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Elaboration of a concept for the cumulative environmental exposure assessment of biocides

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Elaboration of a concept for the cumulative environmental exposure assessment of biocides

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16. Abstract

Article 10(1) of the EU Biocidal Products Directive 98/8/EC (BPD) requires that for the inclusion of an active substance in Annex I, Annex IA or IB, cumulation effects from the use of biocidal products containing the same active substance shall be taken into account, where relevant.

The study proves the feasibility of a technical realisation of Article 10(1) of the BPD and elaborates a first concept for the cumulative environmental exposure assessment of biocides. Existing requirements concerning cumulative assessments in other regulatory frameworks have been evaluated and their applicability for biocides has been examined. Technical terms and definitions used in this context were documented with the aim to harmonise terminology with other frameworks and to set up a precise definition within the BPD. Furthermore, application conditions of biocidal products have been analysed to find out for which cumulative exposure assessments may be relevant. Different parameters were identified which might serve as indicators for the relevance of cumulative exposure assessments. These indicators were then integrated in a flow chart by means of which the relevance of cumulative exposure assessments can be checked. Finally, proposals for the technical performance of cumulative exposure assessments within the Review Programme have been elaborated with the aim to bring the results of the project into the upcoming development and harmonization processes on EU level.

17. Keywords

Annex I inclusion, Biocidal Products Directive, break-even point, combined exposure, consumption, cumulation effects, emission, EUSES, PEClocal, PECregional, tonnage

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16. Zusammenfassung

Artikel 10 (1) der EU-Biozid-Produkte-Richtlinie 98/8/EG (BP-RL) verlangt, dass für die Aufnahme eines aktiven Wirkstoffs in Anhang I, Anhang IA oder IB gegebenenfalls Kumulationseffekte infolge der Verwendung von Biozid-Produkten mit demselben Wirkstoff berücksichtigt werden.
Die Studie untersucht die Machbarkeit einer technischen Umsetzung von Artikel 10 (1) der BP-RL und erarbeitet ein erstes Konzept zur Bewertung der kumulativen Umweltexposition gegenüber Bioziden. Bestehende Anforderungen an kumulative Bewertungen in anderen Regelwerken wurden ausgewertet und auf ihre Anwendbarkeit für Biozide untersucht. In diesem Zusammenhang verwendete technische Begriffe und Definitionen wurden mit dem Ziel dokumentiert, eine Harmonisierung der Terminologie mit anderen Regelwerken herbeizuführen und präzise Definitionen innerhalb der BP-RL zu erstellen. Darüber hinaus wurden Einsatzbedingungen von Biozid-Produkten untersucht, um herauszufinden, für welche Anwendungen kumulative Expositionsbeurteilungen relevant sein könnten. Es wurden verschiedene Parameter identifiziert, die möglicherweise als Indikatoren für die Relevanz der kumulativen Expositionsbeurteilungen dienen könnten. Diese Indikatoren wurden anschließend in ein Flussdiagramm integriert, durch das die Relevanz der kumulativen Expositionsbeurteilung überprüft werden kann.
Schließlich wurden Vorschläge für die technische Durchführung der kumulativen Expositionsbeurteilungen im Rahmen des Review-Programms mit dem Ziel erarbeitet, die Ergebnisse des Projekts in die anstehenden Entwicklungs- und Harmonisierungsprozesse auf EU-Ebene einzubringen.

17. Schlagwörter

Annex I-Aufnahme, Biozid-Produkte-Richtlinie, Break-Even-Punkt, kombinierte Exposition, Verbrauchsmenge, kumulative Effekte, Emissionen, EUSES, PEClocal, PECregional, Tonnage

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BfR	Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)
BPD	Biocidal Products Directive 98/8/EC
BREF	Best Available Technique Reference Document
CA	Competent Authority
CAR	Competent Authority Report
CONCAWE	Conservation of Clean Air and Water in Europe
CORINAIR	CORe Inventory of AIR emissions
DNEL	Derived No-Effect Level
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EFSA	European Food Safety Authority
ESD	Emission Scenario Document
EU	European Union
EUSES	European Union System for the Evaluation of Substances
HPVC	High Production Volume Chemicals
ISEA	International Society of Exposure Science
IUPAC	International Union of Pure and Applied Chemistry
IPCS	International Programme on Chemical Safety
Log K_{ow}	Octanol Water Partition Coefficient
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentrations
OECD	Organisation for Economic Co-operation and Development
PEC	Predicted Environmental Concentration
PNEC	Predicted No-Effect Concentration
PT	Product Type
RA	Risk Assessment
RAR	Risk Assessment Report
REACH	Regulation (EC) No 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals
STP	Sewage Treatment Plant
TGD	Technical Guidance Document
UBA	Umweltbundesamt (Federal Environment Agency of Germany)
US EPA	U.S. Environmental Protection Agency
SETAC	Society of Environmental Toxicology and Chemistry
TNsG	Technical Notes of Guidance
WHO	World Health Organisation

Summary

Article 10(1) of the EU Biocidal Products Directive 98/8/EC (BPD) requires that for the inclusion of an active substance in Annex I, Annex IA or IB, cumulation effects from the use of biocidal products containing the same active substance shall be taken into account, where relevant. Comparable provisions are given in the TNsG on Annex I inclusion requiring that for the first evaluation of the active substance the applicant (in the dossier) and the Competent Authority (in the report) should consider what combination of exposures to the active substance from all the representative uses is realistically possible. However, despite these requirements up to now no agreed methodology on cumulative risk assessments for biocides within the EU Review Programme exists.

Against this background, it has been the objective of the present study to prove the feasibility of a technical realisation of Article 10(1) of the BPD and to elaborate a first concept for the cumulative environmental exposure assessment of biocides. In a first step, existing requirements concerning cumulative assessments in other regulatory frameworks have been evaluated and their applicability for biocides has been examined. Technical terms and definitions used in this context were documented with the aim to harmonise terminology with other frameworks and to set up precise definitions within the BPD. Furthermore, application conditions of biocidal products have been analysed to find out for which cumulative exposure assessments may be relevant. Finally, proposals for the technical performance of cumulative exposure assessments within the Review Programme have been elaborated with the aim to bring the results of the project into the upcoming development and harmonization processes on EU level.

Framework of the BPD and the present study

The BPD sets a clear framework with regard to the aspects that have to be considered within cumulative risk assessments: respective assessments shall focus on the cumulative environmental exposure of biocidal products of the same Product Type (PT) or of different PTs containing the same active substance (i.e. “same biocidal active”). Cumulation effects from the use of biocidal products containing different active substances with a similar mode of action are not explicitly mentioned in the BPD and therefore, have not been considered in the present study. Furthermore, the provisions of the BPD and consequently the investigatory framework of the study comprise only uses within the scope of the BPD; meaning that if active substances are used both in biocidal products and in other use areas like, for example, as plant protection products or industrial chemicals, the emission routes of the latter are not to be considered in the cumulative exposure assessment for biocides according to the existing legislation.

The present study focuses on the technical aspects; it does not discuss the regulatory aspects to be considered with regard to cumulative exposure assessments as for examples the regulatory consequences if cumulative exposure reveals risk for the environment for different applicants.

Existing approaches in other regulatory frameworks

The review of existing approaches and requirements related to cumulative assessments in other regulatory areas revealed that most of them focus on cumulative exposure to multiple chemicals from multiple sources on living organisms. The starting point of those approaches is clearly effect-based. No further information for quantitative assessing of the exposure of biocides from different PTs to the environment has been found in the analysed approaches or in an additionally performed literature search.

Technical terms and definitions

The technical terms and definitions used in the context of cumulative risk assessments have different meanings depending on the regulatory area where they are applied. In many regulatory areas dealing mainly with human health aspects, the risk associated with multiple pathways / routes of exposure to a single chemical is often defined as “aggregate” exposure or risk whereas “cumulative” risk / exposure applies to the impact of multiple chemicals with the same mode of action. In contrast, Article 10(1) of the BPD mentions “cumulation effects” in connection with the use of biocidal products containing the same active substance. It is noted that the term “cumulation effects” refers to both environmental and human health risk assessment and refers to one active substance contained in different products of the same PT or of different PTs. Taking into account the different and not harmonised meanings of “cumulative exposure” in the context of chemicals, pesticides and/or medicinal products, the following definition of the term “cumulative exposure” was defined in the present study in the context of environmental exposure assessments of biocidal active substances considering the specifications in the BPD:

“Cumulative exposure to biocides is the overall exposure to the same biocidal active substance by emissions during the use, service life or waste phase of different biocidal products belonging to the same PT or different PTs.”

For further discussion, however, it has to be kept in mind that this definition is not necessarily in agreement with other regulatory areas, especially those ones dealing with human health aspects.

Relevance of cumulative environmental exposure assessments

According to the provisions given in the BPD cumulative risk assessments shall not be carried out routinely in the Review Programme but only where relevant. Such relevance arises if sufficient scientific support is available indicating that cumulative exposure could lead to additional adverse effects beyond those that have already been estimated in the risk

assessment of the single uses. The necessity of a cumulative risk assessment has to be identified by the respective Rapporteur Member State (CA) on a case by case basis.

In order to reduce the workload for doing cumulative exposure assessments a prioritisation scheme was envisaged. Based on examples of biocidal uses where the performance of a cumulative exposure assessment is considered to be relevant, different parameters were identified which might serve as indicators for the relevance of cumulative exposure assessments. These indicators were then integrated in a flow chart by means of which the relevance of cumulative exposure assessments can be checked (Figure 1).

In a first step it is analysed whether the biocidal use is relevant compared to the inputs from non-biocidal uses from other regulatory areas. A first indicator is whether the substance is included in the list of high production volume chemicals (HPVC), that means it is produced in the EU or imported into the EU in amounts exceeding 1,000 t. Another indicator is whether the active substance is covered by other regulatory areas such as plant protection products, human or veterinary medicinal products, preservatives for cosmetics, food or feed additives etc. If the overall biocides use is lower than a trigger value of e.g. 10%, it can be assumed that emissions to the environment from non-biocidal uses predominate and that therefore a cumulative exposure assessment only for biocides does not seem reasonable. The proposed trigger value of 10% has not been derived on a scientific basis but can be regarded as a first proposal.

An overlap of different biocidal uses in space and time can be considered as a strong indicator of cumulative exposure to the environment. However, these findings depend on the use pattern and exposure scenarios analysed. As there is a considerable gap in knowledge of the use pattern of biocides, the number of PTs for which an active substance is defended has been included as another indicator for possible cumulative exposure. This trigger was set to a value of 4 different PTs. Again, it has to be stressed that the trigger value of > 4 PTs as an immediate indicator for cumulative exposure assessments has no scientific basis but is a first proposal. For those active substances included in 2–4 PTs it is suggested that a rough estimate of the risk quotient ($PEC_{single\ uses}$/PNEC) is carried out. If the risk quotient for one single use exceeds 0.1, for example, a cumulative exposure assessment should be carried out.

In summary, each cumulative exposure assessment must consider the possibility that there might be an overlap in time and space. A level of concern is reached where the risk quotient ($\sum PEC_{single\ uses}$ /PNEC) exceeds 1.

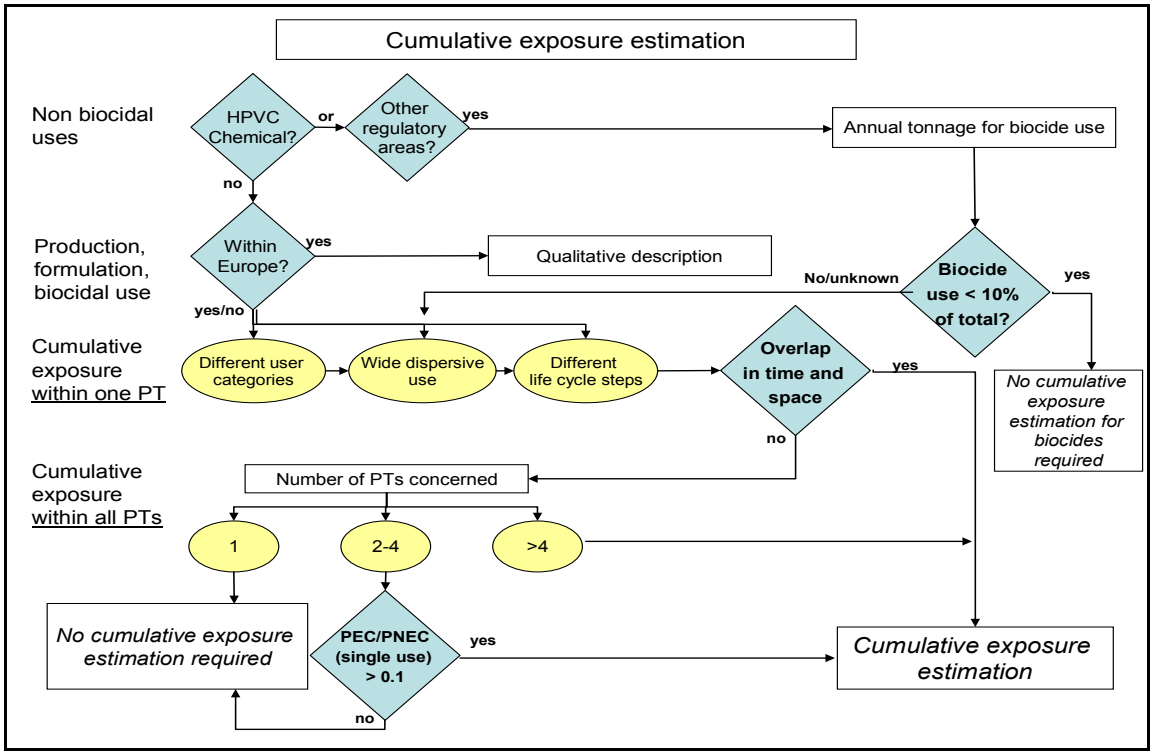

Figure 1 Decision tree to assess the need for cumulative exposure estimations

Proposals for technical guidance on cumulative exposure assessments

In addition to the identification of indicators helping to assess the relevance of cumulative exposure, the present feasibility study examined concrete proposals for the technical realisation of cumulative exposure assessments and discussed their advantages and disadvantages. Different approaches of cumulative environmental exposure assessments are currently under discussion among the technical experts of the CAs. These approaches comprise

1) the addition of the regional background concentration to the local worst case concentration (Clocal (worst case) + PECregional) or
2) the summation of local concentrations of all single uses (∑Clocal).

Example calculations which were performed to illustrate the relation between PEClocal and PECregional revealed that cumulative PEC calculated on basis of the "PECregional approach" are significantly lower than the sum of the Clocal of all single uses. The higher the number of single uses, the higher is the discrepancy between the two approaches. Consequently, the "PECregional approach" might underestimate the environmental concentrations resulting from simultaneous and/or spatial overlapping uses of the same active substance.

Nevertheless, the PECregional approach seems to be a good choice as it represents a mean background concentration resulting from all relevant emissions caused by all potential uses

of an active substance, i.e. the complete emission situation is considered. In addition, adding one PECregional to a local (worst case) PEC is very easily done.

However, to derive a reliable PECregional it is necessary to have a more or less complete picture of uses for one active substance. It is questionable if it is even possible to get all these data. Based on the experiences from the evaluation of existing substances it is known how complex the situation concerning all the different use patterns of substances and the related emissions can be.

Furthermore, the current approach for Annex I inclusion of active substances under BPD requires the assessment of one single, representative use. If for this use no risks are identified the active substance can be included into Annex I. At the same time a cumulative assessment shall be done at Annex I inclusion stage. So it is quite clear that no comprehensive information to derive a sound PECregional is available.

In future, under product authorisation stage more information will become available concerning the use pattern of active substances. This increase in knowledge will allow to derive a better PECregional. However, as product authorization is a national task in each EU Member state a differently detailed level of information will be available. Thus, this may end up in different PECregional for different EU MS and one might question the sense of this situation. A solution would be to centrally derive a PECregional, after a certain time, based on the proceeding knowledge, at least for those products that will have an authorisation in various EU MS. It should also be kept in mind that active substances are included into Annex I for different Product Types and thus, information from product authorization comprising all uses in all product types will be a rather long process regarding time.

For some active substances that are already evaluated as existing substances it could be possible to use for the meantime the PECregional from the EU Risk Assessment Report (RAR). However, it is unclear if this is legally possible as the PECregional is estimated from emissions caused by uses beyond biocidal uses. Nevertheless, from a precautionary point of view this approach would be reasonable.

On the other hand, based on the conclusions drawn from the analyses done in this project PECregional might also underestimate the actual risk resulting from multiple exposures. Thus, the ∑Clocal approach is more conservative and for some cases even more realistic. However, no final conclusion is possible to decide upon which approach describes better a specific emission situation. Also for the ∑Clocal approach the precision is highly depending on the availability of data. A huge disadvantage of the ∑Clocal approach is for sure the summing up of several realistic worst case scenarios. It is questionable if this approach is really satisfactory to derive conclusions of risks and with that on legal consequences for active substances.

Besides comparing the suitability of the two different PEC approaches some further technical details were checked as part of the study:

One technical aspect dealt with the calculation of PEC values on basis of the "∑Clocal approach". It was checked whether the cumulative PEC values have to be calculated by adding up the local emissions / daily release rates to the environmental compartments (e.g. ∑Elocal for surface water) or by adding up the predicted environmental concentrations (PEC values) resulting from the single uses (∑Clocal). On basis of example calculations it could be demonstrated that both approaches lead to analogue results, thus cumulative PEC values may be calculated either by adding up the Clocal values of the single uses or by adding up the emission rates and using the cumulative emission rates for the subsequent PEC calculation with EUSES (or any other appropriate model).

Another technical aspect which was investigated in detail dealt with the question how environmental exposure estimations based on the annual tonnage and based on the average consumption of the biocidal active substance can be combined in cumulative exposure assessments. The following proceeding is proposed whereby two different situations need to be distinguished:

1) For all intended uses that have to be considered in the cumulative exposure assessment, emission scenarios both on basis of the tonnage and the consumption approach are available.
2) For one or several of the intended uses that have to be considered in the cumulative exposure assessment, there are only emission scenarios available on basis of either the consumption or the tonnage approach.

In the first case, for each use it should be estimated by means of the "break-even-calculation" whether the tonnage based or average consumption based approach is more appropriate for the emission estimations. Subsequently, for each use local emission rates (Elocal) and local predicted environmental concentrations (PEClocal) are calculated on basis of the approach identified to be most appropriate by the "break-even-calculation". Then, the Elocal or PEClocal of all uses should be summed up to assess the cumulative exposure.

In the second case, local emission rates (Elocal) and local predicted environmental concentrations (PEClocal) are calculated for each use on basis of the available emission scenario. As explained for the first case, Elocal or PEClocal of all uses should then be summed up to assess the cumulative exposure.

Zusammenfassung

Artikel 10 (1) der EU-Biozid-Produkt-Richtlinie 98/8/EG (BP-RL) verlangt, dass für die Aufnahme eines aktiven Wirkstoffs in Anhang I, Anhang IA oder IB gegebenenfalls Kumulationseffekte infolge der Verwendung von Biozid-Produkten mit demselben Wirkstoff berücksichtigt werden. Vergleichbare Regelungen sind in den TNsG zur Aufnahme in Anhang I vorhanden. Diese fordern, dass für die erstmalige Bewertung eines aktiven Wirkstoffes der Antragsteller (im Dossier) und die zuständige Behörde (im CA-Report) eruieren sollten, welche Kombinationen von Expositionen gegenüber dem Wirkstoff von allen repräsentativen Anwendungen in der Realität möglich sind. Trotz dieser Anforderung ist bislang jedoch noch keine Methode zur kumulativen Risikoabschätzung für Biozide innerhalb des EU-Review-Programms vereinbart worden.

Vor diesem Hintergrund ist es das Ziel der vorliegenden Studie, die Machbarkeit einer technischen Umsetzung von Artikel 10 (1) der BP-RL zu belegen und ein erstes Konzept zur Bewertung der kumulativen Umweltexposition gegenüber Bioziden zu erarbeiten. In einem ersten Schritt wurden die bestehenden Anforderungen an kumulative Bewertungen in anderen Regelwerken ausgewertet und auf ihre Anwendbarkeit für Biozide untersucht. In diesem Zusammenhang verwendete technische Begriffe und Definitionen wurden mit dem Ziel dokumentiert, eine Harmonisierung der Terminologie mit anderen Regelwerken herbeizuführen und präzise Definitionen innerhalb der BP-RL zu erstellen. Darüber hinaus wurden Einsatzbedingungen von Biozid-Produkten untersucht, um herauszufinden, für welche Anwendungen kumulative Expositionsbeurteilungen relevant sein könnten. Schließlich wurden Vorschläge für die technische Durchführung der kumulativen Expositionsbeurteilungen im Rahmen des Review-Programms mit dem Ziel erarbeitet, die Ergebnisse des Projekts in die anstehenden Entwicklungs- und Harmonisierungsprozesse auf EU-Ebene einzubringen.

Rahmen der BP-RL und der vorliegenden Studie

Die BP-RL setzt klare Rahmenbedingungen im Hinblick auf die Aspekte, die in der kumulativen Risikobewertung berücksichtigt werden sollten: die jeweiligen Bewertungen sollen sich auf die kumulative Umweltexposition gegenüber Biozid-Produkten entweder des gleichen Produkttyps (PT) oder unterschiedlicher Produkttypen (PTs) mit demselben Wirkstoff konzentrieren. Kumulationseffekte des Einsatzes von Biozid-Produkten mit verschiedenen Wirkstoffen ähnlicher Wirkungsweise werden in der BP-RL nicht explizit erwähnt und wurden in der vorliegenden Studie auch nicht berücksichtigt. Darüber hinaus beinhalten die Bestimmungen der BP-RL und somit auch der Untersuchungsrahmen der Studie nur Verwendungsarten im Rahmen der BP-RL. Kommen also Wirkstoffe sowohl in Biozid-Produkten als auch in anderen Anwendungsbereichen zum Einsatz, so zum Beispiel als Pflanzenschutzmittel

oder Industriechemikalien, so sind die Emissionswege letzterer Anwendungen nach den bestehenden Rechtsvorschriften nicht in der kumulativen Expositionsbewertung für Biozide zu berücksichtigten.

Die vorliegende Studie konzentriert sich auf die technischen Aspekte, befasst sich jedoch nicht mit regulatorischen Aspekten, die im Zusammenhang mit kumulativen Expositionsbewertungen zu beachten wären. So werden zum Beispiel regulatorische Konsequenzen für den Fall, dass die kumulative Expositionsbewertung ein Risiko für die Umwelt ergibt, außer Acht gelassen.

Ansätze in anderen Rahmenverordnungen

Die Überprüfung der bestehenden Ansätze und Anforderungen in Bezug auf kumulative Bewertungen in anderen Regulierungsbereichen ergaben, dass sich die meisten von ihnen auf die kumulative Exposition von Organismen gegenüber mehreren Chemikalien aus verschiedenen Quellen konzentrieren. Der Ausgangspunkt dieser Ansätze ist eindeutig wirkungsbezogen. Weder in den untersuchten Ansätzen noch in einer darüber hinaus durchgeführten Literaturrecherche wurden weitere Informationen zur quantitativen Beurteilung der Exposition der Umwelt gegenüber Bioziden aus unterschiedlichen PTs gefunden.

Technische Begriffe und Definitionen

Die technischen Begriffe und Definitionen im Zusammenhang mit kumulativen Risikobewertungen haben unterschiedliche Bedeutungen, je nachdem, in welchem Regelungsbereich sie angewendet werden. In vielen Regelungsbereichen, die sich hauptsächlich mit Aspekten der menschlichen Gesundheit beschäftigen, wird das Risiko infolge mehrerer Expositionswege /-pfade gegenüber einer einzigen Chemikalie oft als "aggregierte" Exposition oder aggregiertes Risiko definiert, während "kumulatives" Risiko und "kumulative" Exposition die Auswirkungen mehrerer Chemikalien mit gleicher Wirkungsweise bezeichnen. Im Gegensatz dazu werden in Artikel 10 (1) der BP-RL "Kumulationseffekte" im Zusammenhang mit dem Einsatz von Biozid-Produkten mit demselben Wirkstoff erwähnt. Es ist anzumerken, dass sich der Begriff "Kumulierungseffekte" sowohl auf die Risikobewertung der Umwelt als auch der menschlichen Gesundheit gegenüber einem Wirkstoff, der in verschiedenen Produkten des gleichen PTs oder verschiedener PTs enthalten ist, bezieht. Unter Berücksichtigung der unterschiedlichen und nicht harmonisierten Bedeutungen von "kumulative Exposition" im Kontext von Chemikalien, Pestiziden und / oder Arzneimitteln, wurde in der vorliegenden Studie im Rahmen der Umwelt-Expositionsbewertungen von Biozidwirkstoffen die folgende Definition des Begriffs "kumulative Exposition" unter Beachtung der BP-RL-Angaben erstellt: *"Kumulative Exposition gegenüber Bioziden ist die Gesamtbelastung gegenüber dem gleichen Biozidwirkstoff durch Emissionen während der Anwendung, der Nutzungsdauer oder der Entsorgungsphase von Biozid-Produkten, die zum gleichen PT oder unterschiedlichen PTs gehören."*

Im Hinblick auf die weitere Diskussion ist jedoch zu beachten, dass diese Definition nicht zwingend mit derjenigen anderer Regulierungsbereiche, insbesondere solcher, die Aspekte der menschlichen Gesundheit betreffen, übereinstimmt.

Relevanz kumulativer Umweltexpositionsbeurteilungen

Nach den Bestimmungen der BP-RL sollen kumulative Risikobewertungen nicht routinemäßig, sondern nur dort, wo relevant, im Rahmen des Review-Programms durchgeführt werden. Eine solche Relevanz ergibt sich, wenn hinreichende wissenschaftliche Belege vorhanden sind, die darauf hinweisen, dass die kumulative Exposition zu zusätzlichen schädlichen Auswirkungen führen könnte, die über diejenigen hinausgehen, die bereits im Rahmen der Risikobewertung der Einzelanwendungen beurteilt wurden. Die Notwendigkeit für eine kumulative Risikobewertung ist von dem jeweiligen berichterstattenden Mitgliedstaat (CA) von Fall zu Fall zu ermitteln.

Zur Reduzierung der Arbeitsbelastung ist für die Durchführung kumulativer Expositionsbewertungen ein Priorisierungssystem vorgesehen. Anhand von Beispielen von Biozid-Anwendungen, bei denen die Durchführung einer kumulativen Expositionsbeurteilung als relevant erachtet wurde, wurden verschiedene Parameter identifiziert, die möglicherweise als Indikatoren für die Relevanz der kumulativen Expositionsbeurteilungen dienen könnten. Diese Indikatoren wurden anschließend in ein Flussdiagramm (Abbildung 1) integriert, anhand dessen die Relevanz der kumulativen Expositionsbeurteilung überprüft werden kann.

In einem ersten Schritt wird analysiert, ob der Biozid-Einsatz im Vergleich zu den Einträgen aus Nicht-Biozid-Anwendungen aus anderen Regulierungsbereichen relevant ist. Ein erster Indikator ist, ob der Stoff in der Liste der Chemikalien mit hohem Produktionsvolumen (HPVC) aufgeführt ist, was bedeutet, dass er in Mengen von mehr als 1.000 t in der EU hergestellt oder in die EU importiert wird. Ein weiterer Indikator besteht darin, ob der Wirkstoff in anderen regulatorischen Bereichen wie zum Beispiel den Bereichen Pflanzenschutzmittel, Arzneimittel für Menschen oder Tiere, Kosmetika, Lebensmittel oder Futtermittel-Zusatzstoffe etc. geregelt ist. Liegt die Gesamtmenge des Biozideinsatzes unter einem Grenzwert von beispielsweise 10%, so kann man davon ausgehen, dass Emissionen aus Nicht-Biozid-Anwendungen in die Umwelt überwiegen und eine kumulative Expositionsbewertung nur für Biozide somit keinen Sinn macht. Obgleich der vorgeschlagene Grenzwert von 10% nicht auf wissenschaftlicher Basis abgeleitet wurde, kann dieser als ein erster Vorschlag gelten.

Eine räumliche und zeitliche Überlappung der verschiedenen Biozidanwendungen kann als ein starker Indikator für eine kumulative Umweltexposition betrachtet werden. Allerdings hängen diese Erkenntnisse vom Verwendungsmuster und den analysierten Expositionsszenarien ab. Da eine beträchtliche Wissenslücke über das Verwendungsmuster von Bioziden besteht, wird die Anzahl der PTs, in denen ein Stoff zum Einsatz kommt, als weiterer Indikator für eine mögliche kumulative Exposition aufgenommen. Dieser Trigger wurde auf einen Wert von 4 verschiedenen PTs festgesetzt. Auch hier ist zu beachten, dass der Grenzwert von > 4 PTs als unmittelbarer Indikator für eine kumulative Expositionsbeurteilung keine

wissenschaftliche Grundlage besitzt, sondern es sich um einen ersten Vorschlag handelt. Für Wirkstoffe, die in 2 bis 4 PTs enthalten sind, wird vorgeschlagen, dass eine grobe Berechnung des Risikoquotienten ($PEC_{Einzelanwendungen}$/PNEC) durchgeführt wird. Übersteigt der Risikoquotient für eine Einzelanwendung einen vorgeschlagenen Wert von 0,1, so sollte eine kumulative Expositionsbeurteilung durchgeführt werden.

Zusammenfassend muss jede kumulative Expositionsbeurteilung die Möglichkeit in Betracht ziehen, dass es zu räumlichen und zeitlichen Überschneidungen kommen kann. Anlass zu Besorgnis besteht, sobald der Risikoquotient ($\Sigma PEC_{Einzelanwendungen}$/PNEC) 1 übersteigt.

