**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**
**WASHINGTON, D.C. 20460**

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

**MEMORANDUM**

**16-DEC-2019**

**SUBJECT:** **Naphthalene Acetates:** Draft Human Health Risk Assessment for Registration Review.

**PC Codes:** 056001, 056002, 056003, 056004, 056007, 056008
**Decision No.:** 554023
**Petition No.:** N/A
**Risk Assessment Type:** Single Chemical Aggregate
**TXR No.:** N/A

**MRID No.:** N/A

**DP Barcode:** D453612

**Registration No.:** Numerous
**Regulatory Action:** Registration Review
**Case No.:** 0379
**CAS No.:** 86-86-2, 86-87-3, 15165-79-4, 25545-89-5, 61-31-4, 2122-70-5
**40 CFR:** §180.155

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The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. As part of Registration Review, the Pesticide Re-evaluation Division (PRD) of the Office of Pesticide Programs (OPP) has requested that HED complete a Draft Registration Review Risk Assessment (DRA) for naphthalene acetates. This document contains HED's DRA to support registration review. The hazard characterization and endpoint selection were provided by Yung Yang; the occupational and residential exposure assessments were provided by Monica Hawkins; and the residue chemistry, dietary, and aggregate risk assessments were provided by Amelework Habtemichael. The drinking water assessment was provided by Zoe Ruge of the Environmental Fate and Effects Division (EFED).

The most recent human health risk assessment was completed in 2018 (Memo, B. Cropp-Kohlligian *et al.*, 03-DEC-2018, D445386). The following risk assessment updates have been made:

- The registered residential uses of naphthalene acetates (NAA) have been reevaluated using the revised Standard Operating Procedures for Residential Pesticide Exposure Assessment (Residential SOPs);
- An aggregate exposure assessment was completed, including updated residential exposure estimates;
- A quantitative spray drift assessment was conducted; and
- An occupational exposure assessment for the registered uses was completed reflecting recent updates to the NAA risk assessment points of departure, HED's SOPs, and policy changes for body weight assumptions.

A summary of the findings and an assessment of human risk resulting from the registered uses of naphthalene acetates are provided in this document.

## Table of Contents

## 1.0 Executive Summary

1-Naphthaleneacetic acid, its salts, ester, and acetamide, are plant growth regulators which are collectively referred to as naphthalene acetates and hereafter will be referred to as NAA. They are assessed as a single group because they are structurally related, are metabolized to the acid form, and are eliminated from the body as glycine and glucuronic acid conjugates. NAA products are used to stimulate growth, delay flower induction and leaf drop, prevent preharvest fruit drop, thin fruit, and control sprout formation. NAA is currently registered for use on turf, various orchard and fruit crops and ornamentals as well as commercial and on-farm seed treatment. Registered formulations include wettable powder, flowable concentrate, emulsifiable concentrate, soluble concentrate, and liquid ready-to-use. Products registered for thinning and stop drop are applied using airblast, ground, and aerial equipment. Formulations for control of sprout formation containing NAA are applied by hand-held equipment. NAA products are also applied as a dilute root dip or soil drench with a dip tank and drench equipment.

The NAA registered labels require that applicators and handlers wear baseline attire (i.e., long-sleeved shirts, long pants, shoes, and socks) and chemical-resistant gloves. Additional personal protective equipment (PPE) such as protective eyewear is also listed on several labels.

Tolerances for residues of these naphthalene acetates, measured as 1-NAA (free and conjugated) are currently established in/on a number of commodities ranging from 0.01 ppm to 2.0 ppm (40 CFR §180.155).

The toxicology database is adequate to characterize the toxicity of the NAA. The Hazard and Science Policy Council (HASPOC) recommended that a neurotoxicity battery (acute and subchronic neurotoxicity) and immunotoxicity study are not required; however, an inhalation study is required.

The major target organs were the liver and stomach following subchronic and chronic oral exposure (dogs and rats). In addition to the liver and stomach, the lungs of rats (focal alveolar macrophages) and mice (lung adenomas) were affected following oral exposure. Repeated oral exposure also elicited decreased body weights and body weight gains accompanied by decreased food consumption. Overall, NAA sodium salt was the most toxic form in subchronic and chronic studies. In contrast to oral exposures, repeated dermal exposure to NAA elicited point of contact toxicity in rats; however, produced no evidence of systemic toxicity up to the limit dose.

There is no concern of increased qualitative or quantitative sensitivity/susceptibility following *in utero* exposure to NAA in either the rat or rabbit developmental toxicity studies or following *in utero* and/or post-natal exposure to NAA in the two-generation reproduction study in rats. There is no evidence of neurotoxicity or immunotoxicity in the NAA toxicity database. The risk assessment team recommends that the Food Quality Protection Act (FQPA) Safety Factor be reduced to 1X. However, a 10X database uncertainty factor is applied for inhalation assessment to account for the lack of a route specific inhalation study.

Carcinogenicity studies of NAA acetamide in mice and NAA sodium salt in rats and mice were considered adequate for the evaluation of the carcinogenicity of the NAA group. In these three

studies the tested NAA compounds were not carcinogenic in mice or rats. All mutagenicity studies were negative.

The NAA group has low acute toxicity via the oral, inhalation and dermal routes of exposure (Toxicity Category III or IV). NAA are not a skin irritant (Toxicity Category IV) or a dermal sensitizer. However, eye irritation was severe in animals exposed to naphthaleneacetic acid and NAA sodium salt products (Toxicity Category I), while exposure to NAA ethyl ester and NAA acetamide led to mild, transient irritation (Toxicity Category IV).

An acute reference dose has not been established for either the general population or for females 13-49 years of age since there were no appropriate toxicological effects attributable to a single exposure (dose) in the available toxicity studies. For chronic dietary assessment, a co-critical subchronic and chronic oral toxicity studies in dogs is selected with a NOAEL of 25 mg/kg/day and a LOAEL of 75 mg/kg/day based on gross and histopathologic changes in stomach (slight to moderate necrosis of fundus and pyloric epithelium), and sinusoidal histiocytosis in livers in males. The same co-critical subchronic and chronic oral toxicity studies in dogs is selected for incidental oral, adult oral and inhalation assessments. A quantitative dermal risk assessment is not necessary since no systemic toxicity was observed up to the limit dose (1000 mg/kg/day) in any of the 21-day dermal toxicity study for naphthalene acid and salts (NAA sodium and salt, NAA ethyl ester, and NAA acetamide), and there is no concern for increased sensitivity/susceptibility in the rat and rabbit developmental toxicity studies or the 2-generation rat reproduction study. A total uncertainty factor of 100X (10X for interspecies extrapolation, 10X for intraspecies variation, and 1X for FQPA SF) is applied. Additional 10X database uncertainty factor ($UF_{DB}$) is applied for inhalation assessments to account for the lack of a route specific inhalation study.

The residue chemistry data for NAA are adequate, and no additional data are needed. The terminal residues of concern in plants and livestock (ruminants) are the parent compounds, 1-naphthaleneacetic acid and its conjugates, based on apple, olive, and goat metabolism studies. The residues of concern in drinking water are the parent NAA and conjugates. HED concludes that there is no reasonable expectation of quantifiable residues of NAA in livestock commodities [40 CFR §180.6(a)(3)]. No Codex or Canadian maximum residue limits (MRLs) have been established for residues of 1-naphthaleneacetic acid, its salts, ester, and acetamide on the currently registered commodities. Therefore, there are no harmonization issues at this time.

A revised dietary exposure and risk assessment was not conducted for NAA for this Registration Review since there are no changes to the endpoints, tolerance levels, and estimated drinking water concentrations (EDWCs). The previous dietary assessment assumed tolerance level residues and 100% crop treated (CT). The Environmental Fate and Effects Division (EFED) has confirmed that there were no changes to the EDWCs and the previous EDWC are adequate to cover for the registration review. An acute dietary risk assessment is not required because there were no appropriate toxicological effects attributable to a single exposure (dose) in the available toxicity studies. The previously conducted unrefined chronic dietary (food and water) exposure and risk estimates using tolerance level residues and 100% CT assumptions were below HED's level of concern (<100% of the chronic population adjusted dose (cPAD)) for the general population and all population subgroups. The chronic dietary exposure estimate for the general

population is 5.6% of the cPAD and 15% of the cPAD for all infants (<1-year-old), the most highly-exposed population subgroup.

All registered NAA product labels with residential use sites (e.g., lawns, gardens, and trees) require that handlers wear specific clothing (e.g., long-sleeved shirt/long pants) and/or use PPE. Therefore, HED has made the assumption that these products are not for homeowner use and has not conducted a quantitative residential handler assessment. Residential post-application dermal exposure was not quantitatively assessed since there is no dermal hazard for NAA and a dermal POD was not selected. All incidental oral risk estimates for children 1 to < 2 years old are greater than HED's LOC of 100 (MOEs range from 220,000 to 100,000,000).

