.monsanto.com/products/documents/glyphosate-background-materials/denmark_bkg_05.pdf

Monsanto (2012a). Weed Management in Genuity® Roundup Ready® Corn 2 For Tough-to-Control Weeds in California & Arizona. http://www.monsanto.com/sitecollectiondocuments/wswms-rr-corn-guide.pdf

Monsanto (2012b). "Petition for the Determination of Nonregulated Status for Dicamba-Tolerant Soybean MON 87708." Submitted by Mannion, Rhonda M., Registration Manager. Monsanto Company. St. Louis, MO. http://www.aphis.usda.gov/brs/aphisdocs/10_18801p.pdf

Monsanto (2012c). "Petition for the Determination of Nonregulated Status for Dicamba and Glufosinate-Tolerant Cotton MON 88701." Submitted by Marianne Malven, Registration Manager. Monsanto Company. St. Louis, MO. http://www.aphis.usda.gov/brs/aphisdocs/12_18501p.pdf.

Monsanto (2014). Helping Protect the Monarch Butterfly. http://monsantoblog.com/2014/09/12/helping-protect-the-monarch-butterfly/

Monsanto (2015a). Petition for the Determination of Nonregulated Status for Dicamba and Glufosinate Tolerant MON 87419 Maize. https://www.aphis.usda.gov/brs/aphisdocs/15_11301p.pdf

Monsanto (2015b). Monsanto Reinforces Decades of Data and Regulatory Review Clearly Document Safety of Glyphosate. http://news.monsanto.com/press-release/research-and-development/monsanto-reinforces-decades-data-and-regulatory-review-clearl

Monsanto. (2019, June 27). *Petition for the Determination of Nonregulated Status for Dicamba, Glufosinate, Quizalofop and 2,4-Dichlorophenoxyacetic Acid Tolerant MON 87429 Maize with Tissue-Specific Glyphosate Tolerance Facilitation the Production of Hybrid Maize Seed.* https://www.aphis.usda.gov/brs/aphisdocs/19_31601p.pdf

Montiel-León, J. M., Munoz, G., Vo Duy, S., Do, D. T., Vaudreuil, M.-A., Goeury, K., Guillemette, F., Amyot, M., & Sauvé, S. (2019). Widespread occurrence and spatial distribution of glyphosate, atrazine, and neonicotinoids pesticides in the St. Lawrence and tributary rivers. Environmental Pollution, 250, 29–39. https://doi.org/10.1016/j.envpol.2019.03.125

Moore, L. J., Fuentes, L., Rodgers Jr., J. H., Bowerman, W. W., Yarrow, G. K., Chao, W. Y., & Bridges Jr., W. C. (2012). Relative toxicity of the components of the original formulation of Roundup® to five North American anurans. *Ecotoxicology and Environmental Safety*, *78*, 128–133. http://doi.org/10.1016/j.ecoenv.2011.11.025

Moorman, T. B., Becerril, J. M., Lydon, J., & Duke, S. O. (1992). Production of hydroxybenzoic acids by Bradyrhizobium japonicum strains after treatment with glyphosate. *Journal of Agricultural and Food Chemistry*, *40*(2), 289–293. http://doi.org/10.1021/jf00014a025

Morandin, L.A., Winston, M.L. (2005). Wild Bee Abundance and Seed Production in Conventional, Organic, and Genetically Modified Canola. *Ecological Applications* **15**, 871–881. doi:10.1890/03-5271

Mordor Intelligence. (n.d.). Non-GMO Foods Market | 2022—27 | Industry Share, Size, Growth—Mordor Intelligence. Retrieved 8 June 2022, from https://www.mordorintelligence.com/industry-reports/non-gmo-foods-market

Moreby, S. J., Aebischer, N. J., Southway, S. E., & Sotherton, N. W. (1994). A comparison of the flora and arthropod fauna of organically and conventionally grown winter wheat in southern England. *Annals of Applied Biology*, *125*(1), 13–27. http://doi.org/10.1111/j.1744-7348.1994.tb04942.x

Moretti, M. L., Van Horn, C. R., Robertson, R., Segobye, K., Weller, S. C., Young, B. G., Johnson, W. G., Douglas Sammons, R., Wang, D., Ge, X., d' Avignon, A., Gaines, T. A., Westra, P., Green, A. C., Jeffery, T., Lespérance, M. A., Tardif, F. J., Sikkema, P. H., Christopher Hall, J., … Schulz, B. (2018). Glyphosate resistance in Ambrosia trifida: Part 2. Rapid response physiology and non-target-site resistance. *Pest Management Science*, *74*(5), 1079–1088. https://doi.org/10.1002/ps.4569

Mortensen, D. A., Egan, J. F., Maxwell, B. D., Ryan, M. R., & Smith, R. G. (2012). Navigating a Critical Juncture for Sustainable Weed Management. *BioScience*, *62*(1), 75–84. http://doi.org/10.1525/bio.2012.62.1.12

Motta, E. V. S., Raymann, K., & Moran, N. A. (2018). Glyphosate perturbs the gut microbiota of honey bees. *Proceedings of the National Academy of Sciences*, *115*(41), 10305–10310. https://doi.org/10.1073/pnas.1803880115

Motta, E. V. S., Mak, M., Jong, T. K. D., Powell, J. E., O'Donnell, A., Suhr, K. J., Riddington, I. M., & Moran, N. A. (2020). Oral and topical exposure to glyphosate in herbicide formulation impact the gut microbiota and survival rates of honey bees. *Applied and Environmental Microbiology*. https://doi.org/10.1128/AEM.01150-20

Motta, E. V. S., Powell, J. E., & Moran, N. A. (2022). Glyphosate induces immune dysregulation in honey bees. *Animal Microbiome*, *4*(1), 16. https://doi.org/10.1186/s42523-022-00165-0
Moutinho, M. F., de Almeida, E. A., Espíndola, E. L. G., Daam, M. A., & Schiesari, L. (2020). Herbicides employed in sugarcane plantations have lethal and sublethal effects to larval Boana pardalis (Amphibia, Hylidae). *Ecotoxicology*, *29*(7), 1043–1051. https://doi.org/10.1007/s10646-020-02226-z
MS Technologies. (2020a). *About GT27™ Soybeans*. http://www.gt27soybeans.com/about/
MS Technologies. (2020b). *GT27™*. http://www.mstechseed.com/traits/gt27/
Muller, K., Herrera, K., Talyn, B., & Melchiorre, E. (2021). Toxicological Effects of Roundup® on Drosophila melanogaster Reproduction. *Toxics*, *9*(7), 161. https://doi.org/10.3390/toxics9070161
Müller, B. (2021). Glyphosate—A love story. Ordinary thoughtlessness and response-ability in industrial farming. *Journal of Agrarian Change*, *21*(1), 160–179. https://doi.org/10.1111/joac.12374
Munira, S., Farenhorst, A., Flaten, D., & Grant, C. (2016). Phosphate fertilizer impacts on glyphosate sorption by soil. *Chemosphere*, *153*, 471–477. https://doi.org/10.1016/j.chemosphere.2016.03.028
Muñoz, J. P., Bleak, T. C., & Calaf, G. M. (2021). Glyphosate and the key characteristics of an endocrine disruptor: A review. *Chemosphere*, *270*, 128619. https://doi.org/10.1016/j.chemosphere.2020.128619
Munro, A. (2008). The spatial impact of genetically modified crops. *Ecological Economics*, *67*(4), 658–666. http://doi.org/10.1016/j.ecolecon.2008.01.030
Murschell, T., & Farmer, D. K. (2019). Real-Time Measurement of Herbicides in the Atmosphere: A Case Study of MCPA and 2,4-D during Field Application. *Toxics*, *7*(3), 40. https://doi.org/10.3390/toxics7030040
Muscatine Journal (2016) Midwest Corn Lawsuit continues the fight against Syngenta in court. 14 June 2016. http://muscatinejournal.com/news/local/muscatine/midwest-corn-lawsuit-continues-the-fight-against-syngenta-in-court/article_a3abbcd5-8bb3-5829-b418-372f7aaca854.html?utm_content=buffer1cd48&utm_medium=social&utm_source=twitter.com&utm_campaign=buffer
Murphy, B. P., Larran, A. S., Ackley, B., Loux, M. M., & Tranel, P. J. (2019). Survey of glyphosate-, atrazine- and lactofen-resistance mechanisms in Ohio waterhemp (Amaranthus tuberculatus) populations. *Weed Science*, *67*(3), 296–302. https://doi.org/10.1017/wsc.2018.91
Myers, J. P., Antoniou, M. N., Blumberg, B., Carroll, L., Colborn, T., Everett, L. G., … Benbrook, C. M. (2016). Concerns over use of glyphosate-based herbicides and risks associated with exposures: a consensus statement. *Environmental Health*, *15*(1). http://doi.org/10.1186/s12940-016-0117-0
NABC. (1998). *Vision for Agricultural Research and Development in the 21st Century*. US National Agricultural Biotechnology Council. http://nabc.cals.cornell.edu/Publications/WhitePapers/NABCvision.pdf
Nagy, K., Duca, R. C., Lovas, S., Creta, M., Scheepers, P. T. J., Godderis, L., & Ádám, B. (2020). Systematic review of comparative studies assessing the toxicity of pesticide active ingredients and their product formulations. *Environmental Research*, *181*, 108926. https://doi.org/10.1016/j.envres.2019.108926
Nakayama, Y., & Yamaguchi, H. (2002). Natural hybridization in wild soybean (Glycine max ssp. Soja) by pollen flow from cultivated soybean (Glycine max ssp. Max) in a designed population. *Weed Biology and Management*, *2*, 25–30. https://doi.org/10.1046/j.1445-6664.2002.00043.x
Nam, K.-H., Kim, D. Y., Moon, Y. S., Pack, I. S., Jeong, S.-C., Park, K. W., & Kim, C.-G. (2019). Gene Flow from Transgenic PPO-inhibiting Herbicide-resistant Rice to Weedy Rice, and Agronomic Performance by Their Hybrids. *Journal of Plant Biology*, *62*(4), 286–296. https://doi.org/10.1007/s12374-019-0013-6
Nandula, V. K. (2019). Herbicide Resistance Traits in Maize and Soybean: Current Status and Future Outlook. *Plants*, *8*(9), 337. https://doi.org/10.3390/plants8090337
Nandula, V. K., Reddy, K. N., Duke, S. O., & Poston, D. H. (2005). Glyphosate-Resistant Weeds: Current Status and Future Outlook. *Outlooks on Pest Management*, *16*(4), 183–187. http://doi.org/10.1564/16aug11
Nandula, V. K., Wright, A. A., Bond, J. A., Ray, J. D., Eubank, T. W., & Molin, W. T. (2014). EPSPS amplification in glyphosate-resistant spiny amaranth (Amaranthus spinosus): a case of gene transfer via interspecific hybridization from glyphosate-resistant Palmer amaranth (Amaranthus palmeri). *Pest Management Science*, *70*(12), 1902–1909. http://doi.org/10.1002/ps.3754
Nandula, V. K., Montgomery, G. B., Vennapusa, A. R., Jugulam, M., Giacomini, D. A., Ray, J. D., Bond, J. A., Steckel, L. E., & Tranel, P. J. (2018). Glyphosate-Resistant Junglerice (Echinochloa colona) from Mississippi and Tennessee: Magnitude and Resistance Mechanisms. *Weed Science*, *66*(5), 603–610. https://doi.org/10.1017/wsc.2018.51
Nardi, J., Moras, P. B., Koeppe, C., Dallegrave, E., Leal, M. B., & Rossato-Grando, L. G. (2017). Prepubertal subchronic exposure to soy milk and glyphosate leads to endocrine disruption. *Food and Chemical Toxicology*, *100*, 247–252. https://doi.org/10.1016/j.fct.2016.12.030
National Family Farm Coalition v. USEPA, No. 17–70196 (United States Court of Appeals for the Ninth Circuit June 3, 2020). https://www.courthousenews.com/wp-content/uploads/2020/06/Dicamba.pdf
Nature (2014). A growing problem *Nature*, *510*(7504), 187–187. http://doi.org/10.1038/510187a

Nawaz, M. A., Mesnage, R., Tsatsakis, A. M., Golokhvast, K. S., Yang, S. H., Antoniou, M. N., & Chung, G. (2019). Addressing concerns over the fate of DNA derived from genetically modified food in the human body: A review. *Food and Chemical Toxicology*, *124*, 423–430. https://doi.org/10.1016/j.fct.2018.12.030

NBC News (2015). Monsanto will pay $350K to settle more GM wheat lawsuits. http://www.nbcnews.com/news/us-news/monsanto-pay-350k-settle-more-wheat-related-lawsuits-n326811

NDP (2016) NDP calls for mandatory labelling of genetically modified foods. 14 June 2016. http://www.ndp.ca/news/ndp-calls-mandatory-labelling-genetically-modified-foods

Neeley, T. (2018, February 2). *Dicamba Cases Consolidated in St. Louis—Court: Combining Cases Will Eliminate Duplicative Discovery, Inconsistent Rulings*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/news/article/2018/02/02/complex-issues-seen-factor-decision

Neill, C., Coe, M. T., Riskin, S. H., Krusche, A. V., Elsenbeer, H., Macedo, M. N., … Deegan, L. A. (2013). Watershed responses to Amazon soya bean cropland expansion and intensification. *Phil. Trans. R. Soc. B*, 368(1619), 20120425. http://doi.org/10.1098/rstb.2012.0425

Nelsen A (2017) Glyphosate weedkiller, previously linked to cancer, judged safe by EU watchdog. The Guardian. 15th March 2017. https://www.theguardian.com/environment/2017/mar/15/no-cancer-risk-to-using-glyphosate-weedkiller-says-eu-watchdog?CMP=Share_iOSApp_Other

Neumeister, L. (2014). The risks of the herbicide 2,4-D. Testbiotech, GeneWatch UK, Pesticides Action Network Europe. http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/Risks_of_herbicide_2_4_D.pdf

Newman, M. M., Hoilett, N., Lorenz, N., Dick, R. P., Liles, M. R., Ramsier, C., & Kloepper, J. W. (2016). Glyphosate effects on soil rhizosphere-associated bacterial communities. *Science of The Total Environment*, *543, Part A*, 155–160. http://doi.org/10.1016/j.scitotenv.2015.11.008

New York City Council Member Ben Kallos (2015). Toxic Pesticides in Parks Would be Limited by Council Legislation. http://us3.campaign-archive1.com/?u=9bbabc6df7d331ba5d549651a&id=274840a4eb&e=2386c808b1

NFWF & Monsanto (2015). National Fish and Wildlife Foundation and Monsanto Announce Commitment to Help Monarch Butterflies. http://globenewswire.com/news-release/2015/03/31/720663/10127026/en/National-Fish-and-Wildlife-Foundation-and-Monsanto-Announce-Commitment-to-Help-Monarch-Butterflies.html

Ng, C. H., Wickneswari, R., Salmijah, S., Teng, Y. T., & Ismail, B. S. (2003). Gene polymorphisms in glyphosate-resistant and -susceptible biotypes of Eleusine indica from Malaysia. *Weed Research*, *43*(2), 108–115. http://doi.org/10.1046/j.1365-3180.2003.00322.x

Ngo, T. D., Malone, J. M., Boutsalis, P., Gill, G., & Preston, C. (2018). EPSPS gene amplification conferring resistance to glyphosate in windmill grass (Chloris truncata) in Australia. *Pest Management Science*, *74*(5), 1101–1108. https://doi.org/10.1002/ps.4573

NHNES (2022) National Health and Nutrition Examination Survey. Glyphosate (GLYP) - Urine (SSGLYP_H). June 2022. https://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/SSGLYP_H.htm#Component_Description

Nichols, R. L. (2018). Impacts of Weed Resistance to Herbicides on United States (U.S.) Cotton (*Gossypium Hirsutum*) Production. *Outlooks on Pest Management*, *29*(1), 5–9. https://doi.org/10.1564/v29_feb_02

Nicolas, V., Oestreicher, N., & Vélot, C. (2016). Multiple effects of a commercial Roundup® formulation on the soil filamentous fungus Aspergillus nidulans at low doses: Evidence of an unexpected impact on energetic metabolism. *Environmental Science and Pollution Research International*, *23*(14), 14393–14404. https://doi.org/10.1007/s11356-016-6596-2

Niedobová, J., Skalský, M., Ouředníčková, J., Michalko, R., & Bartošková, A. (2019a). Synergistic effects of glyphosate formulation herbicide and tank-mixing adjuvants on Pardosa spiders. *Environmental Pollution*, *249*, 338–344. https://doi.org/10.1016/j.envpol.2019.03.031

Niedobová, J., Krištofová, L., Michalko, R., Hula, V., Kýnický, J., & Brtnický, M. (2019b). Effects of glufosinate-ammonium herbicide and pod sealant on spider Pardosa agrestis. *Journal of Applied Entomology*, *143*(3), 196–203. https://doi.org/10.1111/jen.12574

Niedobová, J., Ouředníčková, J., Michalko, R., & Skalský, M. (2022). The toxicity of the glyphosate herbicide for Pardosa spiders' predatory activity depends on the formulation of the glyphosate product. Environmental Chemistry Letters, 20(2), 983–990. https://doi.org/10.1007/s10311-022-01391-3

Nishizawa, T., Nakajima, N., Aono, M., Tamaoki, M., Kubo, A., & Saji, H. (2009). Monitoring the occurrence of genetically modified oilseed rape growing along a Japanese roadside: 3-year observations. *Environmental Biosafety Research*, *8*(1), 33–44. http://doi.org/10.1051/ebr/2009001

No. 14-73359 (2015). Oral Argument Not Yet Scheduled United States Court of Appeals for the Ninth Circuit. http://www.biologicaldiversity.org/campaigns/pesticides_reduction/pdfs/2015-11-24_EPA_Voluntary_Vacatur.pdf

Noguera, M. M., Porri, A., Werle, I. S., Heiser, J., Brändle, F., Lerchl, J., Murphy, B., Betz, M., Gatzmann, F., Penkert, M., Tuerk, C., Meyer, L., & Roma-Burgos, N. (2022). Involvement of glutamine synthetase 2 (GS2) amplification and overexpression in Amaranthus palmeri resistance to glufosinate. *Planta*, *256*(3), 57. https://doi.org/10.1007/s00425-022-03968-2

Nolan, E., & Santos, P. (2012). The Contribution of Genetic Modification to Changes in Corn Yield in the United States. *American Journal of Agricultural Economics*, aas069. http://doi.org/10.1093/ajae/aas069

Nomura, H., Hamada, R., Wada, K., Saito, I., Nishihara, N., Kitahara, Y., Watanabe, S., Nakane, K., Nagata, C., Kondo, T., Kamijima, M., & Ueyama, J. (2022). Temporal trend and cross-sectional characterization of urinary concentrations of glyphosate in Japanese children from 2006 to 2015. *International Journal of Hygiene and Environmental Health*, *242*, 113963. https://doi.org/10.1016/j.ijheh.2022.113963

Non-GMO Project (2014). Non-GMO Month 2014 a Resounding Success. http://www.nongmoproject.org/2014/11/14/non-gmo-month-2014-a-resounding-success/

Non-GMO Project (2015). Non-GMO Month 2015 Sets New Records, Generates Further Awareness. Living Non-GMO. http://livingnongmo.org/2015/11/06/wrap-up-non-gmo-month-2015/

Non-GMO Project (2022) Product Verification. https://www.nongmoproject.org/product-verification/

Norsworthy, J. K., Griffith, G., Griffin, T., Bagavathiannan, M., & Gbur, E. E. (2014). In-Field Movement of Glyphosate-Resistant Palmer Amaranth (*Amaranthus palmeri*) and Its Impact on Cotton Lint Yield: Evidence Supporting a Zero-Threshold Strategy. *Weed Science*, *62*(2), 237–249. http://doi.org/10.1614/WS-D-13-00145.1

No-Till Farmer (2016) Scientists: Glyphosate Contributes to Phosphorus Runoff in Lake Erie. 11 June 2016. https://www.no-tillfarmer.com/articles/5793-scientists-glyphosate-contributes-to-phosphorus-runoff-in-lake-erie#sthash.LI6eKmLW.dpuf

NPR (2016) How Monsanto And Scofflaw Farmers Hurt Soybeans In Arkansas. 1 August 2016. http://www.npr.org/sections/thesalt/2016/08/01/487809643/crime-in-the-fields-how-monsanto-and-scofflaw-farmers-hurt-soybeans-in-arkansas

NRDC (2014). Petition to Conduct Interim Administrative Review for the Pesticide Glyphosate, in Light of Serious Harm to Monarch Butterflies. http://docs.nrdc.org/wildlife/files/wil_14022101a.pdf

Nye, M., Hoilett, N., Ramsier, C., Renz, P., & P. Dick, R. (2014). Microbial Community Structure in Soils Amended With Glyphosate-tolerant Soybean Residue. *Applied Ecology and Environmental Sciences*, *2*(3), 74–81. http://doi.org/10.12691/aees-2-3-1

Obidike, I. R., Aka, L. O., Omoja, V. U., Shoyinka, S. V. O., Kamalu, T. N., & Anika, S. M. (2012). Testicular morphology and antispermatogenic effects of 2,4-dichlorophenoxyacetic acid (2,4-D) in male West African Dwarf (WAD) goats. Comparative Clinical Pathology, 21(6), 1457–1462. https://doi.org/10.1007/s00580-011-1314-4

OCA (2015). World's First Public Testing for Monsanto's Glyphosate Begins Today. Organic Consumer Association. https://www.organicconsumers.org/press/world’s-first-public-testing-monsanto’s-glyphosate-begins-today

Odetti, L. M., López González, E. C., Romito, M. L., Simoniello, M. F., & Poletta, G. L. (2020). Genotoxicity and oxidative stress in Caiman latirostris hatchlings exposed to pesticide formulations and their mixtures during incubation period. *Ecotoxicology and Environmental Safety*, *193*, 110312. https://doi.org/10.1016/j.ecoenv.2020.110312