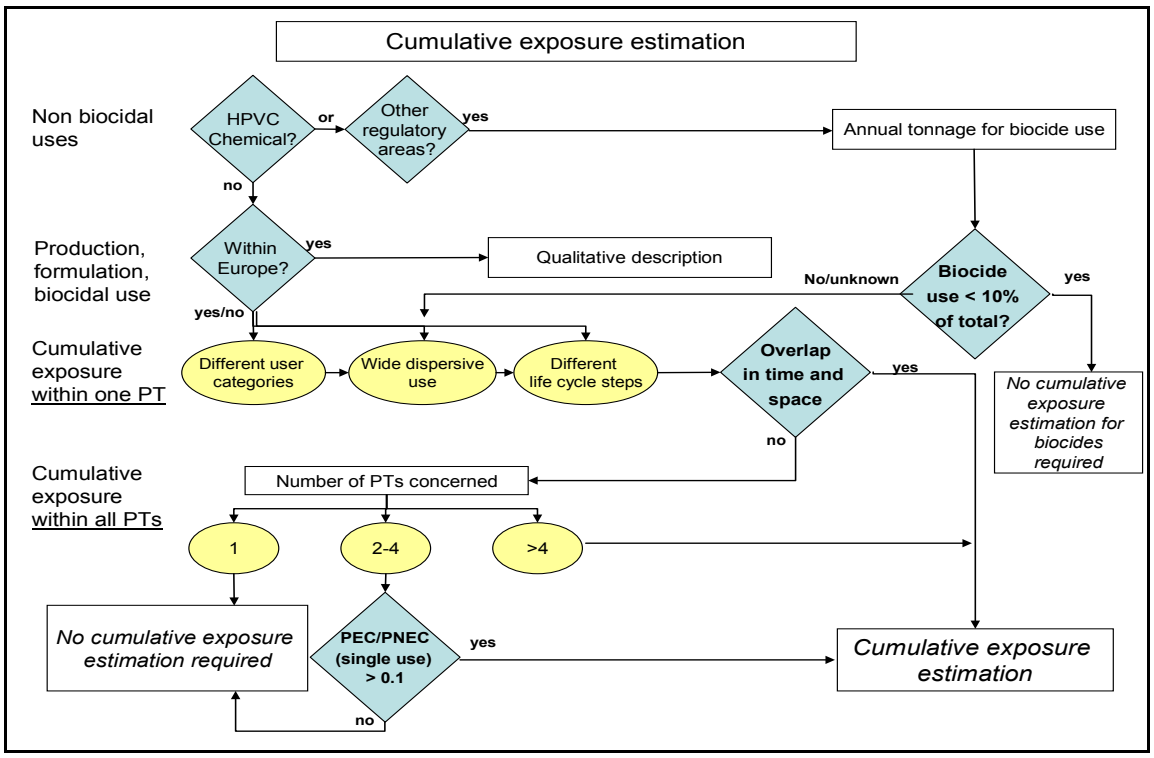

Abbildung 1 Entscheidungsbaum zur Einschätzung der Notwendigkeit einer kumulativen Expositionsbewertung

Vorschläge für eine technische Anleitung zur kumulativen Expositionsbewertung

Neben der Identifizierung von Indikatoren, die der Beurteilung der Relevanz der kumulativen Expositionsbewertung dienen, untersucht die vorliegende Machbarkeitsstudie konkrete Vorschläge für die technische Realisierung von kumulativen Expositionsbewertungen und diskutiert deren Vor- und Nachteile. Unterschiedliche Ansätze kumulativer Umweltexpositionsbewertungen werden derzeit von den Fachleuten der Mitgliedsstaaten in den CA-Meetings diskutiert. Diese Ansätze umfassen:

1) die Summe aus der höchsten lokalen Konzentration (worst case) und der regionalen Hintergrundkonzentration, d.h. (Clocal $_{(worst\ case)}$ + PECregional) oder
2) die Summe der lokalen Konzentrationen aller Einzelanwendungen (∑Clocal).

Anhand von Beispielberechnungen, die das Verhältnis von PEClocal zu PECregional verdeutlichen sollten, wurde gezeigt, dass die kumulierten PEC, die auf Grundlage des "PECregional-Ansatzes" berechnet wurden, deutlich niedriger sind als die Summe der Clocal aller Einzelanwendungen. Je höher die Anzahl der Einzelanwendungen, desto größer ist die Diskrepanz zwischen den beiden Ansätzen. Folglich könnte der "PECregional-Ansatz" die Umweltkonzentrationen aus sich zeitlich und / oder räumlich überlappenden Verwendungen des gleichen Wirkstoffs unterschätzen.

Dennoch scheint der PECregional-Ansatz eine mögliche Option zu sein, da er eine mittlere Hintergrundkonzentration darstellt, verursacht durch alle relevanten Emissionen aller möglichen Verwendungszwecke eines Wirkstoffs, und somit die gesamte Emissionssituation betrachtet. Darüber hinaus kann die Summe aus einem PECregional und einem PEClocal $_{(worst\ case)}$ leicht gebildet werden.

Um jedoch einen zuverlässigen PECregional-Wert abzuleiten, ist es notwendig, einen mehr oder weniger vollständigen Überblick über die Anwendungen eines Wirkstoffes zu haben. Es ist allerdings fraglich, ob es überhaupt möglich ist, alle notwendigen Daten zu erhalten. Durch die Erfahrungen aus der Altstoff-Bewertung ist bekannt, wie komplex die Situation in Bezug auf die unterschiedlichen Verwendungsmuster von Stoffen und den daraus resultierenden Emissionen sein kann.

Darüber hinaus erfordert der derzeitige Ansatz zur Aufnahme von Wirkstoffen in Anhang I unter der BP-RL ausschließlich die Bewertung einer einzigen repräsentativen Anwendung. Werden für diese Anwendung keine Risiken festgestellt, so kann der Wirkstoff in Anhang I aufgenommen werden. Gleichzeitig ist eine kumulative Beurteilung in der Phase der Aufnahme in Anhang I durchzuführen. Augenscheinlich sind also keine umfassenden Informationen zur Ableitung eines fundierten PECregional-Wertes verfügbar.

In Zukunft werden in der Phase der Produktzulassung mehr Informationen zum Verwendungsmuster von Wirkstoffen verfügbar sein. Dieser Wissenszuwachs wird die Ableitung eines verlässlicheren PECregional-Wertes ermöglichen. Da es sich bei der Produktzulassung jedoch um eine nationale Aufgabe eines jeden EU-Mitgliedstaates handelt, wird ein unterschiedliches Genauigkeitsniveau an Informationen vorhanden sein. Dies kann schlussendlich zu verschiedenen PECregional-Werten für die verschiedenen EU-Mitgliedstaaten führen, was den Sinn einer solchen Ableitung fragwürdig erscheinen lässt. Eine Lösung wäre, nach Ablauf einer gewissen Zeit auf Grundlage des fortschreitenden Wissens zumindest für diejenigen Produkte, für die eine Zulassung in mehreren verschiedenen EU-Mitgliedstaaten erlangt wurde, zentral einen PECregional abzuleiten. Ferner ist zu bedenken, dass Wirkstoffe in Anhang I für verschiedene Produkttypen aufgenommen werden und somit die Zusammenstellung von Informationen aus der

Produktzulassung, die alle Anwendungen in allen Produkttypen beinhaltet, einen relativ langwierigen Prozess darstellen wird.

Für einige Wirkstoffe, die bereits als Altstoffe bewertet wurden, könnte man zwischenzeitlich den PECregional-Wert aus dem EU Risk Assessment Report (RAR) nutzen. Es ist jedoch unklar, ob dies rechtlich möglich ist, da der PECregional aus Emissionen berechnet wurde, die über den Einsatz von Bioziden hinausgehen. Dennoch würde dieser Ansatz aus Sicht der Vorsorge Sinn machen.

Andererseits könnte der PECregional, betrachtet man die Schlussfolgerungen aus den Untersuchungen im Rahmen dieses Projektes, das tatsächliche Risiko durch eine mehrfache Exposition auch unterschätzen. Der ∑Clocal-Ansatz ist somit eher konservativ und gibt in einigen Fällen sogar ein realistischeres Bild ab. Schlussfolgernd kann jedoch keine abschließende Entscheidung darüber getroffen werden, welcher Ansatz besser eine spezifische Emissionssituation beschreibt. Auch für den ∑Clocal-Ansatz gilt, dass dessen Genauigkeit in hohem Maße von der Verfügbarkeit der Daten abhängt. Ein großer Nachteil des ∑Clocal-Ansatzes ist sicherlich das Aufaddieren mehrerer realistischer Worst-Case-Szenarien. Es ist fraglich, ob dieser Ansatz zulässt, hinreichende Schlüsse zu Wirkstoffrisiken und zu den rechtlichen Konsequenzen im Hinblick auf diese Wirkstoffe zu ziehen.

Neben dem Vergleich der Eignung der beiden unterschiedlichen PEC-Ansätze wurden einige weitere technische Details im Rahmen der Studie geprüft:

Ein technischer Aspekt betraf die Berechnung der PEC-Werte auf Grundlage des "∑Clocal-Ansatzes". Es wurde überprüft, ob die kumulierten PEC-Werte errechnet werden sollten, indem man die Summe der lokalen Emissionen / täglichen Freisetzungsraten in die Umweltkompartimente bildet (z.B. ∑Elocal für Oberflächenwasser) oder die aus den Einzelanwendungen (∑Clocal) resultierenden vorhergesagten Umweltkonzentrationen (PEC-Werte) aufaddiert. Auf der Grundlage von beispielhaften Berechnungen konnte gezeigt werden, dass beide Ansätze zu analogen Ergebnissen führen. Somit können kumulative PEC-Werte entweder durch Addition der Clocal-Werte der Einzelanwendungen oder durch Addition der Emissionsraten unter Verwendung der kumulativen Emissionsraten für die anschließende PEC-Berechnung mit EUSES (oder mithilfe anderer geeigneter Modelle) berechnet werden.

Ein weiterer technischer Aspekt, der eingehend untersucht wurde, befasst sich mit der Frage, wie Umweltexpositionsschätzungen auf Grundlage der Jahrestonnage und des durchschnittlichen Verbrauchs von Biozid-Wirkstoffen in kumulativen Expositionsbewertungen kombiniert werden können. Die folgende Vorgehensweise, bei der zwei verschiedene Situationen zu unterscheiden sind, wird vorgeschlagen:

1) Für alle Verwendungszwecke, die in der kumulativen Expositionsbewertung berücksichtigt werden müssen, sind Emissionsszenarien sowohl auf Grundlage des Tonnage- als auch des Verbrauchsansatzes vorhanden.

2) Für eine oder mehrere der vorgesehenen Verwendungen, die in der kumulativen Expositionsbewertung berücksichtigt werden muss/müssen, sind lediglich Emissionsszenarien entweder auf Grundlage des Verbrauchs- oder des Tonnageansatzes verfügbar.

Im ersten Fall sollte für jede Anwendung mittels einer "Break-Even-Berechnung“ abgeschätzt werden, ob der auf der Tonnage oder der auf dem Durchschnittsverbrauch basierende Ansatz besser für die Emissionsbewertungen geeignet ist. Anschließend sollten für jede Verwendung lokale Emissionsraten (Elocal) und vorhergesagte lokale Umweltkonzentrationen (PEClocal) auf Grundlage des Ansatzes berechnet werden, der sich anhand der "Break-Even-Berechnung" als der am besten geeignete herausstellt. Zur Bewertung der kumulativen Exposition sollten dann die Elocal oder PEClocal aller Anwendungen aufaddiert werden.

Im zweiten Fall werden lokale Emissionsraten (Elocal) und vorhergesagte lokale Umweltkonzentrationen (PEClocal) für jede Anwendung auf Grundlage des verfügbaren Emissionsszenarios berechnet. Wie für den ersten Fall erläutert, sollten auch hier Elocal oder PEClocal zur Bewertung aller Verwendungen summiert werden.

1 Background

Article 10(1) of the EU Biocidal Products Directive 98/8/EC (BPD) states that for the inclusion of an active substance in Annex I, Annex IA or IB, cumulation effects from the use of biocidal products containing the same active substance shall be taken into account, where relevant. It has to be noted that this refers to both environmental and human health risk assessment and to one active substance contained in different products of the same Product Type (PT) or of different PTs. These provisions have also been considered in Article 8 (3) of the draft Regulation for biocidal products.[1]

Additionally, in the TNsG on Annex I inclusion it is stated that:

"For the first evaluation of the active substance the applicant (in the dossier) and the Competent Authority (in the report) should consider what combination of exposures to the active substance from all the representative uses is realistically possible. This should be based on the combined exposures for each use. A relevant time period for the pattern of use of the products and the nature of the active substance should be decided and explained in each case. The assessment should reflect normal lifestyles and emission patterns. Realistic worst case possible combinations of exposures should also be considered."

During the workshop on Environmental Risk Assessment for PT 1-6 on 11th March 2008 ,the need for the performance of cumulative risk assessment for Annex I inclusion of active substances was extensively discussed (European Commission 2008a). The need for carrying out cumulative risk assessment was generally accepted. It was decided to start performing cumulative risk assessments for PT 01 to 06 with wide dispersive uses based on the available information. An identified risk should be flagged in the Competent Authority Report (CAR). The workshop participants, however, noted that up to now no agreed methodology for cumulative risk assessments for biocides within the EU Review Programme exists.

At the 29th meeting of representatives of Members States Competent Authorities (CAs) for the implementation of the BPD, which took place on 28-30 May 2008, it was suggested that cumulative risk assessments should not be carried out routinely in the Review Programme (European Commission 2008b). It was agreed instead that, for active substances with a cumulative potential, the respective Rapporteur Member State shall decide whether and to what extent a cumulative risk assessment should be included in the CAR. It was recognised once again that more guidance is needed on data requirements and on a methodology how to perform cumulative risk assessments.

[1] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:DKEY=496597:EN:NOT

Against this background, it has been the objective of the present study to prove the feasibility of a technical realisation of Article 10(1) of the BPD and to elaborate a first concept for the cumulative environmental exposure assessment of biocides.

In a first step, existing requirements concerning cumulative assessments in other regulatory frameworks have been evaluated and their applicability for biocides has been examined. Technical terms and definitions used in this context were documented with the aim to harmonise terminology with other frameworks and to set up precise definitions within the BPD. Furthermore, application conditions like for example PT, application areas, emission pathways have been analysed to find out for which cumulative exposure assessments may be relevant. Finally, proposals for the technical performance of cumulative exposure assessments within the Review Programme have been elaborated with the aim to bring the results of the project into the upcoming development and harmonization processes on EU level.

2 Context of cumulative exposure assessment

There are many approaches referred to in the context of cumulative exposure which are not always discriminated from each other in a sound way. This section gives an overview about the different aspects which could be considered when assessing cumulative environmental exposure (see Figure 2).

The present study focuses on the cumulative environmental exposure of biocidal products of the same PT or of different PTs containing the same active substance (i.e. “same biocidal active”). Cumulation effects from the use of biocidal products containing different active substances with a similar mode of action have not been considered in the present study.

Furthermore, the investigatory framework of the study comprised only uses within the scope of the BPD; meaning that if active substances are used both in biocidal products and in other use areas like, for example, as plant protection products or industrial chemicals, the emission routes of the latter are not to be considered in the cumulative exposure assessment for biocides according to the existing legislation.

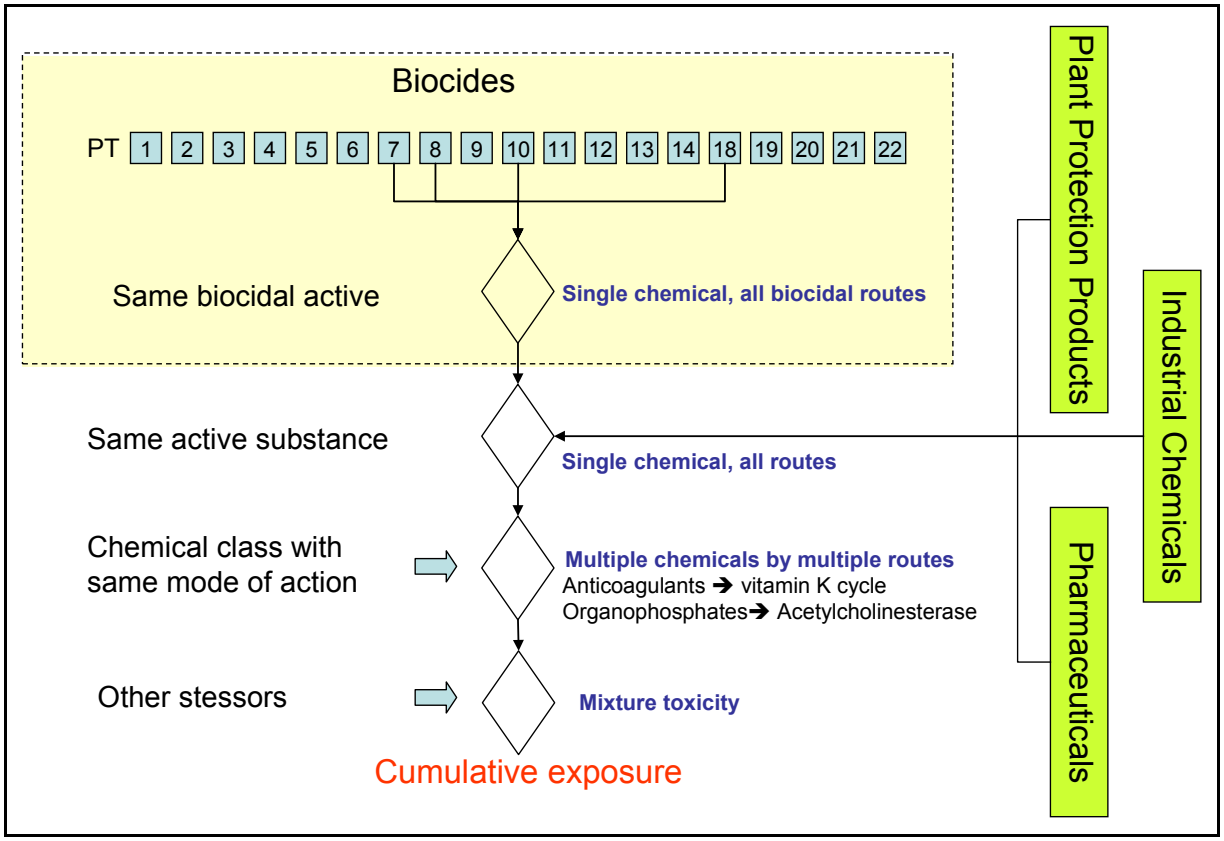

Figure 2 Different approaches for assessing cumulative exposure

In the following, some of the before mentioned aspects are discussed in more detail.

Multiple applicants of the same active substance

Often, more than one applicant supports an active substance for approval. This was observed for biocides as well as for plant protection products and medicinal products.[2] The evaluation of these dossiers in several different assessment reports is laborious and might lead to conflicting conclusions also in the exposure assessment where each applicant uses their own input data. In consequence the competent authorities intend eliminating multiple reviews of the same active substance for multiple dossiers or several PTs by adopting coherent parts of the CAR for all applicants.

[2] In REACH this problem has been avoided by the establishment of SIEFS.

Multiple biocidal product types with the same active substance

A view on the number of biocidal active substances to be assessed in the Review programme reveals that from about 270 different active substances, approximately 716 "active substance – product type" combinations are currently under evaluation. In May 2010, the actualised data basis was provided by the European Commission. This means that one active substance on average is included in three PTs. Some substances, such as glutaraldehyde, 2-biphenylol, or didecyldimethylammonium chloride (DDAC) are included in up to 9 PTs, silver chloride even in 11 PTs.

This problem is addressed in Article 10(1) of the BPD which requires that cumulation effects from the use of biocidal products containing the same active substance shall be taken into account, where relevant. In principle, the different PTs can be considered as different application areas and therefore as different exposure routes of the same chemical to the environment, similar to the provisions of Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Because of the wide dispersive uses of different biocidal applications even in one PT, cumulative exposure assessment is an ambitious task.

Multiple sources of the same active substance from different regulatory areas

The active substances to be assessed are also often used for other purposes outside the scope of the respective regulatory area. A systematic analysis of plant protection and biocidal active substances revealed that about 58 biocidal actives (merely of PT 7-12, 18) are applied as plant protection products. Around 25 biocidal active substances are used as preservatives in cosmetic products not covered by the BPD (Vernon et al 2008).[3] Several oxidizing biocides, such as sodium hypochlorite or hydrogen peroxide are used as bleaching agents e.g. for cleaning purposes. In wastewater treatment, the biocide (and plant protection product) dimethyldithiocarbamate (DMDTC) is used as precipitation agent for precipitation of heavy metals in the presence of complexing agents. Several insecticides are used as veterinary medicinal products against exoparasitic pests. Copper and zinc emissions from the vehicles and building sectors (drinking water distribution) are other examples for important emission sources not covered by the BPD. The biocide 2-Mercaptobenzothiazole (Benzothiazole-2-thiol), too, has its major use as a vulcanization accelerator for the rubber industry.

In the "State of the Art Report on Mixture Toxicity" by Kortenkamp et al. (2009) it was criticised that there is presently no vehicle to deal with exposure to substances that come from areas covered by separate EU regulations, such as cumulative exposure to plant protection products, biocidal products, pharmaceuticals, household chemicals, food additives etc. Each

[3] http://ec.europa.eu/environment/biocides/pdf/cosmetic_products.pdf (Currently, the Commission is discussing a revision of the borderline document between biocides and cosmetic products.)

sector is performing its own risk assessment mostly completely ignoring that there may be contributions from the other sectors. Even in REACH feed additives, veterinary medicines, plant protection products, biocides, and human medicine are not considered.

However, multiple sources from different regulatory areas were out of the scope of this project in accordance with the provisions of the BPD and have not been analysed in detail. Thus, only well-known examples are described in this report.

Same mode of action and mixture toxicity

In scientific literature, cumulative exposure is mainly discussed in the context of exposure to different chemicals with the same mode of action (such as anticoagulants interfering with the vitamin K cycle or organophosphates inhibiting acetylcholinesterase) and/or mixture toxicity of different substances. Mixture toxicity is eventually assessed for authorisation of biocidal products or plant production products (as an example) containing different active substances. As this clearly concerns the part of the risk assessment dealing with effects, it is out of the scope of this project. However, some approaches are discussed in section 3.

Regulatory aspects of cumulative assessments of biocides

Several regulatory questions on practical aspects of cumulative exposure arose in particular in the context of discussions in the framework as, for example, the Arona Workshop on environmental risk assessment (RA) for PTs 1 to 6:[4]

- Should the cumulative RA be carried out already for Annex I inclusion purposes or is it only relevant at the Product Authorisation stage?
- How to deal with an active substance evaluated in the Review Program in more than one PT with different time lines for Annex I inclusion? What are the regulatory consequences if cumulative exposure reveals risks for the environment for the different applicants or PTs?
- Should the PECregional for each active substance be derived as a way forward (at least for wide dispersive uses)?
- Can the PECregional from the final risk assessment report under the EU Existing Substance Regulation be used?
- What data are required with respect to information on the market share or the information on tonnage when several companies apply for different products, for example?
- How to deal with confidential data within the CAR?

[4] CA-Nov08-Doc.6.3

In addition, the reliability of the tonnage due to possible variability during the authorisation period is to be taken into account.

The regulatory aspects to be considered with regard to cumulative exposure assessment as well as the legal consequences of different time lines of dossier evaluation and Annex I inclusion and the management of confidential data have not been object of the project and have therefore not been assessed within the present report.

3 Compilation of existing approaches and requirements related to cumulative assessments

Relevant documents from national, EU, and international sources dealing with cumulative risk assessments have been evaluated and terms and definitions that are used in the context of cumulative assessments have been documented.

Cumulative exposure assessments are required both for environmental and for human health risk assessments. Therefore, the evaluation of existing approaches has not been restricted to documents related to environmental exposure assessments, but has been extended to approaches to cumulative assessments in general, thus also including the human health area.

In addition to the evaluation of scientific documents, information on guidance on cumulative assessments developed in other legal frameworks has been collected in order to check their applicability for biocides.

Nota bene: Different terms and definitions in the context of cumulative exposure assessment are in use. Therefore, these terms and definitions are compiled in chapter 3.3.1. In chapter 3.3.2, a proposal for the use in the context of the BPD is made.

Table 1 gives an overview of existing approaches related to cumulative assessments that were investigated in detail in the present study.

Table 1 Overview of existing approaches related to cumulative assessments

Document / Legal framework	Focus on: Human health or environment	Reference to section
Technical Guidance document (EU TGD), Part II	Environment	Section 3.1
REACH / EC 1907/2006	Human health; environment	Section 3.1.2
Current developments on EU level	Human health	Section 3.1.3
Plant protection products / 91/414/EEC	Human health	Section 3.1.4
Medicinal products 2001/82/EC 2001/83/EC	Human health; environment	Section 3.1.5
US EPA approach for pesticides	Human health	Section 3.1.6
OECD Emission Scenario Documents (ESDs)	Human health; environment	Section 3.1.7
WHO/IPCS activities on risk assesment	Human health	Section 3.1.8

3.1 Existing approaches in detail

3.1.1 EU Technical Guidance Document on Risk Assessment

General guidance on the assessment of environmental exposure of biocidal active substances is provided in the TGD on Risk Assessment (EU TGD 2003).

The **EU TGD (2003) Part II, paragraph 2.3.3.3** deals with "release estimation". On page 43 it is provided that "when assessing the releases on local and regional scales, the following points must be noted: In particular High Production Volume Chemicals (HPVCs) often have more than one application, sometimes in different industrial categories. For these substances, the assessment proceeds by breaking down the production volume for every application according to data from industry. For the local situation, in principle, all stages of the lifecycle need to be considered for each application. Where more than one stage of the lifecycle occurs at one location, the PEClocal shall be calculated by summing all the relevant emissions from that location. For releases to wastewater, only one point source for the local STP is considered. For the regional situation, the emissions to each compartment have to be summed for each stage of the life-cycle and each application. The regional environmental concentrations are used as background concentrations for the local situation."

EU TGD (2003) Part II, Appendix XIII ("Risk assessment of sources not covered by the life-cycle of the substance") states that "*exposure may occur from other sources than the life-cycle of the produced or imported substance under assessment. Such sources have been referred to as "unintentional sources". Examples are substances of natural origin, substances formed in combustion processes and indirect emissions of the substance, e.g. as by-product.*

The recommendation of the EU TGD is that the Rapporteur should clearly list other sources, which can give rise to exposure by the substance being assessed. The risk assessment should include as much readily available information on these sources as possible. In the case that "further information is needed", however, "producers or importers of the substance under examination can not be generally obligated to obtain such information".

Concerning biocides it is stated that "For biocides, sources which include substances of natural origin or releases from other biocidal uses should be taken into account in the risk assessment. When it comes to cumulative effects of a substance used also outside the scope of the BPD (e.g. in plant protection products) and maybe regulated with another Directive there is, at the time of revision of the TGD, still a need for a common EU decision on how to handle such cases. Exclusion of other than only biocidal uses from the assessment causes difficulties, for example, when using monitoring data or comparing measured residue data with Maximum Residue Limits."[5]

3.1.2 Approaches in REACH

REACH deals with the Registration, Evaluation, Authorisation and Restriction of Chemical substances.

REACH is generally based on a single substance approach and places the burden on ensuring the safe use of a substance on the respective substance manufacturer. Annex 1 of the legal text lays out the steps for hazard and exposure assessment and based on this, the risk consideration. The outcome are DNEL values for human health endpoints and PNEC values for environmental endpoints which are used – in combination with estimated exposure values – to demonstrate adequate control for the risks to worker, consumer and the environment.

In this way, REACH requires that all relevant exposure scenarios are investigated for a particular substance: occupational, consumer and environment and also for the exposure from all routes combined:

Annex 1 to Regulation (EC) No. 1907/2006

Identification of DNEL(s) Paragraph 1.4.1

(…)If more than one route of exposure is likely to occur, then a DNEL shall be established for each route of exposure and for the exposure from all routes combined. (…)

[5] This statement has also been included into the revised TNGs Principles and Practical Procedures for the inclusion of active substances in Annexes I, IA and IB, ECB, February 2008

Exposure Estimation Paragraph 5.2.4

(…)Each relevant route of human exposure (inhalation, oral, dermal and combined through all relevant routes and sources of exposure) shall be addressed. Such estimations shall take account of spatial and temporal variations in the exposure pattern.(…)

Risk Characterisation, Paragraph 6.2

(…)In addition, the overall environmental risk caused by the substance shall be reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments.(…)

ECHA Guidance on information requirements and chemical safety assessment

In the respective guidance (ECHA Guidance on information requirements and chemical safety assessment[6]) three relevant guidance chapters were identified as relevant for this project:

- Part E (Risk characterisation),
- Part R 15 (Consumer exposure estimation) and
- Part R 16 (Guidance on environmental exposure estimation)

Starting with **Part E** (Risk characterisation for **human health** (E.3.), the following guiding principle can be found on page 27:

"In situations where the same person is potentially exposed to the same substance in the same setting via different routes of entry into the body or from different products containing the same substance, exposure scenarios reflecting these concomitant exposures should be assessed in the exposure estimation.

Above, there is even some consideration regarding similar acting chemicals required in special cases:

"..in special cases: exposure to several very closely related and similar acting chemicals (e.g. different salts of a metal or closely related derivatives of organic substances) the exposure evaluation and risk characterisation should reflect this".

"If data are available…include...also a scenario concerning this combined exposure".

"One way…add exposures and...use a toxicological descriptor from a representative substance among the analogs".

"If data do not allow for a quantitative assessment an attempt should be made to address this issue in a qualitative manner".

[6] http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_en.htm?time=1258970710#E

"Additionally, in each case the applicant has to assess the need for an assessment of combined exposure, i.e., exposure from different uses of a substance. Normally, occupational exposure will greatly exceed all other exposure, and the contribution from consumer use or from exposure via the environment may not need to be added. However, for substances with consumer use, and which may be present in potential food items (as indicated by the EUSES-modelling), the combined exposure may need to be assessed for the general public exposed both via the food and via consumer products."

For the risk characterisation relating to the **environment** the same principle applies: (page 36, step 5 on combined exposures).

"In special cases, where exposure occurs to a substance as well as to several very closely related and similar acting chemical substances (e.g. different salts of a metal or closely related derivatives of organic substances), the exposure evaluation and risk characterisation should reflect this aspect. If data are available the exposure assessment should also include a scenario concerning this combined exposure. If data do not allow for a quantitative assessment, the issue can be addressed in a qualitative way."

Part R 15 of the REACH guidance on information requirements deals with the consumer exposure estimation. Page 11 specifies that:

"if the same substance (for a single registration) occurs in different consumer products that could reasonably be expected to be used jointly and frequently by an average consumer, it is advised to also calculate the combined exposure to the substance due to exposure to different consumer products, in order to prevent underestimation of the potential exposure."

This is described in more detail on page 20, in the chapter on combined exposure via various exposure routes:

"In cases where consumers are exposed to the substance in the consumer product or products via different exposure routes, each exposure route needs to be calculated separately and considered in the risk characterisation."

"The combined exposure for characterising overall systemic health risks should be assessed by adding up the risk characterisation ratios (RCRs) for the different routes into a total RCR. Common substances (e.g. solvents) are incorporated in several consumer products that could in principle all be used by a consumer. When this is a likely case, not only the exposure routes but also exposure to different products leading to exposure to the same substance should be calculated and combined for a worst-case consumer exposure situation. The overall exposure should be assessed by adding up the risk characterisation ratios (RCRs) for the different routes, (and, if needed, for each type of product) into a total RCR."

See also page 29:

"If a consumer is exposed to a substance in a particular consumer product via different routes, or if the same substance is present in several consumer products that are likely to be used in combination, the contribution of each route or product to the total risk due to exposure can be summed. Normally the summation is done for each time scale separately (acute and long-term). In general, the risk characterisation ratios for the different routes or products will be summed and evaluated for control of risks."