Short-term and chronic aggregate assessments have been completed for NAA. Residential adult exposure was not quantitatively assessed; therefore, the short-term aggregate for adults is equivalent to the chronic dietary exposure and risk estimate for the most highly exposed adult population subgroup (adults 20-49 years old) and is not of concern. The resulting short-term aggregate MOE for children 1 to <2 years old (dietary plus incidental oral post-application exposure) was 1,100 and is not of concern (LOC < 100). The chronic aggregate assessment is equivalent to the chronic dietary (food and drinking water) exposure risk assessment for all population subgroups and is not of concern. No acute endpoint was identified and NAA is classified as "not likely to be carcinogenic to humans;" therefore, acute and cancer aggregate risk assessments were not conducted.

A quantitative spray drift assessment was conducted. A dermal assessment was not conducted due to lack of dermal hazard. Children's (1 to <2 years old) incidental oral risk estimates from exposure to NAA related to spray drift result in no risks of concern at the field edge for aerial, airblast, or groundboom applications.

Only occupational inhalation risks were assessed; a quantitative dermal risk assessment for dermal exposure is not required since a dermal POD was not selected for NAA. The short- and intermediate-term inhalation risk estimates for the occupational handlers are greater than HED's LOC (i.e., MOEs ≥ 1,000) at baseline attire (i.e., no respirator), except for mixing/loading/applying wettable powder formulations for mechanically pressurized handgun applications (drench/soil/ground-directed) when applying 0.0011 lb ai/gallon of NAA to orchard/vineyard (apple, pear); (MOE = 460). With the addition of PPE, such as a protection factor (PF)10 respirator, the MOEs range from 2,100 to 1,100,000,000 and are greater than HED's LOC (i.e., MOEs ≥ 1,000).

For the seed treatment uses of NAA, all of the occupational handler inhalation MOEs are greater than HED's LOC (i.e., MOEs ≥ 1,000) at baseline (i.e., no respirator) the MOEs range from 2,600,000 to 78,000,000.

Occupational post-application dermal exposure was not quantitatively assessed since a dermal POD was not selected for NAA.

Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for NAA at this time. If new policies or

procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for NAA.

The restricted entry interval (REI) listed on the existing NAA labels are based on the acute toxicity of the technical material. NAA has low acute toxicity via the oral, inhalation and dermal routes of exposure (Toxicity Category III or IV). NAA is not a skin irritant (Toxicity Category IV) or a dermal sensitizer. However, eye irritation was severe in animals exposed to naphthaleneacetic acid and NAA sodium salt products (Toxicity Category I), while exposure to NAA ethyl ester and NAA acetamide led to mild, transient irritation (Toxicity Category IV). In accordance with the Worker Protection Standard (WPS), acute Toxicity Category I chemicals require a 48-hour REI. HED recommends an REI of 48 hours for products containing the naphthaleneacetic acid and NAA sodium salt products. The currently registered NAA labels have REIs of 12, 24, or 48 hours.

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from PHED 1.1; the AHETF database; the Outdoor Residential Exposure Task Force (ORETF) database; ExpoSAC Policies 14 and 15.2 (SOPs for Seed Treatment); and the Residential SOPs (Lawns/Turf) are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[1].

## 2.0 Risk Assessment Conclusion

Risk estimates of concern have been identified for occupational handlers based on the label-required PPE. No dietary or aggregate risks of concern were identified.

## 2.1 Data Deficiencies/Data Needs

An analytical reference standard for 1-napthaleneacetic acid (1-NAA) is currently available in the EPA National Pesticide Standards Repository (NPSR) and has an expiration date of 11/5/2020; however, analytical standards for NAA salts; NAA acetamide, NAA potassium salt, NAA sodium salt, NAA ammonium salt and NAA ethyl ester should be submitted to National Pesticide Repository. For the mailing address information, see Appendix H.

## 2.2 Tolerance Considerations

### 2.2.1 Enforcement Analytical Method

A high-performance liquid chromatography (HPLC) method using fluorescence detection (Method NAA-AM-001) for apples and pears and a similar method for olives and olive oil

1 https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure

(Method NAA-AM-002) has been previously submitted for determination of NAA in plant commodities. These methods include extraction with water and incorporate a basic hydrolysis step to release bound residues. These methods do not use benzene or diazomethane which are being discouraged by the Agency for safety reasons. These methods have been subjected to successful independent laboratory validations. Acceptable recoveries were obtained from apples, olives and olive oil fortified with NAA at the method LOQ (0.01 ppm) and at 1.0 ppm. These methods are suitable for enforcement.

### 2.2.2 Recommended & Established Tolerances

The tolerance expression for NAA in 40 CFR §180.155 reflects the S. Knizner memo (HED Interim Guidance on Tolerance Expressions, 27-MAY-2009) and does not need to be updated as a part of Registration Review. However, HED recommends that the tolerance for residues in rambutan be updated to be consistent with the Organization for Economic Co-Operation and Development (OECD) rounding classes. HED's recommendation for a tolerance revision of NAA on the commodity is outlined in Table 2.2.2.

**Table 2.2.2. Tolerance Summary for NAA**

| Commodity | Established/Proposed Tolerance (ppm) | Recommended Tolerance (ppm) | Comments; *Correct Commodity Definition* |
|---|---|---|---|
| *40 CFR §180.155(a)* | | | |
| **Rambutan** | 2.0 | 2 | Corrected value to be consistent with OECD rounding classes |

### 2.2.3 International Harmonization

No Codex or Canadian maximum residue limits (MRLs) have been established for residues of 1-naphthaleneacetic acid, its salts, ester, and acetamide on the currently registered commodities. Therefore, there are no harmonization issues at this time. For the MRL summary, see appendix G.

## 2.3 Label Recommendations

### 2.3.1 Recommendation from Residue Reviews

None.

### 2.3.2 Recommendation from Occupational/Residential Assessment

Risk estimates of concern have been identified for occupational handlers based on the label-required PPE.

HED recommends that PRD ensure that the proper REIs are listed on the registered labels considering the acute toxicity of NAA. In accordance with the WPS, acute Toxicity Category I chemicals require a 48-hour REI. The currently registered labels have REIs of 12, 24, or 48 hours. The REI should be changed to 48 hours for products containing the naphthaleneacetic

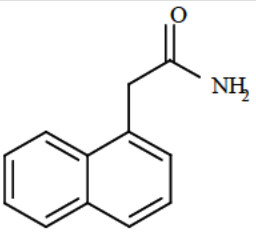
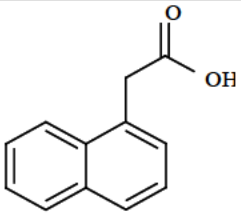
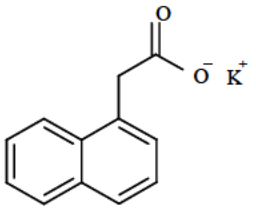
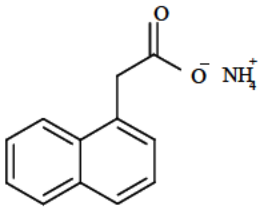
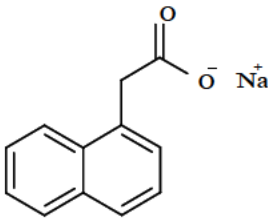
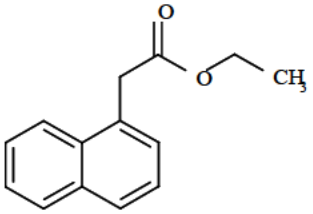
acid and NAA sodium salt products.

## 3.0 Introduction

## 3.1 Chemical Identity

The nomenclature for NAAs is provided in Table 3.1.