Oehen, B., Quiédeville, S., & Stolze, M. (2018). *Socio-economic impacts of GMOs on European Agriculture*. https://www.researchgate.net/publication/323607469_Socio-economic_impacts_of_GMOs_on_European_Agriculture

Okada, E., Pérez, D., De Gerónimo, E., Aparicio, V., Massone, H., & Costa, J. L. (2018). Non-point source pollution of glyphosate and AMPA in a rural basin from the southeast Pampas, Argentina. *Environmental Science and Pollution Research*, *25*(15), 15120–15132. https://doi.org/10.1007/s11356-018-1734-7

Okuzaki, A., & Toriyama, K. (2004). Chimeric RNA/DNA oligonucleotide-directed gene targeting in rice. *Plant Cell Reports*, *22*(7), 509–512. https://doi.org/10.1007/s00299-003-0698-2

Oliva, A., Biasatti, R., Cloquell, S., González, C., Olego, S., & Gelin, A. (2008). Is there any relationship between rural environmental factors and reproductive health in the Pampa Humeda in Argentina? *Cadernos de Saúde Pública*, 24(4), 785–792. http://doi.org/10.1590/S0102-311X2008000400008

Oliveira, A. G., Telles, L. F., Hess, R. A., Mahecha, G. A. B., & Oliveira, C. A. (2007). Effects of the herbicide Roundup on the epididymal region of drakes Anas platyrhynchos. *Reproductive Toxicology (Elmsford, N.Y.)*, *23*(2), 182–191. https://doi.org/10.1016/j.reprotox.2006.11.004

Oliveira, N. P., Moi, G. P., Atanaka-Santos, M., Silva, A. M. C., & Pignati, W. A. (2014). Malformações congênitas em municípios de grande utilização de agrotóxicos em Mato Grosso, Brasil. *Ciência & Saúde Coletiva*, 19(10), 4123–4130. http://doi.org/10.1590/1413-812320141910.08512014

Oliveira, G., & Hecht, S. (2016). Sacred groves, sacrifice zones and soy production: globalization, intensification and neo-nature in South America. *The Journal of Peasant Studies*, 43(2), 251–285. http://doi.org/10.1080/03066150.2016.1146705

Oliveira, R. de C., Boas, L. K. V., & Branco, C. C. Z. (2016). Assessment of the potential toxicity of glyphosate-based herbicides on the photosynthesis of Nitella microcarpa var. Wrightii (Charophyceae). *Phycologia*, *55*(5), 577–584. https://doi.org/10.2216/16-12.1

Oliver, M. (2020, June 4). Broadacre spot spraying kits: All you need to know. *Farmers Weekly*. https://www.fwi.co.uk/machinery/technology/broadacre-spot-spraying-kits-all-you-need-to-know

Ortega, E., Cavalett, O., Bonifácio, R., & Watanabe, M. (2005). Brazilian Soybean Production: Emergy Analysis With an Expanded Scope. *Bulletin of Science, Technology and Society*, 25(4), 323–334. http://doi.org/10.1177/0270467605278367
Ortega, J. L., Rajapakse, W., Bagga, S., Apodaca, K., Lucero, Y., & Sengupta-Gopalan, C. (2018). An intragenic approach to confer glyphosate resistance in chile (Capsicum annuum) by introducing an in vitro mutagenized chile EPSPS gene encoding for a glyphosate resistant EPSPS protein. *PLoS ONE*, *13*(4), e0194666. https://doi.org/10.1371/journal.pone.0194666
Osipova, E., Shi, Y., Kormos, C., Shadie, P., Zwahlen, C., Badman, T. (2014). IUCN World Heritage Outlook 2014: A conservation assessment of all natural World Heritage sites. Gland, Switzerland: IUCN. 64pp.
Osten, J. R., Soares, A. M. V. M., & Guilhermino, L. (2005). Black-bellied whistling duck (Dendrocygna autumnalis) brain cholinesterase characterization and diagnosis of anticholinesterase pesticide exposure in wild populations from Mexico. *Environmental Toxicology and Chemistry*, *24*(2), 313–317. https://doi.org/10.1897/03-646.1
OTA. (1981). Impacts of Applied Genetics: Micro-Organisms, Plants, and Animals (No. NTIS order #PB81-206609). US Office of Technology Assessment. https://ota.fas.org/reports/8115.pdf
OTA (2015). There's more to organic than meets the eye. Organic Trade Association. http://ota.com/sites/default/files/indexed_files/PolicyConference2015_Infographic_8.5x11_1a_0.pdf
Owagboriaye, F. O., Dedeke, G. A., Ademolu, K. O., Olujimi, O. O., Ashidi, J. S., & Adeyinka, A. A. (2017). Reproductive toxicity of Roundup herbicide exposure in male albino rat. Experimental and Toxicologic Pathology, 69(7), 461–468. https://doi.org/10.1016/j.etp.2017.04.007
Owagboriaye, F., Mesnage, R., Dedeke, G., Adegboyega, T., Aladesida, A., Adeleke, M., Owa, S., & Antoniou, M. N. (2021). Impacts of a glyphosate-based herbicide on the gut microbiome of three earthworm species (Alma millsoni, Eudrilus eugeniae and Libyodrilus violaceus): A pilot study. *Toxicology Reports*, *8*, 753–758. https://doi.org/10.1016/j.toxrep.2021.03.021
Packaged Facts (2015). Packaged Facts: Global Non-GMO Food & Beverage Market Reaches $550 Billion, U.S. Sales at $200 Billion. http://www.prnewswire.com/news-releases/packaged-facts-global-non-gmo-food--beverage-market-reaches-550-billion-us-sales-at-200-billion-300127127.html
Padgette, S. R., Biest Taylor, N., Nida, D. L., Bailey, M. R., MacDonald, J., Holden, L. R., & Fuchs, R. L. (1996). The composition of glyphosate-tolerant soybean seeds is equivalent to that of conventional soybeans. *Journal of Nutrition*, *126*(3), 702–716.
Paganelli, A., Gnazzo, V., Acosta, H., López, S. L., & Carrasco, A. E. (2010). Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling. *Chemical Research in Toxicology*, *23*(10), 1586–1595. http://doi.org/10.1021/tx1001749
Página 12 (2016) Cosecha soja, siembra inundación. 27 April 2016. http://www.pagina12.com.ar/diario/sociedad/3-297922-2016-04-27.html
Paixão, F. (2020, November 18). *Transgenic HB4 wheat approved in Argentina has negative side effects*. Brasil de Fato. https://www.brasildefato.com.br/2020/11/18/transgenic-hb4-wheat-approved-in-argentina-generates-negative-side-effects
Pal, E., Almasri, H., Paris, L., Diogon, M., Pioz, M., Cousin, M., Sené, D., Tchamitchian, S., Tavares, D. A., Delbac, F., Blot, N., Brunet, J.-L., & Belzunces, L. P. (2022). Toxicity of the Pesticides Imidacloprid, Difenoconazole and Glyphosate Alone and in Binary and Ternary Mixtures to Winter Honey Bees: Effects on Survival and Antioxidative Defenses. *Toxics*, *10*(3), 104. https://doi.org/10.3390/toxics10030104
Palmeira, C. M., Moreno, A. J., & Madeira, V. M. C. (1995). Thiols metabolism is altered by the herbicides paraquat, dinoseb and 2,4-D: A study in isolated hepatocytes. *Toxicology Letters*, *81*(2), 115–123. https://doi.org/10.1016/0378-4274(95)03414-5
PAN Asia and Pacific (2008) Monograph on Glyphosate. http://www.panap.net/sites/default/files/monograph_glyphosate.pdf
PAN Asia and Pacific (2012) Monogram on Glyphosate: Addendum 2012. http://www.panap.net/sites/default/files/monograph_glyphosate-addendum-2012.pdf
PAN Germany (2017a) The Carcinogenic Hazard of Glyphosate: BfR's "Weight of Evidence Approach". Hamburg, March 2017. http://www.pangermany.org/download/The_Carcinogenic_Hazard_of_Glyphosate.pdf
PAN Germany (2017b) Clean bill of health for glyphosate - a fatal decision of ECHA. 16th March 2017. http://www.pan-germany.org/deu/~news-1445.html
PAN International (2015). Glyphosate confirmed as a probable human carcinogen by the World Health Organization: Pesticide joins international 'highly hazardous' list slated for phaseout. http://www.panap.net/campaigns/hhps/pan-international/post/2653
PAN International. (2019). *PAN International List of Highly Hazardous Pesticides*. Pesticide Action Network International. http://pan-international.org/wp-content/uploads/PAN_HHP_List.pdf
PAN UK & GM Freeze (2013). The Herbicide Treadmill in Roundup Ready Crops. http://www.gmfreeze.org/site_media/uploads/publications/glyphosate_doc_with_PAN.pdf

PAN UK (2017) PAN UK dismayed by ECHA opinion on Glyphosate. 15th March 2017. http://www.pan-uk.org/pan-uk-dismayed-echa-opinion-glyphosate/

Pandolfo, C. E., Presotto, A., Carbonell, F. T., Ureta, S., Poverene, M., & Cantamutto, M. (2016). Transgenic glyphosate-resistant oilseed rape (Brassica napus) as an invasive weed in Argentina: Detection, characterization, and control alternatives. *Environmental Science and Pollution Research*, *23*(23), 24081–24091. https://doi.org/10.1007/s11356-016-7670-5

Pannell, D.J., Tillie, P., Rodríguez-Cerezo, E., Ervin, D., Frisvold, G.B., 2017. Herbicide Resistance: Economic and Environmental Challenges. *AgBioForum* **19**, 5.

Pantsios, A. (2015). Monsanto Demands World Health Organization Retract Report That Says Roundup Is Linked to Cancer. EcoWatch. http://ecowatch.com/2015/03/26/monsanto-demands-who-retract-report/

Park, K., Park, J., Kim, J., & Kwak, I.-S. (2010). Biological and molecular responses of Chironomus riparius (Diptera, Chironomidae) to herbicide 2,4-D (2,4-dichlorophenoxyacetic acid). *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *151*(4), 439–446. https://doi.org/10.1016/j.cbpc.2010.01.009

Parks, C.G., Hoppin, J.A., De Roos, A. J., Costenbader, K. H., Alavanja, M. C., & Sandler, D. P. (2016). Rheumatoid Arthritis in Agricultural Health Study Spouses: Associations with Pesticides and Other Farm Exposures. *Environmental Health Perspectives*, *124*(11), 1728–1734. https://doi.org/10.1289/EHP129

Parrish, J. T. (2015). Investigations into Multiple-Herbicide-Resistant *Ambrosia artemisiifolia* (Common Ragweed) in Ohio and Glyphosate-Resistance Mechanisms. Dissertation. Graduate Program in Horticulture and Crop Science. The Ohio State University.

Parvez, S., Gerona, R. R., Proctor, C., Friesen, M., Ashby, J. L., Reiter, J. L., Lui, Z., & Winchester, P. D. (2018). Glyphosate exposure in pregnancy and shortened gestational length: A prospective Indiana birth cohort study. *Environmental Health*, *17*, 23. https://doi.org/10.1186/s12940-018-0367-0

Pates, M. (2015). Herbicide-resistant weed jumps 60 miles in a year. Grand Forks Herals. http://www.grandforksherald.com/news/agriculture/3809608-herbicide-resistant-weed-jumps-60-miles-year

Paull, J. (2018). Genetically Modified Organisms (GMOs) as Invasive Species. *Journal of Environment Protection and Sustainable Development*, *4*(3), 31–37.

Pavan, F. A., Samojeden, C. G., Rutkoski, C. F., Folador, A., Da Fré, S. P., Müller, C., Hartmann, P. A., & Hartmann, M. T. (2021). Morphological, behavioral and genotoxic effects of glyphosate and 2,4-D mixture in tadpoles of two native species of South American amphibians. *Environmental Toxicology and Pharmacology*, *85*, 103637. https://doi.org/10.1016/j.etap.2021.103637

Peluso, J., Furió Lanuza, A., Pérez Coll, C. S., & Aronzon, C. M. (2021). Synergistic effects of glyphosate- and 2,4-D-based pesticides mixtures on Rhinella arenarum larvae. *Environmental Science and Pollution Research*. https://doi.org/10.1007/s11356-021-16784-0

Peltzer, P. M., Junges, C. M., Attademo, A. M., Bassó, A., Grenón, P., & Lajmanovich, R. C. (2013). Cholinesterase activities and behavioral changes in Hypsiboas pulchellus (Anura: Hylidae) tadpoles exposed to glufosinate ammonium herbicide. *Ecotoxicology*, *22*(7), 1165–1173. https://doi.org/10.1007/s10646-013-1103-8

Peng, W., Lam, S. S., & Sonne, C. (2020). Support Austria's glyphosate ban. *Science (New York, N.Y.)*, *367*(6475), 257–258. https://doi.org/10.1126/science.aba5642

Pengue WA (2017) Cultivos transgénicos, ¿hacia dónde fuimos? Veinte años después de la liberación de soja en la Argentina. 4th January 2017. http://www.biodiversidadla.org/Portada_Principal/Recomendamos/Cultivos_transgenicos_hacia_donde_fuimos_Veinte_anos_despues_de_la_liberacion_de_soja_en_la_Argentina

Pennisi, E. (2021). Are monarchs in trouble? *Science*, *371*(6526), 219–220. https://doi.org/10.1126/science.371.6526.219

Perego, M. C., Caloni, F., Cortinovis, C., Schutz, L. F., Albonico, M., Tsuzukibashi, D., & Spicer, L. J. (2017). Influence of a Roundup formulation on glyphosate effects on steroidogenesis and proliferation of bovine granulosa cells in vitro. *Chemosphere*, *188*, 274–279. https://doi.org/10.1016/j.chemosphere.2017.09.007

Pereira, J. L., Antunes, S. C., Castro, B. B., Marques, C. R., Gonçalves, A. M. M., Gonçalves, F., & Pereira, R. (2009). Toxicity evaluation of three pesticides on non-target aquatic and soil organisms: commercial formulation versus active ingredient. *Ecotoxicology (London, England)*, *18*(4), 455–463. http://doi.org/10.1007/s10646-009-0300-y

Pereira, J. L., Lopes, M. C., Parish, J. B., Silva, A. A., & Picanço, M. C. (2018a). Impact of RR Soybeans and Glyphosate on the Community of Soil Surface Arthropods. *Planta Daninha*, *36*. https://doi.org/10.1590/S0100-83582018360100071

Pereira, A. G., Jaramillo, M. L., Remor, A. P., Latini, A., Davico, C. E., da Silva, M. L., Müller, Y. M. R., Ammar, D., & Nazari, E. M. (2018b). Low-concentration exposure to glyphosate-based herbicide modulates the complexes of the mitochondrial respiratory chain and induces mitochondrial hyperpolarization in the Danio rerio brain. *Chemosphere*, *209*, 353–362. https://doi.org/10.1016/j.chemosphere.2018.06.075

Pereira, J. L., Pereira, R. R., Resende-Silva, G. A., Jakelaitis, A., Silva, A. A., & Picanço, M. C. (2020). Glyphosate Impact on Arthropods Associated to Roundup Ready and Conventional Soybean (*Glycine max* L.). *Planta Daninha*, *38*. https://doi.org/10.1590/S0100-83582020380100047
Pérez, G. L., Vera, M. S., & Miranda, L. A. (2012). Effects of Herbicide Glyphosate and Glyphosate-Based Formulations on Aquatic Ecosystems. Retrieved from http://cdn.intechweb.org/pdfs/12592.pdf
Perez-Jones, A., Park, K. W., Colquhoun, J., Mallory-Smith, C., & Shaner, D. (2005). Identification of glyphosate-resistant Italian ryegrass (Lolium multiflorum) in Oregon. *Weed Science*, *53*(6), 775–779. http://doi.org/10.1614/WS-04-200R.1
Perkins, P. J., Boermans, H. J., & Stephenson, G. R. (2000). Toxicity of glyphosate and triclopyr using the frog embryo teratogenesis assay—Xenopus. *Environmental Toxicology and Chemistry*, *19*(4), 940–945. http://doi.org/10.1002/etc.5620190422
Perkins, C. M., Mueller, T. C., & Steckel, L. E. (2021). Survey of glyphosate-resistant junglerice (Echinochloa colona) accessions in dicamba-resistant crops in Tennessee. *Weed Technology*, *35*(3), 412–418. https://doi.org/10.1017/wet.2020.131
Perocco, P., Ancora, G., Rani, P., Valenti, A. M., Mazzullo, M., Colacci, A., & Grilli, S. (1990). Evaluation of genotoxic effects of the herbicide dicamba using in vivo and in vitro test systems. *Environmental and Molecular Mutagenesis*, *15*(3), 131–135. https://doi.org/10.1002/em.2850150303
Perotti, V. E., Larran, A. S., Palmieri, V. E., Martinatto, A. K., Alvarez, C. E., Tuesca, D., & Permingeat, H. R. (2019). A novel triple amino acid substitution in the EPSPS found in a high-level glyphosate-resistant Amaranthus hybridus population from Argentina. *Pest Management Science*, *75*(5), 1242–1251. https://doi.org/10.1002/ps.5303
Perry, J. N., Firbank, L. G., Champion, G. T., Clark, S. J., Heard, M. S., May, M. J., Hawes, C., Squire, G. R., Rothery, P., Woiwod, I. P., Pidgeon, J. D. (2004). Ban on triazine herbicides likely to reduce but not negate relative benefits of GMHT maize cropping. *Nature*, *428*(6980), 313–316. http://doi.org/10.1038/nature02374
Perry, E. D., Ciliberto, F., Hennessy, D. A., & Moschini, G. (2016). Genetically engineered crops and pesticide use in U.S. maize and soybeans. *Science Advances*, *2*(8), e1600850. https://doi.org/10.1126/sciadv.1600850
Peschard, K. E. (2019, October 31). *Monsanto wins $7.7b lawsuit in Brazil – but farmers' fight to stop its 'amoral' royalty system will continue*. The Conversation. http://theconversation.com/monsanto-wins-7-7b-lawsuit-in-brazil-but-farmers-fight-to-stop-its-amoral-royalty-system-will-continue-125471
Peters, A. (2021, January 9). This farming robot zaps weeds with precision lasers. *FastCompany*. https://www.fastcompany.com/90670773/this-farming-robot-zaps-weeds-with-precision-lasers
Phélinas, P., & Choumert, J. (2017). Is GM Soybean Cultivation in Argentina Sustainable? *World Development*, *99*, 452–462. https://doi.org/10.1016/j.worlddev.2017.05.033
Phillips McDougall (2011). The cost and time involved in the discovery, development and authorisation of a new plant biotechnology derived trait. Brussels, Belgium: Crop Life International.
Phillips, T. M. (2015). Monsanto sued in Los Angeles County for false advertising. Examiner. http://www.examiner.com/article/monsanto-sued-los-angeles-county-for-false-advertising
Pignati, W. A., Machado, J. M. H., & Cabral, J. F. (2007). Acidente rural ampliado: o caso das "chuvas" de agrotóxicos sobre a cidade de Lucas do Rio Verde - MT. *Ciência & Saúde Coletiva*, 12(1), 105–114. http://doi.org/10.1590/S1413-81232007000100014
Pilliod v. Monsanto, JCCP NO. 4953 (Superior Court of the State of California for the County of Alameda May 13, 2019). https://www.baumhedlundlaw.com/pdf/monsanto-documents/Pilliod/Pilliods-Jury-Verdict-Form.pdf
Piñeyro-Nelson, A., Van Heerwaarden, J., Perales, H. R., Serratos-Hernández, J. A., Rangel, A., Hufford, M. B., Gepts, P., Garay-Arroyo, A., Rivera-Bustamente, R., Alvarez-Buylla, E. R. (2009). Transgenes in Mexican maize: molecular evidence and methodological considerations for GMO detection in landrace populations. *Molecular Ecology*, *18*(4), 750–761. http://doi.org/10.1111/j.1365-294X.2008.03993.x
Pingree, C. (2015). http://agri-pulse.com/uploaded/Rep-monarch-letter-32015.pdf
Pinheiro, A., Silva, M., & Kraisch, R. (2010). Presença de pesticidas em águas superficiais e subterrâneas na bacia do Itajaí, SC. *Revista de Gestão de Água Da América Latina*, *7*(2), 17–26. https://doi.org/10.21168/rega.v7n2.p17-26
Pioneer Hi-Bred International (2020) Application for authorisation of genetically modified plants and derived food and feed in accordance with Regulation (EC) No 1829/2003. DP915635 Maize. EFSA-GMO-NL-2020-1xx. Part VII – Summary. Dec. https://www.testbiotech.org/sites/default/files/EFSA-Q-2020-00834-EFSA-GMO-NL-2020-172_%20Summary.pdf
35 Cibus (2022). Our technology. https://www.cibus.com/our-
Pizarro, H., Di Fiori, E., Sinistro, R., Ramírez, M., Rodríguez, P., Vinocur, A., Cataldo, D. (2016). Impact of multiple anthropogenic stressors on freshwater: how do glyphosate and the invasive mussel Limnoperna fortunei affect microbial communities and water quality? *Ecotoxicology* **25**, 56–68. doi:10.1007/s10646-015-1566-x