Chapter R 16 (Guidance on environmental exposure estimation) describes how to deal with multiple emissions (page 15):

"Emissions of a substance may take place from multiple sources at the same time. This results from the manufacturers own production/market volume and the production/market volume of his competitors. Hence single source assessment must take into account that other releases of the same substance may take place at the same time in a near or far distance. However, REACH does not require the registrant to take into account the market volumes of his competitors even if a Consortium performs a joint registration under REACH. But the single manufacturer or importer is obliged to take account of his total market volume and the possibility that total releases may lead to significant higher exposure than calculated or measured at a local single source. There are a number of ways to address this aspect of safety assessment, i.e.:

- *Carry out a very conservative local assessment covering already a situation that several sites emit the substance into the same environment. Unless it is a seasonal use pattern, assume 365 release days, since not all sites will use the substance at the same time.*
- *Carry out a regional background assessment, assuming that 100% of the registrant's market volume is manufactured and applied in the EU standard region as defined in Section R.16.5.4 and sum up the emission factors at the different life stages. Unless it is a seasonal use pattern, assume 365 release days since the use will be spread over the whole year."*

"In a situation where a substance is released through several point sources into the same river, the resulting cumulative concentration may in a first approach be estimated by assuming it to be released from one point source." (Page 68)

PEC regional for the marine environment (Page 91):

(…)

"To assess the potential impacts of multiple point and diffuse sources of substances on the marine environment a river plume in coastal sea water is considered as a marine regional generic environment as follows (…)"

Conclusion

The obligations in the REACH Chemical Safety Assessment (CSA) require manufacturers to include combined exposures from all routes of the same chemical for a specific endpoint. The risk characterisation in Annex 1 (paragraph 6.2) makes it clear that the combined emissions to the environment also need to be integrated.

3.1.3 Current developments on EU level on cumulative risk assessment

The focus of this project lay on the cumulative exposures and the resulting risks of the same biocidal ingredient for the environment. Still, it should be briefly mentioned that there are current discussions taking place at EU level regarding the combination effects of hazardous chemicals. These are mainly aimed at endocrine disrupting chemicals and their potential effects on human health and the environment.

At the Environment Council meeting in October 2009, the EU Swedish presidency agreed to a Danish initiative to draft Council conclusions on cumulative risk assessments and table them for endorsement at the December Environment Council meeting.

The Council can be expected to call on the Commission to consider the combination effects following exposure to multiple (similarly acting) chemicals in existing EU legislation, in particular REACH. Experts regard the predominant chemical-by-chemical approach in risk assessment as insufficient to protect humans and the environment from the risks of combination effects. The conclusions therefore call for more research in the area. Furthermore, the Commission is invited to assess how and whether existing legislation addresses this problem and to suggest appropriate modifications and guidelines, paying attention to the precautionary principle in future legislation. The focus is particularly on endocrine disrupters.

The European Commission provides an own web site concerning the “Combination effects of chemicals” where the discussions among the Council of Environment Ministers is documented.[7] In 2007, the Commission (DG Environment) contracted a study to review the current scientific knowledge and regulatory approaches. The study entitled "State of the Art Report on Mixture Toxicity" describes several examples of synergistic effects of different biocidal active substances which resulted in the conclusion that for biocidal products containing more than one active substance the combined effects should be tested for the biocidal product itself (Kortenkamp et al. 2009). However, while combined risks to humans and the environment resulting from exposure to multiple chemicals are addressed in the report, cumulative exposure to the same chemical from different sources is not considered.

Kortenkamp et al. (2009) define the term “mixture toxicity” as unwanted adverse effects of mixtures of chemicals and as synonym for combined effects. Mixture risk assessments are

[7] http://ec.europa.eu/environment/chemicals/effects.htm; http://www.consilium.europa.eu/showFocus.aspx?id=1&focusId=434&lang=en

applicable for substances that are mixtures themselves, products that contain more than one chemical, chemicals jointly emitted during production, transport, use and disposal and chemicals that might occur together e.g. in environmental compartments or food items.

Kortenkamp et al. (2009) recommend a tiered approach for mixture risk assessment preliminarily based as default concepts on dose (concentration) addition for mixtures composed of chemicals with a similar mode of action. With respect to chemicals with diverse modes of action, the concept of independent action should be applied. The tiered approach is proposed to deal with data gaps and to take account of differing data quality. An evaluation of whether combined exposures are likely to occur is demanded at the lowest tier and it may be concluded that the situation does not present an issue for mixture risk assessment.

Within the evaluation of effects, Kortenkamp et al. (2009) suggest to adopt a specific mixtures assessment factor instead of the usually applied uncertainty factors in order to take into account the possibility of joint effects which are not appropriately covered by the currently applied uncertainty factors. In a subsequent tier, sufficient data may be available to satisfy the assumptions of dose (concentration) addition. In the highest tier it might be possible to address both issues of modes of action and differences in the vulnerability of various species or risk receptors.

Beside of the uncertainty factors, Kortenkamp et al. (2009) also questioned the suitability of the No Observed Adverse Effect Levels (NOAELs) or No Observed Effect Concentrations (NOECs) as the preferred method for defining thresholds of regulatory concern and points of departure. Instead, Kortenkamp et al. (2009) propose the concept of benchmark doses because NOAELs and NOECs are not fixed values, but are highly dependent on the experimental design employed during toxicity studies. Besides, NOAELs and NOECs are associated with varying effects, depending on the statistical resolving power of the underlying experimental studies. Benchmark dose has been developed as a statistical tool to determine acceptable exposures to a chemical. The benchmark dose is a dose that causes a prescribed effect (generally within or close to the experimentally observed range) and that is estimated by fitting a regression model to experimental data. Benchmark doses often produce numerical values similar to NOAELs but produce lower numerical values with data of poor quality.

3.1.4 Approaches in the Review Programme of plant protection products

The evaluation, marketing and use of plant protection products are regulated under Council Directive 91/414/EEC. The Directive has been revised and Regulation (EC) No 1107/2009 on plant protection products will replace the present Council Directive of 15 July 1991.

Neither the old Directive nor the new Regulation concerning the placing of plant protection products on the market explicitly states that cumulative exposure assessments have to be

taken into account for the approval of an active substance in accordance with Annex II to the Regulation.

However, with regard to effects on **human health**, Articles 4(2) and 4(3) state that:

"The residues of the plant protection products, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use, shall meet the following requirements:

(a) they shall not have any harmful effects on human health, including that of vulnerable groups, or animal health, taking into account known cumulative and synergistic effects where the scientific methods accepted by the Authority to assess such effects are available, or on groundwater; (…)"

"A plant protection product, consequent on application consistent with good plant protection practice and having regard to realistic conditions of use, shall meet the following requirements:

(a) it shall be sufficiently effective;

(b) it shall have no immediate or delayed harmful effect on human health, including that of vulnerable groups, or animal health, directly or through drinking water (taking into account substances resulting from water treatment), food, feed or air, or consequences in the workplace or through other indirect effects, taking into account known cumulative and synergistic effects where the scientific methods accepted by the Authority to assess such effects are available; or on groundwater; (…)"

Further reference to cumulative or combined (human health / environmental) risk assessments are not given in the new Plant Protection Products Regulation.

The German Federal Environment Agency (Umweltbundesamt) investigates the combination effects of plant protection products and biocides with regard to the ecotoxicological risk assessment in different research projects. The focus of these investigations lies on the ecotoxicological effects of combination products (i.e. products containing two or more different active substances) and of tank mixtures (i.e. mixtures of two or more products with different active substances in the application tank).

This simultaneous exposition of the environment to more than one active substance (i.e. to pesticide mixtures) has not been regulated by the Plant Protection Products Regulation / Directive to date and thus is not routinely carried out in the Pesticide Review Programme.

The same applies to the cumulative or combined exposure of the environment to different products containing the same active substance: up to now this type of cumulative environmental risk assessment was not considered within the Pesticide Review Programme.

3.1.5 Medicinal products

The assessment of environmental safety for veterinary medicinal products according to Directive 2001/82/EC is carried out in two phases. In the first phase the extent of environmental exposure is estimated and in the second phase the fate and effects of the active residue are assessed. The environmental risk assessment only considers the use of a veterinary medicinal product, but not its production and the waste. The revised guidelines on environmental impact assessment for veterinary medicinal products consider cumulative exposure from different path ways but do not account for cumulative exposure from different sources of different regulatory areas. If excretion data are available, the active substance and relevant metabolites (defined as representing 10% or more of the administered dose and which do not form part of biochemical pathways) should be added to the PEC when it is recalculated (EMEA 2004).

Furthermore, the environmental risk assessment of medicinal products for human use according to Directive 2001/83/EC is routinely applied for all new marketing authorizations for medicinal products for human use. Phase I consists in a pre-screening of the exposure based on consumption data and the log K_{ow}. A $PEC_{surfacewater}$ value of 0.01 µg/L has been defined as action limit value. Usually, the total consumption is used for exposure estimation (tonnage approach). Phase II consists in an initial prediction of risk by a base set aquatic toxicology and fate (Tier A) and a compartment-specific refinement of risks by an extended data set on emission, fate and effects (Tier B). In Phase II the market penetration factor, which represents the proportion of the population being treated daily with a specific drug substance, might be refined by consumption data. The consumption corresponds to the overall consumed amount of the drug substance from all suppliers (tonnage approach). Here, a market share of 100% of the drug substance is assumed for each applicant. However, the market share of several drug substances used for the same indication of a disease is not considered. A cumulative exposure of the active substance is not considered in the guidance document (EMEA 2006).

On the contrary, the US Food Quality Protection Act (FQPA) of 1996 mandates that the U.S. Environmental Protection Agency considers both aggregate and cumulative risks. Aggregate assessments account for multiple sources and routes of exposure for a single chemical. Cumulative assessments combine exposures to two or more chemicals that share a common mechanism of toxicity (Sielken 2000).

3.1.6 US EPA approach

The Food Quality Protection Act (FQPA) of 1996 provides that when determining the safety of a pesticide chemical, US EPA shall base its assessment of the risk posed by the pesticide chemical on aggregate (i.e., total food, drinking water, residential, and other non-occupational) exposure to the pesticide. US EPA is also required to consider available information concerning the combined toxic effects to human health that may result from dietary, residen-

tial, or other non-occupational exposure to chemicals that have a common mechanism of toxicity (US EPA 2002).

A directive to identify chemicals of common mechanism group inducing a common toxic effect by a common mechanism of toxicity was given by the US EPA (1999) for pesticides.[8] Another US EPA document gives further "Information on cumulative risk assessment" (US EPA 2002).[9]

In the first instance, the multiple exposures of men against different pesticide residues are considered. Exposure paths considered were drinking water, food and inhalation. On the basis of four different case studies, cumulative exposure of pesticides was investigated exemplarily:

- In the case study “Cumulative Risk Assessment for Organophosphate Pesticides” (US EPA OPP 2002 and 2006)[10] a first cumulative risk assessment was performed already in 2002. The first document from 2002 comprising about 100 pages was updated in 2006, containing now more than 500 pages. The background was the adaptation of a directive regulating residues in food. In the first study the conclusion was drawn that “Cumulative occupational and ecological risk assessments are not required by FQPA and have not been conducted”. “Occupational and ecological risks were addressed in the individual risk assessments for the Organophosphates”. In the revised study it is concluded that there are almost no methodical changes to the first study. “Exposure”, however, is described in much more detail. Mitigation measures to reduce exposure to these pesticides (Organophosphates) are described and a “technical executive summary“ is included.
- In the second case study, “Triazine Cumulative Risk Assessment” (2006)[11], it is highlighted that exposure is primarily depending on how the chemicals are applied. The exposure path “drinking water” is of significant relevance for this class of substances. Triazines in food are considered negligible.
- In the third case study on “Chloroacetanilide Cumulative Risk Assessment” (2006), risks from food, drinking water, and non-occupational exposure resulting from all registered uses of chloroacetanilide pesticides (e.g. acetochlor, alachlor) were below the Agency's level of concern.[12]

8 http://www.epa.gov/fedrgstr/EPA-PEST/1999/February/Day-05/6055.pdf

9 http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf

10 http://www.epa.gov/oppsrrd1/cumulative/files/guidefinal_4-new.pdf and http://www.epa.gov/fedrgstr/EPA-PEST/2006/August/Day-02/p12343.htm

11 http://www.epa.gov/fedrgstr/EPA-PEST/2006/June/Day-21/p5456.htm

12 http://www.epa.gov/fedrgstr/EPA-PEST/2006/March/Day-29/p4505.htm

- The fourth case study is „N-methyl Carbamate Revised Cumulative Risk Assessment“ (2007)[13]. Reaching another milestone in human health protection and food safety, US EPA has completed its cumulative human health risk assessment for the N-methyl carbamate class of pesticides, which includes: aldicarb, carbaryl, carbofuran, formetanate hydrochloride, methiocarb, methomyl, oxamyl, pirimicarb, propoxur and thiodicarb. Considering the cumulative risks associated with this class of pesticides together with the risk mitigation steps identified in the individual risk management decisions for these pesticides, US EPA concluded that these cumulative risks are below the regulatory level of concern established by the “Food Quality Protection Act of 1996 (FQPA)“.

All four case studies have in common that primarily the exposure of men against the exposure paths drinking water, residues on food and inhalation are considered. Impacts to the environment are not discussed in detail. No cumulative risk to men has been identified for these chemical groups. It seems that cumulative risk assessment is not included in regulatory decisions but is an additional instrument for authorities to quantify the overall risk from the use of pesticides to human health.

3.1.7 OECD

The OECD is developing several Emission Scenario Documents (ESDs), which include biocides, plant protection products and several industrial sectors. The following ESDs for biocides have been published: Antifouling Products, Wood preservatives (4 parts), and Insecticides for Stables and Manure Storage Systems. The principles are described in a guidance document on Emission Scenario Documents.[14] According to this guidance document, an ESD should cover all aspects of the lifecycle of substances used in the area concerned, including production, formulation, processing, use, service life and recovery / disposal. Nevertheless the BPD covers only the application, service life and waste disposal of biocidal products, and their emissions mainly on a local scale. Emissions during the production and formulation of biocides by industry are still being assessed using scenarios developed for new and existing substances and for industrial categories, and therefore are not considered yet.

An emission scenario should include a description of the following subjects:

- description of the industry or use area;
- description of the types of substance used and their function in the industry area;
- identification of the potential points of release in this use area, and estimates of the amounts;

[13] http://www.epa.gov/fedrgstr/EPA-PEST/2007/September/Day-26/p18860.htm

[14] http://www.olis.oecd.org/olis/2000doc.nsf/LinkTo/NT000010DA/$FILE/00081657.PDF

- information on the scale or size of operations in the industry area;
- information on emission control methods for the industry;
- instructions on how to use the information in the document, and examples of calculations.

A survey of approaches in OECD member countries on exposure assessments challenged the need of evaluating cumulative and aggregate exposures (OECD 2005): *"A common limitation of exposure assessments in practice is to examine exposures only to single chemicals at single points in time, or from single sources or products, as if they occur in isolation from other exposures that are in fact relevant to understanding the true nature and magnitude of exposure. … Policies need to ensure that an accurate context is provided within which to judge a particular exposure assessment, one that accounts for factors such as:*

- *production, processing and use of the same chemical by multiple entities;*
- *multiple uses of the chemical leading to actual or potential exposures;*
- *multiple routes of exposure (direct, indirect) to a chemical;*
- *continuous or periodic release of or exposure to a chemical;*
- *exposure to multiple chemicals producing the same/similar effects and/or acting by the same/similar mechanism(s)".*

Anyhow, no activity is known at OECD level concerning the development of guidance documents on cumulative exposure. Mixture toxicity is, however, addressed in several OECD documents (OECD 2001).

3.1.8 The WHO / IPCS Framework

In 2007, the World Health Organization (WHO) convened a workshop on the assessment of risks associated with exposures to multiple chemicals under the umbrella of the International Programme on Chemical Safety (IPCS). The outcome of this WHO/IPCS Workshop on Aggregate / Cumulative Risk Assessment is a framework for risk assessment of combined exposures to multiple chemicals whether or not the components act by similar or different modes of action i.e. "single mode of action" and "multiple modes of action" (WHO/IPCS 2009). The framework describes an iterative process involving stepwise consideration of both exposure and hazard in several tiers depending on the data available to support the analysis.

The differentiation of whether or not a similar mode of action has to be assumed is demanded in its lowest tier based on hypotheses for grouping chemicals into a common group according to their chemical structure, similarity of target tissue and/or similarity in the manifestation of toxicity. The WHO/IPCS report recommends dose addition as risk assessment concept if there is no evidence for interaction of the chemicals (synergisms or antago-

nisms). Prior to any consideration of hazard, considerations of potential for exposure determine the next steps. If there is no or only minimal exposure, there is no need for further assessment. If the result of the initial considerations on the combined risk turns out not to be acceptable, the assessment should be further refined by additional considerations of temporal aspects of the common toxic effect, the presence of a common metabolite, analysis of key biological targets and consideration of information about environmentally relevant mixture ratios and exposure levels. In the highest tier, these aspects would be considered in additional detail (e.g. consideration of environmentally relevant exposure mixture ratios and physiologically based pharmacokinetic modelling) insofar as necessary.

The approach drafted in this report is currently revised and further developed aiming to harmonize global approaches to chemical risk assessment (WHO 2009). The exposure assessment focuses on human exposure i.e. consumer exposure, occupational exposure and man exposed via the environment.

3.2 Projects and literature search

Within the project, a survey of relevant research projects and publications on cumulative exposure has been undertaken. The aim was to analyze whether and where cumulative exposure to the environment is intended to be included in regulatory affairs.

3.2.1 Research Projects

Within CEFIC's "Long-Range Research Initiative" for assessing the potential impact of human activity and man-made substances on the environment and human health[15], a project for identification and evaluation of emission databases in Europe has been carried out by AstraZeneca (Crookes et al. 2004). The aim was to improve the accuracy of estimates of chemical releases by evaluating existing EU and national databases. For this purpose, a detailed review of 15 data sources that have potential for use in the development of emission estimation has been carried out among the reports on industrial areas, compilations of emission factors, pollution inventories and other databases such as the BREF, OECD and CONCAWE documents, the CORINAIR Guidance and Emission Inventory, data from environmental agencies etc. Within the project, some useful flow charts have been developed which partly also cover biocides (e.g. for pulp, paper and board industry, cooling water, personal and domestic uses). Cumulative exposure from different sources is not addressed in this report.

The scientific forum for chemical companies for assessing ecotoxicology and toxicology of chemicals ECETOC publishes a range of reports on test methods, testing strategy and risk assessment. However, according to a screening of the reports published so far, cumulative exposure is not considered in detail.

[15] http://www.cefic-lri.org/

In Germany, the following projects are currently being carried out:

- "Ökotoxische Kombinationswirkungen von Stoffgemischen – Relevanz und angemessene Berücksichtigung in der Umweltrisikobewertung von Pflanzenschutzmitteln und Bioziden" (FKZ 3709 65 404)
- "Entwicklung von ökotoxikologischen Tests mit Biozid-Produkten und Eluaten: Prüfung der Anwendbarkeit des Embryotests mit dem Zebrabärbling (Danio rerio, DarT)" (FKZ 363 04 029)

Both projects focus on mixture toxicity.

3.2.2 Literature

A rough screening of the SETAC Journals "Environmental Toxicology and Chemistry" and "Integrated Environmental Assessment and Management" revealed that cumulative exposure is often addressed (in total 888 hints). However, most articles refer to cumulative effects as identified e.g. by biomarkers or bioaccumulation, case studies with different chemicals, mixture toxicity or general risk assessment.

Cumulative exposure often is analyzed by applying effect based tests to complex mixtures such as the Whole Effluent Assessment (WEA). Here, bio-assays are used for detecting all synergistic or antagonistic interactions between different compounds by the responses of the exposed organisms (Chapman 2000, OSPAR 2007). Kortenkamp et al. (2009) gave an overview on synergistic effects of mixtures of different biocides used as antifouling agents which came to the conclusion that the mixture itself should be tested.

Similarly, in several projects funded by the US EPA, cumulative exposure is assessed using biological markers or living organisms that specifically respond to hormone-signaling pathways (e.g. sex determination among offspring of Daphnia). The results have been presented in several publications (see overview at US EPA 2010).

For assessing cumulative exposure of humans to chemicals, also computer simulation software is applied. The aim is to characterize uncertainty and variability of route-specific doses to a person from one or more sources over time (Price & Chaisson 2005). Environmental media are only considered as further exposure routes to humans. A cumulative risk assessment in human health is conducted to derive acceptable levels of exposure to chemicals that may exist as contaminants in food, drinking water, air or the environment (Mileson et al. 1999). Often, exposure of pesticides to humans via environmental media is referred to as "environmental exposure" (Hoppin et al. 2006).

For environmental risk assessment, several models have been used to predict effects on aquatic organisms resulting from time-varying exposure to one pesticide or a mixture of pesticides (Ashauer et al. 2006, Altenburger & Greco 2009). At ecosystem level, these models have also been used to predict cumulative exposure concentration and to extrapolate the percent species at risk to the episodic exposure (Mortan et al. 2000).

Some publications give interesting information on biocide use with focus on human health and furthermore indirectly provide useful information about the frequency of the application of household pesticides (Nieuwenhuijsen 2005), for instance. Other estimates suggest that in 2010 up to 15% of the total silver released into water in the EU is from biocidal use in plastics and textiles (Blaser et al. 2008). In a market research on biocidal active substances, the following main application areas in washing and cleaning products have been identified in consumer products where the actives are also used for non-biocidal purposes such as bleaching or cleaning (Hahn et al. 2010):

a) surface disinfection (inclusive removal of moulds and films) using sodium hypochlorite (NaOCl), alcohols, quaternary ammonium compounds (QAC) and hydrogen peroxide;
b) laundry disinfection / cleaning clothes using hydrogen peroxide, NaOCl and QAC;
c) machine dishwashing products using dichloroisocyanurates and trichloroisocyanuric acid.

Also, dual use as disinfectant and preservative (e.g. in cosmetic preservatives) has been identified in this study for substances such as triclosan, formaldehyde, glutardialdehyde, benzoic acid, isothiazolin-3-ones, bronopol, 2-phenoxyethanol, and chloroacetamide. This should be considered in exposure assessments.

All these data might be used for refinements of environmental exposure estimates but do not give guidance on how to perform cumulative exposure assessments for the environment.

In summarizing, it can be stated that most of the projects and publications analyzed focus on cumulative exposure to multiple chemicals from multiple sources on living organisms. The starting point of these approaches is clearly effect-based. No further information for quantitative assessing exposure of biocides from different PTs to the environment has been found in the reviewed literature.

3.3 Terms and definitions

3.3.1 Terms and definitions used in the context of cumulative risk assessment

Table 2 compiles the terms and definitions used in the context of cumulative risk assessment. Definitions from the International Society of Exposure Science (ISEA glossary 2005), IUPAC Recommendations (IUPAC 2006) as well as documents from the regulatory authorities US EPA, from the European Food Safety Authority and documents from European (Kortenkamp & Hass 2009) and international panels (WHO/IPCS 2009) have been evaluated. Besides, terms of REACH regulation and the relevant Technical Guidance Documents are listed.

Table 2 Terms and definition in the context of cumulative exposure assessment respectively cumulative risk assessment

Term	Definition (reference)	Comment
Additive Effect	Consequence that follows exposure to two or more physicochemical agents which act jointly but do not interact. The total effect is the simple sum of the effects of separate exposure to the agents under the same conditions (IUPAC 2006; cited from BfR 2009)	EFSA 2008 refers to the IUPAC definition
Aggregated consumer exposure	Exposure to a substance from multiple sources, because products contain many substances and a substance may be present in multiple products in many different forms (EU TGD 2003, Part I)	The term aggregated exposure is used in the EU TGD solely within the scope of consumer exposure assessment.
Aggregate Exposure	Sum total of all exposure to pesticides through inhalation, dermal, oral, or optic contact (IUPAC 2006; cited from BfR 2009)	
	Exposure to one chemical from all sources, for example; total exposure for someone living near to an industrial site from food, air, water and soil (UK Food Standards Agency 2002)	
	The demographic, spatial and temporal characteristics of exposure to a single chemical through all relevant pathways (e.g. food, water, residential uses, occupational) and routes (e.g. oral, dermal, inhalation) (WHO/IPCS 2009)	
	"[…] "aggregate" and "cumulative" are used as adjectives to modify "exposure" or "dose" without further elaboration. Often, "aggregate" and "cumulative" seem to be used interchangeably, suggesting (1) exposures that are from multiple sources, received via multiple exposure pathways, or doses received through multiple routes; (2) exposures or doses that accumulate over time, often over a lifetime; or (3) exposures or doses from more than one chemical or stressor simultaneously or sequentially" (IPCS 2004)	The Exposure Assessment Terminology Working Group [of the IPCS] identified four terms that were particularly difficult to define due to their relatively recent emergence as exposure terms. These are aggregate exposure, aggregate dose, cumulative exposure, and cumulative dose. In studying the literature, the Exposure Assessment Terminology Working Group found very few formal definitions of these terms (IPCS 2004)
Aggregate Exposure Assessment	Aggregate exposure assessment combines exposure from different pathways such as food, air and water and is important in considering the total personal exposure to a given chemical (UK Food Standards Agency 2002)	Focus on human health risk assessment; definition in connection with pesticides
Aggregate Risk	The risk associated with all pathways and routes of exposure to a single chemical (EFSA 2008 according to definition by US EPA 2002; cited from BfR 2009)	
	Aggregate risk is the risk associated with multiple pathways / routes of exposure to a single chemical (WHO/IPCS 2009)	
Aggregate Risk Assessment	Different routes of exposure to the same active substance, which considers: - the use of the same active substance in different biocidal PTs (e.g. wood preservative and insecticide) - the use of the same active substance under different regulations (e.g. biocides, pesticides, veterinary drugs)	Focus on human health risk assessment

Term	Definition (reference)	Comment
	the exposures from food, drinking water, and residential / nonoccupational uses (US EPA 2002; cited from BfR 2009)	
	Risk assessment taking all sources of intake of a given pesticide into account (UK Food Standards Agency 2002; cited from BfR 2009)	UK Food Standards Agency restricts the definition to a given pesticide that might contain several active compounds.
Combined exposure	Combined exposure of humans via two or more routes (EU TGD 2003, Part I); Exposure to a substance under different circumstances (e.g. exposure at the workplace and exposure from consumer products / indirect exposure via the environment) (EU TGD 2003, Part III)	The term “combined exposure” is used in the EU TGD solely within the scope of consumer exposure assessment.
Combination effect, mixture effect, joint effect	The response of a biological system to several chemicals, either after simultaneous or sequential exposure. The terms are used synonymously (Kortenkamp & Hass 2009)	
Concurrent Exposure	Interpreted as potential human exposure by all relevant pathways, durations, and routes that allow one chemical to add to the exposure of another chemical such that the total risk is an estimate of the sum of the exposures to the individual chemicals. This includes simultaneous exposures as well as any sequential exposures that could contribute to the same joint risk, either by overlapping internal doses or by overlapping toxic effects (US EPA 2002, EFSA 2008; cited from BfR 2009)	
Cumulative Assessment Group (CAG)	A group of chemicals that could plausibly act by a common mode of action, not all of which will necessarily do so. Membership of a CAG can usually be refined (reduced) by application of successively higher tiers of the approach described in this Opinion (EFSA 2008; cited from BfR 2009)	
Cumulative ecological risk assessment	A process that involves consideration of the aggregate ecological risk to the target entity caused by the accumulation of risk from multiple stressors (EPA/630/R-95/002F April 1998 Guidelines for Ecological Risk Assessment)	
Cumulative effect	Overall change which occurs after repeated doses of a substance or radiation (IUPAC 2006)	
	Effect resulting from repeated releases of a chemical that gives rise to a “background concentration” in the environment (EU TGD 2003, Part II)	The EU TGD, Part II Environmental Risk Assessment does not mention the term "aggregate" and does not define the terms "combined" and "cumulative". However, unlike the term "cumulative", "combined" rather refers to “multiple chemicals".
Cumulative Exposure	Exposure to multiple chemicals on the basis of whether they have a common mechanism of action (UK Food Standards 2002)	
	Cumulative exposure defines the aggregate exposure to multiple chemicals (WHO/IPCS 2009)	
Cumulative Exposure Assessment	Cumulative [exposure] assessment estimates exposure to multiple chemicals on the basis of whether they have a common mechanism of action (WHO/IPCS 2009)	

Term	Definition (reference)	Comment
	An assessment that describes concurrent spatial and temporal characteristics of exposure performed for a set of chemicals (ILSI 1999; cited from BfR 2009)	
Cumulative Risk	Probability of any defined harmful effect occurring through a common toxic effect associated with concurrent exposure by all relevant pathways and routes of exposure to a group of chemicals that share a common mechanism of toxicity (IUPAC 2006; cited from BfR 2009)	EFSA 2008 also refers to the IUPAC definition, with an additional note: "in the context of this opinion, it is intended more specifically to be the risk deriving from the exposure to compounds that share the same mode of action (dose addition) or that have similar effects but do not act at the same molecular target (response addition) and is contrasted to synergistic risk. Although the term "cumulative risk" has sometimes been used when referring generally to the risk from exposure to more than one pesticide (see EFSA colloquium), in the context of this opinion, it refers more specifically to the risk deriving from combined exposure to compounds that share the same mode of action or that have similar effects but by different modes of action (EFSA 2008; cited from BfR 2009)
	The risk of a common toxic effect associated with concurrent exposure by all relevant pathways and routes of exposure to a group of chemicals that share a common mechanism of toxicity (US EPA 2002; cited from BfR 2009)	
	Cumulative risk is the combined risk from aggregate exposure to multiple chemicals (and may be restricted to chemicals that have a common mechanism of toxicity) (WHO/IPCS 2009)	
Cumulative Risk Assessment	Taking intake of more than one pesticide into account (UK Food Standards Agency 2002; cited from BfR 2009)	
	Risk assessment approaches that consider the impact of multiple chemical exposures, from multiple sources, routes and pathways, over multiple time frames (Kortenkamp & Hass 2009)	Cumulative risk assessment (CRA), mixtures risk assessment: The terms are used synonymously by Kortenkamp & Hass (2009) "It is worth noting that the European use of the term "cumulative risk assessment" encompasses multiple sources, routes and pathways, but restricts considerations to one chemical, not multiple chemicals. For the purposes of this report, the European use of the term is ignored." (Kortenkamp & Hass 2009)
	Exposure to multiple substances by multiple pathways (including food, drinking water, and residential / nonoccupational exposure to air, soil, grass, and indoor surfaces) (US EPA 2002; cited from BfR 2009)	

Term	Definition (reference)	Comment
Effect assessment	Combination of analysis and inference of possible consequences of the exposure to a particular agent (e.g., pesticide) based on knowledge of the dose-effect relationship associated with that agent in a specific target organism, system, or (sub-) population (IUPAC 2006)	
	The effects assessment comprises the following steps of the risk assessment procedure: 1) hazard identification: The aim of the hazard identification is to identify the effects of concern; 2) dose (concentration) – response (effect) assessment: At this step the predicted no effect concentration (PNEC), shall, where possible, be determined. (EU TGD 2003).	
Exposure	Contact between an agent and a target. Contact takes place at an exposure surface over an exposure period (ISEA glossary 2005; cited from BfR 2009)	
	Concentration or amount of a pesticide (or agent) that reaches a target organism, system, or (sub-) population in a specific frequency for a defined duration (IUPAC 2006; cited from BfR 2009)	EFSA 2008 refers to IUPAC 2006
	Relates to the following options: simultaneous and/or sequential exposure, nature of exposure: duration, frequency, timing, magnitude of exposure: exposure concentration and dose (US EPA 2002; cited from BfR 2009)	
	Exposure to the same substance by multiple pathways and routes is likely best described as “Single Chemical, All Routes” (referenced in some jurisdictions as “Aggregate Exposure”). Similarly, it is recommended that exposure to “Multiple Chemicals by a Single Route” be distinguished from “Multiple Chemicals by Multiple Routes”. To this end, the framework being developed addresses “Combined Exposures to Multiple Chemicals” (WHO/IPCS 2009)	
	Exposure *(of the environment) results* from discharges and/or releases of chemicals. (EU TGD 2003)	
Exposure Assessment	The process of estimating or measuring the magnitude, frequency and duration of exposure to an agent, along with the number and characteristics of the population exposed. Ideally, it describes the sources, pathways, routes, and the uncertainties in the assessment (ISEA glossary 2005; cited from BfR 2009)	EFSA 2008 refers to ISEA glossary 2005
	Evaluation of the exposure of an organism, system, or (sub-) population to a pesticide or agent (and its derivatives). Exposure assessment is the third step in the process of risk assessment (IUPAC 2006; cited from BfR 2009)	

Term	Definition (reference)	Comment
	The environment may be exposed to chemical substances during all stages of their life-cycle from production to disposal or recovery. For each environmental compartment (air, soil, water, sediment) potentially exposed, the exposure concentrations should be derived. (EU TGD 2003)	
Exposure Pathway	The course an agent takes from the source to the target (ISEA glossary 2005; cited from BfR 2009)	EFSA 2008 refers to ISEA glossary 2005
	The physical course a substance takes from the source to the organism exposed (e.g., through food or drinking water consumption or residential substance / biocidal uses). (US EPA 2002; cited from BfR 2009)	
Exposure Route	The way an agent enters a target after contact (e.g., by ingestion, inhalation, or dermal absorption) (ISEA glossary 2005; cited from BfR 2009)	EFSA 2008 refers to ISEA glossary 2005; US EPA very similar definition
Exposure Scenario	A combination of facts, assumptions, and inferences that define a discrete situation where potential exposures may occur. These may include the source, the exposed population, the time frame of exposure, microenvironment(s), and activities. Scenarios are often created to aid exposure assessors in estimating exposure (ISEA glossary 2005; cited from BfR 2009)	EFSA 2008 refers to ISEA glossary 2005; US EPA very similar definition
	Generic exposure scenarios assume that substances are emitted into a non-existing model environment with predefined agreed environmental characteristics. These environmental characteristics can be average values or reasonable worst-case values depending on the parameter in question. Generic exposure scenarios have been defined for local emissions from a point source and for emissions into a larger region. When more specific information on the emission of a substance is available, it may well be possible to refine the generic or site-specific assessment. (EU TGD 2003)	
Overall environmental risk	Caused by the substance shall be reviewed by integrating the results for the overall releases, emissions and losses from all sources to all environmental compartments (REACH Annex 1)	
Overall exposure	Overall exposure (combined for all relevant emission/release sources) - Human health (combined for all exposure routes) - Environment (combined for all emission sources) (REACH Annex 1)	
Simultaneity factor	Default number of articles simultaneously treated.	ESD for insecticides, acaricides and products to control other arthropods for household and professional use (OECD 2008)
Source	The origin of an agent for the purposes of an exposure assessment (ISEA glossary 2005)	

3.3.2 Definitions proposed to be used within the Biocidal Products Directive

The overview in

Table 2 shows that terms and definitions used in the context of cumulative risk assessment may have different meanings depending on the regulatory area where they are applied. In many regulatory areas dealing mainly with human health aspects, the risk associated with multiple pathways / routes of exposure to a single chemical is often defined as "aggregate" exposure or risk whereas "cumulative" risk / exposure applies to the impact of multiple chemicals with the same mode of action (e.g. US EPA 2002; EFSA 2008; WHO/IPCS 2009; BfR 2009).