**Table 3.1. NAA Nomenclature**

| | | |
|---|---|---|
| Chemical structure |  |  |
| Common name | NAA acetamide | 1-NAA |
| Molecular Formula | $C_{12}H_{11}NO$ | $C_{12}H_{10}O_2$ |
| Molecular Weight | 185.23 | 186.20 |
| IUPAC name | 2-(1-naphthyl)acetamide | 2-(1-naphthyl)acetic acid |
| CAS name | 1-naphthaleneacetamide | 1-naphthaleneacetic acid |
| CAS # | 86-86-2 | 86-87-3 |
| PC Code | 056001 | 056002 |
| Chemical structure |  |  |
| Common name | NAA potassium salt or NAA-K | NAA ammonium salt |
| Molecular Formula | $C_{12}H_{10}O_2K$ | $C_{12}H_{13}NO_2$ |
| Molecular Weight | 224.31 | 203.24 |
| IUPAC name | potassium-2(1naphthyl)acetate | ammonium-2(1naphthyl)acetate |
| CAS name | 1-naphthalnene acetic acid, potassium salt | 1-naphthaleneacetic acid, ammonium salt |
| CAS # | 15165-79-4 | 25545-89-5 |
| PC Code | 056003 | 056004 |
| Chemical structure |  |  |

| Table 3.1. NAA Nomenclature | | |
|---|---|---|
| Common name | NAA sodium salt | NAA ethyl ester |
| Molecular Formula | $C_{12}H_{10}O_2Na$ | $C_{14}H_{14}O_2$ |
| Molecular Weight | 208.2 | 214.26 |
| IUPAC name | sodium-2(1naphthyl)acetate | ethyl-2(1naphthyl)acetate |
| CAS name | 1-Naphthaleneacetic acid, sodium salt | 1-Naphthaleneacetic acid, ethyl ester |
| CAS # | 61-31-4 | 2122-70-5 |
| PC Code | 056007 | 056008 |

## 3.2 Physical/Chemical Characteristics

A detailed description of the physicochemical properties of the naphthalene acetates are provided in Appendix B. Based on the limited available data, 1-naphthaleneacetic acid and its ester exhibit relatively low or no solubility in water and higher solubility in organic solvents whereas the sodium salt is highly soluble in water and insoluble in organic solutions. 1-Naphthaleneacetic acid has a relatively high vapor pressure (0.3 mmHg), but its salts and esters have lower vapor pressures. 1-Naphthaleneacetic acid is relatively mobile but short lived in terrestrial and aquatic environments. 1-Naphthaleneacetic acid do not present significant concerns for bioaccumulation based on measured bioconcentration factors.

## 3.3 Pesticide Use Pattern

NAA products are used to stimulate growth, delay flower induction and leaf drop, prevent preharvest fruit drop, thin fruit, and control sprout formation. NAA is currently registered for use on turf, various orchard and fruit crops and ornamentals as well as commercial and on-farm seed treatment of potatoes. Registered formulations include wettable powder, flowable concentrate, emulsifiable concentrate, soluble concentrate, and liquid ready-to-use. Thinning and stop drop formulations containing NAA are applied using airblast, ground, and aerial equipment. Formulations for control of sprout formation containing NAA are applied by hand-held equipment. NAA products are also are applied as a dilute root dip or soil drench with a dip tank and drench equipment.

The Biological and Economic Analysis Division (BEAD) provided a comprehensive review of all the currently registered NAA labels. HED has relied on this information along with the review of several labels to populate the maximum single application rates in the use profile table for the NAA products to perform the occupational and residential exposure assessment for Registration Review. Table F.1. in Appendix F provides a list of representative use sites that capture the single maximum application rate for each registered use site. For the purposes of this risk assessment, HED only assessed the single maximum application rates for NAA. Table F.1. in Appendix F summarizes detailed information including use site, type of application equipment, formulation, and required PPE. The NAA registered labels require that applicators and handlers wear baseline attire (i.e., long-sleeved shirts, long pants, shoes, and socks) and chemical-resistant gloves. Additional PPE, such as protective eyewear, is listed on several labels.

### 3.4 Anticipated Exposure Pathways

Humans may be exposed to NAA in food and drinking water, since NAA may be applied directly to growing crops. There are post-application exposures anticipated for workers re-entering treated fields. Exposure to residential handlers is not expected from currently registered uses; however, post-application residential exposures may occur. Occupational exposures are expected from the application (dermal and inhalation) of NAA and its salts. This risk assessment considers all of the aforementioned exposure pathways based on the existing uses of NAA, particularly for the aggregate assessment.

### 3.5 Considerations of Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," (http://epa.gov/compliance/ej/resources/policy/exec_order_12898.pdf). As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey/What We Eat in America, (NHANES/WWEIA), are used in pesticide risk assessments for all registered food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas post-application are evaluated. Spray drift can also potentially result in post-application exposure and it was considered in this analysis. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

## 4.0 Hazard Characterization/Assessment

### 4.1 Toxicology Studies Available for Analysis

The Agency has determined that required toxicity testings on any form should serve for all members of this group of chemicals. The toxicity database for NAA is adequate for a full hazard evaluation except a subchronic inhalation toxicity study. The HASPOC has recommended that neurotoxicity battery (acute and subchronic) and immunotoxicity studies are not required; however, a subchronic inhalation toxicity study is required (K. Rury, 16-OCT-2012, TXR 0056465; J. Leshin, 21-MAY-2014, TXR 0056968).

As part of registration review for NAA, a broad survey of the literature was conducted to identify

studies that report toxicity following exposure to NAA via exposure routes relevant to human health pesticide risk assessment not accounted for in the agency's NAA toxicology database. The search strategy employed terms restricted to the name of the chemical plus any common synonyms, and common mammalian models to capture as broad a list of publications as possible for the chemical of interest. The search strategy returned 28 studies for 1-Naphthaleneacetic acid and 2 studies for 1-Naphthaleneacetamide from the literature. During the title/abstract and/or full text screening of these studies, none of the studies were deemed to contain potentially relevant information (either quantitative or qualitative) for the NAA human health risk assessment. Appendix A.3 has detailed information regarding the literature review.

The toxicology studies for NAA are summarized in Appendix A.1 and A.2. The database includes the following studies:

- Subchronic: 28-day dermal toxicity (rat); 90-day oral toxicity (rat and dog)
- Developmental toxicity: developmental toxicity (rat and rabbit)
- Reproduction: 2-generation reproduction (rat)
- Chronic: chronic oral toxicity/carcinogenicity (rat); carcinogenicity (mouse); one-year oral toxicity (dog)
- Other: acute toxicity battery; mutagenicity battery; metabolism (rat)

## 4.2 Absorption, Distribution, Metabolism and Excretion (ADME)

The absorption, distribution metabolism and excretion of NAA were studied in rats. In one study, rats were given either a single 1 or 100 mg/kg bw oral dose, or a 14-day repeated dose (1 mg/kg/day) of [$^{14}$C] ring labeled NAA acetamide. NAA acetamide was readily absorbed and excreted within 36 hours. Recovery of administered radioactivity was 97-101%. Urinary excretion accounted for 66-74% of the administered radioactivity for single and repeat doses. Repeat doses did not appreciably affect the absorption/excretion processes. Excretion via the feces accounted for the remainder of the administered radioactivity in all treatment groups. Urinary metabolites revealed amide cleavage followed by glycine conjugation with the glycine conjugate being the major metabolite of the low and repeat doses (14-47%). The glucuronide conjugate was also a major metabolite at the low doses (4.5-7%). For feces, the major metabolite detected was the dihydrodiol of NAA acetamide (4-11%). Parent compound was detected at low concentrations (1-2% of administered) only in feces.

In another study, rats were given either a single 1 or 100 mg/kg bw oral dose, or a 14-day repeated dose (1 mg/kg/day) of [$^{14}$C] ring labeled NAA ethyl ester. Recovery of administered radioactivity was 99-101%. NAA ethyl ester was readily absorbed and excreted within 36 - 48 hours following single and repeat doses. Urinary excretion accounted for 68-85% of the administered radioactivity following single or multiple oral low doses and 62-78% following a single high dose. Excretion via the feces accounted for the remainder of the administered radioactivity excreted by all treatment groups. At the high dose, glucuronide conjugation appeared to play a more important role following ester cleavage. Parent compound was detected at low concentrations (0.5-5% of administered) only in feces. For both studies, excretory patterns exhibited no gender-related variability for the low dose groups and only minor gender difference at the high dose. Excretion patterns of the high-dose group reflected delayed absorption. Tissue burdens of parent and metabolites were very low at termination for both

studies. Most components in the matrices examined (urine and feces) were adequately quantified and characterized.

The metabolism studies of the acid and its acetamide and the ethyl ester in animals provide supporting evidence that the toxicity of the naphthalene acetates would be similar since all are metabolized to the acid form and eliminated from the body as glycine and glucuronic acid conjugates within 36 to 48 hours of initial exposure.

### 4.2.1 Dermal Absorption

A dermal penetration study is not available. However, a quantitative dermal risk assessment is not necessary since no systemic toxicity was observed up to the limit dose (1000 mg/kg/day) in any of the 21-day dermal toxicity studies for naphthalene acid and salts (NAA sodium and salt, NAA ethyl ester, and NAA acetamide). There is no concern of increased qualitative or quantitative sensitivity/susceptibility in either the rat or rabbit developmental toxicity studies or in the two-generation reproduction study in rats.

## 4.3 Toxicological Effects

The major target organs were the liver and stomach following subchronic and chronic oral exposure (dogs and rats). Hepatic insult was characterized by inflammation of the tissues around the bile duct, hepatocyte degeneration, sinusoidal histiocytosis, and increased liver weight accompanied by elevated liver enzyme levels, necrosis, extramedullary hematopoiesis, and mononuclear/mixed cell infiltration. The stomach and gastrointestinal tract effects included necrosis of fundus and pyloric epithelium mucosal gland dilation, stomach irritation, ulcerative duodenitis, acute or erosive gastritis, emesis and soft feces. Dogs were the most susceptible mammal to oral subchronic and chronic exposures exhibiting primarily liver and stomach injury. In addition to the liver and stomach, the lungs of rats (focal alveolar macrophages) and mice (lung adenomas) were affected following oral exposure. Repeated oral exposure also elicited decreased body weights and body weight gains accompanied by decreased food consumption. Overall, NAA sodium salt was the most toxic form in subchronic and chronic studies.