Pleasants, J. M., & Oberhauser, K. S. (2012). Milkweed loss in agricultural fields because of herbicide use: effect on the monarch butterfly population: Herbicide use and monarch butterflies. Insect Conservation and Diversity, 6(2), 135–144. http://doi.org/10.1111/j.1752-4598.2012.00196.x
Pleasants, J. (2017). Milkweed restoration in the Midwest for monarch butterfly recovery: Estimates of milkweeds lost, milkweeds remaining and milkweeds that must be added to increase the monarch population. Insect Conservation *and Diversity*, *10*(1), 42–53. https://doi.org/10.1111/icad.12198
Pleasants, J. M., Williams, E. H., Brower, L. P., Oberhauser, K. S., & Taylor, O. R. (2016). Conclusion of No Decline in Summer Monarch Population Not Supported. *Annals of the Entomological Society of America*, sav115. http://doi.org/10.1093/aesa/sav115
Pleasants, J. M., Zalucki, M. P., Oberhauser, K. S., Brower, L. P., Taylor, O. R., & Thogmartin, W. E. (2017). Interpreting surveys to estimate the size of the monarch butterfly population: Pitfalls and prospects. *PLOS ONE*, *12*(7), e0181245. https://doi.org/10.1371/journal.pone.0181245
Plume, K. (2014). ADM sues Syngenta over rejections of GMO corn by China. http://m.stltoday.com/business/local/adm-sues-syngenta-over-rejections-of-gmo-corn-by-china/article_529a7f66-84ec-50d2-8d64-9348e4e2c441.html?mobile_touch=true
Plume, K. (2017, July 13). Tennessee restricts use of Monsanto pesticide as problems spread. *Reuters*. https://www.reuters.com/article/us-tennessee-grains-monsanto-idUSKBN19Y2KE
Pochettino, A. A., Bongiovanni, B., Duffard, R. O., & Evangelista de Duffard, A. M. (2013). Oxidative stress in ventral prostate, ovary, and breast by 2,4-dichlorophenoxyacetic acid in pre- and postnatal exposed rats. *Environmental Toxicology*, *28*(1), 1–10. https://doi.org/10.1002/tox.20690
Pochron, S., Choudhury, M., Gomez, R., Hussaini, S., Illuzzi, K., Mann, M., Mezic, M., Nikakis, J., & Tucker, C. (2019). Temperature and body mass drive earthworm (Eisenia fetida) sensitivity to a popular glyphosate-based herbicide. *Applied Soil Ecology*, *139*, 32–39. https://doi.org/10.1016/j.apsoil.2019.03.015
Poirier, F., Boursier, C., Mesnage, R., Oestreicher, N., Nicolas, V., & Vélot, C. (2017). Proteomic analysis of the soil filamentous fungus Aspergillus nidulans exposed to a Roundup formulation at a dose causing no macroscopic effect: A functional study. *Environmental Science and Pollution Research International*, *24*(33), 25933–25946. https://doi.org/10.1007/s11356-017-0217-6
Polansek, T. (2014a). Cargill sues Syngenta over China rejections of GMO U.S. corn. http://af.reuters.com/article/commoditiesNews/idAFL1N0RD1L020140912
Polansek, T. (2014b). U.S. farmers latest to sue Syngenta over GMO corn rejected by China. http://www.dailymail.co.uk/wires/reuters/article-2782909/U-S-farmers-latest-sue-Syngenta-GMO-corn-rejected-China.html
Polansek, T (2015). REFILE-Syngenta sues Cargill, ADM in GMO corn fight. Reuters. http://www.reuters.com/article/2015/11/20/syngenta-seed-traders-idUSL1N13F18V20151120
Polansek, T. (2020, June 9). Trump administration permits use of weed killer blocked by court. *Reuters*. https://www.reuters.com/article/us-bayer-dicamba-lawsuit-idUSKBN23F31M
Pollack, A. (2014). Altered to Withstand Herbicide, Corn and Soybeans Gain Approval. The New York Times. http://www.nytimes.com/2014/09/18/business/altered-to-withstand-herbicide-corn-and-soybeans-gain-approval.html?_r=2
Pollack, A. (2015). E.P.A. Revokes Approval of New Dow Herbicide for G.M.O. Crops. The New York Times. http://www.nytimes.com/2015/11/26/business/epa-revokes-approval-of-new-dow-herbicide.html?_r=1
Pompermaier, A., Varela, A. C. C., Mozzato, M. T., Soares, S. M., Fortuna, M., Alves, C., Tamagno, W. A., & Barcellos, L. J. G. (2022). Impaired initial development and behavior in zebrafish exposed to environmentally relevant concentrations of widely used pesticides. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *257*, 109328. https://doi.org/10.1016/j.cbpc.2022.109328
Portier, J. et al. (2015). Open letter: Review of the Carciogenicity of Glyphosate by EFSA and BfR. http://www.zeit.de/wissen/umwelt/2015-11/glyphosat-offener-brief.pdf
Portier, C. J. (2020). A comprehensive analysis of the animal carcinogenicity data for glyphosate from chronic exposure rodent carcinogenicity studies. *Environmental Health*, *19*(1), 18. https://doi.org/10.1186/s12940-020-00574-1
Potts, S. G., Biesmeijer, J. C., Kremen, C., Neumann, P., Schweiger, O., & Kunin, W. E. (2010). Global pollinator declines: trends, impacts and drivers. *Trends in Ecology & Evolution*, *25*(6), 345–353. http://doi.org/10.1016/j.tree.2010.01.007
Powles, S. B., Lorraine-Colwill, D. F., Dellow, J. J., & Preston, C. (1998). Evolved resistance to glyphosate in rigid ryegrass (Lolium rigidum) in Australia. *Weed Science*, *46*, 604–607.
Powles, S. B., & Preston, C. (2006). Evolved Glyphosate Resistance in Plants: Biochemical and Genetic Basis of Resistance [1]. *Weed Technology*, *20*(2), 282–289. http://doi.org/10.1614/WT-04-142R.1
Powlson, D. S., Stirling, C. M., Jat, M. L., Gerard, B. G., Palm, C. A., Sanchez, P. A., & Cassman, K. G. (2014). Limited potential of no-till agriculture for climate change mitigation. *Nature Climate Change*, *4*(8), 678–683. http://doi.org/10.1038/nclimate2292

Pratt, S. (2014a). Breeder annoyed GM given credit for yield hikes. The Western Producer. http://www.producer.com/2014/11/breeder-annoyed-gm-given-credit-for-yield-hikes/
Pratt, S. (2014b, December 11). Video: Non-GM flax variety in limbo. *The Western Producer*. https://www.producer.com/2014/12/non-gm-flax-variety-in-limbo/ [accessed: 5 February 2020]
Pratt, S. (2016a, January 8). Herbicide mixes tackle resistant weeds. *The Western Producer*. https://www.producer.com/2016/01/herbicide-mixes-tackle-resistant-weeds/ [accessed: 9 April 2020]
Pratt, S. (2016b, January 29). Herbicide tolerant flax project progressing. *The Western Producer*. https://www.producer.com/2016/01/herbicide-tolerant-flax-project-progressing/ [accessed: 5 February 2020]
Pratt, S. (2016c). Field trials on non-GM, tolerant flax coming soon. Retrieved 29 November 2019, from The Western Producer website: https://www.producer.com/2016/03/field-trials-on-non-gm-tolerant-flax-coming-soon/
Preston, C., Wakelin, A. M., Dolman, F. C., Bostamam, Y., & Boutsalis, P. (2009). A Decade of Glyphosate-Resistant Lolium around the World: Mechanisms, Genes, Fitness, and Agronomic Management. *Weed Science*, *57*(4), 435–441. https://doi.org/10.1614/WS-08-181.1
Price, B., & Cotter, J. (2014). The GM Contamination Register: a review of recorded contamination incidents associated with genetically modified organisms (GMOs), 1997–2013. *International Journal of Food Contamination*, *1*(1), 5. http://doi.org/10.1186/s40550-014-0005-8
Pu, Y., Yang, J., Chang, L., Qu, Y., Wang, S., Zhang, K., Xiong, Z., Zhang, J., Tan, Y., Wang, X., Fujita, Y., Ishima, T., Wang, D., Hwang, S. H., Hammock, B. D., & Hashimoto, K. (2020). Maternal glyphosate exposure causes autism-like behaviors in offspring through increased expression of soluble epoxide hydrolase. *Proceedings of the National Academy of Sciences of the United States of America*, *117*(21), 11753–11759. https://doi.org/10.1073/pnas.1922287117
Pu, Y., Ma, L., Shan, J., Wan, X., Hammock, B. D., & Hashimoto, K. (2021). Autism-like Behaviors in Male Juvenile Offspring after Maternal Glyphosate Exposure. *Clinical Psychopharmacology and Neuroscience*, *19*(3), 554–558. https://doi.org/10.9758/cpn.2021.19.3.554
Pucci, J. (2020, June 15). Corteva, BASF File Motions to Intervene in Dicamba Case. *CropLife*. https://www.croplife.com/crop-inputs/herbicides/corteva-basf-file-motions-to-intervene-in-dicamba-case/
Quartz (2015) This robot kills weeds, and could end the need for herbicides on farms. 18th November 2015. http://qz.com/553383/this-robot-kills-weeds-and-could-end-the-need-for-herbicides-on-farms/
Quist, D., & Chapela, I. H. (2001). Transgenic DNA introgressed into traditional maize landraces in Oaxaca, Mexico. *Nature*, *414*(6863), 541–543. http://doi.org/10.1038/35107068
Ranum, P., Peña-Rosas, J. P., & Garcia-Casal, M. N. (2014). Global maize production, utilization, and consumption. *Annals of the New York Academy of Sciences*, *1312*, 105–112. http://doi.org/10.1111/nyas.12396
Ramirez Haberkon, N. B., Aparicio, V. C., & Mendez, M. J. (2021). First evidence of glyphosate and aminomethylphosphonic acid (AMPA) in the respirable dust (PM10) emitted from unpaved rural roads of Argentina. *Science of The Total Environment*, *773*, 145055. https://doi.org/10.1016/j.scitotenv.2021.145055
Ramsdorf, W., Bordin, E., Munhoz, R., Panicio, P., & Freitas, A. (2021). Transgenerational Effects of Environmentally Relevant Concentrations of Atrazine and Glyphosate Herbicides, Isolated and in Mixture, to Freshwater Microcrustacean Daphnia Magna. https://doi.org/10.21203/rs.3.rs-790734/v1
Raoult, D., Hadjadj, L., Baron, S. A., & Rolain, J.-M. (2021). Role of glyphosate in the emergence of antimicrobial resistance in bacteria? Journal of Antimicrobial Chemotherapy, 76(7), 1655–1657. https://doi.org/10.1093/jac/dkab102
Real Money (2016) There's a Big Harvest of Agribusiness Mergers. 19 May 2016. http://realmoney.thestreet.com/articles/05/19/2016/theres-big-harvest-agribusiness-mergers
Reddy, S. B., Nolan, C. J., & Plautz, C. Z. (2018a). Disturbances in reproduction and expression of steroidogenic enzymes in aquatic invertebrates exposed to components of the herbicide Roundup. *Toxicology Research and Application*, *2*, 2397847318805276. https://doi.org/10.1177/2397847318805276
Reddy, K. N., Cizdziel, J. V., Williams, M. M., Maul, J. E., Rimando, A. M., & Duke, S. O. (2018b). Glyphosate Resistance Technology Has Minimal or No Effect on Maize Mineral Content and Yield. *Journal of Agricultural and Food Chemistry*, *66*(39), 10139–10146. https://doi.org/10.1021/acs.jafc.8b01655
Redo, D., Aide, T. M., & Clark, M. L. (2013). Vegetation change in Brazil's dryland ecoregions and the relationship to crop production and environmental factors: Cerrado, Caatinga, and Mato Grosso, 2001–2009. Journal of Land Use Science, 8(2), 123–153. http://doi.org/10.1080/1747423X.2012.667448
ReliefWeb. (2021, November 3). *FAO Statistical Yearbook 2021—World Food and Agriculture—World | ReliefWeb*. https://reliefweb.int/report/world/fao-statistical-yearbook-2021-world-food-and-agriculture
Relyea, R. A. (2005a). The Impact of Insecticides and Herbicides on the Biodiversity and Productivity of Aquatic Communities. *Ecological Applications*, *15*(2), 618–627. http://doi.org/10.1890/03-5342
Relyea, R. A. (2005b). The lethal impact of roundup on aquatic and terrestrial amphibians. *Ecological Applications*, *15*(4), 1118–1124. http://doi.org/10.1890/04-1291

Relyea, R. A. (2005c). The Lethal Impacts of Roundup and Predatory Stress on Six Species of North American Tadpoles. *Archives of Environmental Contamination and Toxicology*, *48*(3), 351–357. http://doi.org/10.1007/s00244-004-0086-0
Relyea, R. A. (2012). New effects of Roundup on amphibians: Predators reduce herbicide mortality; herbicides induce antipredator morphology. *Ecological Applications*, *22*(2), 634–647. https://doi.org/10.1890/11-0189.1
Relyea, R. A. (2018). The interactive effects of predator stress, predation, and the herbicide Roundup. *Ecosphere*, *9*(11), e02476. https://doi.org/10.1002/ecs2.2476
Relyea, R. A., Schoeppner, N. M., & Hoverman, J. T. (2005). Pesticides and Amphibians: The Importance of Community Context. *Ecological Applications*, *15*(4), 1125–1134. http://doi.org/10.1890/04-0559
Renda, M. (2020a, June 4). *Ninth Circuit Vacates EPA Approval of Dicamba Pesticide*. http://www.courthousenews.com/ninth-circuit-vacates-epa-approval-of-dicamba-pesticide/
Renda, M. (2020b, July 22). *EPA Ordered to Take Fresh Look at Whether Herbicide Harms Butterflies*. https://www.courthousenews.com/epa-ordered-to-take-fresh-look-at-whether-herbicide-harms-butterflies/
Rendón-Aguilar, B., Bernal-Ramírez, L. A., Bravo-Avilez, D., Rocha-Munive, M. G., Rendón-Aguilar, B., Bernal-Ramírez, L. A., Bravo-Avilez, D., & Rocha-Munive, M. G. (2019). Temporal dynamics of detected transgenes in maize landraces in their center of origin. *Revista Mexicana de Biodiversidad*, *90*. https://doi.org/10.22201/ib.20078706e.2019.90.2653
Rendón-Salinas, E., Fernández-Islas, A., Mendoza-Pérez, M. A., Cruz-Piña, M., Mondragón-Contreras, G., & Martínez-Pacheco, A. (2022). *Areas of forest occupied by the colonies of monarch butterflies in Mexico during the 2021-2022 overwintering period | Publications | WWF*. Retrieved 13 June 2022, from https://www.worldwildlife.org/publications/areas-of-forest-occupied-by-the-colonies-of-monarch-butterflies-in-mexico-during-the-2021-2022-overwintering-period
Rendon-von Osten, J., & Dzul-Caamal, R. (2017). Glyphosate Residues in Groundwater, Drinking Water and Urine of Subsistence Farmers from Intensive Agriculture Localities: A Survey in Hopelchén, Campeche, Mexico. *International Journal of Environmental Research and Public Health*, *14*(6), 595. https://doi.org/10.3390/ijerph14060595
Renter, E. (2013). Target To Remove GMOs From Major Food Brand. Natural Society. http://naturalsociety.com/target-to-remove-gmos-from-major-food-brand/
Report on the Status of the Monarch Butterfly Migration and Petition to Include the Monarch Butterfly Biosphere Reserve on the List of World Heritage in Danger (2015). Petition submitted to the World Heritage Committee on behalf of: Grupo de los Cien; Alternare A.C., Danaidas, Conservación y Desarrollo Sustentable; COSTASALVAjE, A.C.; Telar Social México; Natural Resources Defense Council; David Suzuki Foundation. http://docs.nrdc.org/wildlife/files/wil_15040901a.pdf
Reuter, W. (2015). *Toxicology of glyphosate, isoxaflutole, dicamba and possible combination effects* (p. 13). https://www.testbiotech.org/sites/default/files/Tox_Evaluation_Glyphosate_Dicamba_Isoxaflutole.pdf
Reuters (2014). Monsanto critics denied U.S. Supreme Court hearing on seed patents. https://www.reuters.com/article/us-usa-court-monsanto-idUSBREA0C10H20140113
Reuters (2015). French minister calls on shops to stop selling Monsanto's Roundup. http://in.reuters.com/article/2015/06/14/france-monsanto-idINL5N0Z00EH20150614
Reuters (2015b) Brazil soy traders to renegotiate Monsanto royalty deals –Abiove. Dec 2, 2015. http://www.reuters.com/article/brazil-monsanto-idUSL1N13S02Z20151203
Reuters (2016a) European Commission to extend glyphosate license for 18 months. 28 June 2016. http://www.reuters.com/article/us-health-eu-glyphosate-idUSKCN0ZE25B
Reuters (2016b) France to ban some glyphosate weedkillers amid health concerns. 8 April 2016. http://www.reuters.com/article/us-france-glyphosate-idUSKCN0X512S
Reuters (2016c) USDA confirms unapproved GMO wheat found in Washington state. 29 July 2016. http://www.reuters.com/article/us-wheat-washington-gmo-idUSKCN10920K
Reuters. (2021, May 8). Mexican court strikes down Bayer's legal challenge over glyphosate ban. *Reuters*. https://www.reuters.com/business/healthcare-pharmaceuticals/mexican-court-strikes-down-bayers-legal-challenge-over-glyphosate-ban-2021-05-08/ [accessed: 31 December 2021]
REWE Group (2015). REWE Group nimmt Unkrautvernichtungsmittel Glyphosat aus Baumarkt-Sortiment. https://www.rewe-group.com/de/newsroom/pressemitteilungen/1422
Riaño, C., Ortiz-Ruiz, M., Pinto-Sánchez, N. R., & Gómez-Ramírez, E. (2020). Effect of glyphosate (Roundup Active®) on liver of tadpoles of the colombian endemic frog Dendropsophus molitor (amphibia: Anura). *Chemosphere*, *250*, 126287. https://doi.org/10.1016/j.chemosphere.2020.126287
Riar, D.S., Norsworthy, J.K., Steckel, L.E., Stephenson, D.O., Bond, J.A., 2013. Consultant Perspectives on Weed Management Needs in Midsouthern United States Cotton: A Follow-Up Survey. *Weed Technology* **27**, 778–787. doi:10.1614/WT-D-13-00070.1
Richard, S., Moslemi, S., Sipahutar, H., Benachour, N., & Seralini, G.-E. (2005). Differential Effects of Glyphosate and Roundup on Human Placental Cells and Aromatase. *Environmental Health Perspectives*, *113*(6), 716–720.

Ries, L., Zipkin, E. F., & Guralnick, R. P. (2019). Tracking trends in monarch abundance over the 20th century is currently impossible using museum records. *Proceedings of the National Academy of Sciences*, *116*(28), 13745–13748. https://doi.org/10.1073/pnas.1904807116

Rigotto, R. M., Vasconcelos, D. P. e, Rocha, M. M., Rigotto, R. M., Vasconcelos, D. P. e, & Rocha, M. M. (2014). Pesticide use in Brazil and problems for public health. *Cadernos de Saúde Pública*, 30(7), 1360–1362. http://doi.org/10.1590/0102-311XPE020714

Riley, R. (2015). UN's World Heritage Committee Agrees to Examine Plight of Monarch Migration. Switchboard. Natural Resource Defense Council Staff Blog. http://switchboard.nrdc.org/blogs/awetzler/uns_world_heritage_committee_a.html

Rissoli, R. Z., Abdalla, F. C., Costa, M. J., Rantin, F. T., McKenzie, D. J., & Kalinin, A. L. (2016). Effects of glyphosate and the glyphosate based herbicides Roundup Original(®) and Roundup Transorb(®) on respiratory morphophysiology of bullfrog tadpoles. *Chemosphere*, *156*, 37–44. https://doi.org/10.1016/j.chemosphere.2016.04.083

Rizzo, G., Monzon, J. P., Tenorio, F. A., Howard, R., Cassman, K. G., & Grassini, P. (2022). Climate and agronomy, not genetics, underpin recent maize yield gains in favorable environments. *Proceedings of the National Academy of Sciences*, *119*(4), e2113629119. https://doi.org/10.1073/pnas.2113629119

Rizzuto, P., & Vasquez, J. (2020, October 27). *EPA OKs Soybean, Cotton Farmers' Use of Dicamba Weedkiller (2)*. https://news.bloomberglaw.com/environment-and-energy/soybean-cotton-farmers-get-epas-ok-to-use-weedkiller-dicamba

Robinson, C., Portier, C. J., Čavoški, A., Mesnage, R., Roger, A., Clausing, P., Whaley, P., Muilerman, H., & Lyssimachou, A. (2020). Achieving a High Level of Protection from Pesticides in Europe: Problems with the Current Risk Assessment Procedure and Solutions. *European Journal of Risk Regulation*, *11*(3), 450–480. https://doi.org/10.1017/err.2020.18

Robinson, R. A., & Sutherland, W. J. (2002). Post-war changes in arable farming and biodiversity in Great Britain. *Journal of Applied Ecology*, *39*(1), 157–176. http://doi.org/10.1046/j.1365-2664.2002.00695.x

Rodrigues, N. R., & de Souza, A. P. F. (2018). Occurrence of glyphosate and AMPA residues in soy-based infant formula sold in Brazil. Food Additives & Contaminants: Part A, 35(4), 724–731. https://doi.org/10.1080/19440049.2017.1419286

Rodrigues, N. R., Souza, A. P. F. de, Morais, P. P. P., Braga, D. P. V., Crivellari, A. C., Favoretto, L. R. G., & Berger, G. U. (2020). Residues of glyphosate and aminomethylphosphonic acid (AMPA) in genetically modified glyphosate tolerant soybean, corn and cotton crops. *Ciência Rural*, *51*. https://doi.org/10.1590/0103-8478cr20190244

Rodriguez R (2017) Fresno judge rejects Monsanto's bid to block state from listing chemical as cancer causing. Fresno Bee. 27th January 2017. http://www.fresnobee.com/news/business/agriculture/article129228309.html

Rodríguez, E. M., Medesani, D. A., Canosa, I. S., & Avigliano, L. (2021). The Effect of Glyphosate on the Reproduction of Estuarine Crabs: *Neohelice granulata* as a Study Model. *Frontiers in Endocrinology*, *12*. https://www.frontiersin.org/article/10.3389/fendo.2021.643168

Rodríguez-Miguel, A., Hernández-Zamora, M., Martínez-Jerónimo, L., & Martínez-Jerónimo, F. (2021). Exposure to sublethal concentrations of the glyphosate-based herbicide Faena® increases sensitivity in the progeny of the American cladoceran Daphnia exilis (Herrick, 1895). *Environmental Science and Pollution Research International*, *28*(28), 38094–38105. https://doi.org/10.1007/s11356-021-13259-0