In contrast, Article 10(1) of the BPD mentions "cumulation effects" in connection with the use of biocidal products containing the same active substance. It is noted that the term "cumulation effects" refers to both environmental and human health risk assessment and refers to one active substance contained in different products of the same PT or of different PTs.

Taking into account the different and not harmonised meanings of "cumulative exposure" in the context of chemicals, pesticides and/or medicinal products, it is important to define the term "cumulative exposure" in the context of environmental exposure assessments of biocidal active substances considering the specifications in the BPD.

As working definition in the present study dealing with the cumulative environmental exposure assessment of biocides, the following wording is proposed:

"Cumulative exposure" to biocides is the overall exposure to the same biocidal active substance by emissions during the use, service life or waste phase of different biocidal products belonging to the same PT or different PTs.

For further discussion, however, it has to be kept in mind that this definition is not necessarily in agreement with other regulatory areas, especially those ones dealing with human health aspects.

4 Relevance of cumulative exposure assessments

Article 10(1) of the BPD states that for the inclusion of an active substance in Annex I, Annex IA or IB cumulation effects from the use of biocidal products containing the same active substance shall be taken into account, where relevant.

This implies that cumulative risk assessments should not be carried out routinely in the Review Programme (European Commission 2008b). A cumulative exposure assessment is only considered relevant, if the combination of exposure would result in unacceptable risks for the environment. This means that the evaluation of cumulating effects should only be done if sufficient scientific support is available that cumulative exposure could lead to

additional adverse effects beyond those that already have been estimated in the risk assessment of the single uses (European Commission 2007). The necessity of a cumulative risk assessment has to be identified by the respective Rapporteur Member State (CA) on a case by case basis.

Additionally, in the TNsG on Annex I inclusion it is stated "*that it should be considered what combination of exposures to the active substance from all representative uses is realistically possible… The assessment should reflect normal lifestyles and emission patterns. Realistic worst case possible combinations of exposures should also be considered*".

It is the aim of the following section to describe exemplary uses of biocidal active substances where the performance of a cumulative risk assessment is considered to be relevant.

Some of these examples of cumulative risk assessments have already been realised during the EU review programme or have been discussed at workshops on environmental risk assessments for selected PTs (European Commission 2007b and 2008a).

Subsequently, it is evaluated whether certain parameters like for example PT or use area can be indicators for the necessity of cumulative risk assessments.

4.1 Examples discussing the relevance of cumulative exposure assessments

4.1.1 Cumulative exposure estimation within one Product Type

In-can preservatives (PT6)

The following example was discussed at the workshop on environmental risk assessment for PTs 1 to 6 which was held on 11th of March 2008 in Arona, Italy (European Commission 2008a).

The different uses of in-can preservatives can be subdivided into several sub-product types like for example in-can preservatives in washing & cleaning fluids, in detergents, in paints & coatings and in glues & adhesives. For these uses, mainly diffuse sources of emissions are expected (e.g. diffuse releases from households) and the emissions from each of these uses may end up in the same STP. Therefore, it was considered necessary by the workshop participants to carry out a cumulative exposure assessment for all uses of in-can preservatives that may be discharged to a STP.

In general, the environmental emission from biocides used in washing and cleaning fluids, detergents and human hygienic products is very diffuse as these products are used in the majority of all households. After application, the products are usually rinsed or washed off immediately or at a later stage. As the worst case it is assumed that 100% is discharged to the sewage treatment plant (ESD for PT 6). Due to the wide dispersive uses of these products in households (and larger public buildings) and the resulting diffuse releases, the

emissions may end up in the same STP resulting in a cumulative exposure to the same STP and finally to the environment.

In the above given example the relevance of a cumulative exposure results from the wide dispersive use of an active substance in biocidal products of the same PT. The emissions of these uses may end up in the same sewage treatment plant. A combination of emissions is thus realistically possible.

Wood preservatives (PT 8)

The following approach of a cumulative exposure assessment for wood preservatives (PT 8) is described within the Emission Scenario Document (ESD) for Wood Preservatives (OECD 2003). Chapter 4 of Part 1 of the ESD describes the emission estimation for industrial preventive processes of wood preservatives: The emissions to the aquatic environment occurring during the treatment process itself (e.g. emissions resulting from the automated spraying process) and the emissions occurring during the subsequent storage of the treated wood may end up in the same environmental compartment. For the cumulative exposure assessment, the potential release to surface water via the facility drain and via the connected STP from the treatment process has to be added to the release to surface water via run-off from storage sites (see Figure 3).

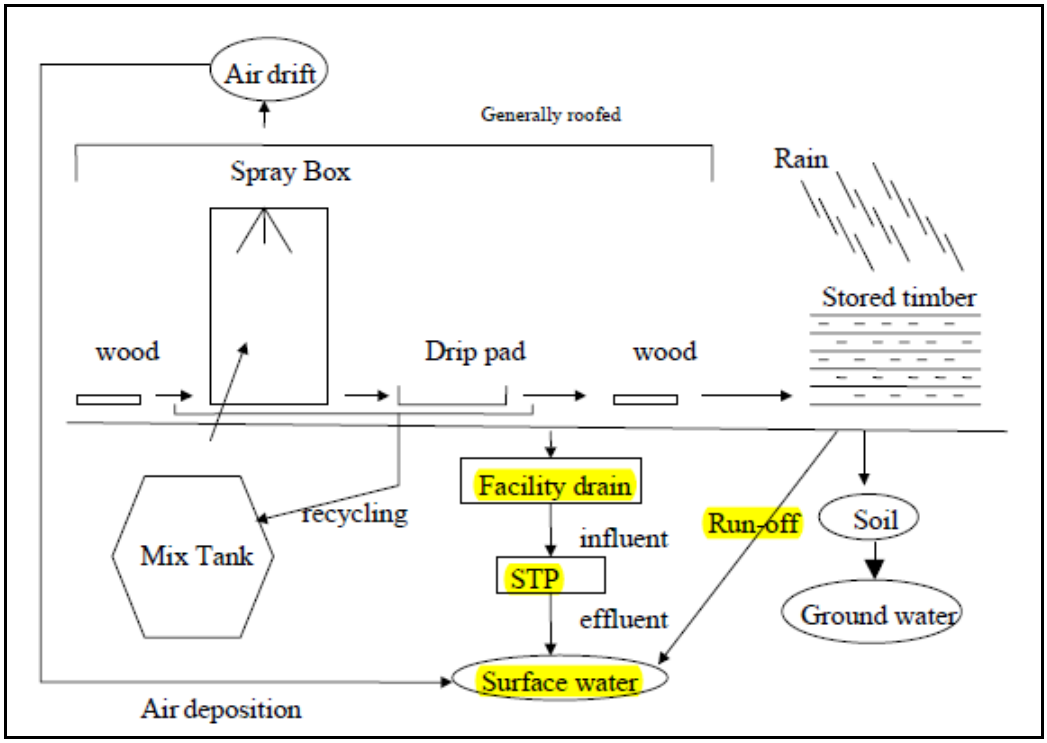

Figure 3 Emission scenario for automated spraying (ESD for Wood Preservatives, Part 1; emission pathways to be cumulated are highlighted yellow)

In the above given example on wood preservatives, the potential cumulative exposure results from the possible spatial and temporal overlapping release of the biocidal product during different lifecycle stages (here: release during the treatment and pre-use phase of treated wood). A combination of emissions is thus realistically possible.

Insecticides, acaricides and products to control other arthropods (PT18)

The following example / approach on a cumulative exposure assessment for PT 18 was discussed at the workshop on environmental risk assessment for insecticides, acaricides and products to control other arthropods (PT 18) which was held on 11th of December 2007 in Brussels, Belgium (European Commission 2007b).

For insecticides that are intended to be used both in households (private use) and larger public buildings like for example hospitals, restaurants, etc. (professional use), a cumulative risk assessment is considered necessary since all releases may end up in the same sewage treatment plant. The requirement for a cumulative exposure assessment depends on the label instruction of the product containing the respective active substance: For example: if the label instruction claims the use of the product both in households and in larger public buildings, a cumulative risk assessment is required for both user categories; if, however, there is no claim for the use of the product in public buildings, first tier exposure assessment will include only emissions from small household buildings. Consequently, in the latter case a cumulative exposure assessment would not be necessary.

At the workshop, the proposal was made to sum up the releases from households and from larger public buildings before they enter the STP (i.e. calculation of a total $Elocal_{water}$ or $Clocal_{influent}$). By summing up all inputs, cumulative $PEClocal_{STP}$ and $PEClocal_{surface\ water}$ can be derived. Such a cumulative exposure assessment for households and professional users should be based on the following exposure scenario as agreed in the Biocides Technical Meeting TM I 2010 on 15–19 February 2010: for outdoor use a number of 2500 households are used as default whereas for indoor use a number of 4000 households serve as default. The treatment area in households is assumed to be 38.5 m². With regard to professional uses, the default number of commercial buildings including hospitals is set to 300. The treatment area in commercial buildings is supposed to be 609 m².

In the above given example, the cumulative exposure results from the simultaneous use of an active substance in biocidal products (of the same or different PT) by different user groups (private and professional users). The emissions of these uses may end up in the same sewage treatment plant. The label claim of the product determines whether and which different user groups need to be considered for the (cumulative) exposure assessment.

The above given example is not only relevant for insecticides (PT 18) but also for other PTs like for example disinfectants or in-can-preservatives[16] (see above).

In the draft CAR for lambda-cyhalothrin, prepared by the Swedish CA (KEMI 2008), the environmental exposure assessment considers combined emissions from small / large buildings and from indoor / outdoor uses for the general use in urban areas. Based on this calculation, risk was identified for the surface water, sediment and soil compartments.

The draft CAR clearly states that Member States should take into account the cumulative exposure of active substance(s) resulting from use in products within the same product group, but also in other PTs when authorising insecticide products. Therefore, when evaluating lambda-cyhalothrin based products, Member States should take into account all biocidal uses of lambda-cyhalothrin both in PT 18 and any other PTs that may be applicable for human and environmental exposure.

In-situ formation of active substances

Another example where cumulative exposure could be assumed is where the active substance is produced in situ from different pre-cursers. This is the case of formaldehyde-releasers such as (Ethylenedioxy)dimethanol, Methenamine 3-chloroallylochloride, 1,3-Bis(hydroxymethyl)-5,5-dimethylimidazolidine-2,4-dione, or Bronopol which all release the same active substance formaldehyde. In total, 12 different compounds are being supported as formaldehyde releasers. The velocity of the release of formaldehyde and the specific efficacy differs among active substances. A Formaldehyde Releasers Evaluation Group (FREG) has been established with the objective to harmonise the data basis and evaluation principles for the different compounds.[17] However, cumulative exposure is not analysed in the different dossiers. Formaldehyde releasers could be considered as a group of active substances with the same or similar mode of action (such as anticoagulant rodenticides). For groups of active substances, the BPD does not envisage cumulative exposure.

4.1.2 Cumulative exposure estimation within different Product Types

Disinfectants (PT 1 and PT 2)

The following example was discussed at the workshop on environmental risk assessment for PTs 1 to 6 (European Commission 2008a). The workshop protocol, however, does not contain a detailed case study, but only a short notice that this example has been discussed during the general discussion.

[16] „DK, FR and NL agreed with this general principle proposed by DE as it also touched other PTs (disinfectants and in can preservatives“ (European Commission 2007b, page10).

[17] CA-Nov07-Doc.8.3: Conclusions of a workshop on formaldehyde releasers, held in Warsaw on 11-12 October 2007.

Emissions of an active substance that is used as PT 1 (human hygiene biocidal product) and PT2 (private area and public health area disinfectant) in the same hospital should be added, as the emissions of the different uses are released in the same sewer ending up in the same STP. It was agreed between the workshop participants that a cumulative risk assessment should be performed.

In the above given example, the relevance of a cumulative exposure results from the spatial (and temporal) overlapping release of an active substance in biocidal products of different PTs. The emissions of these uses may end up in the same STP. A combination of emissions is thus realistically possible.

Disinfectants (PT 1, PT 2 and PT 4)

The environmental part of the draft CAR for a disinfectant, prepared by the German Federal Environment Agency, includes a cumulative environmental exposure assessment. The disinfectant is notified for Annex I inclusion in PT 1 (skin and hand disinfectant in hospitals), PT 2 (disinfection of rooms, furniture and objects in the sanitary sector), and PT 4 (small scale applications / industrial kitchens / meat processing industry). Thus, the intended uses of the disinfectant may take place at the same time. As the main entry pathways into the environment are equal for all applications, a combination of exposures to the disinfectant for all environmental compartments affected is possible and realistic.

The cumulative exposure assessment in the draft CAR is based on the summation of the worst-case local PECs – calculated for each single application - for all PTs.

This approach is slightly different than the approach proposed during the workshop on environmental risk assessment for PT 18 (see above). At the workshop, it was suggested to sum up the releases from different sources (e.g. from households, larger public buildings, etc.) before they enter the STP (i.e. calculation of a total $Elocal_{water}$ or $Clocal_{influent}$). On basis of the combined inputs into the STP cumulative $PEClocal_{STP}$ and $PEClocal_{surface\ water}$ should be calculated (see also Chapter 5.3.3).

Disinfectants and insecticides (PT3 and PT18)

In the following example (that was also discussed at the Arona Workshop for PTs 1 to 6, European Commission 2008a[18]) an active substance is used as a disinfectant in veterinary hygiene (PT3) and as an insecticide (PT 18). The product is applied in stables using the same technique for the same animal category. The application rate for the use as disinfectant is threefold higher than the one for the use as insecticide. The route of environmental exposure is similar for both PTs: application in stables → slurry + manure → soil → groundwater → surface water.

[18] Additional information to this case study has been provided by the German Federal Environment Agency in a personal communication.

The relevance of a cumulative exposure assessment depends on the question whether there is an overlap regarding the time of the application for both uses.

According to the applicant, the time of application differs for the two intended uses: whereas the disinfectant is applied in the winter season, the insecticide is applied in the summer, in addition, degradation in manure is observed; thus, there is no overlap regarding the time of application, also based on the manure application scheme.

Consequently, there is no need to perform a cumulative exposure assessment for the intended uses. In this case, the label claim should clearly prohibit the simultaneous use of the active substance as disinfectant and as insecticide or the additive application of the insecticidal product after disinfection of the stable.

If, however, the use pattern (i.e. the time of application) was identical for both PTs and the products would be used simultaneously, then a cumulative exposure assessment could be relevant. In this case, however, the fact that the application rate for the use as PT 3 is threefold higher than the one for the use as PT 18 most probably renders the cumulative exposure assessment obsolete. The risk assessment for the use as disinfectant most probably also covers the insecticidal use of the product. Thus, it is unlikely that the cumulative exposure would lead to additional adverse effects beyond those that already have been estimated in the risk assessment of the single use as disinfectant.

4.1.3 Cumulative exposure estimation in the case of parent and metabolite

When the metabolite of an active substance itself is used as an active substance, this is a very specific issue. An example is the insecticide Thiamethoxam which is used in PT 8 and 18. According to the draft CAR, one of the relevant metabolites from Thiamethoxam formed in soil is equivalent to the active ingredient Clothianidin, which also is used in PT 8 and 18.

For some major metabolites of an active substance, separate risks assessments have been performed. One example are the metabolites of Tolylfluanid (DMST and N,N-dimethylsulfamide), because these are precursors of the drinking water carcinogen N-nitrosodimethylamine (NDMA) formed during ozonation in treatment of water.

Consequently, it could be discussed whether Thiamethoxam should be considered within a cumulative exposure of Clothianidin.

4.2 Parameters indicating the need / relevance of cumulative risk assessments

The examples in the previous section show that cumulative exposure assessments become relevant when there is a spatial and temporal overlap of emissions from different uses.

In the following, it is evaluated whether certain parameters like PT, user category or entry pathway can be adequate indicators for the necessity of cumulative risk assessments.

In addition, it is analysed whether parameters like tonnage or PNEC can serve as trigger values for a cumulative assessment.

4.2.1 Product type

Product types with predominantly wide dispersive uses

According to the Technical Guidance Document on Risk Assessment (EU TGD 2003), the term “wide dispersive use” should be used for a wide range of activities particularly when end users come into contact with the products, that is to say a large number of small point sources like households or other diffuse releases. Emission reduction measures are usually not common practice for wide dispersive uses.

In contrast, the term “non-dispersive use” refers to chemicals which are used in such a way that only certain groups of workers, with knowledge of the process, come into contact with these chemicals. This means that the use of these chemicals is related to the number (and size) of the emission sources. This main category indicates industrial use at a limited number of sites (i.e. few industrial point sources) where emission reduction measures are often common practice.

Cumulative risk assessments are mainly relevant for wide dispersive uses because it is very likely that the emissions from these diffuse sources may end up in the same STP. For this reason, the participants of the Arona Workshop decided to perform cumulative risk assessments for all PTs with wide dispersive uses in the current and future Review Program (European Commission 2008a).[19]

For non-dispersive uses (like for example applications that are limited to few industrial sites and/or professional users) it is less likely that these point sources emit to the same local STP or environmental compartment. A combination of exposures to the active substance from the intended industrial and/or professional uses is thus considered less relevant.

Exempted from this conclusion are situations where non-dispersive uses and wide dispersive uses take place simultaneously. Then, emissions from non-dispersive uses are to be considered relevant, too.

The use pattern – here: wide dispersive use - is considered as an indicator for the relevance of cumulative exposure to the environment. Thus, the parameter has been included in a decision tree to assess the need for cumulative exposure estimations (see Chapter 4.3).

[19] It was concluded that for PTs that have already been evaluated (i.e. PT8 and PT 14), there is no need to perform retroactively cumulative risk assessment. However, within the next evaluation of these PTs, cumulative risk assessment should be performed, if relevant.

Number of different product types in which the active substance is contained

A rough estimate of the biocidal active substance to be assessed in the Review programme shows that from about 270 different active substances about 716 "active substances / product type" combinations are currently under evaluation. This means that one active substance on average is included in three PTs (data basis provided by the European Commission in May 2010). Some substances such as glutaraldehyde, Biphenyl-2-ol or didecyldimethylammonium chloride are included in 9 different PTs, silver chloride even in 11 PTs.

Figure 4 gives an overview on the active substances that are assessed in the current Review programme and their use in different PTs.

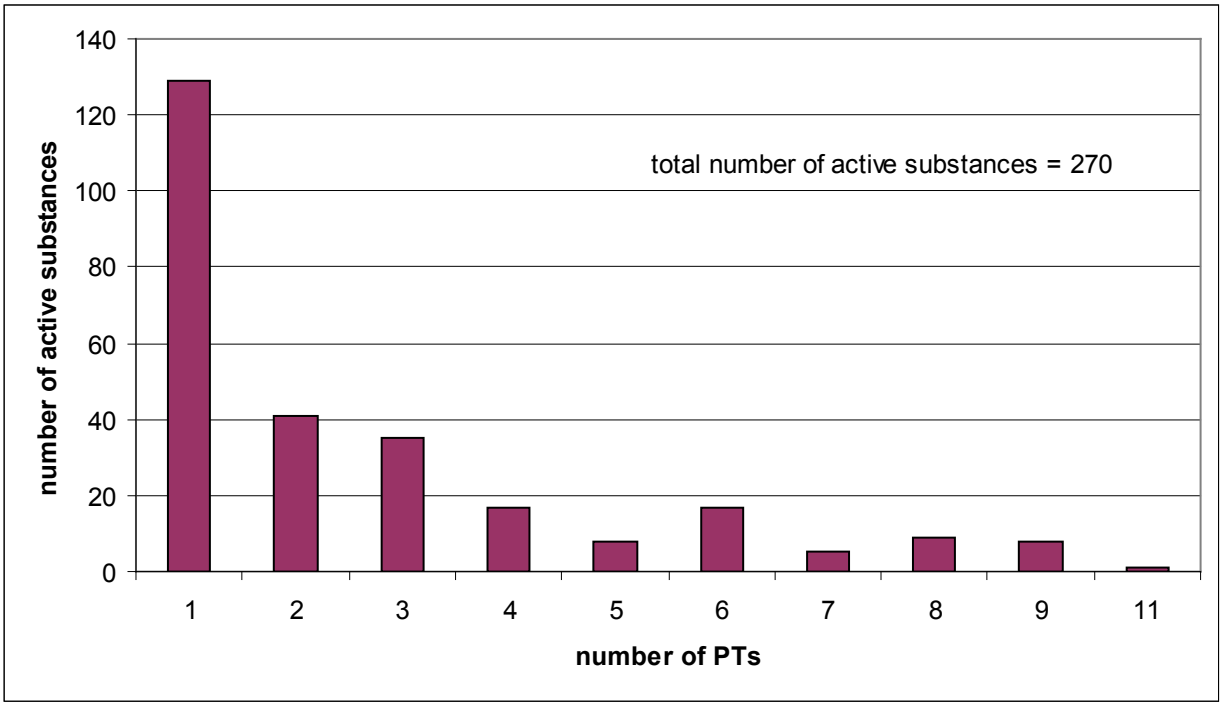

Figure 4 Number of PT per active substance (status May 2010)

Additionally, a systematic analysis of biocides which are considered as high production volume chemicals (HPVC) has been performed. HPVC are those chemicals which are placed on the EU market in volumes exceeding 1000 tonnes per year. The current HPVCs list contains 2,782 substances[20]. The TGD states that in particular HPVCs often have more than one application, sometimes in different industrial categories (European Commission 2003). In total, 74 biocidal active substances are HPVC (see Figure 5).

[20] http://ecb.jrc.ec.europa.eu/esis/

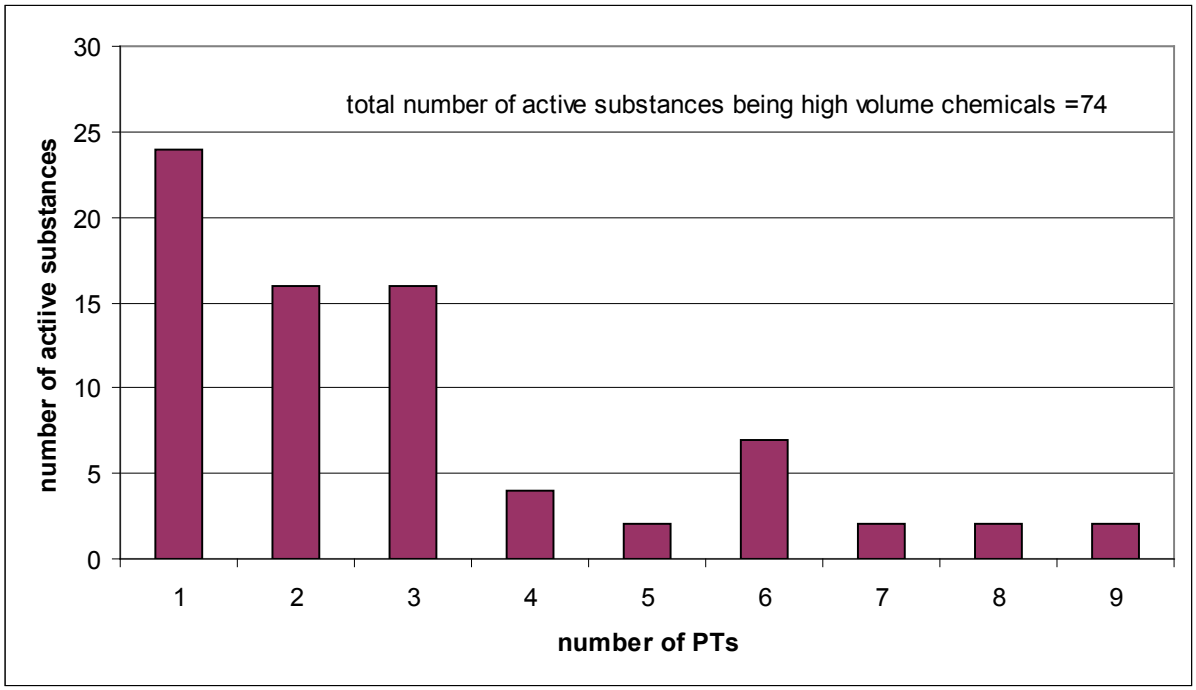

Figure 5 Number of PTs per high volume chemical active substance (status May 2010)

The examples given in Section 4.1 show, however, that the number of different PTs in which the active substance is contained is not a strong indicator for the necessity to perform a cumulative risk assessment. Active substances may only be contained in one PT (e.g. PT 6: In-can preservatives), nevertheless the different uses of this single PT may cause simultaneous emissions of the active substance to the same STP. On the other hand an active substance may be contained in various PTs without having spatial and temporal overlaps of the different uses.

However, the higher the number of different products / PTs in which the active substance is contained, the higher is the probability that spatial and temporal overlapping emissions of the active substance occur and that cumulative exposure assessments become relevant.

The multiple use of biocidal active substances in several main groups (disinfection, preservation, pest control, others) could be a first indicator for the need of a cumulative exposure. In total, 10 active substances are used in three main groups. Among them are Bronopol, Nonanoic acid, Poly(hexamethylendiamine guanidinium chloride, Pyrithione zinc and several QAV. Further 68 active substances are used in two main groups. However, it should be analysed case by case whether the same environmental compartments are affected. For example, there is usually no spatial overlapping of marine antifouling agents with preservatives.

The number of PTs for which an active substance is defended has been included as another indicator in the decision tree for the relevance of cumulative exposure assessment. A

number of >4 PTs is proposed as trigger value for the need of a cumulative risk assessment. It needs to be stressed that this trigger value has no scientific basis but is a first proposal. For those active substances included in 2–4 PTs, it is suggested that a rough estimate of the risk quotient (PECsingle uses /PNEC) is carried out. If the risk quotient for one PT exceeds a PEC / PNEC ratio of 0.1, a refinement of the cumulative exposure assessment should be carried out (see Chapter 4.3).

4.2.2 User category / use sector

With regard to the product application phase it is distinguished between industrial, (trained) professional and private / amateur uses.[21]

Industrial use of biocidal products is usually restricted to (few) industrial point sources and is considered to be non-dispersive (see paragraph “Product types with predominantly wide dispersive uses”). For the industrial use of biocides, cumulative exposure assessments are usually not considered relevant.[22] Exemptions may be preservatives for liquid-cooling and processing systems where different emission routes may be relevant (indirectly from open recirculating cooling systems through STP and directly from once-through cooling systems to surface water).

Professional uses of biocides comprise for example the use of disinfectants in large public buildings like hospitals or restaurants; the use of wood preservatives by pest control technicians or applicators; the use of insecticides by house caretakers, building cleaning professionnals or farmers; the use of antifouling products in dockyards. Depending on the PT, emissions resulting from professional uses may be restricted to few point sources or may be released from several diffuse sources within the same region. Furthermore, biocidal products may be used both by professionals and private users simultaneously (see paragraph „Insecticides, acaricides and products to control other arthropods (PT18)”. Thus, if the label claim of biocidal products includes professional (and private) uses, cumulative risk assessments are often relevant because it cannot be excluded that emissions from various sources may end up in the same STP.

Private uses of biocidal products take place on the scale of households by private consumers. This implies that a large number of small point sources may emit the active substance either into the sewage system or directly into environmental compartments. This type of use is also called “wide dispersive use” (see paragraph “Product types with predominantly wide dispersive uses”). For these wide dispersive uses in households, cumulative risk assessments are often relevant because it is very likely that the emissions from these diffuse

[21] The service life of treated products has not been considered here.

[22] If industrial uses and private uses from households take place simultaneously, emissions from industrial uses have to be considered relevant, too.

sources may end up in the same STP. STPs themselves can be regarded as point sources discharging into one environmental compartment (surface water).

Table 3 gives on overview on the different user categories / use sectors of the different PTs.