In contrast to oral exposures, repeated dermal exposure to the NAA elicited point of contact toxicity in rats, but produced no evidence of systemic toxicity up to the limit dose. NAA ethyl ester administered dermally inducing epidermal hyperplasia and hyperkeratosis, sebaceous gland hyperplasia, and dermal inflammation. Systemic toxicity was not a consequence of dermal exposure to any of the tested naphthalene acetates. None of the naphthalene acetates exhibited dermal irritant properties following acute exposure indicating that skin irritation develops from repeated exposure.

Developmental and offspring toxicity was linked to NAA sodium salt exposure but was not a common observation for the entire NAA group. In the rat developmental study, slightly decreased fetal weight (↓4-8%) and minor skeletal changes were observed at the highest dose where compromised maternal health indicative by statistically significant decreases of maternal body weight in mid- and high-dose groups were observed, although the decreases (<10%) were not considered biologically significant. In the rabbit developmental study, skeletal defects and

variants were observed in rabbit fetuses at same doses that also compromised maternal health. No developmental toxicity was observed in other chemicals of the NAA group. In the 2-generation reproduction study, offspring toxicity from NAA sodium salt manifested as reduced litter survival and pup weight throughout lactation in two generations. These effects coincided with reduced body weight in both parental generations indicating the adults and their young were equally susceptible to NAA sodium salt.

Carcinogenicity studies of NAA acetamide in mice and NAA sodium salt in rats and mice were considered adequate for the evaluation of the oncogenicity of the NAA group. In these three studies the tested NAA compounds were not carcinogenic in mice or rats. All mutagenicity studies were negative. There is no evidence of neurotoxicity and immunotoxicity in the toxicology database for NAA.

NAA have low acute toxicity via the oral, inhalation and dermal routes of exposure (Toxicity Category III or IV). NAA are not a skin irritant (Toxicity Category IV) or a dermal sensitizer. However, eye irritation was severe in animals exposed to naphthaleneacetic acid and NAA sodium salt products (Toxicity Category I), while exposure to NAA ethyl ester and NAA acetamide led to mild, transient irritation (Toxicity Category IV).

## 4.4 Safety Factor for Infants and Children (FQPA Safety Factor)[2]

The risk assessment team recommends that the FQPA Safety Factor be reduced to 1X because (1) the toxicology database for NAA is adequate with regard to FQPA consideration, including the required developmental and reproductive toxicity studies; (2) no signs of neurotoxicity were observed in the database; (3) there is low concern for qualitative or quantitative susceptibility in the rat and rabbit developmental toxicity studies or the 2-generation rat reproduction study (4) there are no residual uncertainties identified in the exposure databases; (5) A 10X database uncertainty factor (FQPA $SF_{DB}$) is retained for inhalation assessment to account for the lack of a route specific inhalation study.

### 4.4.1 Completeness of the Toxicology Database

The toxicity database for NAA is adequate for a full hazard evaluation and is considered adequate to evaluate risks to infants and children. There are acceptable developmental toxicity studies in the rat and rabbit and an acceptable reproduction study in the rat. The HASPOC recommended that the immunotoxicity study and neurotoxicity battery are not required at this time. However, the HASPOC recommended that the subchronic inhalation study is required and a 10X database uncertainty factor ($UF_{DB}$) is applied for inhalation assessments to account for the lack of a route specific study.

[2] HED's standard toxicological, exposure, and risk assessment approaches are consistent with the requirements of EPA's children's environmental health policy (*https://www.epa.gov/children/epas-policy-evaluating-risk-children*).

### 4.4.2 Evidence of Neurotoxicity

There are no neurotoxicity studies available for the current assessment; however, no signs of neurotoxicity or neuropathology were reported in the submitted chronic and subchronic studies. The HASPOC recommended that acute and subchronic neurotoxicity studies are not needed at the present time (K. Rury, 16-OCT-2012, TXR 0056465).

### 4.4.3 Evidence of Sensitivity/Susceptibility in the Developing or Young Animal

There is no concern for increased qualitative or quantitative increased susceptibility in the rat and rabbit developmental toxicity studies or the 2-generation rat reproduction study. Developmental and offspring toxicity was linked to NAA sodium salt exposure but was not a common observation for the entire NAA group. In the rat developmental study, slightly decreased fetal weight (↓4-8%) and minor skeletal changes were observed at the highest dose where compromised maternal health indicative by statistically significant decreases of maternal body weight in mid- and high-dose groups were observed, although the decreases (<10%) were not considered biologically significant. In the rabbit developmental study, skeletal defects and variants were observed in rabbit fetuses after exposure to NAA sodium salt. These effects only occurred at doses that also compromised maternal health. No developmental toxicity was observed in other chemicals of the NAA group. In the 2-generation reproduction study, offspring toxicity from NAA sodium salt manifested as reduced litter survival and pup weight throughout lactation in two generations. These effects coincided with reduced body weight in both parental generations indicating the adults and their young were equally susceptible to NAA sodium salt. There is low concern (and no residual uncertainty) for pre- and/or postnatal toxicity resulting from exposure to the NAA because clear NOAELs and LOAELs were established for the developmental and offspring effects and the POD for all exposure scenarios is protective of these effects.

### 4.4.4 Residual Uncertainty in the Exposure Database

There are no residual uncertainties in the exposure database. The residential exposure assessment incorporates conservative assumptions in the assessment of post-application (incidental oral) exposure assessment for children and will not underestimate actual exposure. The dietary risk assessment is conservative and will not underestimate dietary exposure to NAA.

## 4.5 Toxicity Endpoint and Point of Departure

### 4.5.1 Dose-Response Assessment

Toxicity endpoints and PODs for dietary (food and water), occupational, and residential exposure scenarios have not changed since the last assessment (B. Cropp-Kohlligian *et al.*, 03-DEC-2018, D445386) and are summarized below and in Table 4.5.4.1 and 4.5.4.2.

Acute Dietary Endpoint for the General Population and Females 13-49 Years of Age: An acute reference dose has not been established for either the general population or for females 13-49

years of age since there were no appropriate toxicological effects attributable to a single exposure (dose) in the available toxicity studies.

Chronic Dietary Endpoint for the General Population and Females 13-49 Years of Age: A co-critical subchronic and chronic oral toxicity studies in dogs is selected with a NOAEL of 25 mg/kg/day and a LOAEL of 75 mg/kg/day based on gross and histopathologic changes in stomach (slight to moderate necrosis of fundus and pyloric epithelium), and sinusoidal histiocytosis in livers in males. In the subchronic toxicity study in dogs (MRID 42983801), the NOAEL is 25 mg/kg/day with a LOAEL of 150 mg/kg/day based on lesions of the gastrointestinal tract (ulcerative duodenitis and acute or erosive gastritis) and hypocellularity of the bone marrow. In the chronic toxicity study in dogs (MRID 43744201), the NOAEL is 15 mg/kg/day and the LOAEL is 75 mg/kg/day based on gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers in males. While the chronic toxicity study in dogs has a lower NOAEL for stomach lesions, this was the result of dose selection and the subchronic study in dogs provides a clear NOAEL that is protective of stomach lesions for both durations since the effects and severity were similar between the two studies and there was no evidence of progression with increased exposure duration. An uncertainty factor of 100X (10X for interspecies extrapolation, 10X for intraspecies variation, and 1X for FQPA SF) is applied. The chronic reference dose (cRfD) and chronic population adjusted dose (cPAD) is 0.25 mg/kg/day.

Incidental Oral and Adult Oral Exposure (Short-Term): A co-critical subchronic and chronic oral toxicity studies in dogs is selected with a NOAEL of 25 mg/kg/day and a LOAEL of 75 mg/kg/day based on gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers in males. This study is appropriate for the route and duration of exposure as well as protective of the populations of concern (children and adults) because offspring toxicity from NAA sodium salt manifested as reduced litter survival and pup weight throughout lactation in two generations were observed at higher doses (210 mg/kg/day). An uncertainty factor of 100X (10X for interspecies extrapolation, 10X for intraspecies variation, and 1X for FQPA SF) is applied. LOC=100.

Dermal Exposure (Short- and Intermediate-Term): A quantitative dermal risk assessment is not necessary since no systemic toxicity was observed up to the limit dose (1000 mg/kg/day) in any of the 21-day dermal toxicity study for naphthalene acid and salts (NAA sodium and salt, NAA ethyl ester, and NAA acetamide). There is no concern of increased qualitative or quantitative sensitivity/susceptibility following *in utero* exposure to NAA in either the rat or rabbit developmental toxicity studies or following *in utero* and/or post-natal exposure to NAA in the two-generation reproduction study in rats.