Romano, R. M., Romano, M. A., Bernardi, M. M., Furtado, P. V., & Oliveira, C. A. (2010). Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology. *Archives of Toxicology*, *84*(4), 309–317. http://doi.org/10.1007/s00204-009-0494-z

Romano, R. M., Oliveira, J. M. de, Oliveira, V. M. de, Oliveira, I. M. de, Torres, Y. R., Bargi-Souza, P., Martino Andrade, A. J., & Romano, M. A. (2021). Could Glyphosate and Glyphosate-Based Herbicides Be Associated With Increased Thyroid Diseases Worldwide? *Frontiers in Endocrinology*, *12*. https://www.frontiersin.org/article/10.3389/fendo.2021.627167

Rook, M., & Pates, M. (2021, August 2). *Off-target dicamba damage in 2021 may be the worst year yet in the Upper Midwest*. Agweek. https://www.agweek.com/business/agriculture/7129815-Off-target-dicamba-damage-in-2021-may-be-the-worst-year-yet-in-the-Upper-Midwest

Roseboro, K. (2008): Finding non-GMO soybean seed becoming more difficult: fewer breeding programs for non-GMO soybeans are reducing supplies despite strong demand. The Organic and Non-GMO Report. http://www.non-gmoreport.com/articles/jul08/non-gmo_soybean_seed.php

Roseboro, K. (2012). Scientist says biotech companies encouraging GMO-herbicide treadmill. The Organic and Non-GMO Report. http://www.non-gmoreport.com/articles/april2012/scientist-biotech-gmo-herbicide.php

Roseboro, K. (2015a). Vermont corn trials highlight better non-GMO yields, crop rotations over GMOs. The Organic and Non-GMO Report. http://www.non-gmoreport.com/articles/june-2015/vermont-corn-trials-highlight-better-non-GMO-yields-crop-rotations-over-gmos.php#sthash.lUkIWs66.Hg1sPfhs.dpuf

Roseboro, K. (2015b). More Farmers Predicted to Go Non-GMO and Organic in 2015. Organic Connections. http://organicconnectmag.com/more-farmers-predicted-to-go-non-gmo-and-organic-in-2015/
Rosenblatt et al. (2017) EPA Official Accused of Helping Monsanto 'Kill' Cancer Study. Bloomberg. 14th March 2017. https://www.bloomberg.com/news/articles/2017-03-14/monsanto-accused-of-ghost-writing-papers-on-roundup-cancer-risk
Rosenblatt, J. (2021, March 19). Bayer Won't Ask U.S. Supreme Court to Reverse Roundup Loss. *Bloomberg.Com*. https://www.bloomberg.com/news/articles/2021-03-19/bayer-won-t-ask-u-s-supreme-court-to-reverse-first-roundup-loss [accessed: 12 December 2021]
Rossetti, M. F., Canesini, G., Lorenz, V., Milesi, M. M., Varayoud, J., & Ramos, J. G. (2021). Epigenetic Changes Associated With Exposure to Glyphosate-Based Herbicides in Mammals. *Frontiers in Endocrinology*, *12*. https://www.frontiersin.org/article/10.3389/fendo.2021.671991
Rotam. (2019). Draft Herbicide | Rotam North America. https://www.rotamnorthamerica.com/crop-products/draft-herbicide [Accessed: 27 November 2019]
Rotam. (n.d.). *Draft Label*. Retrieved from https://www.falcoseed.com/wp-content/uploads/2018/09/DraftLabel_US_IdC7F000.pdf [accessed: 8 December 2019]
Royte, E. (2013). The post GMO economy. One mainstream farmer is returning to conventional seed – and he's not alone. Modern Farmer. Retrieved, September, 8. 2014 from http://modernfarmer.com/2013/12/post-gmo-economy/
Rubio, F., Guo, E. And Kamp, L. (2014). Survey of glyphosate residues in honey, corn and soy products. *J. Environ. Anal. Toxicol.* 5 (1) http://dx.doi.org/10.4172/2161- 0525.1000249.
Rueda-Ruzafa, L., Cruz, F., Roman, P., & Cardona, D. (2019). Gut microbiota and neurological effects of glyphosate. *Neurotoxicology*, *75*, 1–8. https://doi.org/10.1016/j.neuro.2019.08.006
Ruiz de Arcaute, C., Soloneski, S., & Larramendy, M. L. (2016). Toxic and genotoxic effects of the 2,4-dichlorophenoxyacetic acid (2,4-D)-based herbicide on the Neotropical fish Cnesterodon decemmaculatus. *Ecotoxicology and Environmental Safety*, *128*, 222–229. https://doi.org/10.1016/j.ecoenv.2016.02.027
Ruiz de Arcaute, C., Larramendy, M. L., & Soloneski, S. (2018). Genotoxicity by long-term exposure to the auxinic herbicides 2,4-dichlorophenoxyacetic acid and dicamba on Cnesterodon decemmaculatus (Pisces: Poeciliidae). *Environmental Pollution*, *243*, 670–678. https://doi.org/10.1016/j.envpol.2018.09.040
Ruuskanen, S., Rainio, M. J., Uusitalo, M., Saikkonen, K., & Helander, M. (2020a). Effects of parental exposure to glyphosate-based herbicides on embryonic development and oxidative status: A long-term experiment in a bird model. *Scientific Reports*, *10*(1), 6349. https://doi.org/10.1038/s41598-020-63365-1
Ruuskanen, S., Rainio, M. J., Gomez-Gallego, C., Selenius, O., Salminen, S., Collado, M. C., Saikkonen, K., Saloniemi, I., & Helander, M. (2020b). Glyphosate-based herbicides influence antioxidants, reproductive hormones and gut microbiome but not reproduction: A long-term experiment in an avian model. *Environmental Pollution*, 115108. https://doi.org/10.1016/j.envpol.2020.115108
Ruuskanen, S., Rainio, M. J., Kuosmanen, V., Laihonen, M., Saikkonen, K., Saloniemi, I., & Helander, M. (2020c). Female Preference and Adverse Developmental Effects of Glyphosate-Based Herbicides on Ecologically Relevant Traits in Japanese Quails. *Environmental Science & Technology*, *54*(2), 1128–1135. https://doi.org/10.1021/acs.est.9b07331
Ryan, C. D. & Smyth, S. J. (2012). Economic Implications of Low-level Presence in a Zero-Tolerance European Import Market: The Case of Canadian Triffid Flax. *AgBioForum*, *15*(1), 21-30. http://www.agbioforum.org/v15n1/v15n1a03-ryan.htm
Rydz, E., Larsen, K., & Peters, C. E. (2021). Estimating Exposure to Three Commonly Used, Potentially Carcinogenic Pesticides (Chlorolathonil, 2,4-D, and Glyphosate) Among Agricultural Workers in Canada. *Annals of Work Exposures and Health*, *65*(4), 377–389. https://doi.org/10.1093/annweh/wxaa109
Sabio y García, C. A., Vera, M. S., Vinocur, A., Graziano, M., Miranda, C., & Pizarro, H. N. (2022). Rethinking the term "glyphosate effect" through the evaluation of different glyphosate-based herbicide effects over aquatic microbial communities. *Environmental Pollution*, *292*, 118382. https://doi.org/10.1016/j.envpol.2021.118382
Sachs, E. (2015). Restoring Natural Habitat for the Monarch. Monsanto Company. http://discover.monsanto.com/posts/restoring-natural-habitat-monarch-butterfly/
Saji, H., Nakajima, N., Aono, M., Tamaoki, M., Kubo, A., Wakiyama, S., … Nagatsu, M. (2005). Monitoring the escape of transgenic oilseed rape around Japanese ports and roadsides. *Environmental Biosafety Research*, *4*(4), 217–222. http://doi.org/10.1051/ebr:2006003
Salas, R. A., Dayan, F. E., Pan, Z., Watson, S. B., Dickson, J. W., Scott, R. C., & Burgos, N. R. (2012). EPSPS gene amplification in glyphosate-resistant Italian ryegrass (Lolium perenne ssp. multiflorum) from Arkansas. *Pest Management Science*, *68*(9), 1223–1230. http://doi.org/10.1002/ps.3342
Salvo, L. M., Malucelli, M. I. C., da Silva, J. R. M. C., Alberton, G. C., & Silva De Assis, H. C. (2015). Toxicity assessment of 2,4-D and MCPA herbicides in primary culture of fish hepatic cells. *Journal of Environmental Science and Health. Part. B, Pesticides, Food Contaminants, and Agricultural Wastes*, *50*(7), 449–455. https://doi.org/10.1080/03601234.2015.1018754

Samanic, C., Rusiecki, J., Dosemeci, M., Hou, L., Hoppin, J. A., Sandler, D. P., Lubin, J., Blair, A., & Alavanja, M. C. R. (2006). Cancer Incidence among Pesticide Applicators Exposed to Dicamba in the Agricultural Health Study. *Environmental Health Perspectives*, *114*(10), 1521–1526. https://doi.org/10.1289/ehp.9204

Sammons, R. D., & Gaines, T. A. (2014). Glyphosate resistance: State of knowledge. *Pest Management Science*, *70*(9), 1367–1377. https://doi.org/10.1002/ps.3743

Sánchez, J. A. A., Barros, D. M., de los Angeles Bistoni, M., Ballesteros, M. L., Roggio, M. A., & Martins, C. D. G. M. (2021). Glyphosate-based herbicides affect behavioural patterns of the livebearer Jenynsia multidentata. *Environmental Science and Pollution Research*, *28*(23), 29958–29970. https://doi.org/10.1007/s11356-020-11958-8

Sandrock, C., Tanadini, M., Tanadini, L. G., Fauser-Misslin, A., Potts, S. G., & Neumann, P. (2014). Impact of Chronic Neonicotinoid Exposure on Honeybee Colony Performance and Queen Supersedure. *PLoS ONE*, *9*(8), e103592. http://doi.org/10.1371/journal.pone.0103592

Sanogo, S., Yang, X. B., & Scherm, H. (2000). Effects of Herbicides on Fusarium solani f. sp. glycines and Development of Sudden Death Syndrome in Glyphosate-Tolerant Soybean. *Phytopathology*, *90*(1), 57–66. http://doi.org/10.1094/PHYTO.2000.90.1.57

Sanogo, S., Yang, X. B., & Lundeen, P. (2001). Field Response of Glyphosate-Tolerant Soybean to Herbicides and Sudden Death Syndrome. *Plant Disease*, *85*(7), 773–779. http://doi.org/10.1094/PDIS.2001.85.7.773

Santadino, M., Coviella, C., & Momo, F. (2014). Glyphosate Sublethal Effects on the Population Dynamics of the Earthworm Eisenia fetida (Savigny, 1826). *Water, Air, & Soil Pollution*, *225*(12), 1–8. http://doi.org/10.1007/s11270-014-2207-3

Santos-Silva, T., Ribeiro, R. I. M. A., Memoriam), S. N. A. (In, Thomé, R. G., & Santos, H. (2021). *Combinatorial Effects of Organophosphate (Temephos), Glyphosate (Roundup) and Sodium Dodecil Sulfate (Sds) on Zebrafish (Danio Rerio) Gills: A Morphometric and Histological Study*. https://doi.org/10.21203/rs.3.rs-185080/v1

Sarangi, D., Tyre, A. J., Patterson, E. L., Gaines, T. A., Irmak, S., Knezevic, S. Z., Lindquist, J. L., & Jhala, A. J. (2017). Pollen-mediated gene flow from glyphosate-resistant common waterhemp (Amaranthus rudis Sauer): Consequences for the dispersal of resistance genes. *Scientific Reports*, *7*, 44913. https://doi.org/10.1038/srep44913

Sarmadi, D. (2015). Pflanzenschutzmittel Glyphosat: Bundesländer fordern EU-Verbot von mutmaßlichem Krebserreger. EurActiv. http://www.euractiv.de/sections/gesundheit-und-verbraucherschutz/pflanzenschutzmittel-glyphosat-bundeslaender-fordern-eu

Saska, P., Skuhrovec, J., Lukáš, J., Chi, H., Tuan, S.-J., & Honěk, A. (2016). Treatment by glyphosate-based herbicide alters life history parameters of the rose-grain aphid Metopolophium dirhodum. *Scientific Reports*, *6*(1), 27801. https://doi.org/10.1038/srep27801

Sauer, N. J., Narváez-Vásquez, J., Mozoruk, J., Miller, R. B., Warburg, Z. J., Woodward, M. J., Mihiret, Y. A., Lincoln, T. A., Segami, R. E., Sanders, S. L., Walker, K. A., Beetham, P. R., Schöpke, C. R., & Gocal, G. F. W. (2016). Oligonucleotide-Mediated Genome Editing Provides Precision and Function to Engineered Nucleases and Antibiotics in Plants[OPEN]. *Plant Physiology*, *170*(4), 1917–1928. https://doi.org/10.1104/pp.15.01696

Saunders, S. P., Ries, L., Neupane, N., Ramírez, M. I., García-Serrano, E., Rendón-Salinas, E., & Zipkin, E. F. (2019). Multiscale seasonal factors drive the size of winter monarch colonies. *Proceedings of the National Academy of Sciences*, *116*(17), 8609–8614. https://doi.org/10.1073/pnas.1805114116

Savitz, D. A., Arbuckle, T., Kaczor, D., & Curtis, K. M. (1997). Male Pesticide Exposure and Pregnancy Outcome. American Journal of Epidemiology, 146(12), 1025–1036.

Schaefer, A. & Carter, A. (2015). GMO trade in a world of fragmented consumer preferences and needs. International Centre for Trade and Sustainable Development. http://www.ictsd.org/bridges-news/biores/news/gmo-trade-in-a-world-of-fragmented-consumer-preferences-and-needs

Schaumburg, L. G., Siroski, P. A., Poletta, G. L., & Mudry, M. D. (2016). Genotoxicity induced by Roundup® (Glyphosate) in tegu lizard (Salvator merianae) embryos. *Pesticide Biochemistry and Physiology*, *130*, 71–78. https://doi.org/10.1016/j.pestbp.2015.11.009

Schiesari, L., & Grillitsch, B. (2011). Pesticides meet megadiversity in the expansion of biofuel crops. Frontiers in Ecology and the Environment, 9(4), 215–221. http://doi.org/10.1890/090139

Schinasi, L., & Leon, M. E. (2014). Non-Hodgkin Lymphoma and Occupational Exposure to Agricultural Pesticide Chemical Groups and Active Ingredients: A Systematic Review and Meta-Analysis. *International Journal of Environmental Research and Public Health*, *11*(4), 4449–4527. https://doi.org/10.3390/ijerph110404449

Schmidt, M., López, V. T., Tobías, M., Grinberg, E., & Merlinsky, G. (2022). Social and environmental conflicts caused by agrochemical use in Salta, Santiago del Estero and Santa Fe, Argentina. *Ciência & Saúde Coletiva*, *27*, 1061–1072. https://doi.org/10.1590/1413-81232022273.04852021

Schoenenberger, N., & D'Andrea, L. (2012). Surveying the occurrence of subspontaneous glyphosate-tolerant genetically engineered Brassica napus L. (Brassicaceae) along Swiss railways. *Environmental Sciences Europe*, *24*(1), 23. http://doi.org/10.1186/2190-4715-24-23

Schreinemachers, D. M. (2003). Birth malformations and other adverse perinatal outcomes in four U.S. Wheat-producing states. *Environmental Health Perspectives*, *111*(9), 1259–1264. https://doi.org/10.1289/ehp.5830

Schroth, M. N., & Hancock, J. G. (1982). Disease-suppressive soil and root-colonizing bacteria. *Science (New York, N.Y.)*, *216*(4553), 1376–1381. http://doi.org/10.1126/science.216.4553.1376

Schulz, A., Krüper, A., & Amrhein, N. (1985). Differential sensitivity of bacterial 5-enolpyruvylshikimate-3-phosphate synthases to the herbicide glyphosate. *FEMS Microbiology Letters*, *28*(3), 297–301. http://doi.org/10.1111/j.1574-6968.1985.tb00809.x

Schulz, R., Bub, S., Petschick, L. L., Stehle, S., & Wolfram, J. (2021). Applied pesticide toxicity shifts toward plants and invertebrates, even in GM crops. *Science*, *372*(6537), 81–84. https://doi.org/10.1126/science.abe1148

Schulze, J., Frauenknecht, T., Brodmann, P., & Bagutti, C. (2014). Unexpected Diversity of Feral Genetically Modified Oilseed Rape (Brassica napus L.) Despite a Cultivation and Import Ban in Switzerland. *PLoS ONE*, *9*(12), e114477. http://doi.org/10.1371/journal.pone.0114477

Schütte, G., Eckerstorfer, M., Rastelli, V., Reichenbecher, W., Restrepo-Vassalli, S., Ruohonen-Lehto, M., Saucy, A.-G.W., Mertens, M. (2017). Herbicide resistance and biodiversity: agronomic and environmental aspects of genetically modified herbicide-resistant plants. *Environmental Sciences Europe* **29**, 5. doi:10.1186/s12302-016-0100-y

Schweizerbauer (2015). Migros kippt Glyphosat aus Sortiment. https://www.schweizerbauer.ch/pflanzen/pflanzenschutz/migros-kippt-glyphosat-aus-sortiment-22482.html

Sciumbato, A. S., Chandler, J. M., Senseman, S. A., Bovey, R. W., & Smith, K. L. (2004). Determining Exposure to Auxin-Like Herbicides. II. Practical Application to Quantify Volatility. *Weed Technology*, *18*(4), 1135–1142. http://doi.org/10.1614/WT-03-229R

Seide, V. E., Bernardes, R. C., Pereira, E. J. G., & Lima, M. A. P. (2018). Glyphosate is lethal and Cry toxins alter the development of the stingless bee Melipona quadrifasciata. *Environmental Pollution*, *243*, 1854–1860. https://doi.org/10.1016/j.envpol.2018.10.020

Seidman, P. (2015). Upfront: Coming to a boil. Debate about using glyphosate to control plants in Marin heats up. Pacific Sun. https://www.pacificsun.com/upfront-coming-to-a-boil/

Selman, A. (2015). Non-GMO premium draws growers. Iowa Farmer Today. http://www.iowafarmertoday.com/news/crop/non-gmo-premium-draws-growers/article_13cee7c4-d88a-11e4-81c7-0fc155a05c10.html

Semmens, B. X., Semmens, D. J., Thogmartin, W. E., Wiederholt, R., López-Hoffman, L., Diffendorfer, J. E., Pleasants, J. M., Oberhauser, K. S., & Taylor, O. R. (2016). Quasi-extinction risk and population targets for the Eastern, migratory population of monarch butterflies (Danaus plexippus). *Scientific Reports*, *6*(1), 23265. https://doi.org/10.1038/srep23265

Séralini, G.-E., Clair, E., Mesnage, R., Gress, S., Defarge, N., Malatesta, M., … Vendômois, J. S. de. (2014). Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. *Environmental Sciences Europe*, *26*(1), 14. http://doi.org/10.1186/s12302-014-0014-5

Séralini, G.-E. (2020). Update on long-term toxicity of agricultural GMOs tolerant to roundup. *Environmental Sciences Europe*, *32*(1), 18. https://doi.org/10.1186/s12302-020-0296-8

Serra, L., Estienne, A., Vasseur, C., Froment, P., & Dupont, J. (2021). Review: Mechanisms of Glyphosate and Glyphosate-Based Herbicides Action in Female and Male Fertility in Humans and Animal Models. *Cells*, *10*(11), 3079. https://doi.org/10.3390/cells10113079

Serratos-Hernández, J.-A., Gómez-Olivares, J.-L., Salinas-Arreortua, N., Buendía-Rodríguez, E., Islas-Gutiérrez, F., & de-Ita, A. (2007). Transgenic proteins in maize in the Soil Conservation area of Federal District, Mexico. *Frontiers in Ecology and the Environment*, *5*(5), 247–252. https://doi.org/10.1890/1540-9295(2007)5[247:TPIMIT]2.0.CO;2

Servizi, J. A., Gordon, R. W., & Martens, D. W. (1987). Acute toxicity of Garlon 4 and Roundup herbicides to Salmon,Daphnia, and trout. *Bulletin of Environmental Contamination and Toxicology*, *39*(1), 15–22. http://doi.org/10.1007/BF01691783

Shalat, S. L., Donnelly, K. C., Freeman, N. C., Calvin, J. A., Ramesh, S., Jimenez, M., Black, K., Coutinho, C., Needham, L. L., Barr, D. B., Ramirez, J. (2003). Nondietary ingestion of pesticides by children in an agricultural community on the US/Mexico border: Preliminary results. *Journal of Exposure Science and Environmental Epidemiology*, *13*(1), 42–50. http://doi.org/10.1038/sj.jea.7500249

Sharma, R., Damgaard, D., Alexander, T. W., Dugan, M. E. R., Aalhus, J. L., Stanford, K., & McAllister, T. A. (2006). Detection of transgenic and endogenous plant DNA in digesta and tissues of sheep and pigs fed Roundup Ready canola meal. *Journal of Agricultural and Food Chemistry*, *54*(5), 1699–1709. http://doi.org/10.1021/jf052459o

Shaw, I. C. (2021). Is it time to round up Roundup®? The changing science of glyphosate. *New Zealand Science Review*, *77*(1), 3–12.