Table 3 Overview on user categories / user groups of different PTs (2010)

Product type	User category (according to ESD)			Remark
	Industrial	Professional / commercial	Private / non professional / households	
PT 1 Human hygiene biocidal products	X	X	X	Hospital is sometimes mentioned as professional use, sometimes as industrial use
PT 2 Private area and public health area disinfectants and other biocidal products	X	X	X	
PT 3 Veterinary hygiene biocidal products		X		
PT 4 Food and feed area disinfectants	X			
PT 05 Drinking water disinfectants	X			
PT 06 In-can preservatives	X	X	X	ESD refers to ESDs of other PTs
PT 07 Film preservatives	X	X	X	
PT 08 Wood preservatives	X	X	X	
PT 09 Fibre, leather, rubber and polymerised materials preservatives	X	X		
PT 10 Masonry preservatives		X	X	
PT 11 Preservatives for liquid-cooling and processing systems	X			
PT 12 Slimicides	X			
PT 13 Metalworking-fluid preservatives	X			
PT 14 Rodenticides		X	X	

Product type	User category (according to ESD)			Remark
	Industrial	Professional / commercial	Private / non professional / households	
PT 15 Avicides		X		Products of this PT may not be authorized in Germany (according to BPD 98/8/EC Article 4(6))
PT 16 Molluscidides		X	X	No ESD available
PT 17 Piscicides				No ESD available; Products of this PT may not be authorized in Germany (according to BPD 98/8/EC Article 4(6))
PT 18 Insecticides, acaricides and products to control other arthropods	X	X	X	There are two important application areas: households and stables; The crosses are made for households; In stables there is only professional use.
PT 19 Repellents and attractants		X	X	No ESD available; using of scenarios of ESD other PTs and if necessary modification of these scenarios or of the EU TGD A-/B-Tables
PT 20 Preservatives for food and feedstocks		X		No ESD available; using of scenarios of ESD other PTs and if necessary modification of these scenarios or of the EU TGD A-/B-Tables
PT 21 Antifouling products		X	X	
PT 22 Embalming and taxidermist fluids		X		
PT 23 Control of other vertebrates				No ESD available; Products of this PT may not be authorized in Germany (according to BPD 98/8/EC Article 4(6))

It can be concluded that the user category or the application area does give an indication on the necessity of a cumulative exposure assessment: private and professional uses of biocidal products which comprise applications in a wide dispersive manner are often relevant for cumulative exposure assessment.

However, regardless of the predominant user category, each application needs to be checked for possible spatial or temporal overlaps. In case of identified overlaps these need to be added up for a cumulative exposure assessment., Although the need for cumulative exposure assessments may be less relevant for the industrial use of biocides, it could be the case, for example, that industrial uses and private uses from households take place simultaneously. In this case, emissions from industrial uses have to be considered as relevant, too.

Consequently, the parameter “user categories” has been included in the decision tree to assess the need for cumulative exposure estimations (see Chapter 4.3).

4.2.3 Entry pathways into the environment

Two main entry pathways into the environment can be distinguished for biocidal products:

1. Direct emission into environmental compartments
2. Release into sewage system / facility drain → STP → environmental compartments[23]

These two entry pathways can be differentiated in terms of whether the emissions are directly released into the environment without passing a STP or whether they pass a STP before entering environmental compartments.

Some PTs are directly and intentionally applied to environmental compartments; other PTs are intentionally used for the preservation of products that are in direct contact with the environment. Both application scenarios result in direct emissions to the environment, for example:

- Insecticides are directly applied to water bodies for mosquito control.
- Timber treated with wood preservatives is used in direct contact with water (e.g. poles of jetty) or in direct contact with soil (e.g. fence poles).
- Preservatives for liquid-cooling systems are directly released to surface water.
- Antifouling products are applied to ship hulls and are thus directly emitted to salt water and freshwater.

Unintentional direct release into environmental compartments may take place if treated or contaminated water does not pass a STP but is directly emitted into surface water.

Indirect emissions of biocidal active substances into the environment can often be attributed to the fact that many biocidal products are released into the sewage system after use. In the STP, the active substances may be partly or completely degraded or otherwise eliminated from the waste water before the effluent water is discharged into the receiving water body.

[23] For veterinary biocidal products used in stables, the entry pathway into to environment is: application in stables → slurry + manure → soil → groundwater → surface water

Sewage sludge containing biocidal residues may be applied to agricultural soil leading to an indirect emission of biocidal active substances into the soil compartment.

Some PTs like veterinary hygiene biocidal products or insecticides are used in stables or other areas in which animals are housed, kept or transported. These biocidal products are for example used for the disinfection of stables and manure storage systems. After use the biocidal residues end up in the dung or liquid manure that are applied to agricultural soils leading to an indirect emission into the soil compartment.

Table 4 summarises the main pathways of environmental exposures to biocides.

Table 4 Main pathways of environmental exposure to biocides (COWI 2009, modified 2010)

Product type	ESD scenarios	Main environmental exposure [a]		
		Environment directly[b]	Via STP	Via waste disposal
Main Group 1: Disinfectants and general biocidal products				
1: Human hygiene biocidal products	Private use		X	
	Professional use		X	
2: Private and public health area disinfectants and other biocidal products	Disinfectants used in the sanitary sector		X	
	Medical sector: Disinfection of rooms, furniture and objects	(X)	X	
	Medical sector: Disinfection of instruments		X	
	Medical sector: Laundry disinfectants		X	
	Medical sector: Hospital waste disinfectants			X
	Disinfection of industrial and institutional areas		X	
	Disinfection of air-conditioning systems	(X)	X	
	Disinfection of chemical toilets		X	
3: Veterinary hygiene biocidal products	Disinfection of animal housing	X	X	
	Disinfection of vehicles used for animal transport	X	X	
	Disinfection for veterinary hygiene: non-medicinal teat dips	X	X	
	Disinfection for veterinary hygiene: footwear and animals' feet	X	X	
	Disinfection in hatcheries	X	X	
4: Food and feed area disinfectants	Disinfection in food, drink and milk industries (FDM)		X	
	Disinfection in large scale catering kitchens, canteens slaughter-houses and butcheries		X	

Product type	ESD scenarios	Main environmental exposure [a]		
		Environment directly[b]	Via STP	Via waste disposal
	Disinfection of milking parlour systems		X	
5: Drinking water disinfectants		(X)	X	
Main Group 2: Preservatives				
6: In-can preservatives	Washing and cleaning fluids, human hygienic products Detergents		X	(X)
	Paints and coatings	X	(X)	X
	Fluids used in paper, textile and leather production	(X)	X	X
	Metal working fluids		X	(X)
	Fuels		(X)	
	Glues and adhesives	(X)	(X)	X
	Preservatives for paper coating and finishing	X	X	(X)
7: Film preservatives	Film preservatives for decorative paints	X	(X)	X
	Preservatives for paper coating and finishing	X	X	(X)
8: Wood preservatives	Industrial preventive product application (Spraying, Dipping, Pressure processes, Storage (all methods))	X	X	(X)
	Service life of treated wood (Use class 3: House, Fence, Noise barrier; Use class 4: Transmission pole, Fence post, Jetty in lake, Sheet piling; Use class 5: Wharf)	X	(X)	(X)
	In-situ application (Fumigation, Brushing, Injection, Foundation treatment)	X		(X)
9: Fibre, leather, rubber, and polymerised materials pre-servatives	Preservatives for rubber, plastics (fibre, leather, paper and other polymeric materials)	X	(X)	X
	Preservatives for leather	X	X	
	Preservatives for paper coating and finishing	X	X	(X)
	Preservatives in textile processing industry (= Preservatives for fibre)	(X)	X	
10: Masonry preservatives		X	X	(X)
11: Preservatives for liquid-cooling and processing systems	Once-through system	X	(X)	
	Open recirculating system	X	X	
	Closed recirculating system	(X)	X	

Product type	ESD scenarios	Main environmental exposure [a]		
		Environment directly[b]	Via STP	Via waste disposal
12: Slimicides	Slimicides in paper production processes	(X)	X	
	Slimicides in the oil extraction processes	X		
13: Metalworking-fluid preservatives			X	
Main Group 3: Pest control				
14: Rodenticides	Sewer system	X	X	(X)
	Buildings (indoor and outdoor)	X	X	(X)
	Open areas	X		
	Waste dumps	X		(X)
15: Avicides	Bait preparation		X	(X)
	Open rural areas	X		(X)
	Buildings (indoor and outdoor)		X	(X)
16: Molluscicides		X		
17: Piscicides		X		
18: Insecticides, acaricides and products to control other arthropods	for household and stable application	X	X	
19: Repellents and attractants	No ESD available; using of scenarios of ESD other PTs and if necessary modification of these scenarios or of the EU TGD A-/B-Tables	X	X	
Main Group 4: Other biocidal products				
20: Preservatives for food and feedstocks		X	X	
21: Antifouling products	Antifouling products	X	(X)	(X)
22: Embalming and taxidermist fluids	Embalming (for humans)	X	X	
	Taxidermy (for animals)	(X)	X	
23: Control of other vertebrates		X	X	(X)

a) Significant routes of exposure are marked with "x", minor exposure routes with "(x)".

b) The "Environment directly" exposure comprises releases to air, soil, water and biota. Discharge of biocides with surface runoff from roads etc. in separate systems is conservatively considered as direct release to the environment (water) as most commonly such runoff is not treated prior to discharge.

The importance of different emission pathways to the aquatic environment can be illustrated by the overall wastewater balance in Germany which is shown in Figure 6.

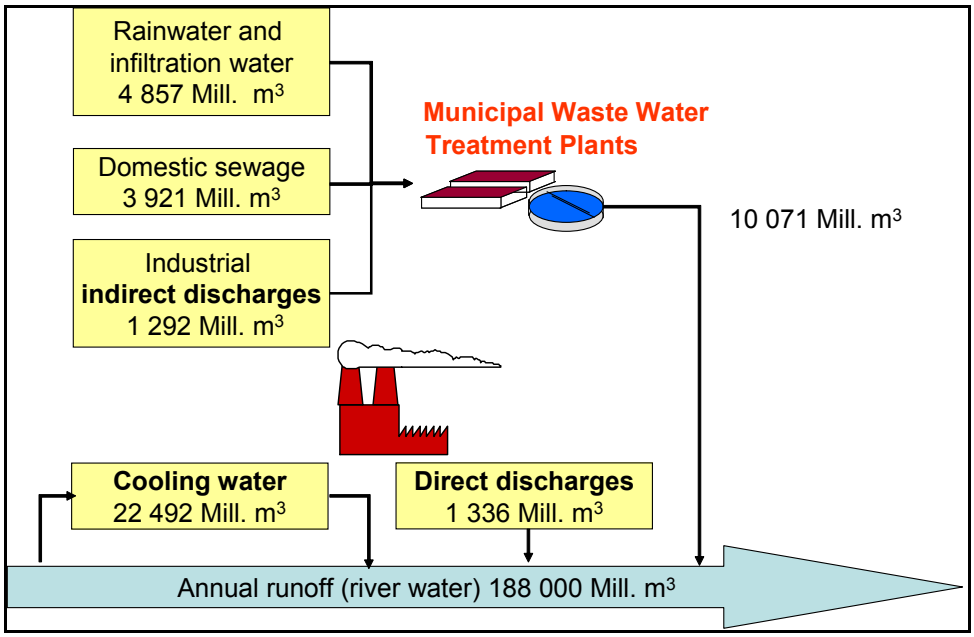

Figure 6 Direct and indirect wastewater discharges in Germany
(wastewater data base from 2007, mean annual runoff from 1969-1990)

In 2007, around 1.3 billion m^3 wastewater per year was directly discharged from industrial sectors to surface water after in-house treatment. In addition, around 22 billion m^3 cooling water per year was discharged directly to surface water mainly originating from once-through cooling systems without chemical treatment (Federal Statistical Office 2009a).

The importance of industrial wastewater discharged into public sewers is often underestimated. The biological treatment of industrial wastewater in municipal treatment plants is very common. In Germany about 1.3 billion m^3 industrial wastewater is discharged indirectly per year after passing a municipal treatment plant, including 0.8 billion m^3 cooling water. Thus, half of the industrial wastewater is discharged directly to surface water and half is discharged indirectly through STPs. This cooling water mainly originates from open circuit cooling systems which usually undergo a chemical treatment. This means that indirectly discharged industrial wastewater is of the same order of magnitude as directly discharged wastewater. When rainwater and infiltration water is ignored, roughly a quarter of the total municipal sewage flow treated in around 10,000 activated sludge plants in Germany is to be attributed to industrial wastewater (Federal Statistical Office 2009b).

According to the water balance of Germany, in total 188 billion m^3 river water per year run off from the borderline of Germany. Thereof, 71 billion m^3 per year originate from upstream riparian and 117 billion m^3 per year from rain runoff.[24] If the contribution of the upstream riparian is disregarded (because it contains also upstream contaminants) the mean dilution

[24] http://www.umweltbundesamt-daten-zur-umwelt.de/umweltdaten/public/find.do „Wasserbilanz“

factor of municipal wastewater in German surface water will be about 1:10 which corresponds to the default average dilution factor recommended in the Technical Guidance Document (Gartiser 1999; European Commission 2003).

Direct emissions often result in higher environmental concentrations in the receiving compartment than indirect emissions via STP, where significant biological degradation and elimination of the biocidal active substances may take place.

If several biocidal products containing the same active substance are directly emitted into the same environmental compartment, it is more likely that the cumulative exposure will lead to higher adverse effects than it would be the case for active substances passing a STP before being discharged into environmental compartments.

However, this does not mean that in the latter case – entry pathway via a STP – cumulation effects are not relevant. As described in chapter 4.2.2, cumulative risk assessments are often relevant for the private use of biocidal products in households because it is very likely that the emissions from these many diffuse sources may end up in the same STP. STPs themselves can be regarded as point sources discharging directly into surface water.

It can be concluded that the entry pathway does not give a clear indication on the necessity of a cumulative exposure assessment. Both for direct emissions into environmental compartments and indirect emissions via STP, cumulation effects from the use of biocidal products containing the same active substance may be relevant.

4.2.4 Tonnage and/or PEC as trigger values

In Phase I of the environmental risk assessments of medicinal products, the PEC for the aquatic compartment (surface water) is calculated on basis of the consumption data. If the $PEC_{surface\ water}$ value is < 0.01 µg/L (regional) and no other environmental concerns are apparent, it is assumed that the medicinal product is unlikely to represent a risk to the environment. Otherwise a refined risk assessment is carried out (Phase II). The basis of this trigger value was derived from a survey of consumption data. The amount required for exceeding this concentration may be recalculated assuming equal distribution of the active substance under consideration in all surface waters generated from the rain runoff in Germany. This amount corresponds to a consumption of 1,170 kg active substance per year.[25]

For biocides, no reliable consumption data are available so far because they are considered confidential. Rough estimates on the biocides market from several sources suggest consumption between 100,000 and 250,000 t of active substances in the EU-15 which corresponds to about 25% of the total pesticides market (Gartiser et al. 2007). An overall

[25] 1170 kg / 117 * 10^9 m^3 = 0.01 mg/m^3 = 0.01 µg/L (see section 4.2.3 for the derivation of the surface water amount generated from the rain run-off in Germany)

evaluation of confidential data submitted with the dossiers by applicants has been carried out within the study “Assessment of different options to address risks from the use phase of biocides” (COWI, 2009). Here, an absolute minimum estimate of 400,000 t active substances production volume in the EU has been calculated. The most detailed study on biocide consumption available in Europe is the Danish inventory of biocides. In total 3,600–5,530 t/a biocidal active substances were consumed in Denmark in 1998 (Lassen et al. 2001). Extrapolating these data from the population of Denmark (5.4 million) to that of the EU-27 (493 million), the total consumption of biocides in the EU-27 can be estimated as being 329,000 to 505,000 t/a which corresponds quite well with the data of the COWI study.

If a total consumption of 400,000 t active substances is reasonable to assume, a mean consumption of around 1,500 t per active substance (n=270) could be expected. However, there are several high production volume actives such as chlorine[26] and others like rodenticides which are used in low quantities of a few tonnes (total consumption of all 14 rodenticidal active substances in the EU 4.1 t according to the COWI estimate).

Adapting the trigger value of medicinal products to biocides, a $PEC_{surface\ water}$ of 0.01 µg/L (regional) or a corresponding consumption rate of about 1 ton per year could be considered as one decision tool for cumulative exposure assessment of biocides. As the regional PEC usually is far lower than the local PEC for biocides, a trigger value of e.g. $PEC_{surface\ water}$ of 0.1 µg/L (local) could be defined. This value corresponds to the groundwater Pollutant Quality Standard for pesticides (plant protection products and biocides) defined in Directive 2006/118/EC on the protection of groundwater against pollution and deterioration. In Germany, the limit value for pesticides in drinking water has also been set at 0.1 µg/L (TrinkwV 2001).[27]

The US Department of Health and Human Services (1998) suggested another model for estimating the concentration of pharmaceuticals in the aquatic environment by considering the main point of entry that is the outflow of municipal treatment plants. The expected introduction concentration (EIC) of an active moiety into the aquatic environment is calculated as follows:

EIC-Aquatic (ppb) = A x B x C x D

where

A = kg/year produced for direct use (as active moiety),
B = 1/liters per day entering STP,
C = year/365 days,
D = 10^9 µg/kg (conversion factor).

[26] Total chlorine production capacity in the EU is about 13 million tonnes disinfectants, of which 13.7% are used as disinfectants, for water treatment, or for paint pigments according to EUROCHLOR http://www.eurochlor.org/upload/documents/document352.pdf

[27] http://www.gesetze-im-internet.de/bundesrecht/trinkwv_2001/gesamt.pdf

Again, the consumption of the active substance is the main input parameter for deriving the PEC surface water. The water entering the STP and the average dilution factor with surface water can be derived from the statistic on water supply and wastewater treatment (Figure 6).

To sum up, data on the tonnage of an active substance used in the biocide sector may give a first indication about the order of magnitude of emissions to the environment which could be used for pre-selecting scenarios for cumulative exposure. However, this approach has a weak scientific basis because neither the distribution behaviour nor the ecotoxicity of the substance is considered. Therefore, the tonnage has not been included as separate indicator in the decision tree to assess the need for cumulative exposure estimations.

4.2.5 PNEC as a trigger value

The PNEC of a substance of interest clearly indicates a hazard which might cause a risk when exposure to the environment occurs. However, the PNEC does not consider the emission pathways or the distribution in environmental compartments. Furthermore, contaminants with a very low PNEC might effectively be removed during waste water treatment in STPs. Thus, the PNEC alone is not considered as suitable trigger value for the performance of cumulative risk assessments (see section 4.2.6).

4.2.6 Risk quotient as a trigger value

The environmental risk characterisation for biocidal active substances in the context of Article 5 and Annex VI of the BPD involves inter alia the comparison of the predicted environmental concentration (PEC) and the predicted no effect values (PNEC) for relevant environmental compartments. While risk quotients (= PEC/PNEC) > 1 clearly indicate a risk, some researchers also assume that a PEC/PNEC of > 0.1 still indicates a residual probability that adverse effects can occur.[28]

Article 17 of the proposal for a Regulation on Biocidal Products describes criteria for low-risk biocidal products. Again, “low-risk” is defined where the risk quotient for any given environmental compartment is lower than 0.1.

The same conclusion can be found in the TNsG on Annex I inclusion (2002) stating that “*an active substance shows effects of concern if PEC/PNEC ratio is lower than 1 but higher than 0.1 (the result of the risk assessment indicates a residual probability that adverse effects can occur)*”.

In the “State of the Art Report on Mixture Toxicity” by Kortenkamp et al. (2009), regulatory experts concluded that there is no vehicle at the moment to deal with exposure to substances that come from areas that are currently covered by separate EU regulations, for

[28] Dr David Aston, Arch Timber Protection, UK; The Regulator’s view about alternative approaches to PEC/PNEC comparisons in environmental risk assessment; http://www.bfafh.de/inst4/43/ppt/3regulat.pdf

example, cumulative exposure to pesticides (both plant protection products and biocides), pharmaceuticals, household chemicals, food additives etc. Each sector is making its own risk assessment completely neglecting the fact that the other sectors' contributions may affect the own risk assessment. Thus, it has been proposed that, as a general approach, a maximum of the PEC/PNEC ratio of 0.1 for each chemical should be allowed for exposure both to humans and the environment. While this conclusion refers to the exposure to chemicals from different regulatory areas, a PEC/PNEC ratio of 0.1 could also be applied as a rough trigger value for cumulative exposure of biocides from different PTs. This risk quotient should be defined as a PEC(local)/PNEC thus considering both cumulating exposure within one PT and of more than one PT.

Risk based models (and monitoring data) have been used for the pre-selection of priority substances in water policy according to the Water Framework Directive. According to the "Combined monitoring-based and modelling-based priority setting" scheme (COMMPS), the risk based approach clearly is the most scientific decision tool for deciding whether combined exposure of biocides should be evaluated. The knowledge of monitoring data would be an additional decision tool, however only few biocides are included in routine monitoring programmes so far.

Considering the above given facts, a risk quotient PEC/PNEC of > 0.1 for the single use has been suggested as trigger value in the decision tree for cumulative exposure assessments. For those active substances that are included in 2 - 4 PTs it is suggested that a rough estimate of the risk quotient ($PEC_{single\ use}$ / PNEC) is carried out. If the risk quotient PEC/PNEC exceeds 0.1, a cumulative exposure assessment should be carried out (see Chapter 4.3).

4.3 Decision tree to assess the need / relevance of cumulative exposure estimation

A decision tree to assess the need / relevance of cumulative exposure estimations is proposed in Figure 7.

In a first step it is analysed whether the biocidal use is relevant compared to the inputs from non-biocidal uses from other regulatory areas. A first indicator is whether the substance is included in the list of high production volume chemicals (HPVC), that means it is produced in the EU or imported into the EU in amounts exceeding 1,000 t. About 70 biocidal active substances are listed as HPVC. Another indicator is whether the active substance is covered by other regulatory areas such as plant protection products, human or veterinary medicinal products, preservatives for cosmetics, food or feed additives etc. If the overall biocides use is lower than a trigger value of e.g. 10%, it can be assumed that emissions to the environment from non-biocidal uses predominate and that therefore a cumulative exposure assessment

only for biocides does not seem reasonable. The proposed trigger value of 10% has not been derived on a scientific basis but can be regarded as a first proposal.

An overlap of different biocidal uses in space and time can be considered as a strong indicator of cumulative exposure to the environment. However, these findings depend on the use pattern and exposure scenarios analysed. As there is a considerable gap in knowledge of the use pattern of biocides, the number of PTs for which an active substance is defended has been included as another indicator for possible cumulative exposure. Again, it has to be stressed that the trigger value of > 4 PTs as an immediate indicator for cumulative exposure assessments has no scientific basis but is a first proposal. For those active substances included in 2–4 PTs it is suggested that a rough estimate of the risk quotient (PECsingle use / PNEC) is carried out. If the risk quotient for one single use exceeds 0.1, for example, a cumulative exposure assessment should be carried out. The PEC/PNEC value of 0.1 has been suggested by several researchers and guidance documents (see chapter 4.2.6).

In total, 48 active substances are included in > 4 PTs and 93 active substances in 2 - 4 PTs. Thus, a considerable workflow for cumulative exposure assessment can be expected.

In summary, each cumulative exposure assessment must consider the possibility that there might be an overlap in time and space. A level of concern is reached where the risk quotient (∑PECsingle use / PNEC) exceeds 1.

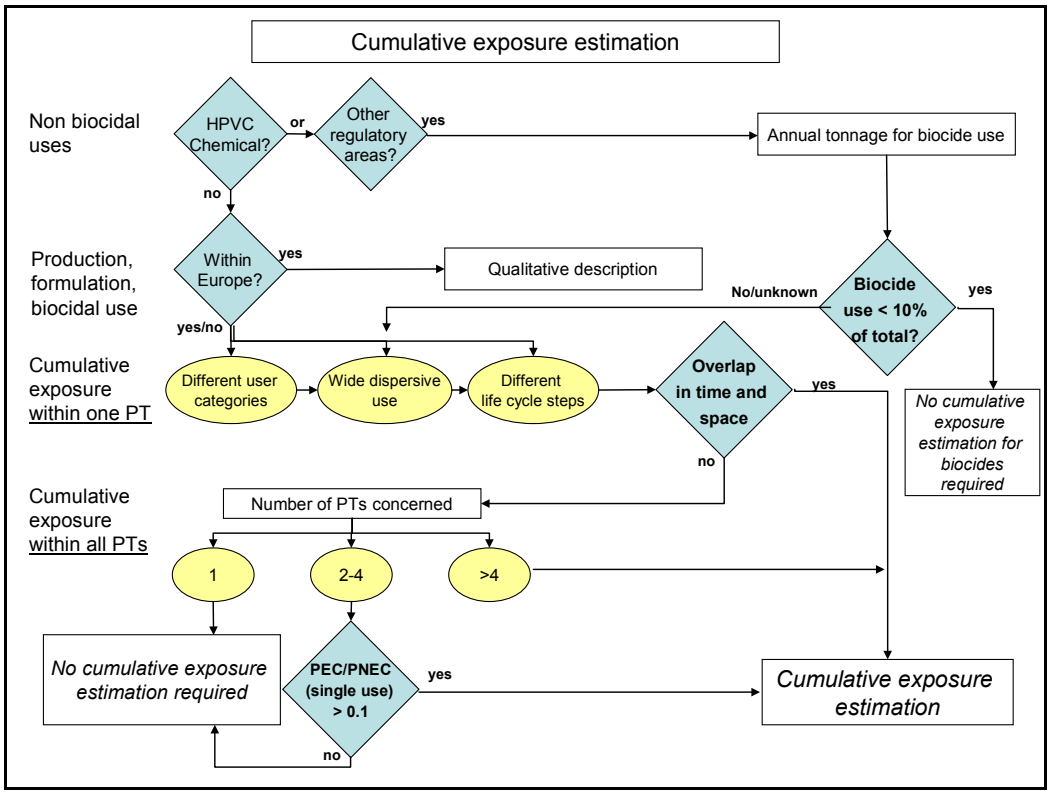

Figure 7 Decision tree to assess the need for cumulative exposure estimations

4.4 Model based pre-selection of surface water contaminants

An alternative approach for ranking chemicals with potential relevance for surface water consists in widening the tonnage approach by a distribution model of contaminants. Götz et al. (2010) proposed a simple exposure based methodology for pre-selecting microcontaminants according to their potential to occur in the water phase of surface waters. The method is based on the annual consumption of the pollutants, physical-chemical properties and information about degradation and input dynamics. The distribution behaviour between different environmental media is estimated via a Mackay-type model (Level III fugacity model, Mackay et al. 1991). The method requires input of publicly available data only based on the chemicals' distribution behaviour between different environmental media, degradation data, and input dynamics. Missing data are estimated with quantitative structure-property relationships. Ranking is based on a chemical's potential to occur in the water phase of surface waters. The three filters used consist in (1) the distribution between media (water soluble, volatile or strongly sorbing chemicals), (2) the chemicals' biodegradation half-life in water, and (3) the input dynamics (continuously or repeated pulse input). The goal of this categorization methodology is to support the selection of compounds for water protection policy guidance and the identification of appropriate monitoring strategies. For biocidal applications with releases to municipal treatment plants, a similar approach could be used to pre-select the need for cumulative assessments: Substances with a higher potential as surface water contaminants would require higher attention with regard of cumulative exposure. However, ecotoxicity data are not considered in this approach.

This approach might be useful for an exposure based ranking of biocides whose cumulative exposure might be relevant for surface water. It only covers the environmental exposure part of the risk characterisation. Total consumption of the active substances is one of the most important input parameters.

5 Proposals for technical guidance on cumulative exposure assessments

Within the framework of the present feasibility study, proposals for a technical guidance should be elaborated on how to perform a cumulative exposure assessment.

With regard to the technical guidance, it is important to specify which data and information are required for the performance of a cumulative exposure assessment. In the following section, it is furthermore checked whether all required data and information are included in the dossiers for active substances which are submitted by the applicants to the respective CA of the Member States. In this context, it must also be considered whether the required data and information are submitted within the review programme of existing substances (i.e.

as part of the dossier for the active substance) or within the applications for product authorisations at a national level in Member States.

Data and information that are required for the application of cumulative exposure assessments but are not yet part of the dossiers for active substances or biocidal products are identified.

5.1 General Guidance on Risk Assessment in the BPD

According to the TNsG on product evaluation, the BPD requires that the risks from biocidal products must be assessed. Guidance on the assessment of active substances contained in biocidal products is found in the TNsG on Annex I inclusion and the EU TGD (2003). For the life cycle stages "production of the active substance" and "formulation of the biocidal product" the BPD refers to REACH (see Figure 8). REACH does not exclude biocidal active substances from its scope. Active substances used in biocidal products are considered substances for the purposes of REACH.[29]

On the 22nd CA meeting (7-8 September 2006), a guidance on "Exposure associated with manufacture" has been confirmed. This guidance states that while the BPD is unclear with regard to how far the production process is covered and CAs do not have a harmonised point of view on this question, the BPD only addresses the placing on the market of biocidal products, whilst, for example, the protection of workers, or, the manufacture and placing on the market of chemical substances, are already addressed by other pieces of legislation. Information on the production process can only be required when manufacturing takes place within the European Economic Area (EEA). Therefore, it has been recommended that Member States should take into account that this is already addressed through other pieces of legislation. Only in the case when the substance is exclusively manufactured for biocidal purposes within the EEA, this information should be required in great detail.[30]

The German Federal Environment Agency recently checked the legal aspects and identified a gap between BPD and REACH when dealing with environmental risks in the life cycle stages "production" and "formulation". Neither BPD nor REACH allow for a complete intervention when risks are identified. In future, a clarification of the legal gap should be intended.

[29] CA-Nov07-Doc.13.2. Inter-linkages between the REACH Regulation and the Biocides Directive (98/8/EC)

[30] http://ecb.jrc.ec.europa.eu/DOCUMENTS/Biocides/TECHNICAL_NOTES_FOR_GUIDANCE/Additional_Guidance_Exposure_Associated_with_Manufacture.pdf

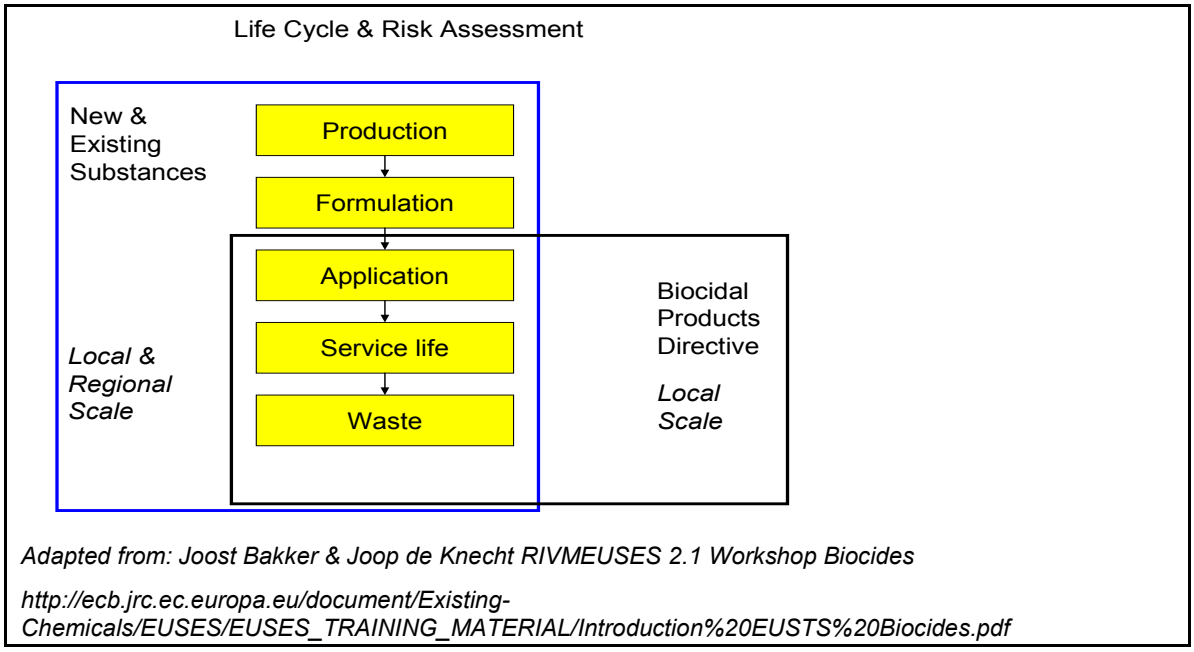

Figure 8 Life cycle stages of biocides covered by the BPD

5.2 Availability of specific data required for the performance of cumulative exposure assessments

5.2.1 Tonnage

If no specific information on use or emission per capita is available for the estimation of PECregional according to the EU TGD, a default factor of 10% of the European production is often assumed as input parameter for the regional system (see Chapter 5.3.1). Thus, for the assessment of PECregional sound data on the total production / consumption are required. However, reliable data on the quantities of biocidal active substances and products produced or sold are often missing.