Inhalation Exposure (Short and Intermediate-Term): No data from a route-specific inhalation study is available other than an acute inhalation study. The HASPOC has recommended that a subchronic inhalation toxicity study is required for inhalation assessments. For inhalation assessment, a co-critical subchronic and chronic oral toxicity studies in dogs is selected for inhalation assessment with a NOAEL of 25 mg/kg/day and a LOAEL of 75 mg/kg/day based on gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers in males. A total uncertainty factor of 1000X (10X for interspecies extrapolation, 10X for intraspecies variation, and 10X for database uncertainty) is applied. A 10X database uncertainty factor

($UF_{DB}$) is applied for inhalation assessments to account for the lack of a route specific study. LOC =1000.

### 4.5.2 Recommendations for Combining Exposure Routes

According to FQPA (1996), when there are potential residual exposures to a pesticide, a risk assessment must consider exposures from 3 major routes: oral, dermal, and inhalation. PODs for the oral and inhalation routes are derived from same studies and endpoints; therefore, oral and inhalation routes can be combined. No dermal risk assessment is needed since there is no dermal hazard identified.

### 4.5.3 Classification of Carcinogenic Potential

A published NCI (National Cancer Institute) carcinogenicity study of NAA acetamide in mice, a guideline chronic/oncogenicity study of NAA sodium salt in rats, and a chronic/carcinogenicity study of NAA sodium salt mice were considered adequate for the evaluation of the carcinogenicity of the NAA group. In these three studies, the tested NAA compounds were not carcinogenic in mice or rats. There is no evidence of mutagenicity. The cancer classification is "Not Likely to be Carcinogenic to Humans".

### 4.5.4 Summary of Points of Departure Used in Risk Assessment

Toxicological doses/endpoints selected for NAA risk assessment are provided in Tables 4.5.4.1 and 4.5.4.2.

**Table 4.5.4.1. Summary of Toxicological Endpoints of NAA for Use in Dietary and Non-Occupational Human Health Risk Assessments**

| Exposure/Scenario | Point of Departure | Uncertainty Factor/ FQPA SF | RfD, PAD, LOC for Risk Assessment | Study and Toxicological Effects |
|---|---|---|---|---|
| Acute Dietary (all Populations) | An acute reference dose has not been established for either the general population or for females 13-49 years of age since there were no appropriate toxicological effects attributable to a single exposure (dose) in the available toxicity studies. | | | |
| Chronic Dietary (All Populations) | NOAEL= 25 mg/kg/day | $UF_A$= 10X<br>$UF_H$=10X<br>FQPA SF= 1X | cRfD = 0.25 mg/kg/day<br><br>cPAD = 0.25 mg/kg/day | Co-critical studies:<br>Subchronic oral toxicity (dog)<br>(MRID 42983801)<br>Chronic oral toxicity (dog)<br>(MRID 43744201)<br>LOAEL = 75 mg/kg/day based on gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers in males |
| Incidental and Adult Oral Short-term (1-30 Days) | NOAEL= 25 mg/kg/day | $UF_A$= 10X<br>$UF_H$=10X<br>FQPA SF= 1X | LOC for MOE < 100 | Co-critical studies:<br>Subchronic oral toxicity (dog)<br>(MRID 42983801)<br>Chronic oral toxicity (dog)<br>(MRID 43744201)<br>LOAEL = 75 mg/kg/day based on gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers in males |

| | | | | |
|---|---|---|---|---|
| Dermal<br>All Durations | A quantitative dermal risk assessment for dermal exposure is not necessary since no systemic toxicity was observed at the limit dose in a 21-day dermal toxicity study for any of the naphthalene acid and salts. There is no concern for sensitivity/susceptibility in the developing or young animal. | | | |
| Inhalation<br>Short- (1-30 days) and intermediate-term (1-6 months) | Oral<br>NOAEL= 25 mg/kg/day<br><br>Inhalation assumed equivalent to oral | $UF_A$ = 10X<br>$UF_H$ = 10X<br>FQPA $SF_{DB}$= 10X | LOC for MOE < 1000 | Co-critical studies:<br>Subchronic oral toxicity (dog)<br>(MRID 42983801)<br>Chronic oral toxicity (dog)<br>(MRID 43744201)<br>LOAEL = 75 mg/kg/day based on gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers in males. |
| Cancer | Not Likely to Be Carcinogenic to Humans | | | |

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. $UF_A$ = extrapolation from animal to human (interspecies). $UF_H$ = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. PAD = population adjusted dose (c = chronic). RfD = reference dose. FQPA $SF_{DB}$ for inhalation accounts for the lack of an inhalation study.

**Table 4.5.4.2. Summary of Toxicological Endpoints of NAA for Assessing Occupational Human Health Risk Assessments**

| Exposure Scenario[1] | Dose Used in Risk Assessment, UF | Uncertainty Factor/ FQPA SF | LOC for Risk Assessment | Study and Toxicological Effects |
|---|---|---|---|---|
| Dermal<br>Short, Intermediate, and Long-term | A quantitative dermal risk assessment for dermal exposure is not necessary since no systemic toxicity was observed at the limit dose in a 21-day dermal toxicity study for any of the naphthalene acid and salts. There is no concern for sensitivity/susceptibility in the developing or young animal. | | | |
| Inhalation<br>Short- (1-30 days) and intermediate-term (1-6 months) | Oral<br>NOAEL= 25 mg/kg/day<br><br>Inhalation assumed equivalent to oral | $UF_A$ = 10X<br>$UF_H$ = 10X<br>$UF_{DB}$ = 10X | LOC for MOE < 1000 | Co-critical studies:<br>Subchronic oral toxicity (dog)<br>(MRID 42983801)<br>Chronic oral toxicity (dog)<br>(MRID 43744201)<br>LOAEL = 75 mg/kg/day based on gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers in males. |
| Cancer | Not Likely to Be Carcinogenic to Humans | | | |

Point of Departure (POD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. $UF_A$ = extrapolation from animal to human (interspecies). $UF_H$ = potential variation in sensitivity among members of the human population (intraspecies). $UF_{DB}$= database uncertainty factor: lack of an inhalation specific study. LOC = level of concern.

## 4.6 Endocrine Disruption

As required by Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and Federal Food, Drug, and Cosmetic Act (FFDCA), EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, subchronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be

susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent reregistration decision for NAA, EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), NAA is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

EPA has developed the EDSP to determine whether certain substances (including pesticide active and other ingredients) may have an effect in humans or wildlife similar to an effect produced by a "naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." The EDSP employs a two-tiered approach to making the statutorily required determinations. Tier 1 consists of a battery of 11 screening assays to identify the potential of a chemical substance to interact with the estrogen, androgen, or thyroid (E, A, or T) hormonal systems. Chemicals that go through Tier 1 screening and are found to have the potential to interact with E, A, or T hormonal systems will proceed to the next stage of the EDSP where EPA will determine which, if any, of the Tier 2 tests are necessary based on the available data. Tier 2 testing is designed to identify any adverse endocrine-related effects caused by the substance, and establish a dose-response relationship between the dose and the E, A, or T effect.

Under FFDCA section 408(p), the Agency must screen all pesticide chemicals. Between October 2009 and February 2010, EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. A second list of chemicals identified for EDSP screening was published on June 14, 2013[3] and includes some pesticides scheduled for registration review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors.

For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[4]

## 5.0 Dietary Exposure and Risk Assessment

### 5.1 Residues of Concern Summary and Rationale

The nature of the residues of NAA in in the currently registered primary crops, rotational crops, and animals have been adequately understood. Previously residues of concern were determined by the HED risk assessment team for NAA. The terminal residues of concern in plants and ruminants are the parent compounds, 1-naphthaleneacetic acid and its conjugates, based on apple, olive, and goat metabolism studies. There are no poultry feed items associated with

3 See http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2009-0477-0074 for the final second list of chemicals.
4 http://www.epa.gov/endo/

currently registered food uses of NAA; thus, a poultry metabolism study is not required at this time (G. Otakie, 18-NOV-2003, D293239).

**Table 5.1. NAA Residues of Concern in Plants and Ruminants.**

| Matrix | | Residues of Concern | |
|---|---|---|---|
| | | For Risk Assessment | For Tolerance Expression |
| Plants | Primary and Rotational crops | NAA and Conjugates | NAA and Conjugates |
| Livestock | Ruminant | NAA and Conjugates | NAA and Conjugates |
| Drinking Water | | NAA and Conjugates | N/A |

N/A = Not Applicable

## 5.2 Food Residue Profile

Adequate residue chemistry data are available for the registration review of NAA and its salts. NAA and its salts are currently registered for use on various orchard and fruit crops and ornamental trees. Sufficient metabolism (crops and livestock), storage stability, magnitude of residue and processing data are available to support the registered uses. There are sufficient storage stability data for apples, pears and olives.