Shehata, A. A., Schrödl, W., Aldin, A. A., Hafez, H. M., & Krüger, M. (2013). The Effect of Glyphosate on Potential Pathogens and Beneficial Members of Poultry Microbiota In Vitro. *Current Microbiology*, *66*(4), 350–358. http://doi.org/10.1007/s00284-012-0277-2

Sherwani, S. I., Arif, I. A., & Khan, H. A. (2015). Modes of Action of Different Classes of Herbicides. *Herbicides, Physiology of Action, and Safety*. https://doi.org/10.5772/61779

Shi, G., Chavas, J.-P., & Lauer, J. (2013). Commercialized transgenic traits, maize productivity and yield risk. *Nature Biotechnology*, *31*(2), 111–114. http://doi.org/10.1038/nbt.2496

Shimatani, Z., Kashojiya, S., Takayama, M., Terada, R., Arazoe, T., Ishii, H., Teramura, H., Yamamoto, T., Komatsu, H., Miura, K., Ezura, H., Nishida, K., Ariizumi, T., & Kondo, A. (2017). Targeted base editing in rice and tomato using a CRISPR-Cas9 cytidine deaminase fusion. *Nature Biotechnology*, *35*(5), 441–443. https://doi.org/10.1038/nbt.3833

Shimono, A., Kanbe, H., Nakamura, S., Ueno, S., Yamashita, J., & Asai, M. (2020). Initial invasion of glyphosate-resistant Amaranthus palmeri around grain-import ports in Japan. *PLANTS, PEOPLE, PLANET*, *2*(6), 640–648. https://doi.org/10.1002/ppp3.10156

Shinabarger, D. L., & Braymer, H. D. (1986). Glyphosate catabolism by Pseudomonas sp. strain PG2982. *Journal of Bacteriology*, *168*(2), 702–707.

Shrestha, S., Parks, C. G., Goldner, W. S., Kamel, F., Umbach, Ward, M. H., Lerro, C. C., Koutros, S., Hofmann, J. N., Freeman, L. E., & Sandler, D. P. (2018). Pesticide Use and Incident Hypothyroidism in Pesticide Applicators in the Agricultural Health Study. *Environmental Health Perspectives*, *126*(9), 097008. https://doi.org/10.1289/EHP3194

Shukla, V. K., Doyon, Y., Miller, J. C., DeKelver, R. C., Moehle, E. A., Worden, S. E., Mitchell, J. C., Arnold, N. L., Gopalan, S., Meng, X., Choi, V. M., Rock, J. M., Wu, Y.-Y., Katibah, G. E., Zhifang, G., McCaskill, D., Simpson, M. A., Blakeslee, B., Greenwalt, S. A., … Urnov, F. D. (2009). Precise genome modification in the crop species Zea mays using zinc-finger nucleases. *Nature*, *459*(7245), 437–441. https://doi.org/10.1038/nature07992

Silva, J. F. S. da, Silva, A. M. C. da, Lima-Luz, L., Aydos, R. D., & Mattos, I. E. (2015). Correlação entre produção agrícola, variáveis clínicas-demográfcas e câncer de próstata: um estudo ecológico. *Ciência & Saúde Coletiva*, 20(9), 2805–2812. http://doi.org/10.1590/1413-81232015209.00582015

Silver, M. K., Shao, J., Li, M., Ji, C., Chen, M., Xia, Y., Lozoff, B., & Meeker, J. D. (2019). Prenatal exposure to the herbicide 2,4-D is associated with deficits in auditory processing during infancy. *Environmental Research*, *172*, 486–494. https://doi.org/10.1016/j.envres.2019.02.046

Silver, M. K., Fernandez, J., Tang, J., McDade, A., Sabino, J., Rosario, Z., V, élez V. C., Alshawabkeh, A., Cordero, J. F., & Meeker, J. D. (2021). Prenatal Exposure to Glyphosate and Its Environmental Degradate, Aminomethylphosphonic Acid (AMPA), and Preterm Birth: A Nested Case–Control Study in the PROTECT Cohort (Puerto Rico). *Environmental Health Perspectives*, *129*(5), 057011. https://doi.org/10.1289/EHP7295

Simon, F (2017a) EFSA boss: Trust in integrity of science has a cost. Euractiv. 16th January 2017. http://www.euractiv.com/section/science-policymaking/interview/efsa-boss-trust-in-integrity-of-science-has-a-cost/

Simon, F (2017b) EFSA: Glyphosate ban debate 'legitimate' but not about science. 16th January 2017. http://www.euractiv.com/section/science-policymaking/news/efsa-glyphosate-ban-debate-legitimate-but-not-about-science/?nl_ref=28998550

Sineiro, C. C., & Berger, M. (2012). Citizens' Rights and Environmental Genocide. *Environmental Justice*, 5(2), 105–110. http://doi.org/10.1089/env.2011.0011

Singh, S., Kumar, V., Datta, S., Wani, A. B., Dhanjal, D. S., Romero, R., & Singh, J. (2020). Glyphosate uptake, translocation, resistance emergence in crops, analytical monitoring, toxicity and degradation: A review. *Environmental Chemistry Letters*, *18*(3), 663–702. https://doi.org/10.1007/s10311-020-00969-z

Slaby, S., Titran, P., Marchand, G., Hanotel, J., Lescuyer, A., Leprêtre, A., Bodart, J.-F., Marin, M., & Lemiere, S. (2020). Effects of glyphosate and a commercial formulation Roundup® exposures on maturation of Xenopus laevis oocytes. *Environmental Science and Pollution Research*, *27*(4), 3697–3705. https://doi.org/10.1007/s11356-019-04596-2

Slager, R. E., Poole, J. A., LeVan, T. D., Sandler, D. P., Alavanja, M. C. R., & Hoppin, J. A. (2009). Rhinitis associated with pesticide exposure among commercial pesticide applicators in the Agricultural Health Study. Occupational and Environmental Medicine, 66(11), 718–724. http://doi.org/10.1136/oem.2008.041798

Smagghe, D. (2015). McDonald's: dans notre poulet, ni antibiotiques activateurs de croissance, ni OGM. Le Plus. http://leplus.nouvelobs.com/contribution/1353598-mcdonald-s-dans-notre-poulet-ni-antibiotiques-activateurs-de-croissance-ni-ogm.html

Smith, K. L., Doherty, R. C., Bullington, J. A., Meier, J. R., & Bagavathiannan, M. V. (2012). Seed Production Potential of Palmer Amaranth in Arkansas. In *Summaries of Arkansas Cotton Research 2011*.

Smith, P. (2016, December 19). *Dicamba Lawsuit—Missouri Farmer Sues Monsanto*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/news/business-inputs/article/2016/12/19/missouri-farmer-sues-monsanto

Smith, A. M., Smith, M. T., La Merrill, M. A., Liaw, J., & Steinmaus, C. (2017). 2,4-dichlorophenoxyacetic acid (2,4-D) and risk of non-Hodgkin lymphoma: A meta-analysis accounting for exposure levels. *Annals of Epidemiology*, *27*(4), 281-289.e4. https://doi.org/10.1016/j.annepidem.2017.03.003

Smith, D. F. Q., Camacho, E., Thakur, R., Barron, A. J., Dong, Y., Dimopoulos, G., Broderick, N. A., & Casadevall, A. (2021). Glyphosate inhibits melanization and increases susceptibility to infection in insects. PLOS Biology, 19(5), e3001182. https://doi.org/10.1371/journal.pbio.3001182

Smyth, S., Khachatourians, G. G., Philips, P. W. B. (2002). Liabilities and economics of transgenic crops. *Nature Biotechnology*, vol. 20, 537-541.

Snow, A. (2009). Unwanted transgenes re-discovered in Oaxacan maize. *Molecular Ecology*, *18*(4), 569–571. http://doi.org/10.1111/j.1365-294X.2008.04063.x

Soares, C., Pereira, R., Spormann, S., & Fidalgo, F. (2019). Is soil contamination by a glyphosate commercial formulation truly harmless to non-target plants? – Evaluation of oxidative damage and antioxidant responses in tomato. *Environmental Pollution*, *247*, 256–265. https://doi.org/10.1016/j.envpol.2019.01.063

Sobjak, T. M., Romão, S., do Nascimento, C. Z., Dos Santos, A. F. P., Vogel, L., & Guimarães, A. T. B. (2017). Assessment of the oxidative and neurotoxic effects of glyphosate pesticide on the larvae of Rhamdia quelen fish. *Chemosphere*, *182*, 267–275. https://doi.org/10.1016/j.chemosphere.2017.05.031

Sohn, S.-I., Pandian, S., Oh, Y.-J., Kang, H.-J., Ryu, T.-H., Cho, W.-S., Shin, E.-K., & Shin, K.-S. (2021). A Review of the Unintentional Release of Feral Genetically Modified Rapeseed into the Environment. *Biology*, *10*(12), 1264. https://doi.org/10.3390/biology10121264

Soil Association (2015). Soil Association calls for ban on Glyphosate: the world's most widely sold weedkiller. http://www.soilassociation.org/news/newsstory/articleid/8110/soil-association-calls-for-ban-on-glyphosate-the-world-s-most-widely-sold-weedkiller

Soloneski, S., Ruiz de Arcaute, C., & Larramendy, M. L. (2016). Genotoxic effect of a binary mixture of dicamba- and glyphosate-based commercial herbicide formulations on Rhinella arenarum (Hensel, 1867) (Anura, Bufonidae) late-stage larvae. *Environmental Science and Pollution Research International*, *23*(17), 17811–17821. https://doi.org/10.1007/s11356-016-6992-7

Soltani, N., Oliveira, M. C., Alves, G. S., Werle, R., Norsworthy, J. K., Sprague, C. L., Young, B. G., Reynolds, D. B., Brown, A., & Sikkema, P. H. (2020). Off-target movement assessment of dicamba in North America. *Weed Technology*, *34*(3), 318–330. https://doi.org/10.1017/wet.2020.17

Song, X., Wang, Z., Zuo, J., Huangfu, C., & Qiang, S. (2010). Potential gene flow of two herbicide-tolerant transgenes from oilseed rape to wild B. juncea var. Gracilis. *Theoretical and Applied Genetics*, *120*(8), 1501–1510. https://doi.org/10.1007/s00122-010-1271-3

Song, X., Wang, Z., & Qiang, S. (2011). Agronomic performance of F1, F2 and F3 hybrids between weedy rice and transgenic glufosinate-resistant rice. *Pest Management Science*, *67*(8), 921–931. https://doi.org/10.1002/ps.2132

Sørensen, M. T., Poulsen, H. D., Katholm, C. L., & Højberg, O. (2021). Review: Feed residues of glyphosate – potential consequences for livestock health and productivity. *Animal*, *15*(1), 100026. https://doi.org/10.1016/j.animal.2020.100026

Sosnoskie, L. M., & Culpepper, A. S. (2014). Glyphosate-Resistant Palmer Amaranth (*Amaranthus palmeri*) Increases Herbicide Use, Tillage, and Hand-Weeding in Georgia Cotton. *Weed Science*, *62*(2), 393–402. http://doi.org/10.1614/WS-D-13-00077.1

Southey, F. (2021, February 11). *Behind the push for GMO transparency on-pack: 'Non-GMO food labelling closes a loophole in EU legislation'*. Foodnavigator.Com. https://www.foodnavigator.com/Article/2021/02/11/ENGA-pushes-for-non-GMO-food-labelling-across-Europe

Sparling, D. W., & Fellers, G. M. (2009). Toxicity of two insecticides to California, USA, anurans and its relevance to declining amphibian populations. *Environmental Toxicology and Chemistry*, *28*(8), 1696–1703. https://doi.org/10.1897/08-336.1

Spaunhorst, D. J., Nie, H., Todd, J. R., Young, J. M., Young, B. G., & Johnson, W. G. (2019). Confirmation of herbicide resistance mutations Trp574Leu, ΔG210, and EPSPS gene amplification and control of multiple herbicide-resistant Palmer amaranth (Amaranthus palmeri) with chlorimuron-ethyl, fomesafen, and glyphosate. *PLOS ONE*, *14*(3), e0214458. https://doi.org/10.1371/journal.pone.0214458

Spinaci, M., Nerozzi, C., Tamanini, C. lo, Bucci, D., & Galeati, G. (2020). Glyphosate and its formulation Roundup impair pig oocyte maturation. *Scientific Reports*, *10*(1), 12007. https://doi.org/10.1038/s41598-020-68813-6

Spisák, S., Solymosi, N., Ittzés, P., Bodor, A., Kondor, D., Vattay, G., Barták, B. K., Sipod, F., Galamb, O., Tulassay, Z., Szállási, Z., Rasmussen, S., Sicheritz-Ponten, T., Brunak, S., Molnár, B., Csabai, I. (2013). Complete Genes May Pass from Food to Human Blood. *PLoS ONE*, *8*(7). http://doi.org/10.1371/journal.pone.0069805

Sprinkle, R. H., & Payne-Sturges, D. C. (2021). Mixture toxicity, cumulative risk, and environmental justice in United States federal policy, 1980–2016. *Environmental Health*, *20*(1), 104. https://doi.org/10.1186/s12940-021-00764-5
Stauffer Chemical Co (1964), Aminomethylenephosphinic acids, salts thereof, and process for their production. U.S. Patent 3,160,632
Stebbins-Boaz, B., Fortner, K., Frazier, J., Piluso, S., Pullen, S., Rasar, M., Reid, W., Sinclair, K., & Winger, E. (2004). Oocyte maturation in Xenopus laevis is blocked by the hormonal herbicide, 2,4-dichlorophenoxy acetic acid. *Molecular Reproduction and Development*, *67*(2), 233–242. https://doi.org/10.1002/mrd.10396
Steed. (2018, February 2). *Dicamba cases in 4 states, including Arkansas, moved to 1 court*. Arkansas Online. https://www.arkansasonline.com/news/2018/feb/02/11-dicamba-cases-moved-to-1-court-20180/
Stempel, J. (2022, June 17). U.S. EPA ordered to reassess glyphosate's impact on health, environment. *Reuters*. https://www.reuters.com/business/environment/us-agency-ordered-reassess-glyphosates-impact-health-environment-2022-06-17/
Stenoien, C., Nail, K. R., Zalucki, J. M., Parry, H., Oberhauser, K. S., & Zalucki, M. P. (2018). Monarchs in decline: A collateral landscape-level effect of modern agriculture. *Insect Science*, *25*(4), 528–541. https://doi.org/10.1111/1744-7917.12404
Stoate, C., Boatman, N. D., Borralho, R. J., Carvalho, C. R., Snoo, G. R. de, & Eden, P. (2001). Ecological impacts of arable intensification in Europe. *Journal of Environmental Management*, *63*(4), 337–365. http://doi.org/10.1006/jema.2001.0473
Storkey, J., Meyer, S., Still, K. S., & Leuschner, C. (2011). The impact of agricultural intensification and land-use change on the European arable flora. *Proceedings of the Royal Society B: Biological Sciences*, rspb20111686. http://doi.org/10.1098/rspb.2011.1686
Strandberg, B., Sørensen, P. B., Bruus, M., Bossi, R., Dupont, Y. L., Link, M., & Damgaard, C. F. (2021). Effects of glyphosate spray-drift on plant flowering. *Environmental Pollution*, *280*, 116953. https://doi.org/10.1016/j.envpol.2021.116953
Straw, E. A., Carpentier, E. N., & Brown, M. J. F. (2021). Roundup causes high levels of mortality following contact exposure in bumble bees. *Journal of Applied Ecology*, *58*(6), 1167–1176. https://doi.org/10.1111/1365-2664.13867
Strom, S. (2015). Similac Advance Infant Formula to Be Offered G.M.O.-Free. The New York Times. http://www.nytimes.com/2015/05/26/business/similac-advance-infant-formula-to-be-offered-gmo-free.html?_r=0
Strom, P. (2020, January 24). ADM Files Class Action for GMO MIR 162 Syngenta Corn Seed Lawsuit. Strom Law Firm. https://stromlaw.com/adm-files-class-action-for-gmo-mir-162-syngenta-corn-seed-lawsuit/
Struger, J., Thompson, D., Staznik, B., Martin, P., McDaniel, T., & Marvin, C. (2008). Occurrence of Glyphosate in Surface Waters of Southern Ontario. *Bulletin of Environmental Contamination and Toxicology*, *80*(4), 378–384. http://doi.org/10.1007/s00128-008-9373-1
Sudianto, E., Beng-Kah, S., Ting-Xiang, N., Saldain, N. E., Scott, R. C., & Burgos, N. R. (2013). Clearfield® rice: Its development, success, and key challenges on a global perspective. *Crop Protection*, *49*, 40–51. https://doi.org/10.1016/j.cropro.2013.02.013
Sulukan, E., Köktürk, M., Ceylan, H., Beydemir, Ş., Işik, M., Atamanalp, M., & Ceyhun, S. B. (2017). An approach to clarify the effect mechanism of glyphosate on body malformations during embryonic development of zebrafish (Daino rerio). *Chemosphere*, *180*, 77–85. https://doi.org/10.1016/j.chemosphere.2017.04.018
Sun, Y., Zhang, X., Wu, C., He, Y., Ma, Y., Hou, H., Guo, X., Du, W., Zhao, Y., & Xia, L. (2016). Engineering Herbicide-Resistant Rice Plants through CRISPR/Cas9-Mediated Homologous Recombination of Acetolactate Synthase. *Molecular Plant*, *9*(4), 628–631. https://doi.org/10.1016/j.molp.2016.01.001
Suppa, A., Kvist, J., Li, X., Dhandapani, V., Almulla, H., Tian, A. Y., Kissane, S., Zhou, J., Perotti, A., Mangelson, H., Langford, K., Rossi, V., Brown, J. B., & Orsini, L. (2020). Roundup causes embryonic development failure and alters metabolic pathways and gut microbiota functionality in non-target species. *Microbiome*, *8*(1), 170. https://doi.org/10.1186/s40168-020-00943-5
Supreme Court of Western Australia (2014). Marsh v Baxter [2014] WASC 187 (CIV 1561 of 2012). Judgment summary. http://www.supremecourt.wa.gov.au/_files/Judgment%20Summary%20-%20Marsh%20v%20Baxter%20(CIV%201561%20of%202012)%2028%20May%202014.pdf
Sustainable Pulse (2014). Glyphosate Herbicide Sales Boom Powers Global Biotech Industry. http://sustainablepulse.com/2014/08/21/glyphosate-sales-boom-powers-global-biotech-industry/#.VKsgGb46XbK
Sustainable Pulse (2015a). WSU researcher Find Glyphosate-Free Breast Milk for Monsanto. http://sustainablepulse.com/2015/07/24/wsu-researchers-find-glyphosate-free-breast-milk-for-monsanto/#.VbOxKr7DrbI

Sustainable Pulse (2015b). Slack Science Destroys Monsanto Breast Milk Study. http://sustainablepulse.com/2015/07/27/slack-science-destroys-monsanto-breast-milk-study/#.VbXJqChuKTN

Sustainable Pulse (2015d). Dutch Parliament Bans Glyphosate Herbicide for Non-Commercial Use. http://sustainablepulse.com/2014/04/04/dutch-parliament-bans-glyphosate-herbicides-non-commercial-use/#.Vb92Ub7DrbJ

Sustainable Pulse. (2020, July 20). *Bayer Investors Investigate Company's Directors for Possible Securities Fraud over Roundup Cancer Cases*. Sustainable Pulse. https://sustainablepulse.com/2020/07/20/bayer-investors-investigate-companys-directors-for-possible-securities-fraud-over-roundup-cancer-case/

Sustainable Pulse. (2021, July 29). *Bayer Confirms End of Sale of Glyphosate-Based Herbicides for US Lawn & Garden Market*. Sustainable Pulse. https://sustainablepulse.com/2021/07/29/bayer-confirms-end-of-sale-of-glyphosate-based-herbicides-for-us-lawn-garden-market/ [accessed: 31 December 2021]

Svitashev, S., Young, J. K., Schwartz, C., Gao, H., Falco, S. C., & Cigan, A. M. (2015). Targeted Mutagenesis, Precise Gene Editing, and Site-Specific Gene Insertion in Maize Using Cas9 and Guide RNA[OPEN]. *Plant Physiology*, *169*(2), 931–945. https://doi.org/10.1104/pp.15.00793

Svitashev, S., Schwartz, C., Lenderts, B., Young, J. K., & Mark Cigan, A. (2016). Genome editing in maize directed by CRISPR–Cas9 ribonucleoprotein complexes. *Nature Communications*, *7*. https://doi.org/10.1038/ncomms13274

Sweeney, F., Testorf, J., 2017. Dose Response of *D. Magna* and *C. Elegans* Exposed to Glyphosate. Presented at the 2017 AAAS Annual Meeting (February 16-20, 2017), aaas. https://aaas.confex.com/aaas/2017/webprogram/Paper19936.html

Tan, S., Evans, R. R., Dahmer, M. L., Singh, B. K., & Shaner, D. L. (2005). Imidazolinone-tolerant crops: History, current status and future. *Pest Management Science*, *61*(3), 246–257. https://doi.org/10.1002/ps.993

Tan, Z., Zhou, J., Chen, H., Zou, Q., Weng, S., Luo, T., & Tang, Y. (2016). Toxic effects of 2,4-dichlorophenoxyacetic acid on human sperm function *in vitro* . *The Journal of Toxicological Sciences*, *41*(4), 543–549. https://doi.org/10.2131/jts.41.543

Tan, S., Li, G., Liu, Z., Wang, H., Guo, X., & Xu, B. (2022). Effects of glyphosate exposure on honeybees. *Environmental Toxicology and Pharmacology*, *90*, 103792. https://doi.org/10.1016/j.etap.2021.103792

Tanaka, J., Yamashita, M., Yamashita, M., Matsuo, H., & Yamamoto, T. (1998). Two cases of glufosinate poisoning with late onset convulsions. *Veterinary and Human Toxicology*, *40*(4), 219–222.