According to Annex II A, point 5.8 of the BPD, industry should provide data on the likely tonnage to be placed on the market. These data, which are considered confidential, have been evaluated in COWI (2009) and revealed very useful information about the biocide market. However, evaluation is too aggregated for allowing an interpretation of use patterns.

Regulation (EC) No 1185/2009 concerning statistics on pesticides does not consider biocides so far, but indicates that the scope may be expanded at a later stage so as to include biocides. The argument for the postponement was that the *"effects of the Directive 98/8/EC will not become apparent until the first evaluation of active substances for use in biocidal products is finalised"* and that *"neither the Commission nor most Member States currently*

have sufficient knowledge or experience to propose further measures regarding biocides." However, it is *"anticipated that, taking into account the results of the evaluation of Directive 98/8/EC and on the basis of an impact assessment, the scope of this Regulation will be extended to cover biocidal products*."

The previous draft versions of the Regulation on statistic in Article 3 imposed reporting obligations to suppliers on the products placed on the market and to professional users on records to be kept on the use of plant protection products.[31] These obligations have now been shifted from the final version of Regulation (EC) No 1185/2009 to Article 67 of Regulation (EC) No 1107/2009 concerning the placing of plant protection products on the market.

Although, according to the Commission, tonnage data are considered as being confidential and the generation of such data as being costly,[32] any data that improve knowledge about production, use pattern, typical applications and consumption data would be very useful for the risk assessment of biocides. Similar to the crop-specific data collection of plant protection products in the biocide area, PT specific data are required.

These data would also be required for the evaluation of candidates of priority substances in water policy according to the Water Framework Directive 2000/60/EC. The advisory group coordinated by the European Chemicals Bureau elaborated a new concept for an optimised prioritisation strategy for future ranking. For substances for which monitoring data are not available at the required quality level, a modelling-based approach to assess potential exposure needs to be implemented. Information such as overall tonnage used, fractions of this tonnage going to particular uses and emissions from these uses may be used as input to a simple partitioning model (Lepper et al. 2008).

The inclusion of biocides into the scope of the Directive on statistics on plant protection products is therefore recommended by the consultants in order to obtain these data bases urgently needed for the development of suitable indicators.

National approaches for collecting data on use and consumption of biocides would improve the basis for cumulative exposure assessments. Many Member States routinely collect data on biocides. The most detailed study on biocide consumption available in Europe is the Danish inventory of biocides drawn up on the basis of information from the Danish Pesticide Statistics (Lassen et al. 2001). In Finland, retailers, distributors and producers have to provide data on biocidal products to the national authorities on a yearly basis. The data covers information on production, import / export and sales. Romania too collects data on import and export volumes as well as data on sales, general use, professional and non-professional use. According to COWI (2009), Spain, Belgium, Slovenia and Sweden collect

[31] http://www.insee.fr/ue2008/en/documents/COM-(2006)-778.pdf

[32] CA-Nov07-Doc.6.3: Note on the provision of information concerning tonnage of active substances/biocidal products placed on the market

data on sales of some active substances from specific PTs (mainly PT 8, 14, 18) or with specific properties (toxic and very toxic, CMR).

5.2.2 Entry pathways

A detailed description of the intended uses is required in order to derive the entry pathways of the active substance into the environment. Although the description of the intended uses belongs to the common core data set for active substances (Dossier, Annex IIA, V. Effectiveness against target organisms and intended uses), the information provided by the applicant is often insufficient.

In this context, reference is made to the "Application Codes for Encoding PTs".[33] These application codes have been developed with the aim of offering guidance in the preparation of application documents for Annex I inclusion of active substances and for the authorisation of products. They contain the specific terminology for each PT, listing inter alia all possible fields of use as well as the methods of application and the user category. This document is intended to be used by the applicants (and the competent authorities) to exactly specify the intended uses of their active substances and/or biocidal products in a harmonised way. The specification of the intended uses on basis of these application codes helps to provide information on the possible entry pathways of the active substance into the environment.

5.3 Relation between PEClocal and PECregional

Different approaches of cumulative environmental exposure assessments are under discussion. For example, at the Arona Workshop for PTs 1 to 6 (European Commission 2008a), the question was raised whether the PECregional (e.g. taken from the risk assessment reports (RAR) compiled under the Existing Substance Regulation) could be used for the cumulative exposure assessment (at least for wide dispersive uses).[34]

Another possible approach would be the summation of PEClocal of all single uses.

In this respect, it is discussed whether the calculation of a regional background level (deriving either from biocidal applications only or deriving both from biocidal and non-biocidal applications) is sufficient for a cumulative exposure assessment of biocidal active substances or whether a summation of all local concentrations of single uses is more appropriate.

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[33] http://ecb.jrc.ec.europa.eu/biocides/
Application Codes for Encoding Wood Preservatives (PT 08) (2004);
Application Codes for Encoding Rodenticides (PT 14) (2004);
Application Codes for Encoding PT 18, PT 19 and 20 (2008).

[34] http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=ora

5.3.1 Background

The Technical Guidance Document on Risk Assessment for chemical substances (EU TGD, 2003) distinguishes between predicted environmental concentrations on the local scale, e.g. at the site where the use of the biocide takes place (PEClocal) and on the regional scale to assess the distribution in a larger area with several sources (PECregional).

The PEClocal represents the concentration expected in the vicinity of a point source on a day when discharge occurs. The local concentration of a substance is calculated for each identified application and – in the case of chemicals regulated under REACH[35]– for each life-cycle step of the substance separately. If more than one stage of the life-cycle occurs at one location, the PEClocal shall be calculated by summing all the relevant emissions from that location (EU TGD 2003). STPs receiving emissions from wide dispersive uses in households can themselves be regarded as point sources discharging into one environmental compartment, namely surface water and soil via sludge application.

The regional concentration for each environmental compartment is calculated from the sum of releases from all uses in all life cycle stages of the substance in a particular region. The regional system is an area of 200 by 200 km with 20 million inhabitants. Unless specific information on use or emission per capita is available, it is assumed that 10% of the European production and use of a chemical takes place within this area, i.e. 10% of the estimated emission is used as input for the region. PECregional are so-called steady-state concentrations, i.e. the concentration obtained at emissions and fate processes taking place over infinite time.

PECregional provides a background concentration which should be added to the local scale concentration resulting of emissions from a single site or a single use. In other words, the local scale receives the background concentration from the regional scale.

For substances with many relatively small point sources, this background concentration may represent a significant addition to the concentration from a local source.

The relationship between local and regional scale emissions is illustrated in Figure 9.

[35] In contrast, the BPD covers only the life-cycle stages application, service-life and waste (see Figure 9).

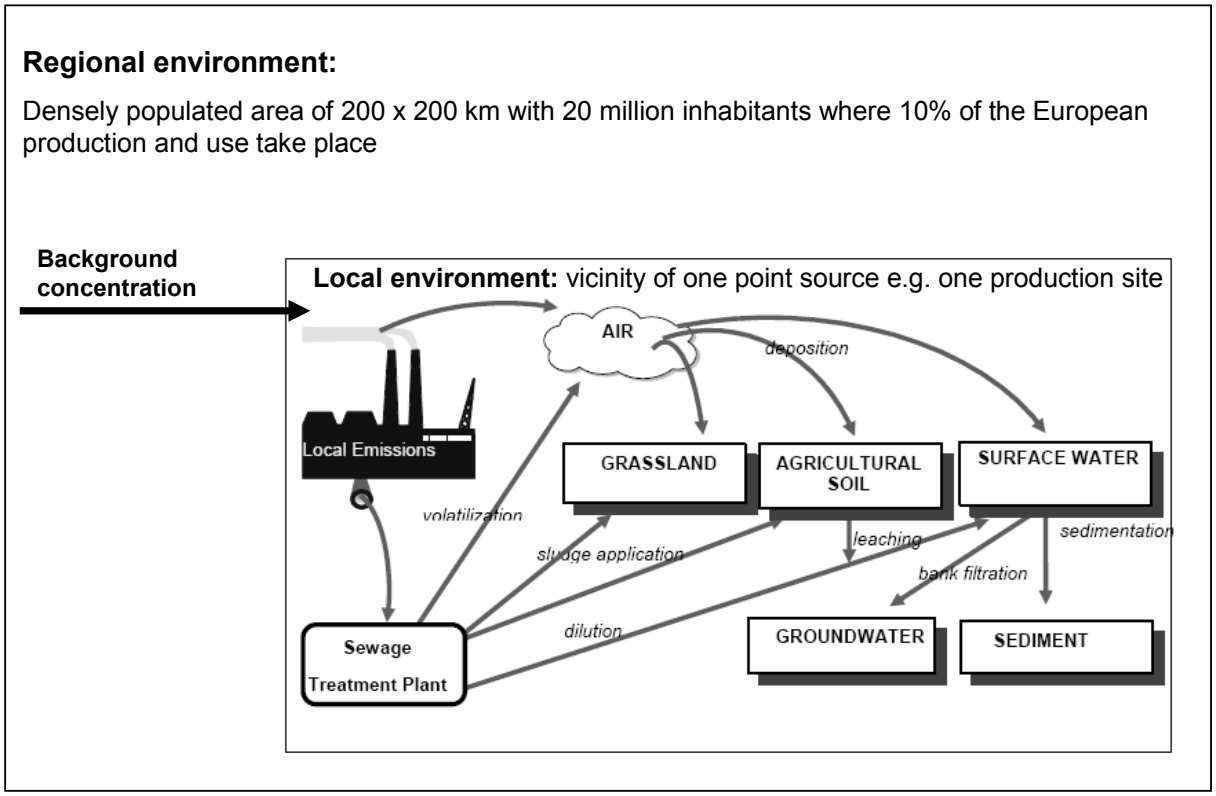


Figure 9 Relationship between regional and local scale (adapted from EU TGD 2003)

In the EU TGD (2003), the PEClocal is calculated by summing up the concentration at the local scale (Clocal) and the regional background concentration (PECregional):

PEClocal = Clocal + PECregional

However, within the scope of the BPD, the regional background concentration (PECregional) is not yet considered in the environmental exposure assessment by default.

Here, PECregional is usually set to “0” resulting in PEClocal = Clocal.

This is mainly due to the fact that data required for the calculation of PECregional (e.g. sound data on total releases of all sources) are often not made available during the registration process. Furthermore, the total tonnage of most active substances brought onto the market does not exceed 10 t per year which is considered as trigger value for the calculation of regional (and continental) concentrations.[36]

[36] In general, regional (and continental) concentrations should be considered if the total tonnage of the active substance brought on the market exceeds 10 t per year (EU TGD 2003; Part II, Chapter 2.1.2).

5.3.2 Guidance on calculation of PEClocal and PECregional in environmental risk assessments

The following guidance for the calculation of PEClocal and PECregional of chemical substances (including biocidal active substances) is given in the Technical Guidance Document on Risk Assessment, Part II (EU TGD 2003) and in the ECHA Guidance on information requirements and chemical safety assessment, Chapter R.16 (ECHA 2008).

PEClocal

- PEClocal is calculated for each identified local point source.
- PEClocal is always calculated on the basis of a daily release rate; it represents the concentration expected at a certain distance from the source on a day when discharge occurs. The discharge is always assumed to be continuous over the 24-hour period. For discharges with varying magnitude over the day, the daily average concentration is typically used in the further assessment.
- The concentrations of substances released from point sources are assessed for a generic local environment. This is not an actual site, but a hypothetical site with predefined, agreed environmental characteristics, the so-called “standard environment”.
- The B-tables in Appendix I of EU TGD (2003) are used for the determination of the releases from point sources for the evaluation of PEClocal. They provide the fraction of the total volume released that can be assumed to be released through a single point source, and the number of days during which the substance is released, thus allowing the daily release rate at a main point source to be calculated.
- For substances that have more than one application / use, the exposure assessment proceeds by breaking down the production volume for every application according to data from industry. For the local situation, in principle, all stages of the lifecycle need to be considered for each application. Where more than one stage of the lifecycle occurs at one location, the PEClocal shall be calculated by summing up all the relevant emissions from that location. For releases to wastewater, only one point source for the local STP is considered (EU TGD 2003, page 35).
- For the life cycle stage professional use of substances (in preparations) and private use of substances or preparations, substances will usually be released into the central public sewage system and be locally released after treatment. Emissions to water could be treated in an on-site sewage treatment plant or in a public STP. STPs are available as an RMM for local industrial emissions. Substances or preparations used directly in the environment will possibly not pass any kind of abatement technique before entering the environmental media. Hence, there is no connection to sewer (ECHA 2008).

- In case of diffuse emissions, the local concentration in fresh water is calculated based on a standard scenario: Diffuse emissions to water are processed in a default sewage treatment (with default number of inhabitants and sewage flow per inhabitant). A fixed dilution factor is applied to the effluent concentration. Dilution factors are dependent on flow rates and the industry-specific discharge flow.
- In a situation where a substance is released through several point sources into the same river, the resulting (local) cumulative concentration may in a first approach be estimated by assuming it to be released from one point source (EU TGD 2003, page 76).
- Local PECs are based on the concentrations from the local distribution model, adding the concentrations from the regional scale as background:
- EU TGD: PEClocal = Clocal + PECregional
- Within the scope of the BPD, however, regional background concentrations (PECregional) are not yet considered in the environmental exposure assessment by default. Here, PECregional is usually set to “0” resulting in PEClocal = Clocal. This is mainly due to the fact that data required for the calculation of PECregional (e.g. sound data on total releases of all sources) are often not made available during the registration process. Furthermore, the total tonnage of most active substances brought onto the market does not exceed 10 t per year which is considered as trigger value for the calculation of regional (and continental) concentrations (see last bullet point of the following paragraph).

PECregional

- The regional concentration mainly serves as estimate for background levels, the estimates of these levels describing the so-called steady-state concentration, i.e. the concentration obtained at emissions and fate processes taking place over infinite time (ECHA 2008, page 48).
- The regional concentration for each environmental compartment is calculated from the sum of releases from all uses in all life cycle stages of the substance in a particular region. The emissions are assumed to be a constant and continuous flux during the year (ECHA 2008, page 19).
- PECregional is calculated using the annual release rate; it represents the steady-state concentration to be expected, regardless of when the discharge occurred (EU TGD 2003, page 35).
- The concentrations of substances released from point and diffuse sources over a wider area are assessed for a generic regional environment. The PECregional takes into account the further distribution and fate of the chemical upon release. It also provides a

background concentration to be incorporated in the calculation of the PEClocal (EU TGD 2003, page 16).

- PECregional are calculated for a standardised regional environment which is a densely populated area of 200x200 km with 20 million inhabitants. Within this area, 10% of the European production and use takes place, i.e. 10% of the estimated emission is used as input for the region. Thus, sound data on total consumption of all sources are required for assessing PECregional.
- Computations of regional environmental concentrations are done by means of the multimedia fate model SimpleBox which is incorporated in the software tool EUSES. The model is a box model consisting of a number of compartments which are considered homogeneous and well mixed. A substance released into the model scenario is distributed between the compartments according to the properties of both the substance and the model environment. Substance input to the model is regarded as continuous and equivalent to continuous diffuse emission. The results from the model are steady-state concentrations, which can be regarded as estimates of long-term average exposure levels.
- For the PECregional calculation, an average connection rate to STPs of 80% is assumed. This leads to a more realistic estimation of the likely background concentration on a regional scale.
- In general, regional (and continental) concentrations should be considered if the total tonnage of the active substance brought on the market exceeds 10t per year (EU TGD 2003; Part II, Chapter 2.1.2)[37].

5.3.3 PEClocal versus PECregional in cumulative exposure assessments

At the Arona Workshop, as described above, the question was raised whether PECregional should be used for the cumulative exposure assessment (at least for wide dispersive uses). Another possible approach for the assessment of the cumulative exposure is the summation of the local emission rates or local PECs calculated for the single uses.

In the following section it is therefore discussed whether the cumulative exposure assessment of biocidal active substances can be covered by the addition of the regional background concentration to the local (worst case) concentration resulting from a single use or whether a summation of all local concentrations is more appropriate.

In short form, these two different approaches may be described as:

1) PECregional approach": Clocal (worst case) + PECregional

[37] EU TGD (2003), Part II, Chapter 2.1.2: „When determining a PEC for new substances at base-set level, or at the 10 tonnes per annum production level, Annex III, paragraph 3.4 of Directive 93/67 foresees that such estimates will usually focus on the generic local environment to which releases may occur."

2) "Sum Clocal approach": ∑Clocal

An example calculation with the software tool EUSES 2.1 (2008) and the calculation of PECregional with the model SimpleBox 2.0 was performed to illustrate the relation between Clocal, PEClocal and PECregional (see Table 5).

The calculation was performed for a biocidal active substance that is used in the following applications:

PT1: Human hygiene biocidal product; professional use

PT2: Medical disinfectant in accommodations, professional use

PT2: Disinfectant in sanitary sector, private use

PT6: In-can preservative in washing and cleaning fluids, private use

It was assumed that the active substance is used at a tonnage of 200 or 400 tonnes per year in the respective application (PT) within the EU.

The calculation was sequentially done for one, two, three and four simultaneous uses of the biocidal active substance. After application the active substance is released into the waste water ending up in a STP. The calculation of the daily emission rates into the waste water is based on the respective emission scenarios incorporated in EUSES for the respective PTs.

The results for the aquatic compartment (surface water) are given in form of the calculated local emission to waste water [kg/d]; the PECregional in surface water [µg/L]; the concentration in surface water (PEClocal) after passing the STP [µg/L] (see Table 5).

In addition, the concentrations in soil and ground water after sludge application and atmospheric deposition have been calculated (Table 6)[38].

In a second step, the figures of the "PECregional approach" – calculated for the environmental compartment surface water – were compared with those obtained by the "Sum Clocal approach" (Table 7).

The figures listed in Table 7 illustrate that the cumulative PEC calculated on basis of the "PECregional approach" is significantly lower than the sum of the Clocal of all single uses. The higher the number of single uses, the higher is the discrepancy between the two approaches. Consequently, the "PECregional approach" underestimates the environmental concentrations resulting from simultaneous and/or spatial overlapping uses of the same active substance.

These results are to be kept in mind for the following discussion of the advantages and disadvantages of the "PECregional" and the "Sum Clocal approach".

There are several advantages and disadvantages comparing the both approaches "PECregional approach" and "Sum Clocal approach".

[38] Exposure of soil and groundwater to biocides results from application of sewage sludge in agriculture and from dry and wet deposition from the atmosphere.

In general, the PECregional approach seems to be a good choice as it represents a mean background concentration resulting from all relevant emissions caused by all potential uses of an active substance, i.e. the complete emission situation is considered. In addition, adding one PECregional to a local (worst case) PEC is very easily done.

However, to derive a reliable PECregional it is necessary to have a more or less complete picture of uses for one active substance. It is questionable if this is even possible to get all these data. Based on the experiences from the evaluation of existing substances it is known how complex the situation concerning all the different use patterns of substances and the related emissions can be.

Furthermore, the current approach for Annex I inclusion of active substances under BPD requires the assessment of one single, representative use. If for this use no risks are identified the active substance can be included into Annex I. At the same time a cumulative assessment shall be done at Annex I inclusion stage. So it is quite clear that no comprehensive information to derive a sound PECregional is available.

In future, under product authorisation stage more information will become available concerning the use pattern of active substances. This increase in knowledge will allow deriving a better PECregional. However, as product authorization is a national task in each EU Member state a differently detailed level of information will be available. Thus, this may end up in different PECregional for different EU MS and one might question the sense of this situation. A solution would be to centrally derive a PECregional, after a certain time, based on the proceeding knowledge. It should also be kept in mind that active substances are included into Annex I for different Product Types and thus, information from product authorization comprising all uses in all product types will be a rather long process regarding time.

For some active substances that are already evaluated as existing substances it could be possible to use for the meantime the PECregional from the EU RAR. However, it is unclear if this is legally possible as the PECregional is estimated from emissions caused by uses beyond biocidal uses. Nevertheless, from a precautionary point of view this approach would be reasonable. The Scientific Steering Committee's Working Group on Harmonisation of Risk Assessment Procedures advising the European Commission points out that exposure assessments usually follow the respective legislation, but not an integrated approach. Thus, only a certain use of a chemical, e.g. in plant protection, is considered in the respective risk assessment regardless of whether the same chemical is used for other purposes or whether exposure takes place by other media than those in the focus of legislation. A realistic description of the exposures of consumers and environment requires a stratification of input-data in relation to ways and means of primary production and primary products and the full life-cycle of the product. When different pathways can be envisioned, there is a need to take all of these into consideration. Interaction between the different scientific committees and regulatory agencies in this regard is an important issue (European Commission 2000b).

On the other hand, based on the conclusions drawn from the analyses done in this project PECregional might also underestimate the actual risk resulting from multiple exposures. Thus, the ∑Clocal approach is more conservative and for some cases even more realistic. However, no final conclusion is possible to decide upon which approach describes better a specific emission situation. Also for the ∑Clocal approach the precision is highly depending on the availability of data. On huge disadvantage of the ∑Clocal approach is for sure the summing up of several realistic worst case scenarios. It is questionable if this approach is really satisfactory to derive conclusions of risks and with that on legal consequences for active substances.

Table 5 Relation between Clocal, PEClocal and PECregional: Concentration in surface water after passing STP

Relevant tonnage in EU [tonnes]				Local emission to waste water (Elocal water) [kg/d]				Concentration in surface water after passing STP									
								PECreg_sw [ng/L]	Clocal surface water [µg/L]				Clocal surface water with PECregional [µg/L]				∑Clocal surface water [µg/L]
Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)	Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)		Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)	Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)	
200	-	-	-	0.384	-	-	-	0.0707	6.18	-	-	-	6.18	-	-	-	-
200	200	-	-	0.384	0.404	-	-	0.145	6.18	6.51	-	-	6.18	6.51	-	-	12.69
200	200	200	-	0.384	0.404	0.11	-	0.165	6.18	6.51	1.77	-	6.18	6.51	1.77	-	14.46
200	200	200	400	0.384	0.404	0.11	0.219	0.206	6.18	6.51	1.77	3.53	6.18	6.51	1.77	3.53	17.99

Table 6 Relation between Clocal, PEClocal and PECregional: Concentration in soil and ground water after sludge application

Concentration in dry sewage sludge [mg/kg]				Annual average total deposition flux (DEPtotal_ann) [mg/(m² · d)]				Concentration in soil and ground water after sludge application								
								PECregional$_{soil}$ [µg/kg]	Clocal$_{soil}$ [µg/kg] (= Clocal without PECregional)				Clocal$_{ground\ water}$ [µg/L] (= Clocal without PECregional)			
Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)	Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)		Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)	Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)
0.211	-	-	-	8.72E-07	-	-	-	1.55E-03	0.232	-	-	-	0.426	-	-	-
0.211	0.222	-	-	8.72E-07	9.2E-07	-	-	3.18E-03	0.232	0.244	-	-	0.426	0.448	-	-
0.211	0.222	0.0603	-	8.72E-07	9.2E-07	2.49E-07	-	3.62E-03	0.232	0.244	0.066	-	0.426	0.448	0.122	-
0.211	0.222	0.0603	0.121	8.72E-07	9.2E-07	2.49E-07	5E-07	4.50E-03	0.232	0.244	0.066	0.133	0.426	0.448	0.122	0.244

Table 7 Comparison of "PECregional approach" and "Sum Clocal approach" for the environmental compartment surface water (figures calculated on basis of the example calculation summarised in Table 5)

Example Scenarios	$PEC_{surface\ water}$ [µg/L]
Cumulative PEC for 2 biocide uses	
PECregional	0.000145
PECregional approach (Clocal worst-case + PECregional)	6.51
Sum Clocal approach (∑Clocal)	12.69
Cumulative PEC for 3 biocide uses	
PECregional	0.000165
PECregional approach (Clocal worst-case + PECregional)	6.51
Sum Clocal approach (∑Clocal)	14.46
Cumulative PEC for 4 biocide uses	
PECregional	0.000206
PECregional approach (Clocal worst-case + PECregional)	6.51
Sum Clocal approach (∑Clocal)	17.99

5.3.4 Calculation of cumulative PEClocal

In principle, there are two different options to calculate cumulative PEC values on basis of the "Sum Clocal approach":

1) Cumulative PEC values may be calculated by adding up the local emissions to the environmental compartments surface water, air and soil (i.e. ∑Elocal for surface water; $\sum C_{sludge}$ + DEPtotal_ann for soil and groundwater), i.e. the daily release rates of the different uses are cumulated. On basis of this cumulative release rates the resulting predictive environmental concentrations are calculated.
2) The predicted environmental concentrations resulting from the single uses are added up to obtain cumulative PEC values (∑Clocal).

With regard to the surface water compartment, the local emissions to the STP and the resulting Clocal are linear (see Table 5); thus, cumulative $PEC_{surface\ water}$ values may be calculated either by adding up Elocal or Clocal.

Exposure of soil and groundwater to biocides results from application of sewage sludge in agriculture and from dry and wet deposition from the atmosphere. The results of the example calculation in Table 6 were used to calculate cumulative PEC values for soil and groundwater (Table 8 and Table 9, respectively). First, Clocal soil or Clocal gw values were added up to obtain cumulative PEC values (i.e. summation $Clocal_{soil}$ or $Clocal_{groundwater}$). Secondly, the concentration in dry sewage sludge (C_{sludge}) and the annual average total deposition flux (DEPtotal_ann) were added up, respectively, and the cumulated values $\sum C_{sludge}$ and

∑DEPtotal_ann were used as input parameters in EUSES for the calculation of cumulative PECs. The resulting cumulative PEC values (Clocal calculated by summation of C_{sludge} and DEPtotal_ann) are almost identical to the values obtained by summation of $Clocal_{soil}$ or $Clocal_{groundwater}$, respectively. Thus, cumulative PEC_{soil} and $PEC_{groundwater}$ values may also be calculated either by adding up the Clocal values of the single uses or by adding up the emission rates and using the cumulative emission rates for the subsequent PEC calculation with EUSES (or any other appropriate model).

Table 8 Results for cumulative $PEClocal_{soil}$ (figures calculated on basis of the example calculation in Table 6)

Example Scenarios	Value	Unit
Cumulative PEC for 2 biocide uses		
Summation $Clocal_{soil}$	**0.476**	µg/kg
Summation C_{sludge}	0.433	mg/kg
Summation DEPtotal_ann	17.92	x 10^{-07} mg/(m² · d)
$Clocal_{soil}$ calculated by summation of C_{sludge} and DEPtotal_ann	**0.477**	µg/kg
Cumulative PEC for 3 biocide uses		
Summation $Clocal_{soil}$	**0.542**	µg/kg
Summation C_{sludge}	0.493	mg/kg
Summation DEPtotal_ann	20.412	x 10^{-07} mg/(m² · d)
$Clocal_{soil}$ calculated by summation of C_{sludge} and DEPtotal_ann	**0.543**	µg/kg
Cumulative PEC for 4 biocide uses		
Summation $Clocal_{soil}$	**0.675**	µg/kg
Summation C_{sludge}	0.614	mg/kg
Summation DEPtotal_ann	25.412	x 10^{-07} mg/(m² · d)
$Clocal_{soil}$ calculated by summation of C_{sludge} and DEPtotal_ann	**0.676**	µg/kg

Table 9 Results for cumulative PEClocal$_{groundwater}$ (figures calculated on basis of the example calculation in Table 6)

Example Scenarios	Value	Unit
Cumulative PEC for 2 biocide uses		
Summation Clocal$_{groundwater}$	**0.874**	µg/L
Summation C$_{sludge}$	0.433	mg/kg
Summation DEPtotal_ann	17.92	x 10^{-07} mg/(m² · d)
Clocal$_{groundwater}$ calculated by summation of C$_{sludge}$ and DEPtotal_ann	**0.874**	µg/L
Cumulative PEC for 3 biocide uses		
Summation Clocal$_{groundwater}$	**0.996**	µg/L
Summation C$_{sludge}$	0.493	mg/kg
Summation DEPtotal_ann	20.412	x 10^{-07} mg/(m² · d)
Clocal$_{groundwater}$ calculated by summation of C$_{sludge}$ and DEPtotal_ann	**0.995**	µg/L
Cumulative PEC for 4 biocide uses		
Summation Clocal$_{groundwater}$	**1.24**	µg/L
Summation C$_{sludge}$	0.614	mg/kg
Summation DEPtotal_ann	25.412	x 10^{-07} mg/(m² · d)
Clocal$_{groundwater}$ calculated by summation of C$_{sludge}$ and DEPtotal_ann	**1.239**	µg/L

5.4 Use of tonnage and average consumption data in cumulative exposure assessments

Environmental exposure estimations are either based on the annual tonnage applied for the respective use or the average consumption of the biocidal active substance.

In the following chapter the differences between these two approaches are examined in detail. Furthermore, a method is described to select the most appropriate approach in case the respective ESDs include scenarios which are based both on the tonnage and the consumption. In addition, the question is discussed whether these two approaches can be combined in cumulative exposure assessments.

5.4.1 Background

In the tonnage approach it is assumed that the use of the biocidal products is evenly distributed over a particular region. Usually, only the tonnage used within the EU is known whereas the regional tonnage is unknown. In that case the regional tonnage is derived from the EU tonnage by multiplication with a production factor of 0.1 assuming that 10% of the amount that is produced and used in the EU is produced / used within a region (so called 10% rule; EU TGD 2003).