An orange processing data, as well as, data-collection method and storage stability data were submitted to fulfil the required storage stability data of NAA in/on the processed commodities of apples (or citrus fruits) and citrus processing study. These data were reviewed and deemed adequate (B. Cropp-Kohlligian, 28-NOV-2018, D448272). The registrant, AMVAC also requested a waiver for the requirement of "Olive oil" storage stability data for NAA, NAD and NAA-ET as a part of DCI requirement and proposes to use the frozen storage stability data of NAA and its salts on orange dry pulp, juice, and oil (MRID 50827801), with emphasis on the approximately 2 year storage stability data for orange can cover for other vegetables and fruit oils, including olive oil. Available data indicates that residues of NAA are relatively stable under frozen storage conditions in olives for up to 365 day (G Otakie, 06-NOV-2003, D217162). HED has reviewed the available olive RAC data and submitted orange oil processing study and concludes that the combination of the orange oil (154 days) and olive (12 months) storage stability data are adequate to validate the 10-month olive oil storage interval. HED notes that it is not necessary to extrapolate the 154 days orange oil data for a greater interval (2 years). The recoveries of the orange oil in the submitted study were 96-111% (D455451, A. Habtemichael, 16-DEC-2019).

Residues of NAA in livestock were previously tentatively classified under category 180.6(a)(3). There were no new animal studies submitted for registration review at this time. No new tolerance for citrus dried pulp was recommended based on the submitted citrus processing study and the previously established tolerance did not change; therefore, no new dietary burden calculation was conducted and the 180.6(a)(3) classification for NAA is still appropriate (i.e., no reasonable expectation of finite residues of concern in meat and milk).

## 5.3 Water Residue Profile

No new EDWCs were provided by EFED. EFED has determined in the memo:

"*Naphthaleneacetic Acid and Its Sodium, Potassium, and Ammonium Salts, Ethyl Ester, and Acetamide: Drinking Water Assessment (DWA) for Registration Review"* (Z. Ruge, 05-NOV-2019, D454904) that previously calculated EDWCs are adequate for the Registration Review (J. Melendez, 04-MAY-2015, D423410 and M. Ruhman, 21-AUG-2018, D445385).

In the previous assessment (J. Melendez, 04-MAY-2015, D423410), the Estimated Drinking Water Concentrations (EDWCs) were calculated using the Tier 1 aquatic model PRZM-GW (ground water; v.1.07) and the Tier 1 aquatic model FIRST (surface water; v.1.1.1). The maximum allowable rates were modeled for pomegranate (7.2 lb a.e./A). The resultant ground water EDWCs were 789 ppb of NAA for the acute value and 646 ppb of NAA for the chronic value, and the surface water EDWCs were 440 ppb of NAA for the acute value and 65.1 ppb of NAA for the chronic value.

In 2018 memo (M. Ruhman, 21-AUG-2018, D445385), a Drinking Water Assessment for the Section 3 New Use on Citrus and Olives was conducted which recalculated surface water EDWCs using the Tier 2 aquatic model PRZM/EXAMS (surface water; v.3.12/v.2.98.04.02) interfaced through the Pesticide in Water Calculator (version 1.52). The maximum allowable rates were modeled for pomegranate (7.2 lb a.e./A) and mandarin (0.75 lb a.e./A). The resultant surface water EDWCs were 39.4 ppb of NAA for the acute value and 0.694 ppb of NAA for the chronic value. Lower results than the 2015 EDWCs are directly related to the use of Tier 2 modeling instead of Tier 1. The ground water EDWCs did not need to be revised. Therefore, it was determined that the 2015 EDWCs still applied.

**Table 5.3. Table 1. Estimated Drinking Water Concentrations (EDWCs) for Naphthalene Acetates (J. Melendez, 04-MAY-2015, D423410)**

| DRINKING WATER SOURCE (MODEL USED) | SCENARIO (rate modeled per crop cycle) | MAXIMUM ESTIMATED DRINKING WATER CONCENTRATION (EDWC) (ppb) | |
|---|---|---|---|
| 2015 Groundwater (PRZM-GW) | WI sand (7.2 lb a.e./A/yr) | Acute | 789 |
| | WI sand (7.2 lb a.e./A/yr) | Chronic | 646 |
| 2015 Surface water (FIRST) | Index Reservoir (7.2 lb a.e./A/yr) | Acute | 440 |
| | Index Reservoir (7.2 lb a.e./A/yr) | Chronic | 65.1 |

*The abbreviations: A = acre; a.e.= acid equivalents (*i.e.*, the lbs of NAA ethyl ester, expressed as lbs of NAA acid); ppb = parts per billion (µg/L).

## 5.4 Dietary and Drinking Water Exposure and Risk

### 5.4.1 Description of Residue Data Used in Dietary Assessment

An unrefined screening-level chronic dietary (food and drinking water) exposure and risk assessment for naphthalene acetates was last conducted in 2015 (T. Morton, 18-NOV-2015, D426996) using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID), Version 3.16, which incorporates 2003-2008 food consumption data from USDA's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA). The analysis was performed to support a Section 3 request for use of NAA on pomegranate. The previous assessment assumed tolerance level residues and 100% crop treated. No quantitative acute dietary exposure risk assessment was conducted because no toxicological endpoint for acute dietary exposure was identified. Water residues were

incorporated into the DEEM-FCID food categories of "water, direct, all sources" and "water, indirect, all sources. EFED indicated that the previous drinking water assessment is adequate for registration review; therefore, the previously conducted dietary exposure (food and water) and risk assessment (T. Morton, 18-NOV-2015, D426996) for NAA is adequate for registration review.

### 5.4.2 Percent Crop Treated Used in Dietary Assessment

The 2015 dietary assessment assumed 100% crop treated for all commodities.

### 5.4.3 Acute Dietary and Drinking Water Analysis

There were no toxicological effects attributable to a single exposure (dose) of NAA observed in oral toxicity studies including the developmental toxicity studies in rats or rabbits. Therefore, a dose and an endpoint for acute dietary exposure were not identified for NAA and a quantitative acute dietary exposure assessment was not conducted.

### 5.4.4 Chronic Dietary and Drinking Water Analysis

The 2015 chronic dietary (food and drinking water) exposure and risk assessment is considered an unrefined screening-level assessment and the exposure and risk estimates are considered conservative. No population subgroup exceeds HED's level of concern. The U.S. population occupied 5.6% of the cPAD, while the most highly exposed population subgroup, all infants (<1 year old), occupied 15% of the cPAD. The exposure and risk estimates are presented in Table 5.4.6.

### 5.4.5 Cancer Dietary Risk Assessment

Naphthalene acetates is considered "not likely to be carcinogenic to humans;" therefore, quantification of human cancer risk is not required.

### 5.4.6 Summary Table

**Table 5.4.6. Summary of Chronic Dietary Exposure and Risk for Napthelene Acetates**

| Population Subgroup | cPAD (mg/kg/day) | Chronic | |
|---|---|---|---|
| | | Exposure (mg/kg/day) | % cPAD |
| General U.S. Population | 0.25 | 0.013977 | 5.6 |
| **All Infants (< 1 year old)** | | **0.036203** | **15** |
| Children 1-2 years old | | 0.022367 | 8.9 |
| Children 3-5 years old | | 0.018232 | 7.3 |
| Children 6-12 years old | | 0.012575 | 5.0 |
| Youth 13-19 years old | | 0.010202 | 4.1 |
| Adults 20-49 years old | | 0.013738 | 5.5 |
| Adults 50-99 years old | | 0.013583 | 5.4 |
| Females 13-49 years old | | 0.013701 | 5.5 |

T. Morton, 18-NOV-2015, D426996
**Population subgroup with highest exposure is in bold.**

## 6.0 Residential Exposure/Risk Characterization

Occupational and Residential Exposure Memo: M. Hawkins, 16-DEC-2019, D454588

There are existing residential uses that have been reassessed in this document to reflect updates to HED's 2012 Residential SOPs[5] along with policy changes for body weight assumptions. The revision of residential exposures will impact the human health aggregate risk assessment for NAA.

### 6.1 Residential Handler Exposure/Risk Estimates

All registered NAA product labels with residential use sites (e.g., lawns, garden and trees) require that handlers wear specific clothing (e.g., long-sleeved shirt/long pants) and/or use PPE. Therefore, HED has made the assumption that these products are not for homeowner use and has not conducted a quantitative residential handler assessment.

### 6.2 Residential Post-application Exposure/Risk Estimates

There is the potential for post-application exposure for individuals exposed as a result of being in an environment that has been previously treated with NAA. Residential post-application dermal exposure was not quantitatively assessed since there is no dermal hazard for NAA and a dermal POD was not selected. The quantitative exposure/risk assessment for residential post-application exposures (incidental oral) to turf is based on the scenarios listed in Table 6.2.1.

The lifestages selected for each post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs[2]. While not the only lifestage potentially exposed for these post-application scenarios, the lifestage that is included in the quantitative assessment is health protective for the exposures and risk estimates for any other potentially exposed lifestage.