Tang, X., Sretenovic, S., Ren, Q., Jia, X., Li, M., Fan, T., Yin, D., Xiang, S., Guo, Y., Liu, L., Zheng, X., Qi, Y., & Zhang, Y. (2020). Plant Prime Editors Enable Precise Gene Editing in Rice Cells. *Molecular Plant*, *13*(5), 667–670. https://doi.org/10.1016/j.molp.2020.03.010

Tapkir, S. D., Kharat, S. S., Kumkar, P., & Gosavi, S. M. (2019). Impact, recovery and carryover effect of Roundup® on predator recognition in common spiny loach, Lepidocephalichthys thermalis. *Ecotoxicology*, *28*(2), 189–200. https://doi.org/10.1007/s10646-018-02011-z

Tayeb, W., Nakbi, A., Trabelsi, M., Attia, N., Miled, A., & Hammami, M. (2010). Hepatotoxicity induced by sub-acute exposure of rats to 2,4-Dichlorophenoxyacetic acid based herbicide "Désormone lourd." *Journal of Hazardous Materials*, *180*(1), 225–233. https://doi.org/10.1016/j.jhazmat.2010.04.018

Tayeb, W., Nakbi, A., Trabelsi, M., Miled, A., & Hammami, M. (2012). Biochemical and histological evaluation of kidney damage after sub-acute exposure to 2,4-dichlorophenoxyacetic herbicide in rats: Involvement of oxidative stress. *Toxicology Mechanisms and Methods*, *22*(9), 696–704. https://doi.org/10.3109/15376516.2012.717650

Tayeb, W., Nakbi, A., Cheraief, I., Miled, A., & Hammami, M. (2013). Alteration of lipid status and lipid metabolism, induction of oxidative stress and lipid peroxidation by 2,4-dichlorophenoxyacetic herbicide in rat liver. *Toxicology Mechanisms and Methods*, *23*(6), 449–458. https://doi.org/10.3109/15376516.2013.780275

Taylor, N. B., Fuchs, R. L., MacDonald, J., Shariff, A. R., & Padgette, S. R. (1999). Compositional Analysis of Glyphosate-Tolerant Soybeans Treated with Glyphosate. *Journal of Agricultural and Food Chemistry*, *47*(10), 4469–4473. http://doi.org/10.1021/jf990056g

Taylor, O. R. J., Pleasants, J. M., Grundel, R., Pecoraro, S. D., Lovett, J. P., & Ryan, A. (2020). Evaluating the Migration Mortality Hypothesis Using Monarch Tagging Data. *Frontiers in Ecology and Evolution*, *0*. https://doi.org/10.3389/fevo.2020.00264

Tehranchian, P., Nandula, V., Jugulam, M., Putta, K., & Jasieniuk, M. (2018). Multiple resistance to glyphosate, paraquat and ACCase-inhibiting herbicides in Italian ryegrass populations from California: Confirmation and mechanisms of resistance. *Pest Management Science*, *74*(4), 868–877. https://doi.org/10.1002/ps.4774

Telesur (2015). Colombia May Prohibit Fumigations with Monsanto's Glyphosate. http://www.telesurtv.net/english/news/Colombia-May-Prohibit-Fumigations-with-Monsantos-Glyphosate-20150502-0015.html

Telesur (2017) Colombia Restarts Controversial Glyphosate Fumigation of Coca. 11th January 2017. http://www.telesurtv.net/english/news/Colombia-Restarts-Controversial-Glyphosate-Fumigation-of-Coca-20170111-0030.html

Terazono, E. (2015). Ukraine set to become top corn exporter to China in first half. Financial Times. http://www.ft.com/cms/s/0/989c82ba-20cc-11e5-ab0f-6bb9974f25d0.html#axzz3ezsvZWEj

Testbiotech (2013). High levels of residues from spraying with glyphosate found in soybeans in Argentina. Testbiotech Background, http://www.testbiotech.de/en/node/926

The Progressive Farmer (2016) More Herbicide Heartburn. 14 July 2016. https://www.dtnpf.com/agriculture/web/ag/news/article/2016/07/14/dicamba-injury-reports-mount?referrer=twitter#.V4pW7iEmuEc.twitter

The Sydney Morning Herald (2008). GM canola 'contaminated' Canadian farms. http://www.smh.com.au/national/gm-canola-contaminated-canadian-farms-20080204-1pzh.html

Then, C. & Tippe, R. (2014). European patents on plants and animals – is the patent industry taking control of our food? No Patents on Seeds. http://www.no-patents-on-seeds.org/sites/default/files/news/european_patents_on_plants_and_animals_2014.pdf

Thogmartin, W. E., Wiederholt, R., Oberhauser, K., Drum, R. G., Diffendorfer, J. E., Altizer, S., Taylor, O. R., Pleasants, J., Semmens, D., Semmens, B., Erickson, R., Libby, K., & Lopez-Hoffman, L. (2017). Monarch butterfly population decline in North America: Identifying the threatening processes. *Royal Society Open Science*, *4*(9), 170760. https://doi.org/10.1098/rsos.170760

Thongprakaisang, S., Thiantanawat, A., Rangkadilok, N., Suriyo, T., & Satayavivad, J. (2013). Glyphosate induces human breast cancer cells growth via estrogen receptors. *Food and Chemical Toxicology*, *59*, 129–136. http://doi.org/10.1016/j.fct.2013.05.057

Tian, S., Jiang, L., Cui, X., Zhang, J., Guo, S., Li, M., Zhang, H., Ren, Y., Gong, G., Zong, M., Liu, F., Chen, Q., & Xu, Y. (2018). Engineering herbicide-resistant watermelon variety through CRISPR/Cas9-mediated base-editing. *Plant Cell Reports*, *37*(9), 1353–1356. https://doi.org/10.1007/s00299-018-2299-0

Tillie, P., Rodríguez-Cerezo, E. (2015). Markets for non-Genetically Modified Identity-Preserved soybean in the EU. JRC Science and Policy Report, Europena Commission. http://publications.jrc.ec.europa.eu/repository/bitstream/JRC95457/report.pdf

Times of Malta (2016) Malta set to ban probable carcinogenic weedkiller. 15 July 2016. http://www.timesofmalta.com/articles/view/20160715/local/malta-set-to-ban-probable-carcinogenic-weedkiller.618884

Today in Bermuda (2015). Health Minister: Importation of Roundup Weed Spray Suspended. http://www.todayinbermuda.com/news/health/item/1471-health-minister-importation-of-roundup-weed-spray-suspended

Torretta, V., Katsoyiannis, I. A., Viotti, P., & Rada, E. C. (2018). Critical Review of the Effects of Glyphosate Exposure to the Environment and Humans through the Food Supply Chain. *Sustainability*, *10*(4), 950. https://doi.org/10.3390/su10040950

Townsend, M., Peck, C., Meng, W., Heaton, M., Robison, R., O'Neill, K. (2017). Evaluation of various glyphosate concentrations on DNA damage in human Raji cells and its impact on cytotoxicity. *Regul. Toxicol. Pharmacol.* **85**, 79–85. doi:10.1016/j.yrtph.2017.02.002

Trasande, L., Zoeller, R. T., Hass, U., Kortenkamp, A., Grandjean, P., Myers, J. P., DiGangi, J., Bellanger, M., Hauser, R., Legler, J., Skakkebaek, N. E., Heindel, J. J. (2015). Estimating Burden and Disease Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. *The Journal of Clinical Endocrinology & Metabolism*, jc.2014–4324. http://doi.org/10.1210/jc.2014-4324

Tresnakova, N., Stara, A., & Velisek, J. (2021). Effects of Glyphosate and Its Metabolite AMPA on Aquatic Organisms. *Applied Sciences*, *11*(19), 9004. https://doi.org/10.3390/app11199004

Tscharntke, T., Clough, Y., Wanger, T. C., Jackson, L., Motzke, I., Perfecto, I., … Whitbread, A. (2012). Global food security, biodiversity conservation and the future of agricultural intensification. *Biological Conservation*, **151**(1), 53–59. http://doi.org/10.1016/j.biocon.2012.01.068

Tsui, M. T. K., & Chu, L. M. (2003). Aquatic toxicity of glyphosate-based formulations: comparison between different organisms and the effects of environmental factors. *Chemosphere*, **52**(7), 1189–1197. http://doi.org/10.1016/S0045-6535(03)00306-0

Tsui, M. T. K., & Chu, L. M. (2004). Comparative Toxicity of Glyphosate-Based Herbicides: Aqueous and Sediment Porewater Exposures. *Archives of Environmental Contamination and Toxicology*, *46*(3), 316–323. http://doi.org/10.1007/s00244-003-2307-3

Tu, P., Gao, B., Chi, L., Lai, Y., Bian, X., Ru, H., & Lu, K. (2019). Subchronic low-dose 2,4-D exposure changed plasma acylcarnitine levels and induced gut microbiome perturbations in mice. *Scientific Reports*, *9*(1), 4363. https://doi.org/10.1038/s41598-019-40776-3

Turner, H. (2015a). Another Month, Another 300 Syngenta Lawsuits. Lawyers and Settlements. http://www.lawyersandsettlements.com/articles/gmo-corn-seed/syngenta-lawsuits-viptera-lawsuit-gmo-corn-4-20650.html#.VW1j5r7UTbK

Turner, C. (2015b). Weedkiller alert over cancer link. The Telegraph. http://www.telegraph.co.uk/news/science/science-news/11487118/Weedkiller-alert-over-cancer-link.html

Tush, D., Meyer, M.T., 2016. Polyoxyethylene Tallow Amine, a Glyphosate Formulation Adjuvant: Soil Adsorption Characteristics, Degradation Profile, and Occurrence on Selected Soils from Agricultural Fields in Iowa, Illinois, Indiana, Kansas, Mississippi, and Missouri. Environ. Sci. Technol. 50, 5781–5789. doi:10.1021/acs.est.6b00965

Twellman, B. (2021, November 29). *Non-GMO U.S. Soy Production Competes with High Commodity Prices*. U.S. Soy. https://ussoy.org/non-gmo-u-s-soy-production-competes-with-high-commodity-prices/?persona=importers&pillar=exceptional-supply&region=americas&goal=inform-educate

UNCTAD (2013). Trade and Environment Review 2013 - Wake up before it is too late. Make agriculture truly sustainable now for food security in a changing climate. http://unctad.org/en/PublicationsLibrary/ditcted2012d3_en.pdf

UNEP (2013). The Emission Gap Report 2013. United Nations Environment Programme (UNEP), Nairobi.

UNESCO (2008). World Heritage list. Monarch butterfly biosphere reserve. http://whc.unesco.org/en/list/1290.

Unglesbee E (2017) Second Dicamba Lawsuit. The Progressive Farmer. 16th February 2017. https://www.dtnpf.com/agriculture/web/ag/news/crops/article/2017/02/16/class-action-lawsuit-filed-monsanto-2

Unglesbee, E. (2018, June 8). *New Bayer Today; BASF Takes Over "Old" Bayer Traits, Seeds – DTN*. AgFax. https://agfax.com/2018/06/08/new-bayer-today-basf-takes-over-old-bayer-traits-seeds-dtn/

Unglesbee, E. (2020a, June 5). *Weed Control Minus Dicamba—Xtend Weed Control Options Without Dicamba*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/article/2020/06/05/xtend-weed-control-options-without

Unglesbee, E. (2020b). *Dicamba Not Controlling Some Tennessee Palmer Amaranth Populations*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/02/27/dicamba-controlling-tennessee-palmer

Unglesbee, E. (2020c, July 14). *The Future of Dicamba—Dicamba Use Faces Trio of Threats: Courts, Weeds and Farmer Fatigue*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/07/14/dicamba-use-faces-trio-threats-weeds

Unglesbee, E. (2020d, December 17). *Dicamba Settlement Is a Go—$300 Million Dicamba Settlement Finalized, Claim Filing to Start Shortly*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/12/17/300-million-dicamba-settlement-claim

Unglesbee, E. (2020e, June 8). *Dicamba Legal Update—Here's What We Know About the Legal Status of Dicamba*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/06/04/know-legal-status-dicamba

Unglesbee, E. (2020f, June 4). *Dicamba Registrations Vacated—The Ninth Circuit Vacates Three Dicamba Registrations*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/06/04/ninth-circuit-vacates-three-dicamba

Unglesbee, E. (2020g, June 8). *The States of Dicamba—States Enter Uncertain Legal Territory With Conflicting Dicamba Decisions*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/06/08/states-enter-uncertain-legal-dicamba

Unglesbee, E. (2020h, June 12). *Dicamba Use Challenged—Plaintiffs Ask Federal Court to Halt Dicamba Spraying, Hold EPA in Contempt*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/06/12/plaintiffs-ask-federal-court-halt

Unglesbee, E. (2020i, June 19). *Dicamba Use to Continue—Ninth Circuit Denies Petition to Halt Dicamba Use*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/06/20/ninth-circuit-denies-petition-halt

Unglesbee, E. (2020j, June 5). *Weed Control Minus Dicamba—Xtend Weed Control Options Without Dicamba*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/article/2020/06/05/xtend-weed-control-options-without

Unglesbee, E. (2020k, June 25). *No Reversal on Dicamba—Judges Deny BASF's Motion, Dicamba Registrations Remain Vacated*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/06/26/judges-deny-basfs-motion-dicamba

Unglesbee, E. (2020l, July 21). *Dicamba Fight Continues—Companies Ask Ninth Circuit Court to Re-Hear Dicamba Case*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/07/21/companies-ask-ninth-circuit-court-re

Unglesbee, E. (2020m, September 24). *EPA's Dicamba To-Do List — Dicamba Decision Time for EPA: What's on the Table?* DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/09/24/dicamba-decision-time-epa-table
Unglesbee, E. (2020n, July 14). *The Future of Dicamba—Dicamba Use Faces Trio of Threats: Courts, Weeds and Farmer Fatigue*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/07/14/dicamba-use-faces-trio-threats-weeds
Unglesbee, E. (2020o, June 10). *Production Blog—Enlist Duo Herbicide Also Under Scrutiny in the Ninth Circuit*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/blogs/production-blog/blog-post/2020/06/10/enlist-duo-herbicide-also-scrutiny
Unglesbee, E. (2020p, July 22). *Enlist Duo Ruling—Ninth Circuit Court Ruling Upholds Enlist Duo Registration*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/07/22/ninth-circuit-court-ruling-upholds
Unglesbee, E. (2021a, February 17). *Glufosinate-Resistant Palmer Amaranth Confirmed in Arkansas*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2021/02/17/glufosinate-resistant-palmer
Unglesbee, E. (2021b, July 21). *Hebricide Injury on the Rise—Battle Lines Drawn as Dicamba Injury Surfaces Once Again*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2021/07/21/battle-lines-drawn-dicamba-injury
Unglesbee, E. (2022a, March 29). *Court Asks EPA for Agency's Long-Term Dicamba Plan*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2022/03/29/court-asks-epa-agencys-long-term
Unglesbee, E. (2022b, July 1). *Court Asked to Kickstart Lawsuit to Vacate Dicamba Registrations*. DTN Progressive Farmer. https://www.dtnpf.com/agriculture/web/ag/crops/article/2022/01/07/court-asked-kickstart-lawsuit-vacate
Union of Concerned Scientists. (2012). *High and Dry: Why Genetic Engineering Is Not Solving Agriculture's Drought Problem in a Thirsty World*. https://www.ucsusa.org/sites/default/files/2019-09/high-and-dry-report.pdf
United States District Court Northern District of California (2017) Plaintiffs' Reply in Support of Motion to Compel Deposition of Jess Rowland. In Re: Roundup Products Liability Litigation. Case No. 16-md-02741-VC. MDL No. 2741. 27th February, 2017
University of California, Division of Agriculture and Natural Resources. (2021). Carotenoid Biosynthesis Inhibitors. Herbicide Symptoms. http://herbicidesymptoms.ipm.ucanr.edu/MOA/Carotenoid_biosynthesis_inhibitors [accessed: 4th January, 2022]
University of Nebraska CropWatch (2015). Glyphosate-resistant Palmer amaranth confirmed in SW Nebraska. http://www.agprofessional.com/news/glyphosate-resistant-palmer-amaranth-confirmed-sw-nebraska?utm_content=bufferdd1d0&utm_medium=social&utm_source=twitter.com&utm_campaign=buffer
Univox (2015). Agrarbericht 2015. http://www.agrarbericht.ch/de/mensch/gesellschaft/einschaetzungen-der-bevoelkerung
Upamalika, S. W. A. M., Wannige, C. T., Vidanagamachchi, S. M., Gunasekara, S. C., Kolli, R. T., De Silva, P. M. C. S., Kulasiri, D., & Jayasundara, N. (2022). A review of molecular mechanisms linked to potential renal injury agents in tropical rural farming communities. *Environmental Toxicology and Pharmacology*, *92*, 103850. https://doi.org/10.1016/j.etap.2022.103850
Uren Webster, T.M., Santos, E.M. (2015). Global transcriptomic profiling demonstrates induction of oxidative stress and of compensatory cellular stress responses in brown trout exposed to glyphosate and Roundup. BMC Genomics 16, 32. doi:10.1186/s12864-015-1254-5
USDA. (2021, June 7). Austria: Parliament Adopts Partial Ban on Glyphosate. USDA Foreign Agricultural Service. https://www.fas.usda.gov/data/austria-austrian-parliament-adopts-partial-ban-glyphosate
USDA APHIS. (2013). *Determination of nonregulated status for Bayer Event FG72 soybean*. United States Department of Agriculture. https://www.aphis.usda.gov/brs/aphisdocs/09_32801p_det.pdf
USDA APHIS. (2014). *Dow AgroScience LLC; Determination of Nonregulated Status of Herbicide Resistant Corn and Soybeans*. United States Department of Agriculture. https://www.federalregister.gov/documents/2014/09/22/2014-22409/dow-agrosciences-llc-determination-of-nonregulated-status-of-herbicide-resistant-corn-and-soybeans
USDA APHIS (2014a). Monsanto Petitions (10-188-01p and 12-185-01p) for Determinations of Nonregulated Status for Dicamba Resistant Soybean and Cotton Varieties. Final Environmental Impact Statement. https://www.aphis.usda.gov/brs/aphisdocs/dicamba_feis.pdf
USDA APHIS (2014b). Dow AgroSciences Petitions (09-233- 01p, 09-349-01p, and 11-234-01p) for Determinations of Nonregulated Status for 2,4-D-Resistant Corn and Soybean Varieties. Final Environmental Impact Statement. https://www.aphis.usda.gov/brs/aphisdocs/24d_feis.pdf
USDA APHIS. (2015). *Determination of Nonregulated Status for Dow AgroSciences DAS-8191Ø-7 Cotton*. United States Department of Agriculture. https://www.aphis.usda.gov/brs/aphisdocs/13_26201p_det.pdf

USDA APHIS. (2016a). USDA Announces Comment Period for GE Creeping Bentgrass Petition. http://content.govdelivery.com/accounts/USDAAPHIS/bulletins/12e98b6
USDA APHIS. (2016b). *Determination of Nonregulated Status for Monsanto MON 87419 Maize*. United States Department of Agriculture. https://www.aphis.usda.gov/brs/aphisdocs/15_11301p_det.pdf
USDA APHIS. (2018). *Determination of Nonregulated Status for Bayer CropScience GHB811 Cotton*. United States Department of Agriculture. https://www.aphis.usda.gov/brs/aphisdocs/17_13801p_det.pdf
USDA APHIS. (2020) “Am I Regulated” Process. https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/am-i-regulated
USDA NASS (2014). Genetically engineered varieties of corn, upland cotton, and soybeans, by State and for the United States, 2000-14.
USDA NASS (2015). 2012 Census of Agriculture. Organic Survey (2014). Volume 3, Special Studies, Part 4. http://www.agcensus.usda.gov/Publications/2012/Online_Resources/Organics/ORGANICS.pdf
USDA RMA (n.d.). Contract Price Addendum Eligibility by Commodity. http://www.rma.usda.gov/news/currentissues/organics/cpa_eligibility.html
USDA RMA (2013). Contract Price Addendum (CPA) -- 2014 and succeeding crop years. http://www.rma.usda.gov/policies/2014/14cpa-r.pdf
USDA RMA (2016). Contract Price Addendum. Fact Sheet. http://www.rma.usda.gov/pubs/rme/addendum.pdf
US EPA (1991). Second Peer Review of Glyphosate. United States Environmental Protection Agency. Office of Pesticides and Toxic Substances. http://www.epa.gov/opp00001/chem_search/cleared_reviews/csr_PC-103601_30-Oct-91_265.pdf
US EPA. (1998). *Pesticide Fact Sheet*. United States Environmental Protection Agency, Office of Prevention, Pesticides and Toxic Substances. https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-123000_15-Sep-98.pdf
US EPA. (2004). *EFED risk assessment for the reregistration eligibility document for2,4-dichlorophenoxyaceticacid(2,4-D).* United States Environmental Protection Agency. https://www3.epa.gov/pesticides/endanger/litstatus/effects/24d/attachment-b.pdf
US EPA (2009). National Primary Drinking Water Regulations. http://water.epa.gov/drink/contaminants/upload/mcl-2.pdf
US EPA (2014). EPA Announces Final Decision to Register Enlist Duo, Herbicide Containing 2,4-D and Glyphosate/Risk assessment ensures protection of human health, including infants, children. http://yosemite.epa.gov/opa/admpress.nsf/0/72FDE554930F3F6985257D7200591180
US EPA. (2018a). *Registration Decision for the Continuation of Uses of Dicamba on Dicamba Tolerant Cotton and Soybean*. United States Environmental Protection Agency. US EPA https://www.regulations.gov/document?D=EPA-HQ-OPP-2016-0187-0968
US EPA. (2018b, December 21). *Registration of Enlist Duo*. US EPA https://www.epa.gov/ingredients-used-pesticide-products/registration-enlist-duo#precautions
US EPA (2019a). *Glyphosate: Response to Comments, Usage, and Benefits (PC Codes: 103601, 103604, 103605, 103607, 103608, 103613, 417300)*. United States Environmental Protection Agency. https://www.epa.gov/sites/default/files/2019-04/documents/glyphosate-response-comments-usage-benefits-final.pdf
US EPA. (2019b). *Notice of Pesticide: Registration*. United States Environmental Protection Agency; 12/28/2021. https://www.mda.state.mn.us/sites/default/files/inline-files/taviumlabel.pdf
US EPA. (2020). *Alite 27 Herbicide Registration 7969-433*. United States Environmental Protection Agency. https://www3.epa.gov/pesticides/chem_search/ppls/007969-00433-20200326.pdf
US EPA (2021a). Final National Level Listed Species Biological Evaluation for Glyphosate [Collections and Lists]. https://www.epa.gov/endangered-species/final-national-level-listed-species-biological-evaluation-glyphosate
US EPA, OIG (2021b, May 24). *Report: EPA Deviated from Typical Procedures in Its 2018 Dicamba Pesticide Registration Decision* [Reports and Assessments]. https://www.epa.gov/office-inspector-general/report-epa-deviated-typical-procedures-its-2018-dicamba-pesticide
US Right to Know (2017a) MDL Monsanto Glyphosate Cancer Case Key Documents & Analysis. 21st March 2017. https://usrtk.org/pesticides/mdl-monsanto-glyphosate-cancer-case-key-documents-analysis/
US Right to Know (2017b) U.S. Right to Know Sues EPA for Release of Glyphosate Documents. 9th March 2017. https://usrtk.org/pesticides/u-s-right-to-know-sues-epa-for-release-of-glyphosate-documents/
Valente (2009) ARGENTINA: Countryside No Longer Synonymous with Healthy Living. IPSNews. 4th March 2009. http://www.ipsnews.net/2009/03/argentina-countryside-no-longer-synonymous-with-healthy-living/
Vallaeys, V., Tyson, R.C., Lane, W.D., Deleersnijder, E., Hanert, E. (2017). A Lévy-flight diffusion model to predict transgenic pollen dispersal. *Journal of The Royal Society Interface* **14**, 20160889. doi:10.1098/rsif.2016.0889