The formula for the calculation of the emission rate to wastewater on basis of the tonnage approach is given here exemplarily for a disinfectant used for sanitary purposes (PT2; van der Poel, 2001):

$Elocal_{water} = TONNAGE_{reg} \bullet F_{water} \bullet F_{mainsource} \bullet 1{,}000 / T_{emission}$

where:

$Elocal_{water}$ = Emission rate to wastewater [kg/d]
$TONNAGE_{reg}$ = Relevant tonnage in the region for this application [t]
$F_{mainsource}$ = Fraction of the main source [-]
F_{water} = Fraction released to wastewater [-]
$T_{emission}$ = Number of emission days [d]

The consumption approach is based on the average consumption per capita and uses post-consumer release predictions. An example of the average consumption is the use of soaps and detergents for cleaning and washing. The emission estimation applies the consumption of the biocidal product per capita, the concentration of the active substance in the product as well as the penetration factor of the product (i.e. the fraction of the biocidal product on the market containing the active substance).

In compliance with the above given example, the formula for the calculation of the emission rate to wastewater on basis of the consumption approach is given here for a disinfectant used for sanitary purposes (PT2; van der Poel, 2001):

$Elocal_{water} = Nlocal \bullet V_{form} \bullet C_{form} \bullet F_{penetr} \bullet F_{water}$

where

$Elocal_{water}$ = Emission rate to wastewater [kg/d]
Nlocal = Number of inhabitants feeding one STP [cap]
V_{form} = Consumption per capita [$L.cap^{-1}.d^{-1}$] or consumption point source [$kg.y^{-1}$]
C_{form} = Concentration of active substance in biocidal product [$kg.L^{-1}$]
F_{penetr} = Penetration factor of biocidal product [-]
F_{water} = Fraction released to wastewater [-]

For some PTs or certain applications, there are only emission scenarios available on basis of either the consumption approach or – in few cases – the tonnage approach. Table 10 gives an exemplary overview on the availability of tonnage and/or consumption scenarios in existing ESDs for biocidal products Main Group 1 “Disinfectants and general biocidal products”.

Table 10 Availability of tonnage and/or consumption scenarios for disinfectants and general biocidal products (Main Group 1)

Product type	ESD scenarios	Tonnage Scenario	Consumption Scenario
Main Group 1: Disinfectants and general biocidal products			
1: Human hygiene biocidal products	Private use	X	X
	Professional use (hospitals)	X	X
2: Private and public health area disinfectants and other biocidal products	Disinfectants used in the sanitary sector	X	X
	Medical sector: Disinfection of rooms, furniture and objects	X	X
	Medical sector: Disinfection of instruments	–	X
	Medical sector: Laundry disinfectants	–	X
	Medical sector: Hospital waste disinfectants	–	–
	Disinfection of industrial and institutional areas	X	X
	Disinfection of air-conditioning systems	–	X
	Disinfection for chemical toilets	–	X
3: Veterinary hygiene biocidal products	Disinfection of animal housing	–	X
	Disinfection of vehicles used for animal transport	–	X
	Disinfection for veterinary hygiene: non-medicinal teat dips	–	X
	Disinfection for veterinary hygiene: footwear and animals’ feet	–	X
	Disinfection in hatcheries	–	X
4: Food and feed area disinfectants	Disinfection in food, drink and milk industries (FDM)	–	X
	Disinfection in large scale catering kitchens, canteens slaughterhouses and butcheries	–	X
	Disinfection of milking parlour systems	–	X
5: Drinking water disinfectants		–	X

5.4.2 Advantages and disadvantages related to the tonnage and consumption approach

The main advantages (pros) and disadvantages (cons) related to these two different approaches have been discussed at the workshop on environmental risk assessment for PTs 1 to 6 (European Commission 2008a). The results are as follows:

Tonnage approach

Pros:

- The tonnage approach allows presenting the total consumption which is useful when information on the detailed use is lacking.
- The emission is directly related to the volume of use.
- The tonnage approach allows cumulation effects from the use of biocidal products.
- The applicants often have information only on the total value of the amount of the active substance placed on the market.

Cons:

- Tonnage information is confidential.
- Precise figures on tonnages relevant for the different uses may not be available to the applicants who are in the first place producers of the active substance (a.s.) and do not hold detailed information on the downstream end-users market.
- The fraction reaching the different relevant environmental compartments may be unknown.
- For most scenarios, a tonnage based environmental emission calculation is not defined in the current ESDs. Only for wide dispersive uses, a tonnage based calculation could be applied depending on the outcome of the “break-even calculations” (see below).
- If MS should take other biocidal uses into consideration, this must include other PTs and will require harmonised and agreed guidance at EU level.

Further Cons – not discussed at the workshop – are:

- The Annex I listing of an active substance lasts for up to 10 years. During this period significant market fluctuations may occur influencing significantly the tonnage actually used. Thus, the basis of the risk assessment (i.e. the tonnage value) may not be valid throughout the complete duration of the registration.
- Frequently, registration dossiers are submitted by only one applicant. In these cases, the registration dossiers do not reflect the total tonnage available on the market.

Consumption approach

Pros:

- It is simple as it requires only an emission factor, the amount of product used and the concentration of substance in a product.
- Many ESDs have been agreed upon and are based on this approach.
- It is transparent as default values can be modified if this is fully justified.

Cons:

- Using only the average consumption approach in specific exposure scenarios may underestimate the exposure to the environment as only one use is specified. Several uses of the same active substance should be added when considering the emission to the same STP and finally the environment.
- Lack of reliable data (e.g. of average consumption or market penetration) leads to uncertain estimates.
- No direct relation with actual volume for the application in case of diffuse emission.

At the workshop it was concluded that both approaches have their pros and cons and that the RMS will use the tonnage approach to assess the validity of the average consumption approach and in particular the default values used in the models.

5.4.3 Relation between tonnage and consumption approach

Van der Poel (2001) mentioned the following general differences between tonnage and consumption scenarios:

For the diffuse emissions, i.e. emissions caused by use by the public at large (e.g. households), the scenario with the average consumption will give a fixed value whereas the scenario with the tonnage will give the emission as a linear relation to the quantity.

With regard to point sources, there may be a situation that the use of the tonnage scenario is underestimating the emission. For example, if considering a cleaner with a disinfectant for sanitary purposes, the various manufacturers of such products may apply different active substances. While one hospital applies the disinfectant assessed, another applies a product with a different active substance. The tonnage scenario, however, will distribute the whole amount of an active substance over all hospitals by using the fraction of its relative size. The emissions by a single hospital (= point source) may, however, be higher than the assumed average amount. Thus, there is a certain tonnage below which the consumption scenario provides more realistic emission estimations for the point source under consideration.

By means of the so-called “break-even-calculation” (developed by van der Poel, 2001) it is possible to estimate which of the above described approaches, tonnage based or average consumption by inhabitant based, is more appropriate for the intended emission estimation (European Commission 2010a).

The break-even point for PT2 (see Chapter 5.4.1) can be calculated as follows:

$Elocal_{water\ /\ Tonnage} = TONNAGE_{reg} \bullet F_{water} \bullet F_{mainsource} \bullet 1{,}000 / T_{emission}$

$Elocal_{water\ /\ Consumption} = Nlocal \bullet V_{form} \bullet C_{form} \bullet F_{penetr} \bullet F_{water}$

$\Rightarrow TONNAGE_{reg} \bullet F_{water} \bullet F_{mainsource} \bullet 1{,}000 / T_{emission} = Nlocal \bullet V_{form} \bullet C_{form} \bullet F_{penetr} \bullet F_{water}$

$\Rightarrow \mathbf{TONNAGE_{reg} = (Nlocal \bullet V_{form} \bullet C_{form} \bullet F_{penetr} \bullet T_{emission}) / (1{,}000 \bullet F_{mainsource})}$

where:

$TONNAGE_{reg}$ = Relevant tonnage in the region for this application [t]
Nlocal = Number of inhabitants feeding one STP [cap]
V_{form} = Consumption per capita [$L.cap^{-1}.d^{-1}$]
C_{form} = Concentration of active substance in biocidal product [$kg.L^{-1}$]
F_{penetr} = Penetration factor of biocidal product [-]
$T_{emission}$ = Number of emission days [d]
$F_{mainsource}$ = Fraction of the main source [-]

Above a certain tonnage (i.e. the break-even point), the scenario based on tonnage is more appropriate, since the scenario based on consumption would underestimate the actual amount of disinfectant reaching the STP. Below the “break-even tonnage”, however, the scenario based on consumption is considered more appropriate for the release estimation.

The determination of the break-even point is exemplarily illustrated in two example calculations in Appendix 8.2 and Appendix 8.3.

Apart from the “break-even-calculation” RMS propose to calculate both tonnage and consumption scenarios – provided that respective emission scenarios are available in the ESDs – and then to choose the worst-case PEC values for the environmental risk assessment. With regard to the performance of cumulative risk assessments this means that release estimations are made for each single use both by the tonnage and the average consumption approach; in each case the worst case release estimation is chosen and the resulting worst case values are used to assess the cumulative PEC values.

The procedure proposed by the RMS is illustrated by means of a sample calculation. The basis for this calculation is the example in Chapter 5.3.3 dealing with a biocidal active substance that is used in the following applications:

PT1: Human hygiene biocidal product; professional use

PT2: Medical disinfectant in accommodations, professional use

PT6: In-can preservative in washing and cleaning fluids, private use

PT2: Disinfectant in sanitary sector, private use

The calculation was done with the software tool EUSES both on basis of an estimated tonnage in the region (assumed tonnages are given in Table 5) and on basis of the average consumption rates for each application as given in the respective ESDs in EUSES (assumed input parameters are summarised in Appendix 8.1). PECregional was estimated by applying SimpleBox 2.0 model separately.

Table 11 summarises the results of the calculated local emission to waste water and the resulting local concentrations in surface water. Because of their completely different character, calculations on basis of the tonnage and the average consumption scenarios often provide outcomes which may be quite different and the selection of either the tonnage or the average consumption approach may significantly influence the outcome of the emission calculation. In the example given in Table 11 the consumption approach delivers worst-case emission rates and Clocal values for three out of four different uses (namely Use 1 / PT 1; Use 3 / PT 6; Use 4 / PT 2). For Use 2 (PT 2), the tonnage approach yields higher (i.e. worst case) values.

Table 11 Comparison of $Elocal_{water}$ and $Clocal_{surface\ water}$ calculated on basis of the tonnage and the consumption approach

Approach	**Local emission to waste water (Elocal water) [kg/d]**				**Concentration in surface water after passing STP**								
					$PECreg\_{surface\ water}$ [ng/L]	**$Clocal_{surface\ water}$ [µg/L]**				**$Clocal_{surface\ water}$ with PECregional [µg/L]**			
	Use 1 (PT1)[39]	Use 2 (PT2)[39]	Use 3 (PT6)	Use 4 (PT2)		Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)	Use 1 (PT1)	Use 2 (PT2)	Use 3 (PT6)	Use 4 (PT2)
Tonnage [a)]	0.384	0.404	0.11	0.219	0.206	6.18	6.51	1.77	3.53	6.18	6.51	1.77	3.53
Consumption [b)]	6.00	0.375	0.25	0.25	1.27	96.7	6.05	4.03	4.03	96.70	6.05	4.03	4.03

a) Assumed tonnages are given in Table 5.

b) Assumed input parameters (according to the emission scenarios in EUSES) are summarised in Appendix 8.1.

[39] See also example calculation in Appendix 8.2 and 8.3

According the procedure proposed by the RMS, the worst case release estimation should be chosen for each use and the resulting worst case values should be added to assess the cumulative PEC values. With regard to the example given in Table 11 this would imply that figures derived from both approaches have to be combined in the cumulative exposure assessments.

Thus, a closer look should be given to the question whether release rates or predicted environmental concentrations calculated on basis of the tonnage approach can be combined with release rates or PEC values obtained by average consumption scenarios.

The results of the example calculations in Table 11 as well as in Appendix 8.2 and 8.3 demonstrate that both the tonnage and the consumption approach provide local emission rates (e.g. to waste water (Elocal water) expressed in [kg/d]) which serve as input values for the subsequent PEC calculations. As each of these local emission rates is considered to be an independent and reliable value expressed in the same unit, from the scientific point of view no obstacle is seen to combine these values. Therefore, we conclude that release rates or predicted environmental concentrations calculated on basis of the tonnage approach can be combined with release rates or PEC values obtained by average consumption scenarios.

In general, the following proceeding is proposed whereby two different situations need to be distinguished:

1) For all intended uses that have to be considered in the cumulative exposure assessment, emission scenarios both on basis of the tonnage and the consumption approach are available.
2) For one or several of the intended uses that have to be considered in the cumulative exposure assessment, there are only emission scenarios available on basis of either the consumption or the tonnage approach.

In the first case, for each use it should be estimated by means of the “break-even-calculation” whether the tonnage based or average consumption based approach is more appropriate for the emission estimations (see example calculations in Appendix 8.2 and 8.3). Subsequently, for each use local emission rates (Elocal) and local predicted environmental concentrations (PEClocal) are calculated on basis of the approach identified to be most appropriate by the “break-even-calculation”. Then, the Elocal or PEClocal of all uses should be summed up to assess the cumulative exposure (see Chapter 5.3.3 “Sum Clocal approach”).

In the second case, local emission rates (Elocal) and local predicted environmental concentrations (PEClocal) are calculated for each use on basis of the available emission scenario. As explained for the first case, Elocal or PEClocal of all uses should then be summed up to assess the cumulative exposure (see Chapter 5.3.3 “Sum Clocal approach”).

6 Outlook and recommendations for further research

The research conducted in the present study has led to conclusions and recommendations on how the provisions of the Biocidal Product Directive concerning cumulative environmental exposure could be assessed. However it has also uncovered several areas that need further attention. The purpose of this chapter is therefore to identify and discuss the need for further research in the area of cumulative risk assessments.

Harmonisation of terms and definitions

The review of existing approaches related to cumulative assessments in other regulatory areas revealed that the technical terms and definitions used have different meanings depending on the regulatory area where they are applied. A harmonisation of terminology across regulatory areas should be envisaged. This is of even greater relevance if cumulative exposure assessment does not only focus on single regulations but is done trans-sectorial considering all uses of an active substance as suggested by many European experts (see below).

Data and information requirements

Sound data on the total production / consumption of the active substance as well as a detailed description of the intended uses and use pattern are a prerequisite for cumulative exposure assessments. Up to now, these data are often lacking which makes cumulative assessments difficult.

One possibility to obtain such data would be the inclusion of biocides into the scope of Regulation (EC) No 1185/2009 concerning statistics on pesticides.[40] Similar to the crop-specific data collection of plant protection products, in the biocide area PT specific data are required.

In addition, national approaches for collecting data on use and consumption of biocides would improve the basis for cumulative exposure assessments. Several Member States do already collect data on biocides (e.g. Denmark, Finland, Spain, Belgium, Slovenia and

[40] Regulation (EC) No 1185/2009 concerning statistics on pesticides does not consider biocides so far, but indicates that the scope may be expanded at a later stage so as to include biocides. The argument for the postponement was that the *"effects of the Directive 98/8/EC will not become apparent until the first evaluation of active substances for use in biocidal products is finalised"* and that *"neither the Commission nor most Member States currently have sufficient knowledge or experience to propose further measures regarding biocides."* However, it is *"anticipated that, taking into account the results of the evaluation of Directive 98/8/EC and on the basis of an impact assessment, the scope of this Regulation will be extended to cover biocidal products."*

Sweden). Other MS should follow these examples and implement their own national data collection programmes.

Legal consequence

The regulatory aspects to be considered with regard to cumulative exposure assessment as well as the legal consequences or the management of confidential data have not been object of the project and have therefore not been assessed within the present report. Nevertheless, these aspects need further consideration in the future.

Guidance is required how to deal with an active substance evaluated in the Review Program in more than one PT with different time lines for Annex I inclusion. For example, several active substances are included in PTs for which the evaluation is finalised whereas or for which the evaluation has not yet started.

Further guidance is necessary to clarify the regulatory consequences with regard to an Annex I inclusion if cumulative exposure reveals unacceptable risks for the environment.

Challenges beyond single regulations

The BPD limits the framework for cumulative risk assessments of biocidal active substances to their uses within the scope of the BPD; meaning that if the same active substance is used both in biocidal products and in other use areas like, for example, as plant protection products or industrial chemicals, the emission routes of the latter are not to be considered in the cumulative exposure assessment for biocides according to the existing legislation.

However, the compounds that make up chemical exposure in the real-world do not belong to a single regulatory group (i.e. not all of them are biocides, not all of them are pesticides, etc.). This trans-sectorial nature of “chemical mixtures” in the environment poses a major challenge for the current regulatory system. In this context, Backhaus et al. (2010) state that media-oriented pieces of legislation, such as the Water Framework Directive, may potentially provide a useful platform to tackle this problem effectively, and substance-oriented pieces of regulation seem to provide options for the complementary assessment of particular scenarios as can be seen from the recent revision of the legislation on plant protection products.

Kortenkamp et al. (2009) argue along these lines in their “State of the Art Report on Mixture Toxicity”. They criticise that there is presently no vehicle to deal with exposure to substances that come from areas covered by separate EU regulations, such as cumulative exposure to plant protection products, biocidal products, pharmaceuticals, household chemicals, food additives etc. Each sector is performing its own risk assessment mostly completely ignoring that there may be contributions from the other sectors.

Therefore, cumulative exposure and risk assessments within one regulatory area like the BPD can only be a starting point. Future work is required to develop a concept considering all releases into the environment from all uses of a substance.

Cumulative exposure and mixture toxicity of similar acting substances

In a broader context also the requirement of cumulative exposure and toxicity of different substances with similar mode of action has been challenged. Examples are anticoagulants interfering with the vitamin K cycle or organophosphates inhibiting acetylcholinesterase. Mixture toxicity is eventually assessed for authorisation of biocidal products or plant production products containing different active substances. Guidance on how and when assessing cumulative exposure and mixture toxicity of different substances is mainly missing.

7 References

Altenburger & Greco 2009 — Altenburger, R., Greco, W.R.; Extrapolation Concepts for Dealing with Multiple Contamination in Environmental Risk Assessment. Integrated Environmental Assessment and Management 5(1), 2009, 62–68

Ashauer et al. 2006 — Ashauer, R. Boxall, A., Brown, C.; Predicting effects on aquatic organisms from fluctuating or pulsed exposure to pesticides. Environmental Toxicology and Chemistry 25(7), 2006, 1899–1912

BfR 2009 — Bundesamt für Risikobewertung – BfR (Ed.); Thought Starter for Revision of the TNsG on Annex I Inclusion Chapter 4.4: Cumulative and Aggregate Risk Assessment, personal communication

Blaser et al. 2008 — Blaser, S.A.; Scheringer, M.; MacLeod, M.; Hungerbühler, K.; Estimation of cumulative aquatic exposure and risk due to silver: Contribution of nano-functionalized plastics and textiles; Science of The Total Environment 390 (2-3), 2008, 396-409

Chapman 2000 — Chapman, P.M.; Whole effluent toxicity testing – Usefulness, level of protection, and risk assessment", Environmental Toxicology and Chemistry, 19(1), 2000, 3-13

COWI 2009 — COWI A/S Denmark (Ed.); Assessment of different options to address risks from the use phase of biocides. Final report on behalf of the European Commission, DG ENV (CA-Feb09-Doc.5.3.1); Kongens Lyngby 2009;
http://ec.europa.eu/environment/biocides/pdf/report_use.pdf

Crookes et al. 2004 — Crookes, J.; Quarterman, P.; Brooke, D.N.; Murray-Smith, R.J.; Data sources for use in emission estimation – Version 1.02 Client report number 218177 prepared for CEFIC Long-Range Research Initiative, June 2004

ECHA 2008a — European Chemical Agency – ECHA (Ed.); Guidance on information requirements and chemical safety assessment, Part E: Risk Characterisation; May 2008

ECHA 2008b — European Chemical Agency – ECHA (Ed.); Guidance on information requirements and chemical safety assessment, Chapter R.15: Consumer exposure estimation; May 2008

ECHA 2008c — European Chemical Agency – ECHA (Ed.); Guidance on information requirements and chemical safety assessment, Chapter R.16: Chapter R.16: Environmental Exposure Estimation; May 2008

EFSA 2008 — European Food Safety Authority – EFSA (Ed.); Opinion of the Scientific Panel on Plant Protection products and their Residues to evaluate the suitability of existing methodologies and, if appropriate, the identification of new approaches to assess cumulative and synergistic risks from pesticides to human health with a view to set MRLs for those pesticides in the frame of Regulation (EC) 396/2005; The EFSA Journal 704, 2008, 1-84

EMEA 2006 — European Medicines Agency – EMEA (Ed.); Guideline on the environmental risk assessment of medicinal products for human use; Committee for Medicinal Products for Human Use (CHMP); London, 01 June 2006; http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500003978.pdf

EMEA 2008 — European Medicines Agency – EMEA (Ed.); Revised guideline on environmental impact assessment for veterinary medicinal products in support of the VICH Guidelines GL6 AND GL 38; Committee for medicinal products for veterinary use, Doc. Ref. EMEA/CVMP/ERA/418282/2005-Rev.1; http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004386.pdf

EU TGD 2003 — European Commission (Ed.); Technical Guidance Document in Support of Directive 93/67/EEC on Risk Assessment of New Notified Substances and Regulation (EC) No. 1488/94 on Risk Assessment of Existing Substances (Parts I, II, III and IV); Luxembourg, Office for the Official Publications of the European Community, 2003

European Commission 2003 — European Commission (Ed.); Technical Guidance Document in Support of Directive 93/67/EEC on Risk Assessment of New Notified Substances and Regulation (EC) No. 1488/94 on Risk Assessment of Existing Substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market (Part II Chapter 3 Environmental Risk Assessment); http://ecb.jrc.ec.europa.eu/documents/TECHNICAL_GUIDANCE_DOCUMENT/EDITION_2/tgdpart2_2ed.pdf

European Commission 2007a — European Commission (Ed.); 27th meeting of representatives of Member States' competent authorities for the implementation of Directive 98/8/EC concerning the placing of biocidal products on the market. Notes on the provision of information concerning tonnage of active substances/biocidal products placed on the market; CA-Nov07-Doc.6.3; 2007

European Commission 2007b — European Commission (Ed.); Workshop on environmental risk assessment for insecticides, acaricides and products to control other arthropods (Product Type 18); A workshop for technical experts evaluating PT 18 active substances for the Competent Authorities implementing the Biocidal Products Directive 98/8/EC; Arona, Italy, 11 March 2008

European Commission 2008a — European Commission (Ed.); Workshop on environmental risk assessment for Product Types 1 to 6; A workshop for technical experts evaluating PTs 1 to 6 active substances for the Competent Authorities implementing the Biocidal Products Directive 98/8/EC; Brussels, Belgium, 11 December 2007

European Commission 2008b — European Commission (Ed.); 29th meeting of representatives of Members States Competent Authorities for the implementation of Directive 98/8/EC concerning the placing of biocidal products on the market: Cumulative (Combined) risk assessment; CA-May08-Doc6.3; 2008

European Commission 2010a — European Commission (Ed.); Technical Notes for Guidance: Supplement to the methodology for risk evaluation of biocides; Supplement to the Emission Scenario Document for Product Type 2: Private and public health area disinfectant and other biocidal products; 2010; http://ec.europa.eu/environment/biocides/pdf/ESD%20PT2_public%20consultation.pdf

European Commission 2010b — Combination Effects of Chemicals (Ed.); Science for Environment Policy, DG Environment News Alert Service, June 2010; http://ec.europa.eu/environment/integration/research/newsalert/pdf/21si.pdf

EUSES 2008 — European Commission (Ed.); European Union System for the Evaluation of Substances – EUSES, Version 2.1 (2008); http://tcsweb3.jrc.it/euses/

Federal Statistical Office 2009a — Statistisches Bundsamt Deutschland (Ed.); Nichtöffentliche Wasserversorgung und Abwasserbeseitigung 2007; Fachserie 19 Reihe 2.2; Wiesbaden, September 2009

Federal Statistical Office 2009b — Statistisches Bundesamt Deutschland; Öffentliche Wasserversorgung und Abwasserbeseitigung 2007; Fachserie 19 Reihe 2.1; Wiesbaden, September 2009

Gartiser 1999 — Gartiser, S.; Abschätzung des Beitrages kommunaler Kläranlagen an Schadstoffkonzentrationen in Oberflächengewässern; Diskussionsbeiträge: Abwasser; Zeitschrift für Umweltchemie und Ökotoxikologie 11(3), 1999, 157–162

Gartiser et al. 2007 — Gartiser, S.; Reuther, R.; Reihlen, A.; Lüskow, H.; Vernon, J.; Zarogiannis, P.; Study on Impact of the Implementation of Directive 98/8/EC concerning the Placing on the Market of Biocidal Products; Final Report for DG Environment, European Commission, October 10th 2007; http://ec.europa.eu/environment/biocides/study.htm

Götz et al. 2010 — Götz, C.W.; Stamm, C.; Fenner, K.; Singer, H.; Schärer, M.; Hollender, J.; Targeting aquatic microcontaminants for monitoring: exposure categorization and application to the Swiss situation; Environmental Science and Pollution Research 17(2), 2010, 341-54

Hahn et al. 2010 — Hahn, S.; Schneider, K.; Gartiser, S.; Heger, W.; Mangelsdorf, I.; 2010 Consumer exposure to biocides – identification of relevant sources and evaluation of possible health effects; Environmental Health 2010, 9:7; http://www.ehjournal.net/content/9/1/7

Hoppin et al. 2006 — Hoppin, J.A.; Adgate, J.L.; Eberhart, M.; Nishioka, M.; Ryan, P.B.; Environmental Exposure Assessment of Pesticides in Farmworker Homes; Environmental Health Perspectives 114(6), 2006, 929-935

Hughes 2002 — Hughes, I.; Risk Assessment of Mixtures of Pesticides and Similar Substances; Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment; September 2002; http://cot.food.gov.uk/pdfs/reportindexed.pdf

IPCS 2004 — World Health Organization (Ed.); International Program on Chemical Safety – IPCS – Harmonization Project Document No. 1, IPCS Risk Assessment Terminology; Part 1: IPCS/OECD Key Generic Terms used in Chemical Hazard/Risk Assessment; Part 2: IPCS Glossary of Key Exposure Assessment Terminology; Geneva 2004

ISEA glossary 2005 — Zartarian, V.; Bahadori, T.; McKone, T.; Adoption of an official ISEA glossary; Journal of exposure Analysis and Environmental Epidemiology 15, 2005, 1-5

IUPAC 2006 — Stephenson, G.R.; Ferris, I.G.; Holland, P.T.; Nordberg, M.; Glossary of Terms Relating to Pesticides (IUPAC Recommendations 2006); Pure Appl. Chem. 78(11), 2006, 2075–2154

Kortenkamp & Hass 2009 — Kortenkamp, A.; Hass, U.; Expert workshop on combination effects of chemicals, 28-30 January 2009, Hornbæk, Denmark. Workshop Report organized under the auspices of the Danish Ministry of the Environment and the Danish Environmental Protection Agency; June 2009; http://www.mim.dk/NR/rdonlyres/C59693B7-2421-4748-89F0-5937496E0A28/0/BILAG_2_Expertworkshop.pdf

Kortenkamp et al. 2009 — Kortenkamp, A.; Backhaus, T.; Faust, M.; State of the Art Report on Mixture Toxicity. Study Contract Number 070307/2007/485103/ETU/D.1; Final Report from 22 December 2009; http://ec.europa.eu/environment/chemicals/pdf/report_Mixture%20toxicity.pdf

Lassen et al. 2001 — Lassen, C.; Skårup, S.; Mikkelsen, S.H.; Kjølholt, J.; Nielsen, P.J.; Samsøe-Petersen, L.; Inventory of biocides used in Denmark. Environmental Project No. 585. Danish EPA; Copenhagen 2001; http://www2.mst.dk/udgiv/Publications/2001/87-7944-383-4/pdf/87-7944-384-2.pdf

Lepper et al. 2008 — Lepper, P.; Daginnus, K.; De Coen, W.; Deviller, G.; Netzeva, T.; Pavan, M.; Sobanska, M.; Worth, A.; Paya Perez, A.; Eisenreich, S.; Selection of Priority Substances in the context of the European Water Framework Directive; European Commission, Joint Research Centre; 21 May 2008; http://ecb.jrc.ec.europa.eu/documents/QSAR/INFORMATION_SOURCES/PRESENTATIONS/Priority_setting_WFD.pdf

Mackay et al. 1991 — Mackay D.; Paterson S.; Evaluating the multimedia fate of organic chemicals: a level III fugacity model. Environmental Science and Technology 25, 1991, 427–436

Mileson et al. 1999 — Mileson, B.; Faustman, E.; Olin, S.; Ryan, P.B.; Ferenc, S.; Burke, T.; A Framework for cumulative risk assessment. An ILSI Risk Science Institute workshop report; International Life Sciences Institute; Washington 1999

Morton et al. 2000 — Morton, M.G.; Dickson, K.L.; Waller, W.T.; Acevedo, M.F.; Mayer, F.L.; Ablan, M.; Methodology for the evaluation of cumulative episodic exposure to chemical stressors in aquatic risk assessment; Environmental Toxicology and Chemistry 19 (4,2), 2000, 1213–1221

Nieuwenhuijsen et al. 2005 — Nieuwenhuijsen, M.J.; Grey, C.N.B.; Golding, J.; Exposure Misclassification of Household Pesticides and Risk Perception and Behaviour; Annals of Occupational Hygiene 49(8), 2005, 703–709; http://annhyg.oxfordjournals.org/cgi/content/full/49/8/703

OECD 2001 — OECD (Ed.); OECD Series on Testing and Assessment Number 30; Detailed review document on hazard classification systems for mixtures, 23 July 2001

OECD 2003 — OECD (Ed.); OECD Series on Emission Scenario Documents Number 2; Emission Scenario Document for Wood Preservatives, Part 1; 2003

OECD 2005 — OECD (Ed.); OECD Series on Testing and Assessment Number 51; Approaches to exposure assessment in OECD member countries. Report from the Policy Dialogue on Exposure Assessment in June 2005

OSPAR 2007a
OSPAR Hazardous Substances Committee (Ed.); OSPAR's practical Guidance Document on Whole Effluent Assessment; OSPAR Intersessional Expert Group on Whole Effluent Assessment (WEA), OSPAR Hazardous Substances Series 316; http://www.ospar.org/documents/dbase/publications/p00316_WEA%20Guidance%20Document.pdf

Price & Chaisson 2005
Price, P.S.; Chaisson, C.F.; A conceptual framework for modelling aggregate and cumulative exposures to chemicals; Journal of Exposure Analysis and Environmental Epidemiology, 2005(5), 473–481; http://www.nature.com/jes/journal/v15/n6/pdf/7500425a.pdf

REACH 2006
European Commission (Ed.); Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACh), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC

Sielken 2000
Sielken R.L.; Risk Metrics and Cumulative Risk Assessment Methodology for the FQPA. Regulatory Toxicology and Pharmacology 31(3); 300-307 (only abstract available)

TNsG on Annex I inclusion 2002
European Commission (Ed.); Technical Notes for Guidance (TNsG) in Support of Directive 98/8/EC of the European Parliament and the Council Concerning the Placing of Biocidal Products on the Market; Principles and Practical Procedures for the inclusion of active substances in Annexes I, IA and IB; April 2002

U.S. Department of Health and Human Services 1998
U.S. Department of Health and Human Services (Ed.); Environmental Assessment of Human Drug and Biologics Applications - Guidance for Industry; Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Revision 1, July 1998