Residential Post-application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential post-application risk assessment. Each assumption and factor is detailed in the 2012 Residential SOPs[2].

*Application Rate:* The single maximum application rate for turf (EPA Reg. No. 90866-4) uses is listed in Table F.1. in Appendix F.

*Exposure Duration:* Residential exposure is expected to be short-term in duration. Intermediate-term exposures are not likely because of the intermittent nature of applications by homeowners. For NAA, short-term exposures are protective of intermediate-term exposures since the PODs are the same.

5 Available: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

Residential Post-application Non-Cancer Exposure and Risk Equations

The algorithms used to estimate residential post-application exposure and dose can be found in the 2012 Residential SOPs[6].

Summary of Residential Post-application Non-Cancer Exposure and Risk Estimates

All incidental oral risk estimates for children 1 to < 2 years old are greater than HED's LOC (i.e., MOEs ≥ 100), from post-application exposure to turf. The MOEs range from 220,000 to 100,000,000.

**Table 6.2.1. Residential Post-application Non-cancer Exposure and Risk Estimates for NAA.**

| Lifestage | Post-application Exposure Scenario | | Application Rate[1] | Dose (mg/kg/day)[2] | MOEs[3] |
|---|---|---|---|---|---|
| | Use Site | Route of Exposure | | | |
| **Lawns and Turf** | | | | | |
| Child 1 to <2 years | Lawns/Turf | Hand to Mouth-Liquid | 0.0074 lb ai/A | 0.0001 | 220,000 |
| | | Object to Mouth-Liquid | | 0.0000034 | 7,300,000 |
| | | Soil ingestion- Liquid | | 0.00000025 | 100,000,000 |

1 Based on registered labels (See Table F.1).
2 Dose (mg/kg/day) algorithms provided in 2012 Residential SOPs (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 MOE = POD (25 mg/kg/day) ÷ Dose (mg/kg/day). LOC for MOE = 100.

Turf Transferable Residue (TTR): In accordance with 40CFR158, TTR data are required for all occupational (e.g., sod farms, golf courses, parks, and recreational areas) or residential turf uses that could result in post-application exposure to turf. HED developed a waiver policy for TTR studies. The MOEs from the assessment, using default TTR values, are evaluated. If those are 10 times higher than the level of concern (LOC), the TTR studies can be waived.

Since the estimated residential turf post-application exposure for incidental oral exposure *(hand-to-mouth; liquid formulations)* using default TTR values for NAA is minimal in comparison to the level of concern (i.e., the calculated MOE is greater than 10 times higher than the level of concern, MOE =220,000 compared to the LOC of 100); EPA is waiving the 40CFR TTR data requirement. In this instance, it is unlikely that chemical-specific TTR data would be needed to further refine exposure assessments or would add appreciably to our general understanding of the availability of turf transferable pesticide residues.

## 6.3 Residential Risk Estimates for Use in Aggregate Assessment

Table 6.3.1 reflects the residential risk estimates that are recommended for use in the aggregate assessment for NAA.

- The recommended residential exposure for use in the children 1<2 years old aggregate assessment is hand-to-mouth exposures from post-application exposure to turf.

6 http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

| Table 6.3.1. Recommendations for the Residential Exposures for the NAA Aggregate Assessment. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Lifestage | Exposure Scenario | Dose (mg/kg/day)[1] | | | | MOE[2] | | | |
| | | Dermal | Inhalation | Oral | Total | Dermal | Inhalation | Oral | Total |
| Child | Residential Post-Application to Turf | N/A | N/A | 0.0001 | 0.0001 | N/A | N/A | 220,000 | 220,000 |

1 Dose = the highest dose for each applicable lifestage of all residential scenarios assessed. Total = dermal + inhalation + incidental oral (where applicable).

2 MOE = the MOEs associated with the highest residential doses. Total = 1 ÷ (1/Dermal MOE) + (1/Inhalation MOE) + (1/Incidental Oral MOE), where applicable.

## 7.0 Aggregate Exposure/Risk Characterization

In accordance with the FQPA, HED must consider and aggregate pesticide exposures and risks from three major sources: food, drinking water, and residential exposures (dermal and inhalation). In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or the risks themselves can be aggregated. When aggregating exposures and risks from various sources, HED considers both the route and duration of exposure. The short-term aggregate assessment includes the combined exposure from dietary and incidental oral exposures. The dermal contribution is omitted because endpoints were not selected for dermal exposure. An acute aggregate exposure and risk assessment was not conducted because a dose and an endpoint for acute dietary exposure was not identified for NAA. NAA is classified as "not likely to be carcinogenic to humans," therefore, a cancer aggregate assessment was not conducted.

### 7.1 Short-Term Aggregate Risk

The short-term aggregate risk assessment includes estimated exposure from dietary and non-dietary sources. Since NAA is registered for use on turf, post-application residential exposure is expected. The dietary (food plus drinking water) exposure estimates are based on a conservative, unrefined chronic dietary exposure assessment (see Table 5.4.6).

No adult scenario was recommended for the inclusion in the short-term aggregate, therefore, the short-term aggregate assessment for adults is equivalent to the chronic dietary exposure and risk estimate for the most highly exposed adult population subgroup, adults 20-49 years old, and is not of concern (5.5% cPAD; see Section 5.4.6).

For children (1 to <2 years old), the short-term aggregate routes of exposure include dietary (food and water) and incidental oral exposure. For NAA, the child lifestage with the highest dietary exposure (all infants < 1 year old) does not match the child lifestage with the highest residential exposure (children 1 to <2 years old). The lifestages selected for each residential post-application scenario are based on an analysis provided as an Appendix in the 2012 *Residential SOPs*[7]. This analysis provides quantitative and qualitative basis for why children 1 to <2 years old are the representative lifestage for most residential post-application scenarios

7 Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

involving young children, as well as reasons why a residential assessment is not conducted for infants. For children, therefore, the NAA aggregate assessment only combines the residential exposure estimates for children 1 to <2 years old with the dietary exposure estimates for that same lifestage, children 1-2 years old.

Short-term aggregate risk estimates (MOEs) for the most highly exposed child population, children 1 to<2 years old, are not of concern to HED (i.e., MOEs are ≥ 100). See Table 7.2.

**Table 7.2. Short-Term Aggregate Risk Calculations for NAA**

| Population | LOC for Aggregate Risk[1] | Dietary exposure (food + drinking water)[2] | Inhalation[2] | Incidental Oral[3] | Total Exposure | Aggregate MOE (food and residential)[4] |
|---|---|---|---|---|---|---|
| Children (1 to <2 years old) | 100 | 0.022367 | NA | 0.0001 | 0.022467 | 1100 |

1 Level of Concern = 100 (based on inter- and intra- species uncertainty factors, each at 10X).
2 Dietary exposure (mg/kg/day) = chronic dietary exposure from Table 5.4.6.
3 Residential exposure (incidental oral exposure) based on recommendations from Table 6.3.1
4 Aggregate MOE = POD (25 mg/kg/day) ÷ Combined dose (dietary + residential, mg/kg/day).

## 7.2 Chronic Aggregate Risk

Chronic aggregate exposures include food plus drinking water exposures. As demonstrated under Section 5.4.4, chronic aggregate risks are not of concern.

# 8.0 Non-Occupational Spray Drift Exposure and Risk Estimates

Off-target movement of pesticides can occur via many types of pathways and it is governed by a variety of factors. Sprays that are released and do not deposit in the application area end up off-target and can lead to exposures to those it may directly contact. They can also deposit on surfaces where contact with residues can eventually lead to indirect exposures (e.g., children playing on lawns where residues have deposited next to treated fields). The potential risk estimates from these residues can be calculated using drift modeling coupled with methods employed for residential risk assessments for turf products.

The approach to be used for quantitatively incorporating spray drift into risk assessment is based on a premise of compliant applications which, by definition, should not result in direct exposures to individuals because of existing label language and other regulatory requirements intended to prevent them. Direct exposures would include inhalation of the spray plume or being sprayed directly. Rather, the exposures addressed here are thought to occur indirectly through contact with impacted areas, such as residential lawns, when compliant applications are conducted. Given this premise, exposures for children (1 to 2 years old) and adults who have contact with turf where residues are assumed to have deposited via spray drift thus resulting in an indirect exposure are the focus of this analysis analogous to how exposures to turf products are considered in risk assessment.

In order to evaluate the drift potential and associated risks, an approach based on drift modeling coupled with techniques used to evaluate residential uses of pesticides was utilized. Essentially, a residential turf assessment based on exposure to deposited residues has been completed to address drift from the agricultural applications of NAA**.** In the spray drift scenario, the deposited residue value was determined based on the amount of spray drift that may occur at varying distances from the edge of the treated field using the AgDrift (v2.1.1) model and the *Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift Policy*. Once the deposited residue values were determined, the remainder of the spray drift assessment was based on the algorithms and input values specified in the recently revised (2012) *Standard Operating Procedures for Residential Risk Assessment (SOPs)*.