Van Bruggen, A. H. C., He, M. M., Shin, K., Mai, V., Jeong, K. C., Finckh, M. R., & Morris, J. G. (2018). Environmental and health effects of the herbicide glyphosate. *Science of The Total Environment*, *616–617*, 255–268. https://doi.org/10.1016/j.scitotenv.2017.10.309

Van Bruggen, A. H. C., Finckh, M. R., He, M., Ritsema, C. J., Harkes, P., Knuth, D., & Geissen, V. (2021). Indirect Effects of the Herbicide Glyphosate on Plant, Animal and Human Health Through its Effects on Microbial Communities. *Frontiers in Environmental Science*, *9*. https://www.frontiersin.org/article/10.3389/fenvs.2021.763917

Van Buskirk, J. (2002). A comparative test of the adaptive plasticity hypothesis: Relationships between habitat and phenotype in anuran larvae. *The American Naturalist*, *160*(1), 87–102. https://doi.org/10.1086/340599

Van Buskirk, J., McCollum, S. A., & Werner, E. E. (1997). Natural Selection for Environmentally Induced Phenotypes in Tadpoles. *Evolution*, *51*(6), 1983–1992. https://doi.org/10.2307/2411018

Van der Zee, R., Pisa, L., Andonov, S., Brodschneider, R., Charrière, J.-D., Chlebo, R., … Wilkins, S. (2012). Managed honey bee colony losses in Canada, China, Europe, Israel and Turkey, for the winters of 2008-9 and 2009-10. *Journal of Apicultural Research*, *51*(1), 100–114. http://doi.org/10.3896/IBRA.1.51.1.12

Van Engelsdorp, D., Hayes, J., Jr., Underwood, R. M., & Pettis, J. (2008). A Survey of Honey Bee Colony Losses in the U.S., Fall 2007 to Spring 2008. *PLoS ONE*, *3*(12), e4071. http://doi.org/10.1371/journal.pone.0004071

Van Horn, C. R., Moretti, M. L., Robertson, R. R., Segobye, K., Weller, S. C., Young, B. G., Johnson, W. G., Schulz, B., Green, A. C., Jeffery, T., Lespérance, M. A., Tardif, F. J., Sikkema, P. H., Hall, J. C., McLean, M. D., Lawton, M. B., Sammons, R. D., Wang, D., Westra, P., & Gaines, T. A. (2018). Glyphosate resistance in Ambrosia trifida: Part 1. Novel rapid cell death response to glyphosate. *Pest Management Science*, *74*(5), 1071–1078. https://doi.org/10.1002/ps.4567

Vanlaeys, A., Dubuisson, F., Seralini, G.-E., & Travert, C. (2018). Formulants of glyphosate-based herbicides have more deleterious impact than glyphosate on TM4 Sertoli cells. *Toxicology in Vitro*, *52*, 14–22. https://doi.org/10.1016/j.tiv.2018.01.002

Vanloqueren, G., & Baret, P. V. (2009). How agricultural research systems shape a technological regime that develops genetic engineering but locks out agroecological innovations. *Research Policy*, *38*(6), 971–983. https://doi.org/10.1016/j.respol.2009.02.008

Varayoud, J., Durando, M., Ramos, J. G., Milesi, M. M., Ingaramo, P. I., Muñoz-de-Toro, M., & Luque, E. H. (2017). Effects of a glyphosate-based herbicide on the uterus of adult ovariectomized rats. *Environmental Toxicology*, *32*(4), 1191–1201. https://doi.org/10.1002/tox.22316

Vázquez, D. E., Ilina, N., Pagano, E. A., Zavala, J. A., & Farina, W. M. (2018). Glyphosate affects the larval development of honey bees depending on the susceptibility of colonies. *PLOS ONE*, *13*(10), e0205074. https://doi.org/10.1371/journal.pone.0205074

Vázquez, D. E., Latorre-Estivalis, J. M., Ons, S., & Farina, W. M. (2020). Chronic exposure to glyphosate induces transcriptional changes in honey bee larva: A toxicogenomic study. *Environmental Pollution*, *261*, 114148. https://doi.org/10.1016/j.envpol.2020.114148

Vázquez, M. B., Moreno, M. V., Amodeo, M. R., & Bianchinotti, M. V. (2021). Effects of glyphosate on soil fungal communities: A field study. *Revista Argentina de Microbiología*, *53*(4), 349–358. https://doi.org/10.1016/j.ram.2020.10.005

Veillet, F., Perrot, L., Chauvin, L., Kermarrec, M.-P., Guyon-Debast, A., Chauvin, J.-E., Nogué, F., & Mazier, M. (2019). Transgene-Free Genome Editing in Tomato and Potato Plants Using Agrobacterium-Mediated Delivery of a CRISPR/Cas9 Cytidine Base Editor. *International Journal of Molecular Sciences*, *20*(2), 402. https://doi.org/10.3390/ijms20020402

Velasques, R. R., Sandrini, J. Z., & da Rosa, C. E. (2016). Roundup® in Zebrafish: Effects on Oxidative Status and Gene Expression. *Zebrafish*, *13*(5), 432–441. https://doi.org/10.1089/zeb.2016.1259

Vennet, B. V., Schneider, S., & Dessein, J. (2016). Different farming styles behind the homogenous soy production in southern Brazil. *The Journal of Peasant Studies*, 43(2), 396–418. http://doi.org/10.1080/03066150.2014.993319

Vera, M.S., Lagomarsino, L., Sylvester, M., Pérez, G.L., Rodríguez, P., Mugni, H., Sinistro, R., Ferraro, M., Bonetto, C., Zagarese, H., Pizarro, H. (2010). New evidences of Roundup (glyphosate formulation) impact on the periphyton community and the water quality of freshwater ecosystems. *Ecotoxicology* **19**, 710–721. doi:10.1007/s10646-009-0446-7

Verrière, P. (2014). Preventing GMO Contamination. An Overview of National "Coexistence" Measures in the EU. IFOAM EU Group. http://www.ifoam-eu.org/sites/default/files/ifoameu_policy_gmos_dossier_201412.pdf

Viazmenski, M.R., Griggs, G.E., Miller, S.A. (2017). Observing the Effects of Roundup Exposure on the Activity Levels of *C. Elegans*. Presented at the 2017 AAAS Annual Meeting (February 16-20, 2017), aaas. https://aaas.confex.com/aaas/2017/webprogram/Paper19793.html

Vicini, J. L., Jensen, P. K., Young, B. M., & Swarthout, J. T. (2021). Residues of glyphosate in food and dietary exposure. *Comprehensive Reviews in Food Science and Food Safety*, *20*(5), 5226–5257. https://doi.org/10.1111/1541-4337.12822

Vidal, O., López-García, J., & Rendón-Salinas, E. (2014). Trends in Deforestation and Forest Degradation after a Decade of Monitoring in the Monarch Butterfly Biosphere Reserve in Mexico. Conservation Biology, 28(1), 177–186. http://doi.org/10.1111/cobi.12138

Vidal, O., & Rendón-Salinas, E. (2014). Dynamics and trends of overwintering colonies of the monarch butterfly in Mexico. Biological Conservation, 180, 165–175. http://doi.org/10.1016/j.biocon.2014.09.041

Vieira, B. C., Luck, J. D., Amundsen, K. L., Werle, R., Gaines, T. A., & Kruger, G. R. (2020). Herbicide drift exposure leads to reduced herbicide sensitivity in Amaranthus spp. *Scientific Reports*, *10*(1), 2146. https://doi.org/10.1038/s41598-020-59126-9

Vila-Aiub, M. M., Balbi, M. C., Gundel, P. E., Ghersa, C. M., & Powles, S. B. (2007). Evolution of Glyphosate-Resistant Johnsongrass (*Sorghum halepense*) in Glyphosate-Resistant Soybean. *Weed Science*, 55(6), 566–571.

Vila-Aiub, M. M., Vidal, R. A., Balbi, M. C., Gundel, P. E., Trucco, F., & Ghersa, C. M. (2008). Glyphosate-resistant weeds of South American cropping systems: an overview. *Pest Management Science*, 64(4), 366–371. http://doi.org/10.1002/ps.1488

Vila-Aiub, M. M., Balbi, M. C., Distéfano, A. J., Fernández, L., Hopp, E., Yu, Q., & Powles, S. B. (2012). Glyphosate resistance in perennial Sorghum halepense (Johnsongrass), endowed by reduced glyphosate translocation and leaf uptake. *Pest Management Science*, *68*(3), 430–436. https://doi.org/10.1002/ps.2286

Vila-Aiub, M. M., Goh, S. S., Gaines, T. A., Han, H., Busi, R., Yu, Q., & Powles, S. B. (2014). No fitness cost of glyphosate resistance endowed by massive EPSPS gene amplification in Amaranthus palmeri. *Planta*, *239*(4), 793–801. https://doi.org/10.1007/s00425-013-2022-x

Vila-Aiub, M. M., Yu, Q., & Powles, S. B. (2019). Do plants pay a fitness cost to be resistant to glyphosate? *New Phytologist*, *223*(2), 532–547. https://doi.org/10.1111/nph.15733

Villar, J. & Freese, B. (2008). Who benefits from GM crops? The rise in pesticide use. Friends of the Earth International.

Viljoen, C. D., Koortzen, B. J., & Sreenivasan Tantuan, S. (2021). Determining the presence of glyphosate and glyphosate-tolerant events in maize and soybean food products in South Africa. *Food Additives & Contaminants: Part B*, *14*(2), 91–97. https://doi.org/10.1080/19393210.2021.1872713

Vilperte, V., Agapito-Tenfen, S.Z., Wikmark, O.-G., Nodari, R.O. (2016). Levels of DNA methylation and transcript accumulation in leaves of transgenic maize varieties. *Environmental Sciences Europe* **28**, 29. doi:10.1186/s12302-016-0097-2

Vin, V. D., Slozina, N. M., & Nikitin, A. I. (1990). Nature of the estrous cycle, incidence of anovulation, chromosome gametopathies and fetal death in female rats with 2,4-dichlorophenoxyacetic acid (2,4-D) before pregnancy. *Arkhiv Anatomii, Gistologii I Embriologii*, *99*(9), 69–73.

Vincent, K., & Davidson, C. (2015). The toxicity of glyphosate alone and glyphosate-surfactant mixtures to western toad (Anaxyrus boreas) tadpoles. *Environmental Toxicology and Chemistry / SETAC*. http://doi.org/10.1002/etc.3118

Viriato, C., França, F. M., Santos, D. S., Marcantonio, A. S., Badaró-Pedroso, C., & Ferreira, C. M. (2021). Evaluation of the potential teratogenic and toxic effect of the herbicide 2,4-D (DMA® 806) in bullfrog embryos and tadpoles (Lithobates catesbeianus). *Chemosphere*, *266*, 129018. https://doi.org/10.1016/j.chemosphere.2020.129018

Vivian, R., Reis, A., Kálnay, P. A., Vargas, L., & Mariani, A. C. C. F. and F. (2013). Weed Management in Soybean — Issues and Practices. InTech. http://www.intechopen.com/books/soybean-pest-resistance/weed-management-in-soybean-issues-and-practices

VLOG (2016) Verfügbarkeit von gentechnikfreiem Soja aus Brasilien gesichert. 30 May 2016. http://www.ohnegentechnik.org/aktuelles/nachrichten/2016/mai/verfuegbarkeit-von-gentechnikfreiem-soja-aus-brasilien-gesichert/

VLOG. (2022a). Products sold for over 13 billion euros: Maintaining the successful 'Ohne Gentechnik' label. https://www.ohnegentechnik.org/en/press/articles/products-sold-for-over-13-billion-euros-maintaining-the-successful-ohne-gentechnik-label

VLOG. (2022b, January 7). Significantly more non-GMO soybean cultivation in Brazil. https://www.ohnegentechnik.org/en/news/article/significantly-more-non-gmo-soybean-cultivation-in-brazil

Wagner, N., Reichenbecher, W., Teichmann, H., Tappeser, B., Lötters, S. (2013). Questions concerning the potential impact of glyphosate-based herbicides on amphibians. *Environmental Toxicology and Chemistry* **32**, 1688–1700. doi:10.1002/etc.2268

Wagner, N., Veith, M., Lötters, S., & Viertel, B. (2017). Population and life-stage-specific effects of two herbicide formulations on the aquatic development of European common frogs (Rana temporaria). *Environmental Toxicology and Chemistry*, *36*(1), 190–200. https://doi.org/10.1002/etc.3525

Wakelin, A. M., Lorraine-Colwill, D. F., & Preston, C. (2004). Glyphosate resistance in four different populations of Lolium rigidum is associated with reduced translocation of glyphosate to meristematic zones. *Weed Research*, *44*(6), 453–459. http://doi.org/10.1111/j.1365-3180.2004.00421.x

Wakelin, A., & Preston, C. (2006). A target-site mutation is present in a glyphosate-resistant Lolium rigidum population. *Weed Research*, *46*(5), 432–440. http://doi.org/10.1111/j.1365-3180.2006.00527.x

Walsh, L. P., McCormick, C., Martin, C., & Stocco, D. M. (2000). Roundup inhibits steroidogenesis by disrupting steroidogenic acute regulatory (StAR) protein expression. *Environmental Health Perspectives*, *108*(8), 769–776.

Walsh, M., Ouzman, J., Newman, P., Powles, S., & Llewellyn, R. (2017). High Levels of Adoption Indicate That Harvest Weed Seed Control Is Now an Established Weed Control Practice in Australian Cropping. *Weed Technology*, *31*(3), 341–347. https://doi.org/10.1017/wet.2017.9

Wang, K.-J., Li, X.-H., Zhang, J.-J., Chen, H., Zhang, Z.-L., & Yu, G.-D. (2010). Natural introgression from cultivated soybean (Glycine max) into wild soybean (Glycine soja) with the implications for origin of populations of semi-wild type and for biosafety of wild species in China. *Genetic Resources and Crop Evolution*, *57*(5), 747–761. https://doi.org/10.1007/s10722-009-9513-4

Wang, W., Xia, H., Yang, X., Xu, T., Si, H. J., Cai, X. X., Wang, F., Su, J., Snow, A. A., & Lu, B.-R. (2014). A novel 5-enolpyruvoylshikimate-3-phosphate (EPSP) synthase transgene for glyphosate resistance stimulates growth and fecundity in weedy rice (Oryza sativa) without herbicide. *The New Phytologist*, *202*(2), 679–688. https://doi.org/10.1111/nph.12428

Wang, M., Liu, Y., Zhang, C., Liu, J., Liu, X., Wang, L., Wang, W., Chen, H., Wei, C., Ye, X., Li, X., & Tu, J. (2015). Gene Editing by Co-Transformation of TALEN and Chimeric RNA/DNA Oligonucleotides on the Rice OsEPSPS Gene and the Inheritance of Mutations. *PLOS ONE*, *10*(4), e0122755. https://doi.org/10.1371/journal.pone.0122755

Wang, S., Seiwert, B., Kästner, M., Miltner, A., Schäffer, A., Reemtsma, T., Yang, Q., & Nowak, K. M. (2016a). (Bio)degradation of glyphosate in water-sediment microcosms – A stable isotope co-labeling approach. *Water Research*, *99*, 91–100. https://doi.org/10.1016/j.watres.2016.04.041

Wang, C., Lin, X., Li, L., & Lin, S. (2016b). Differential Growth Responses of Marine Phytoplankton to Herbicide Glyphosate. *PLOS ONE*, *11*(3), e0151633. https://doi.org/10.1371/journal.pone.0151633

Wang, C., Lin, X., Li, L., Lin, L., & Lin, S. (2017a). Glyphosate Shapes a Dinoflagellate-Associated Bacterial Community While Supporting Algal Growth as Sole Phosphorus Source. *Frontiers in Microbiology*, *8*, 2530. https://doi.org/10.3389/fmicb.2017.02530

Wang, Y., Ezemaduka, A.N., Li, Z., Chen, Z., Song, C. (2017b). Joint Toxicity of Arsenic, Copper and Glyphosate on Behavior, Reproduction and Heat Shock Protein Response in Caenorhabditis elegans. *Bull Environ Contam Toxicol* **98**, 465–471. doi:10.1007/s00128-017-2042-5

Wang, M., Wang, Z., Mao, Y., Lu, Y., Yang, R., Tao, X., & Zhu, J.-K. (2019). Optimizing base editors for improved efficiency and expanded editing scope in rice. *Plant Biotechnology Journal*, *17*(9), 1697–1699. https://doi.org/10.1111/pbi.13124

Wang, F., Xu, Y., Li, W., Chen, Z., Wang, J., Fan, F., Tao, Y., Jiang, Y., Zhu, Q.-H., & Yang, J. (2020). Creating a novel herbicide-tolerance OsALS allele using CRISPR/Cas9-mediated gene editing. *The Crop Journal*, *9*(2), 305–312. https://doi.org/10.1016/j.cj.2020.06.001

Wang, Z., Wan, L., Qiang, X., Xiaohui, Z., Song, Y., Wang, P., Hong, D., Fan, Z., & Yang, G. (2021). Optimising glyphosate tolerance in rapeseed (Brassica napus L.) by CRISPR/Cas9-based geminiviral donor DNA replicon system with Csy4-based single-guide RNA processing. *Journal of Experimental Botany*, *72*. https://doi.org/10.1093/jxb/erab167

Wang, X., Lu, Q., Guo, J., Ares, I., Martínez, M., Martínez-Larrañaga, M.-R., Wang, X., Anadón, A., & Martínez, M.-A. (2022a). Oxidative Stress and Metabolism: A Mechanistic Insight for Glyphosate Toxicology. Annual Review of Pharmacology and Toxicology, 62(1), 617–639. https://doi.org/10.1146/annurev-pharmtox-020821-111552

Wang, B., Jiang, L., Pan, B., & Lin, Y. (2022b). Toxicity of glufosinate-ammonium in soil to earthworm (*Eisenia fetida*). *Journal of Soils and Sediments*, *22*(5), 1469–1478. https://doi.org/10.1007/s11368-022-03146-7

Warren (2013). Argentines link health problems to agrochemicals. AP. October 20, 2013. https://apnews.com/article/b2747c2f2a0743f2a365ed1ccd706175

Washington Times (2016) Obama signs bill overturning Vermont's GMO labeling law. 2 August 2016. http://www.washingtontimes.com/news/2016/aug/2/obama-signs-bill-overturning-vermonts-gmo-labeling/

Watanabe, T. (1997). Apoptosis induced by glufosinate ammonium in the neuroepithelium of developing mouse embryos in culture. *Neuroscience Letters*, *222*(1), 17–20. https://doi.org/10.1016/S0304-3940(97)13330-4

Watanabe, T., & Iwase, T. (1996). Developmental and dysmorphogenic effects of glufosinate ammonium on mouse embryos in culture. *Teratogenesis, Carcinogenesis, and Mutagenesis*, *16*(6), 287–299. https://doi.org/10.1002/(SICI)1520-6866(1996)16:6<287::AID-TCM1>3.0.CO;2-E

Watanabe, T., & Sano, T. (1998). Neurological effects of glufosinate poisoning with a brief review. *Human & Experimental Toxicology*, *17*(1), 35–39. https://doi.org/10.1177/096032719801700106

Watkinson, A. R., Freckleton, R. P., Robinson, R. A., & Sutherland, W. J. (2000). Predictions of Biodiversity Response to Genetically Modified Herbicide-Tolerant Crops. *Science*, *289*(5484), 1554–1557. http://doi.org/10.1126/science.289.5484.1554

Wechsler, S. J., McFadden, J. R., & Smith, D. J. (2016). Into the Weeds: A Structural Model of Herbicide Demand and Glyphosate Resistance on U.S. Corn Farms. In *2016 Annual Meeting, July 31-August 2, Boston, Massachusetts* (No. 235998; 2016 Annual Meeting, July 31-August 2, Boston, Massachusetts). Agricultural and Applied Economics Association. https://ideas.repec.org/p/ags/aaea16/235998.html

Wechsler, S., Smith, D., Mcfadden, J., Dodson, L., & Williamson, S. (2019). *USDA ERS - The Use of Genetically Engineered Dicamba-Tolerant Soybean Seeds Has Increased Quickly, Benefiting Adopters but Damaging Crops in Some Fields*. Retrieved June 26, 2020, from https://www.ers.usda.gov/amber-waves/2019/october/the-use-of-genetically-engineered-dicamba-tolerant-soybean-seeds-has-increased-quickly-benefiting-adopters-but-damaging-crops-in-some-fields/

Wee, J., Lee, Y.-S., Kim, Y., Lee, Y. H., Lee, S.-E., Hyun, S., & Cho, K. (2021). Multigeneration toxicity of Geunsami® (a glyphosate-based herbicide) to Allonychiurus kimi (Lee) (Collembola) from sub-individual to population levels. *Environmental Pollution*, *291*, 118172. https://doi.org/10.1016/j.envpol.2021.118172

WEF (2013). Global Risks 2013. Section 2. The Dangers of Hubris on Human Health.