UK Food Standards Agency 2002
UK Food Standards Agency (Ed.), Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment; Risk Assessment of Mixtures of Pesticides and Similar Substances; September 2002

US EPA 2002
U.S. Environmental Protection Agency (Ed.); Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity; Office of Pesticide Programs, U.S. Environmental Protection Agency Washington, D.C.; January 14, 2002; http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf

US EPA 2010
U.S. Environmental Protection Agency (Ed.); Systems Approach to Assessing Cumulative Exposure to Endocrine Disrupting Chemicals. EPA Grant Number: R832739, North Carolina State University; EPA 2010; http://cfpub.epa.gov/ncer_abstracts/index.cfm/fuseaction/display.abstractDetail/abstract/7845/report/0

US EPA OPP 2002
U.S. Environmental Protection Agency – EPA, Office of Pesticide Programs – OPP (Ed.); Status of cumulative risk assessment for organophosphate pesticides; January 15, 2002, Revised Draft; http://www.epa.gov/oppsrrd1/cumulative/files/guidefinal_4-new. pdf

Van de Meent et al. 1996
Van de Meent, D.; Brandes, L.J.; den Hollander, H.; SimpleBox 2.0: a nested multimedia fate model for evaluating the environmental fate of chemicals; National institute of public health and the environment (RIVM) NL for the European Commission, DG ENV; Bilthoven 1996

Van der Aa & Balk 2004
Van der Aa, E.; Balk, F.; Supplement to the methodology for risk evaluation of biocides: Environmental Emission Scenarios for biocides used as human hygiene biocidal products (Product type 1); National institute of public health and the environment (RIVM) NL for the European Commission, DG ENV; Bilthoven 2004

Van der Poel 2001
Van der Poel, P.; Supplement to the methodology for risk evaluation of biocides; Emission Scenarios Document for Product Type 2: Private and public health area disinfectants and other biocidal products (sanitary and medical sector); National institute of public health and the environment (RIVM) NL, report 601 450 008, for the European Commission, DG ENV; Bilthofen 2001

Vernon et al. 2008
Vernon, J.; Tuffnell, N.; Gartiser, S.; Zamparutti, T.; White, O.; Pozo, E.; Assessing the Impact of the Revision of Directive 98/8/EC concerning the Placing of Biocidal Products on the Market. Final Report prepared for the European Commission, DG Environment, August 2008; http://ec.europa.eu/environment/biocides/pdf/rev_ias_report.pdf

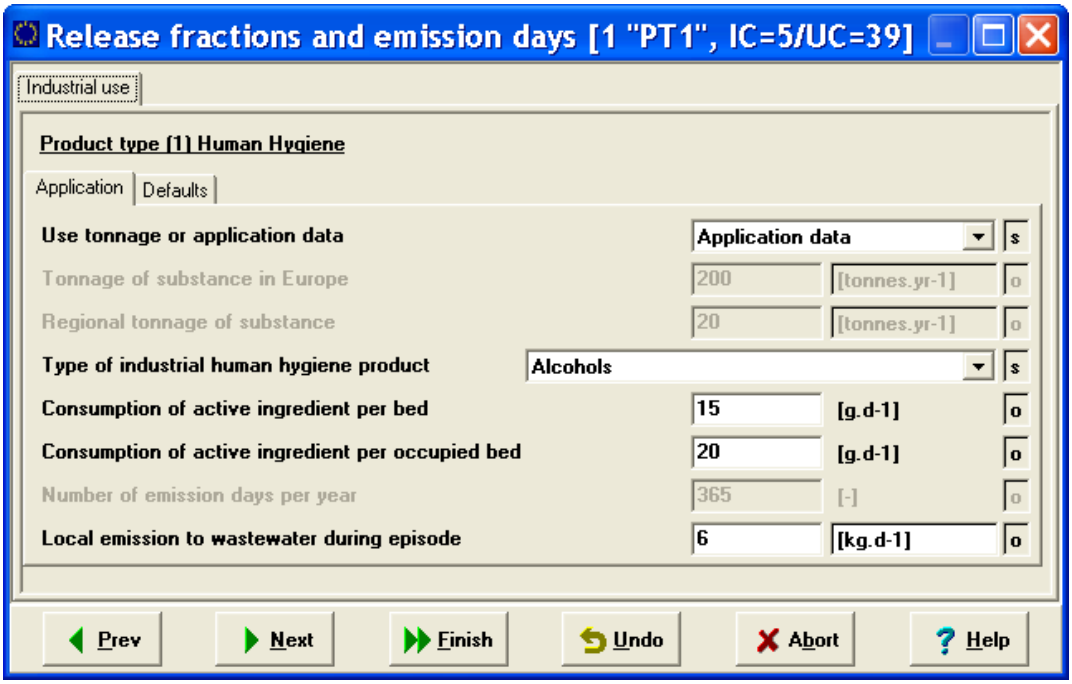
WHO 2009
World Health Organisation – WHO (Ed.); Risk assessment of combined exposures to multiple chemicals: a WHO / IPCS Framework Harmonization Project draft document for public and peer review; 2009; http://www.who.int/ipcs/methods/harmonization/areas/combinedexposure.pdf

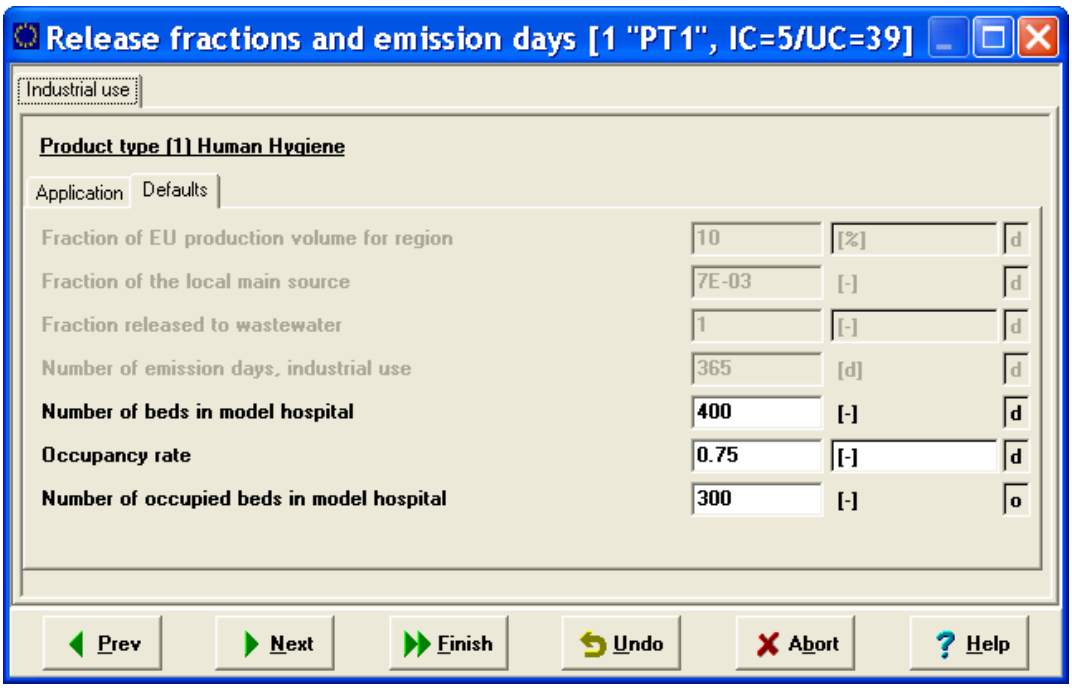
WHO/IPCS 2009
World Health Organisation – WHO (Ed.); Assessment of combined exposures to multiple chemicals: Report of a WHO/IPCS international workshop on aggregate/cumulative risk assessment; IPCS harmonization project document no. 7; WHO 2009

8 Appendices

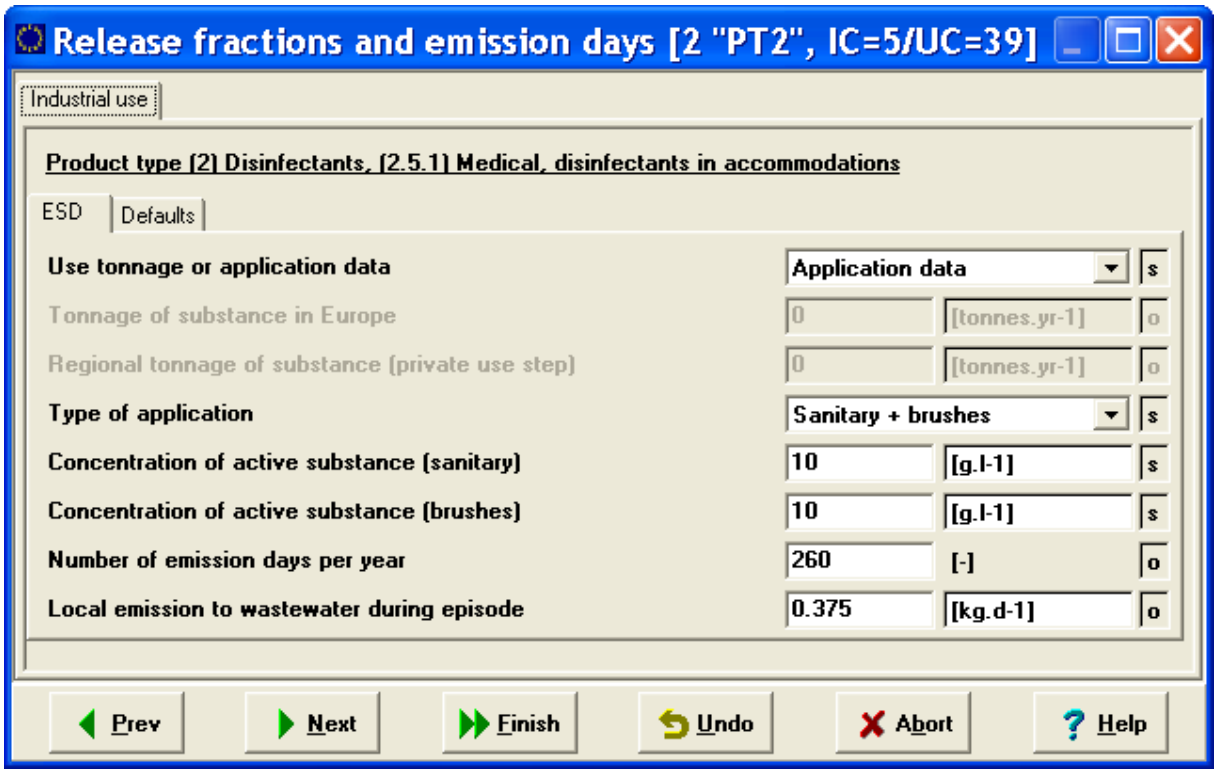
8.1 Appendix 1: EUSES input data: Example calculation on basis of the consumption approach

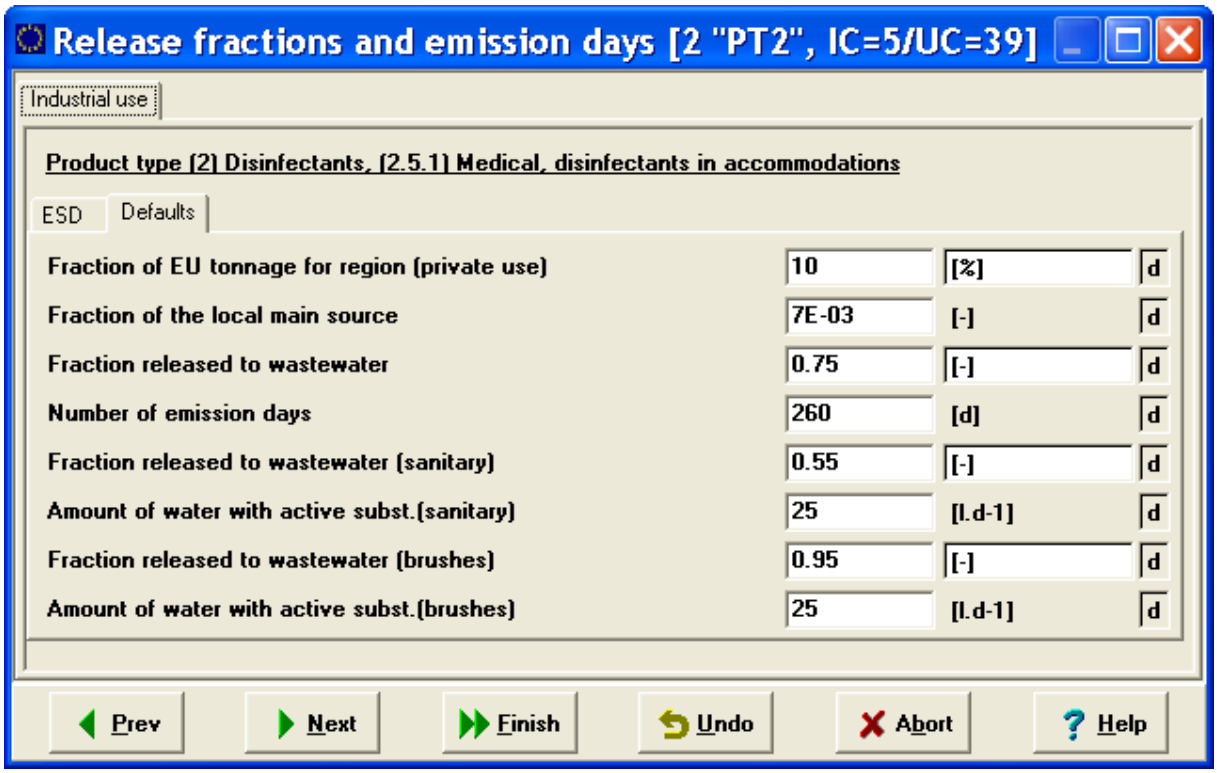
Input for PT1: Human hygiene biocidal product; professional use



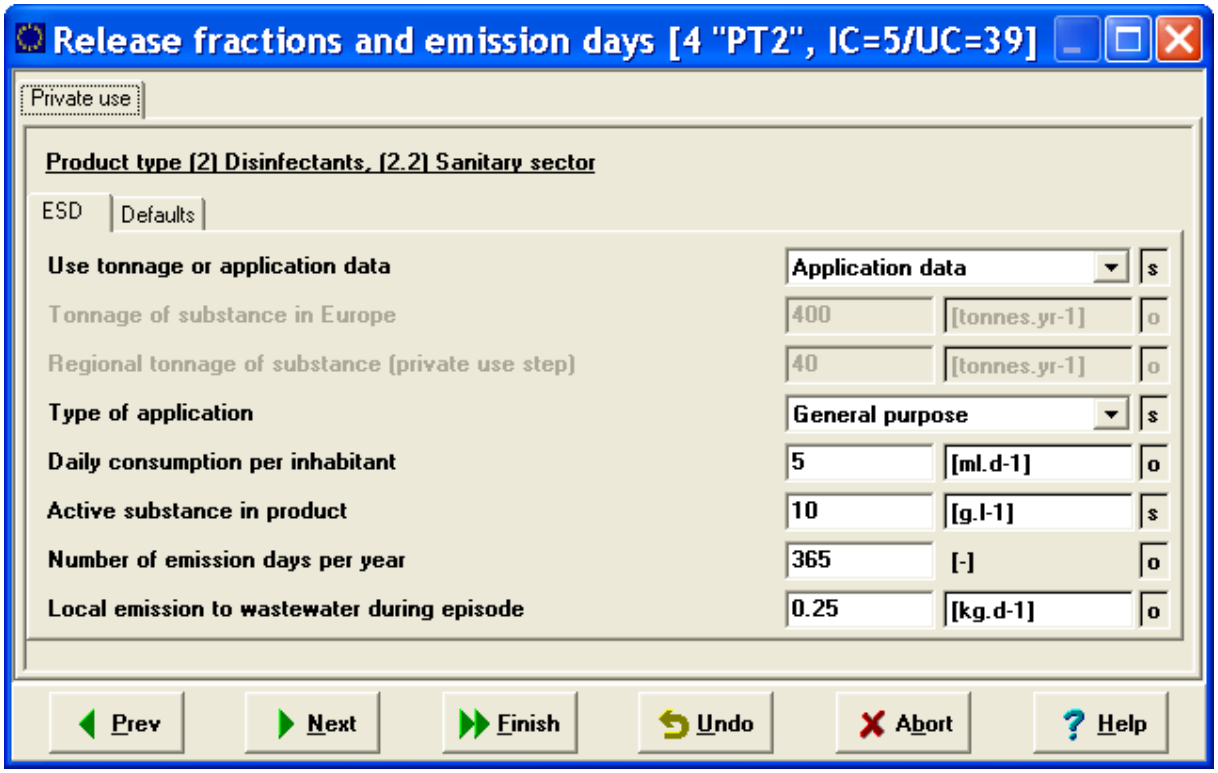


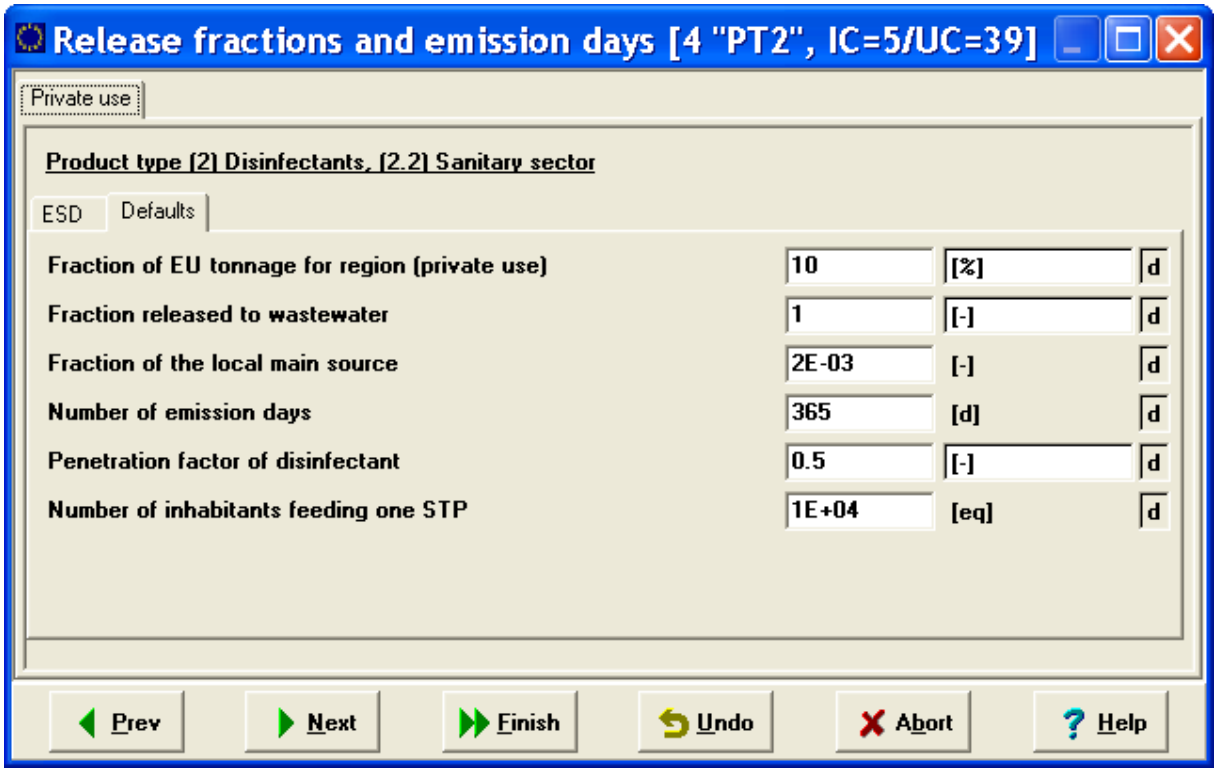
Input for PT2: Medical disinfectant in accommodations, professional use



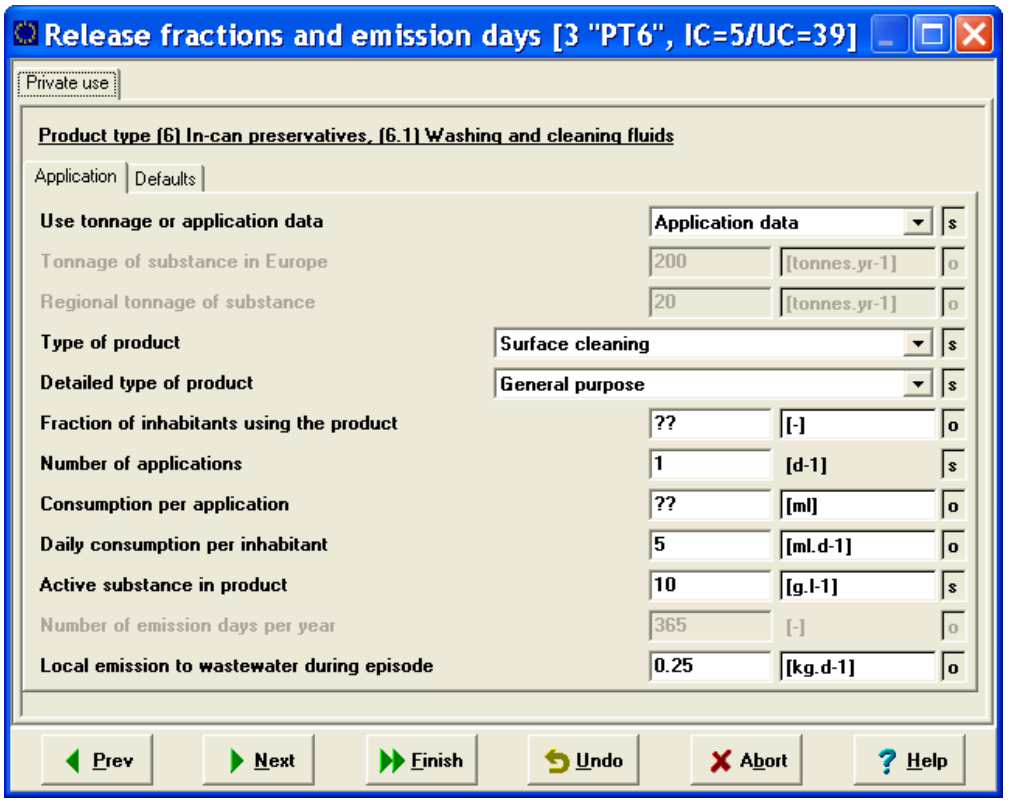


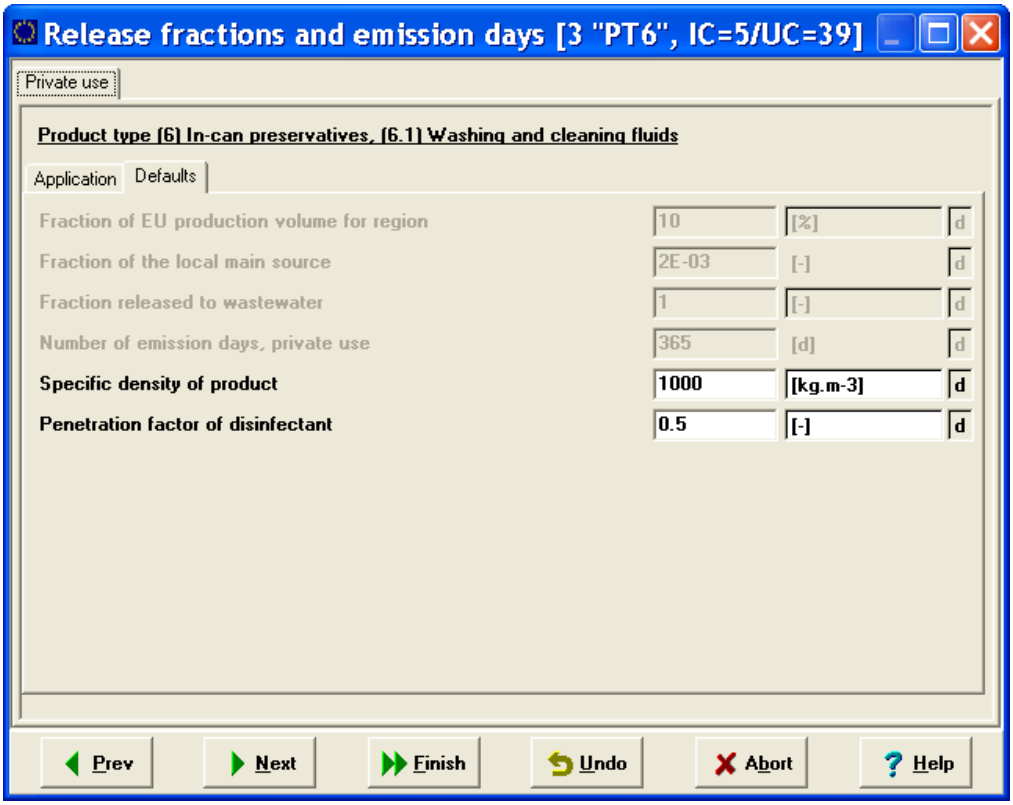
Input for PT2: Disinfectant in sanitary sector, private use





Input for PT6: In-can preservative in washing and cleaning fluids, private use





8.2 Appendix 2: Environmental Emission Scenarios for biocides used as human hygiene biocidal products (PT 1)

8.2.1 Emission scenario for calculating the releases of disinfectants used for skin and hand application in hospitals

Consumption approach (van der Aa & Balk 2004)

Variable/parameter	Unit	Symbol	Default	S/D/O/P
Input				
A) Number of beds in model hospital	[-]	Nbedspres	400	D
Occupancy rate	[-]	Foccup	0.75	D
B) Number of occupied beds in model hospital	[-]	Nbedsoccup	300	D
Fraction released to wastewater	[-]	Fwater	1	D
C) Consumption of active ingredient per bed	[g.d-1]	Qsubstpres_bed	15	P
D) Consumption of active ingredient per occupied bed	[g.d-1]	Qsubstoccup_bed	20	P
Output				
Emission rate to wastewater	[kg.d-1]	Elocalwater		
Model calculations				
A + C) Elocalwater = Nbedspres * Qsubstpres_bed * 0.001 * Fwater				6.00
A + D) Elocalwater = Nbedspres * Foccup * Qsubstoccup_bed * 0.001 * Fwater				6
B + C) Elocalwater = Nbedsoccup * Qsubstpres_bed * Foccup * 0.001 * Fwater				3.375
B + D) Elocalwater = Nbedsoccup * Qsubstoccup_bed * 0.001 * Fwater				6

Tonnage approach (van der Aa & Balk, 2004)

Variable/parameter	Unit	Symbol	Default	S/D/O/P
Input				
A) Relevant tonnage in EU for this application	[tonnes.yr-1]	TONNAGE	200	S
B) Relevant tonnage in the region for this application	[tonnes.yr-1]	TONNAGEreg	20	O
Fraction for the region		$Fprodvol_{reg}$	0.1	D
A + B)				
Fraction of the main source (STP)	[-]	Fmainsource	0.007	D
Fraction released to wastewater	[-]	F_{water}	1	D
Number of emission days for application	$[d.yr^{-1}]$	Temission	365	D
Output				
Emission rate to wastewater	$[kg.d^{-1}]$	$Elocal_{water}$		
Intermediate calculations				
B) Relevant tonnage in the region for this application (tonnes.yr-1)				
TONNAGEreg = Fprodvolreg * TONNAGE				20
End calculations				
A + B)				
Elocalwater = TONNAGEreg * 1000 * Fmainsource * Fwater / Temission				**0.38**

Calculation of break-even point

Tonnage: Elocalwater = TONNAGEreg * 1000 * Fmainsource * Fwater / Temission

Consumption: Elocalwater = Nbedspres * Qsubstpres_bed * 0.001 * Fwater

⇨ TONNAGEreg * 1000 * Fmainsource ~~* Fwater~~ / Temission = Nbedspres * Qsubstpres_bed * 0.001 * ~~Fwater~~

⇨ TONNAGEreg * 1000 * Fmainsource / Temission = Nbedspres * Qsubstpres_bed * 0.001

⇨ **TONNAGEreg = Nbedspres * Qsubstpres_bed * 0.001 * Temission / (1000 * Fmainsource) = 313 t/a**

8.3 Appendix 3: Emission Scenario Document for PT 2: Private and public health area disinfectants and other biocidal products (sanitary and medical sector)

8.3.1 Emission scenario for calculating the releases of disinfectants used for sanitary purposes

Consumption approach (van der Poel, 2001)

Parameters	Nomenclature	Value	Unit	Origin
Input				
Number of inhabitants feeding one STP	*Nlocal*	10000	[cap]	D A)
Fraction released to wastewater	*F4,water* B)	1	[-]	D
Concentration of active substance in biocidal product	*Cform*	*0.01*	[kg.l-1]	S
Consumption per capita				
General purpose (tiles, floors, sinks)	*Vform*	0.005	[l.cap-1.d-1]	D
Lavatory	*Vform*	0.002	[l.cap-1.d-1]	D
Fraction of substance disintegrated during or after application (before release to the sewer system)	*Fdis*	0	[-]	D
Penetration factor of disinfectant	*Fpenetr*	0.5	[-]	D
Output				
Emission rate to wastewater	*Elocal4,water* B)		[kg.d-1]	O
Calculation				
Elocal,water = Nlocal • Vform • Cform • Fpenetr • (1 - Fdis) • Fwater				**0.25**

Tonnage approach (van der Poel, 2001)

Parameters	Nomenclature	Value	Unit	Origin
Input				
A) Relevant tonnage in the EU for this application	*TONNAGE A)*	400	[t.yr^{-1}]	S
Fraction for the region	*Fprodvolreg*	0.1	[-]	D
B) Relevant tonnage in the region for this application	*TONNAGEreg A)*	40	[t.yr^{-1}]	S/O
A + B)				
Fraction of the main source (sewage treatment plant - STP)	*Fmainsource4* B)	0.002	[-]	D
Fraction of substance disintegrated during or after application (before release to the sewer system)	*Fdis*	0	[-]	D
Fraction released to wastewater	*F4,water* B)	1	[-]	D
Number of emission days for life cycle stage 4 (private use)	*Temission4* B)	365	[d.yr^{-1}]	D
Output				
Emission rate to wastewater	*Elocal4,water* B)		[kg.d^{-1}]	O
Intermediate calculation				
B) Relevant tonnage in the region for this application				
TONNAGEreg = Fprodvolreg • TONNAGE [t.yr-1]				40
End calculation				
A + B)				
Elocal,water = TONNAGEreg • 1,000 • Fmainsource • Fwater / Temission				**0.219**

Calculation of break-even point

Tonnage: $Elocal_{,water} = TONNAGEreg \cdot 1{,}000 \cdot Fmainsource \cdot F_{water} / Temission$

Consumption: $Elocal_{,water} = Nlocal \cdot Vform \cdot Cform \cdot Fpenetr \cdot F_{water}$

⇨ TONNAGEreg • 1,000 • Fmainsource • ~~Fwater~~ / Temission = Nlocal • Vform • Cform • Fpenetr • (1 - Fdis) • ~~Fwater~~

⇨ TONNAGEreg • 1,000 • Fmainsource / Temission = Nlocal • Vform • Cform • Fpenetr

⇨ **TONNAGEreg = Nlocal•Vform•Cform•Fpenetr•Temission / (1,000•Fmainsource) = 45.625 t/a**