Wegier, A., Piñeyro-Nelson, A., Alarcón, J., Gálvez-Mariscal, A., Alvarez-Buylla, E. R., & Piñero, D. (2011). Recent long-distance transgene flow into wild populations conforms to historical patterns of gene flow in cotton (Gossypium hirsutum) at its centre of origin. *Molecular Ecology*, *20*(19), 4182–4194. http://doi.org/10.1111/j.1365-294X.2011.05258.x

Weidenmüller, A., Meltzer, A., Neupert, S., Schwarz, A., & Kleineidam, C. (2022). Glyphosate impairs collective thermoregulation in bumblebees. Science, 376(6597), 1122–1126. https://doi.org/10.1126/science.abf7482

Weisenburger, D. D. (2021). A Review and Update with Perspective of Evidence that the Herbicide Glyphosate (Roundup) is a Cause of Non-Hodgkin Lymphoma. Clinical Lymphoma Myeloma and Leukemia, 21(9), 621–630. https://doi.org/10.1016/j.clml.2021.04.009

Weller, D. M. (2007). Pseudomonas Biocontrol Agents of Soilborne Pathogens: Looking Back Over 30 Years. *Phytopathology*, *97*(2), 250–256. http://doi.org/10.1094/PHYTO-97-2-0250

Wepprich, T. (2019). Monarch butterfly trends are sensitive to unexamined changes in museum collections over time. *Proceedings of the National Academy of Sciences*, *116*(28), 13742–13744. https://doi.org/10.1073/pnas.1903511116

Weselak, M., Arbuckle, T. E., Wigle, D. T., Walker, M. C., & Krewski, D. (2008). Pre- and post-conception pesticide exposure and the risk of birth defects in an Ontario farm population. *Reproductive Toxicology (Elmsford, N.Y.)*, *25*(4), 472–480. http://doi.org/10.1016/j.reprotox.2008.05.060

Wesz Jr, V. J. (2016). Strategies and hybrid dynamics of soy transnational companies in the Southern Cone. *The Journal of Peasant Studies*, 43(2), 286–312. http://doi.org/10.1080/03066150.2015.1129496

Wheeler, A. R. (2020). *Final Cancellation Order for Three Dicamba Products (Xtendimax with Vaporgrip Technology, Engenia, and FeXapan)*. United States Environmental Protection Agency. https://www.epa.gov/sites/production/files/2020-06/documents/final_cancellation_order_for_three_dicamba_products.pdf

Where is Glyphosate Banned? (2022, March). Baum Hedlund Aristei & Goldman. https://www.baumhedlundlaw.com/toxic-tort-law/monsanto-roundup-lawsuit/where-is-glyphosate-banned-/

WHO (2014). Antimicrobial Resistance: Global Report on Surveillance. https://apps.who.int/iris/handle/10665/112642

WHO. (2020, July 31). Antibiotic resistance. https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

Whole Foods Market (2013). Whole Foods Market commits to full GMO transparency. Company News. http://media.wholefoodsmarket.com/news/whole-foods-market-commits-to-full-gmo-transparency

Wiersma, A. T., Gaines, T. A., Preston, C., Hamilton, J. P., Giacomini, D., Buell, C. R., … Westra, P. (2014). Gene amplification of 5-enol-pyruvylshikimate-3-phosphate synthase in glyphosate-resistant Kochia scoparia. *Planta*, *241*(2), 463–474. http://doi.org/10.1007/s00425-014-2197-9

Wilke, R. A., Qamar, M., Lupu, R. A., Gu, S., & Zhao, J. (2019). Chronic Kidney Disease in Agricultural Communities. *The American Journal of Medicine, 132*(10), e727. https://doi.org/10.1016/j.amjmed.2019.03.036

Williamson (2008) Rural communities in Paraguay endangered by soya pesticides. Pesticide News 81, 12-15. http://www.pan-uk.org/pestnews/Issue/pn81/pn81_p12-15.pdf

Wines, M. (2014). Migration of Monarch Butterflies Shrinks Again Under Inhospitable Conditions. The New York Times. http://www.nytimes.com/2014/01/30/us/monarch-butterflies-falter-under-extreme-weather.html

WNAX. (2018). $1.5 Billion Settlement Reached in Syngenta MIR 162 Lawsuit. *Radio 570 WNAX*. http://wnax.com/news/180081-1-5-billion-settlement-reached-in-syngenta-mir-162-lawsuit/

Wozniacka, G. (2019, June 24). Roundup's Other Problem: Glyphosate is Sourced from Controversial Mines. *Civil Eats*. https://civileats.com/2019/06/24/roundups-other-problem-glyphosate-is-sourced-from-controversial-mines/

Wróbel, M. H., Młynarczuk, J., & Rękawiecki, R. (2022). Do commonly used herbicides (atrazine and glyphosate) have the potential to impair the contractions, prostaglandin releasing and conducting of oxytocin signal at the bovine cervix in vitro? *Theriogenology*, *183*, 26–35. https://doi.org/10.1016/j.theriogenology.2022.02.011

WSU (2015). WSO researchers find U.S. breast milk is glyphosate free. https://news.wsu.edu/2015/07/23/wsu-researchers-find-u-s-breast-milk-is-glyphosate-free/#.VbOxcr7DrbI
Wu, J., Chen, C., Xian, G., Liu, D., Lin, L., Yin, S., Sun, Q., Fang, Y., Zhang, H., & Wang, Y. (2020). Engineering herbicide-resistant oilseed rape by CRISPR/Cas9-mediated cytosine base-editing. *Plant Biotechnology Journal*, *18*(9), 1857–1859. https://doi.org/10.1111/pbi.13368
WWF Mexico & Fondo Monarca (2013). Degradación Forestal en la Zona Núcleo de la Reserva Biosfera Mariposa Monarca 2012-2013. http://www.wwf.org.mx/que_hacemos/mariposa_monarca/publicaciones/
Xu, J., Smith, S., Smith, G., Wang, W., & Li, Y. (2019). Glyphosate contamination in grains and foods: An overview. *Food Control*, *106*, 106710. https://doi.org/10.1016/j.foodcont.2019.106710
Xu, R., Li, J., Liu, X., Shan, T., Qin, R., & Wei, P. (2020). Development of Plant Prime-Editing Systems for Precise Genome Editing. *Plant Communications*, *1*(3), 100043. https://doi.org/10.1016/j.xplc.2020.100043
Xu, S., Liu, Y., Zhang, J., & Gao, B. (2021). Proteomic mechanisms for the combined stimulatory effects of glyphosate and antibiotic contaminants on Microcystis aeruginosa. *Chemosphere*, *267*, 129244. https://doi.org/10.1016/j.chemosphere.2020.129244
Yamada, T., Kremer, R. J., de Camargo e Castro, P. R., & Wood, B. W. (2009). Glyphosate interactions with physiology, nutrition, and diseases of plants: Threat to agricultural sustainability? *European Journal of Agronomy*, *31*(3), 111–113. http://doi.org/10.1016/j.eja.2009.07.004
Yamamoto, E., Zeng, L., & Baird, W. V. (1998). Alpha-tubulin missense mutations correlate with antimicrotubule drug resistance in Eleusine indica. *The Plant Cell*, *10*(2), 297–308. https://doi.org/10.1105/tpc.10.2.297
Yan, B., Lei, L., Chen, X., Men, J., Sun, Y., Guo, Y., Yang, L., Wang, Q., Han, J., & Zhou, B. (2022). Glyphosate and glufosinate-ammonium in aquaculture ponds and aquatic products: Occurrence and health risk assessment. *Environmental Pollution*, *296*, 118742. https://doi.org/10.1016/j.envpol.2021.118742
Yang, M., Wen, Z., Fazal, A., Hua, X., Xu, X., Yin, T., Qi, J., Yang, R., Lu, G., Hong, Z., & Yang, Y. (2020). Impact of a G2-EPSPS & GAT Dual Transgenic Glyphosate-Resistant Soybean Line on the Soil Microbial Community under Field Conditions Affected by Glyphosate Application. *Microbes and Environments*, *35*(4), ME20056. https://doi.org/10.1264/jsme2.ME20056
Yang, C., Lim, W., & Song, G. (2021). Reproductive toxicity due to herbicide exposure in freshwater organisms. *Comparative Biochemistry and Physiology. Toxicology & Pharmacology: CBP*, *248*, 109103. https://doi.org/10.1016/j.cbpc.2021.109103
Yanniccari, M., Gomez Lobato, E., Istilart, C., Natalucci, C., Giménez, D., & Castro, A. (2017). Mechanism of Resistance to Glyphosate in Lolium perenne from Argentina. *Frontiers in Ecology and Evolution*, *5*, 123. https://doi.org/10.3389/fevo.2017.00123
Yanniccari, M., Istilart, C., Giménez, D., & Castro, A. (2018). Dynamics of Glyphosate Resistance in Lolium perenne: Pollen-Mediated Gene Flow under Field Conditions in Argentina. *Agronomy*, *8*(12), 286. https://doi.org/10.3390/agronomy8120286
Yanniccari, M., Vázquez-García, J. G., Gómez-Lobato, M. E., Rojano-Delgado, A. M., Alves, P. L. da C. A., & De Prado, R. (2021). First Case of Glyphosate Resistance in Bromus catharticus Vahl.: Examination of Endowing Resistance Mechanisms. *Frontiers in Plant Science*, *12*, 198. https://doi.org/10.3389/fpls.2021.617945
Yield10 Bioscience. (2022, March 3). *Yield10 Bioscience Announces an Update on the Camelina Line E3902 Development Program for Producing Low-carbon Feedstock Oil for Renewable Diesel | Press Release*. https://www.yield10bio.com/press/yield10-bioscience-announces-an-update-on-the-camelina-line-e3902-development-program-for-producing-low-carbon-feedstock-oil-for-renewable-diesel
Yook, M.-J., Park, H.-R., Zhang, C.-J., Lim, S.-H., Jeong, S.-C., Chung, Y. S., & Kim, D.-S. (2021). Environmental risk assessment of glufosinate-resistant soybean by pollen-mediated gene flow under field conditions in the region of the genetic origin. *Science of The Total Environment*, *762*, 143073. https://doi.org/10.1016/j.scitotenv.2020.143073
Young, F., Ho, D., Glynn, D., Edwards, V. (2015). Endocrine disruption and cytotoxicity of glyphosate and roundup in human Jar cells *in vitro*. Integrative Pharmacology, Toxicology and Genotoxicology. Vol. 1(1): 12-19. doi: 10.15761/IPTG.1000104.
Young, S. L. (2012). True integrated weed management. *Weed Research*, *52*(2), 107–111. https://doi.org/10.1111/j.1365-3180.2012.00903.x
Yu, Q., Jalaludin, A., Han, H., Chen, M., Sammons, R. D., & Powles, S. B. (2015). Evolution of a Double Amino Acid Substitution in the 5-Enolpyruvylshikimate-3-Phosphate Synthase in Eleusine indica Conferring High-Level Glyphosate Resistance. *Plant Physiology*, *167*(4), 1440–1447. https://doi.org/10.1104/pp.15.00146
Yu, Z., Lu, C., Hennessy, D. A., Feng, H., & Tian, H. (2020). Impacts of tillage practices on soil carbon stocks in the US corn-soybean cropping system during 1998 to 2016. *Environmental Research Letters*, *15*(1), 014008. https://doi.org/10.1088/1748-9326/ab6393

Yu, H., Peng, J., Cao, X., Wang, Y., Zhang, Z., Xu, Y., & Qi, W. (2021). Effects of microplastics and glyphosate on growth rate, morphological plasticity, photosynthesis, and oxidative stress in the aquatic species Salvinia cucullata. *Environmental Pollution*, *279*, 116900. https://doi.org/10.1016/j.envpol.2021.116900

Yuan, G. (2021, September 23). *Ranking List of Global Top 20 Agrochemical Enterprises for FY2020 / 15 Realize Sales Growth, 11 Chinese Enterprises Contribute to 37% of Total Sales*. Grainews. http://news.agropages.com/News/Detail-40437.htm

Zaller, J. G., Heigl, F., Ruess, L., & Grabmaier, A. (2014). Glyphosate herbicide affects belowground interactions between earthworms and symbiotic mycorrhizal fungi in a model ecosystem. *Scientific Reports*, *4*. http://doi.org/10.1038/srep05634

Zalucki, M. P., & Lammers, J. H. (2010). Dispersal and egg shortfall in Monarch butterflies: what happens when the matrix is cleaned up? *Ecological Entomology*, *35*(1), 84–91. http://doi.org/10.1111/j.1365-2311.2009.01160.x

Zebral, Y. D., Costa, P. G., de Castro Knopp, B., Lansini, L. R., Zafalon-Silva, B., Bianchini, A., & Robaldo, R. B. (2017). Effects of a glyphosate-based herbicide in pejerrey Odontesthes humensis embryonic development. *Chemosphere*, *185*, 860–867. https://doi.org/10.1016/j.chemosphere.2017.07.069

Zebral, Y. D., Lansini, L. R., Costa, P. G., Roza, M., Bianchini, A., & Robaldo, R. B. (2018). A glyphosate-based herbicide reduces fertility, embryonic upper thermal tolerance and alters embryonic diapause of the threatened annual fish Austrolebias nigrofasciatus. *Chemosphere*, *196*, 260–269. https://doi.org/10.1016/j.chemosphere.2017.12.196

Zhang, N., Linscombe, S., & Oard, J. (2003). Out-crossing frequency and genetic analysis of hybrids between transgenic glufosinate herbicide-resistant rice and the weed, red rice. *Euphytica*, *130*(1), 35–45. https://doi.org/10.1023/A:1022371104679

Zhang, W., Linscombe, S. D., Webster, E., Tan, S., & Oard, J. (2006). Risk assessment of the transfer of imazethapyr herbicide tolerance from Clearfield rice to red rice (Oryza sativa). *Euphytica*, *152*(1), 75–86. https://doi.org/10.1007/s10681-006-9180-x

Zhang, C.-J., Yook, M.-J., Park, H.-R., Lim, S.-H., Kim, J.-W., Song, J.-S., Nah, G., Song, H.-R., Jo, B.-H., Roh, K. H., Park, S., Jang, Y.-S., Noua, I.-S., & Kim, D.-S. (2018a). Evaluation of maximum potential gene flow from herbicide resistant Brassica napus to its male sterile relatives under open and wind pollination conditions. *Science of The Total Environment*, *634*, 821–830. https://doi.org/10.1016/j.scitotenv.2018.03.390

Zhang, J., Kang, Y., Valverde, B. E., Dai, W., Song, X., & Qiang, S. (2018b). Feral rice from introgression of weedy rice genes into transgenic herbicide-resistant hybrid-rice progeny. *Journal of Experimental Botany*, *69*(16), 3855–3865. https://doi.org/10.1093/jxb/ery210

Zhang, R., Liu, J., Chai, Z., Chen, S., Bai, Y., Zong, Y., Chen, K., Li, J., Jiang, L., & Gao, C. (2019). Generation of herbicide tolerance traits and a new selectable marker in wheat using base editing. *Nature Plants*, *5*(5), 480–485. https://doi.org/10.1038/s41477-019-0405-0

Zhang, W., Wang, J., Song, J., Feng, Y., Zhang, S., Wang, N., Liu, S., Song, Z., Lian, K., & Kang, W. (2021a). Effects of low-concentration glyphosate and aminomethyl phosphonic acid on zebrafish embryo development. *Ecotoxicology and Environmental Safety*, *226*, 112854. https://doi.org/10.1016/j.ecoenv.2021.112854

Zhang, R., Chen, S., Meng, X., Chai, Z., Wang, D., Yuan, Y., Chen, K., Jiang, L., Li, J., & Gao, C. (2021b). Generating broad-spectrum tolerance to ALS-inhibiting herbicides in rice by base editing. *Science China Life Sciences*, *64*(10), 1624–1633. https://doi.org/10.1007/s11427-020-1800-5

Zhang, L., Liu, L., Fang, Z., Shen, W., Dai, Y., Jia, R. Z., liang, jingang, & Liu, B. (2022a). *Risk assessment of hybrids between genetically modified soybean and its wild relatives* [Preprint]. Preprints. https://doi.org/10.22541/au.164268047.71439409/v1

Zhang, Q., Liu, X., Gao, M., Li, X., Wang, Y., Chang, Y., Zhang, X., Huo, Z., Zhang, L., Shan, J., Zhang, F., Zhu, B., & Yao, W. (2022b). The study of human serum metabolome on the health effects of glyphosate and early warning of potential damage. *Chemosphere*, *298*, 134308. https://doi.org/10.1016/j.chemosphere.2022.134308

Zhao, L., Zhang, J., Yang, L., Zhang, H., Zhang, Y., Gao, D., Jiang, H., Li, Y., Dong, H., Ma, T., Wang, X., Wu, M., Wang, A., Jin, Y., Yuan, Y., & Chen, H. (2021). Glyphosate exposure attenuates testosterone synthesis via NR1D1 inhibition of StAR expression in mouse Leydig cells. *Science of The Total Environment*, *785*, 147323. https://doi.org/10.1016/j.scitotenv.2021.147323

Zheng, W., Scott, J. W., Holm, N., & Machesky, M. L. (2018). *Occurrence and Fate of the Herbicide Glyphosate in Tile Drainage and Receiving Rivers in East Central Illinois*. Illinois Sustainable Technology Center. http://hdl.handle.net/2142/101912

Zhou, M., Xu, H., Wei, X., Ye, Z., Wei, L., Gong, W., Wang, Y., & Zhu, Z. (2006). Identification of a glyphosate-resistant mutant of rice 5-enolpyruvylshikimate 3-phosphate synthase using a directed evolution strategy. *Plant Physiology*, *140*(1), 184–195. https://doi.org/10.1104/pp.105.068577

Zhou, X., Larson, J.A., Lambert, D.M., Roberts, R.K., English, B.C., Bryant, K.J., Mishra, A.K., Falconer, L.L., Hogan Jr., R.J., Johnson, J.L., & Reeves, J.M. (2015). Farmer experience with weed resistance to herbicides in cotton production. *AgBioForum*, *18*(1), 114-125.

http://agbioforum.org/v18n1/v18n1a12-zhou.htm
Zhou, Z., Ni, X., Wu, Z., & Tang, J. (2022). Physiological and transcriptomic analyses reveal the threat of herbicides glufosinate and glyphosate to the scleractinian coral Pocillopora damicornis. *Ecotoxicology and Environmental Safety*, *229*, 113074. https://doi.org/10.1016/j.ecoenv.2021.113074
Zhu, T., Peterson, D., Tagliani, L., Clair, G., Baszczynski, C., & Bowen, B. (1999). Targeted Manipulation of Maize Genes in vivo Using Chimeric RNA/DNA Oligonucleotides. *Proceedings of the National Academy of Sciences*, *96*. https://doi.org/10.1073/pnas.96.15.8768
Zhu, T., Mettenburg, K., Peterson, D. J., Tagliani, L., & Baszczynski, C. L. (2000). Engineering herbicide-resistant maize using chimeric RNA/DNA oligonucleotides. *Nature Biotechnology*, *18*(5), 555–558. https://doi.org/10.1038/75435
Zhu, L., Li, W., Zha, J., & Wang, Z. (2015). Dicamba affects sex steroid hormone level and mRNA expression of related genes in adult rare minnow (Gobiocypris rarus) at environmentally relevant concentrations. *Environmental Toxicology*, *30*(6), 693–703. https://doi.org/10.1002/tox.21947
Zilberman, D., Sexton, S. E., Marra, M. C., & Fernandez-Cornejo, J. (2010). The Economic Impact of Genetically Engineered Crops. *Choices*, *25*(2). Retrieved from http://ideas.repec.org/a/ags/aaeach/94769.htm
Zobiole, L. H. S., Bonini, E. A., Jr, R. S. de O., Kremer, R. J., & Ferrarese-Filho, O. (2010a). Glyphosate affects lignin content and amino acid production in glyphosate-resistant soybean. *Acta Physiologiae Plantarum*, *32*(5), 831–837. http://doi.org/10.1007/s11738-010-0467-0
Zobiole, L. H. S., Jr, R. S. de O., Huber, D. M., Constantin, J., Castro, C. de, Oliveira, F. A. de, & Jr, A. de O. (2010b). Glyphosate reduces shoot concentrations of mineral nutrients in glyphosate-resistant soybeans. *Plant and Soil*, *328*(1-2), 57–69. http://doi.org/10.1007/s11104-009-0081-3
Zobiole, L. H. S., Oliveira, R. S., Visentainer, J. V., Kremer, R. J., Bellaloui, N., & Yamada, T. (2010c). Glyphosate Affects Seed Composition in Glyphosate-Resistant Soybean. *Journal of Agricultural and Food Chemistry*, *58*(7), 4517–4522. http://doi.org/10.1021/jf904342t
Zobiole, L.H.S., Kremer, R.J., Jr, R.S. de O., Constantin, J. (2010d). Glyphosate affects photosynthesis in first and second generation of glyphosate-resistant soybeans. *Plant Soil* **336**, 251–265. doi:10.1007/s11104-010-0474-3
Zobiole, L. H. S., Kremer, R. J., Oliveira, R. S., & Constantin, J. (2011). Glyphosate affects micro-organisms in rhizospheres of glyphosate-resistant soybeans. *Journal of Applied Microbiology*, *110*(1), 118–127. http://doi.org/10.1111/j.1365-2672.2010.04864.x
Zobiole, L. H. S., Kremer, R. J., de Oliveira Jr., R. S., & Constantin, J. (2012). Glyphosate effects on photosynthesis, nutrient accumulation, and nodulation in glyphosate-resistant soybean. *Journal of Plant Nutrition and Soil Science*, *175*(2), 319–330. http://doi.org/10.1002/jpln.201000434
Zong, Y., Song, Q., Li, C., Jin, S., Zhang, D., Wang, Y., Qiu, J.-L., & Gao, C. (2018). Efficient C-to-T base editing in plants using a fusion of nCas9 and human APOBEC3A. *Nature Biotechnology*, *36*(10), 950–953. https://doi.org/10.1038/nbt.4261