A screening approach was developed based on the use of the AgDrift model in situations where specific label guidance that defines application parameters is not available.[8] AgDrift is appropriate for use only when applications are made by aircraft, airblast orchard sprayers, and groundboom sprayers. When AgDrift was developed, a series of screening values (i.e., the Tier 1 option) were incorporated into the model and represent each equipment type and use under varied conditions. The screening options specifically recommended in this methodology were selected because they are plausible and represent a reasonable upper bound level of drift for common application methods in agriculture. These screening options are consistent with how spray drift is considered in a number of ecological risk assessments and in the process used to develop drinking water concentrations used for risk assessment. In all cases, each scenario is to be evaluated unless it is not plausible based on the anticipated use pattern (e.g., herbicides are not typically applied to tree canopies) or specific label prohibitions (e.g., aerial applications are not allowed).

NAA products have an existing label for use on turf, thus it was considered whether the risk assessment for that use may be considered protective of any type of exposure that would be associated with spray drift. If the maximum application rate on crops adjusted by the amount of drift expected is less than or equal to existing turf application rates, the existing turf assessment is considered protective of spray drift exposure. The currently registered maximum single application rate of NAA for orchard/vineyard (olive) is 0.33 lb ai/A. The highest degree of spray drift noted for any application method immediately adjacent to a treated field (Tier 1 output from the aerial application using fine to medium spray quality) results in a deposition fraction of 0.26 of the application rate. A quantitative spray drift assessment for NAA is required because the maximum application rate to a crop/target site multiplied by the adjustment factor for drift of 0.26 is more than the maximum direct spray residential turf application rate (0.0074 lb ai/A)[9] for any NAA products. Section 8.1. provides the screening level drift related risk estimates.
In many cases, risks are of concern when the screening level estimates for spray drift are used as the basis for the analysis. In order to account for this issue and to provide additional risk management options additional spray drift deposition fractions were also considered. These drift estimates represent plausible options for pesticide labels.

8 https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#AgDrift
9 0.33 lb ai/A x 0.26 > 0.0074 lb ai/A

### 8.1. Risk Estimates from Lawn Deposition Adjacent to Applications

The spray drift risk estimates are based on an estimated deposited residue concentration as a result of the screening level agricultural application scenarios. The spray drift assessment was conducted using the highest registered application rate of 0.33 lb ai/A. The recommended drift scenario screening level options are listed below:

- **Groundboom applications** are based on the AgDrift option for high boom height and using very fine to fine spray type using the 90th percentile results.
- **Orchard airblast applications** are based on the AgDrift option for Sparse (Young/Dormant) tree canopies.
- **Aerial applications** are based on the use of AgDrift Tier 1 aerial option for a fine to medium spray type and a series of other parameters which will be described in more detail below (e.g., wind vector assumed to be 10 mph in a downwind direction for entire application/drift event).[10]

There are no short- or intermediate-term dermal PODs. Only incidental oral risk estimates were evaluated. The total applicable LOC is 100, so MOEs <100 would be of concern. Children (1 to <2 years old) incidental oral risk estimates from exposure to NAA related to spray drift result in no risks of concern at the field edge for aerial, airblast, or groundboom applications (See Table 8.1.1. below; drift algorithms are provided in Appendix D; all drift calculations are provided in the Appendix E).

**Table 8.1.1. Children (1 to <2 years old) Risk Estimates (MOEs) Related to Indirect Incidental Oral Spray Drift Exposure for NAA[1].**

| Application Equipment | Spray Type/ Nozzle Configuration | Application Rate (lb ai/A) | Estimated TTR ($ug/cm^2$)[1] | At Field Edge |
|---|---|---|---|---|
| | | | | Incidental Oral MOE (LOC = 100) |
| Orchard/Vineyard (Olive) | | | | |
| Aerial | ***Fine to Medium*** | 0.33 | 0.0366795 | 19,000 |
| Orchard/Vineyard (Olive) | | | | |
| Groundboom | ***High Boom Very fine to Fine*** | 0.33 | 0.0366795 | 27,000 |
| Orchard/Vineyard (Olive) | | | | |
| Airblast | ***Sparse*** | 0.5 | 0.0366795 | 35,000 |

1. Algorithms and inputs related to the spray drift assessment can be found in Appendix D.

### 9.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates

Volatilization of pesticides may be a source of post-application inhalation exposure to individuals nearby pesticide applications. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0687-

10 AgDrift allows for consideration of even finer spray patterns characterized as very fine to fine. However, this spray pattern was not selected as the common screening basis since it is used less commonly for most agriculture.

0037). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (http://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for NAA.

## 10.0 Cumulative Exposure/Risk Characterization

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to NAA and any other substances and NAA does not appear to produce a toxic metabolite produced by other substances. For the purposes of this action, therefore, EPA has not assumed that NAA has a common mechanism of toxicity with other substances. In 2016, EPA's Office of Pesticide Programs released a guidance document entitled, *Pesticide Cumulative Risk Assessment: Framework for Screening Analysis* [https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/pesticide-cumulative-risk-assessment-framework]. This document provides guidance on how to screen groups of pesticides for cumulative evaluation using a two-step approach beginning with the evaluation of available toxicological information and if necessary, followed by a risk-based screening approach. This framework supplements the existing guidance documents for establishing common mechanism groups (CMGs)[11] and conducting cumulative risk assessments (CRA)[12]. During Registration Review, the agency will utilize this framework to determine if the available toxicological data for NAA suggests a candidate CMG may be established with other pesticides. If a CMG is established, a screening-level toxicology and exposure analysis may be conducted to provide an initial screen for multiple pesticide exposure.

## 11.0 Occupational Exposure and Risk Estimates

Occupational and Residential Exposure Memo: M. Hawkins, 16-DEC-2019, D454588

### 11.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the registered uses. Refer to Table 11.1.1. below for the individual risk estimates.

[11] *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)
[12] *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)

Occupational Handler Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor is detailed below on an individual basis.

*Application Rate*: The representative single maximum application rates for the currently registered uses reviewed by HED are listed in Table F.1. in Appendix F.

*Unit Exposures:*

Foliar Uses: It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include PHED 1.1, the AHETF database, the Outdoor Residential Exposure Task Force (ORETF) database, or other registrant-submitted occupational exposure studies. Some of these data are proprietary (e.g., AHETF data), and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table[13]", which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at the Agency website[14].

Seed Treatment Uses: Unit exposures are from ExpoSAC Policy 14: SOPs for Seed Treatment (01-MAY-2003), which are based on data for open mixing/loading/application systems.

*Area Treated or Amount Handled:*

Foliar Uses: The area treated/amount handled are based on ExpoSAC Policy 9.1.

Seed Treatment Uses: The amount of seed handled (for both primary/treater and secondary/planter handlers) is based on HED ExpoSAC Policy 15.2.

Refer to Table 11.1.1. and Table 11.1.2. for these assumptions for each scenario.

*Exposure Duration:* HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site. For most agricultural uses, it is reasonable to believe that occupational handlers will not apply the same chemical every day for more than a one-month time frame; however, there may be a large agribusiness and/or commercial applicators who may apply a product over a period of weeks (e.g., completing multiple applications for multiple clients within a region). For NAA, based on the registered uses, short- and intermediate-term exposure(s) is expected for occupational handlers.

13 Available: https://www.epa.gov/sites/production/files/2018-06/documents/opp-hed-pesticide-handler-surrogate-unit-exposure-table-june-2018.pdf
14 Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

*Personal Protective Equipment:* Estimates of inhalation exposure were calculated for various levels of PPE. Results are presented for "baseline," defined as a single layer of clothing consisting of a long-sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator, as well as baseline with various levels of PPE as necessary (e.g., gloves, respirator, etc). The NAA product labels direct mixers, loaders, applicators and other handlers to wear baseline attire and chemical-resistant gloves. Additional PPE, such as a protective eyewear, is listed on several labels.

Occupational Handler Non-Cancer Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix C.

Combining Exposures/Risk Estimates:

Only inhalation risks were quantitatively assessed since a dermal POD was not selected for NAA.

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates

Only occupational inhalation risks were assessed since a dermal POD was not selected for NAA. The short- and intermediate-term inhalation risk estimates for the occupational handlers are greater than HED's LOC (i.e., MOEs ≥ 1,000) at baseline attire (i.e., no respirator), except for mixing/loading/applying wettable powder formulations for mechanically pressurized handgun applications (drench/soil/ground-directed) when applying 0.0011 lb ai/gallon of NAA to orchard/vineyard (apple, pear); (MOE = 460). With the addition of PPE, such as a protection factor (PF)10 respirator, the MOEs range from 2,100 to 1,100,000,000 and are greater than HED's LOC (i.e., MOEs ≥ 1,000).

For the seed treatment uses of NAA, all of the occupational handler inhalation MOEs are greater than HED's LOC (i.e., MOEs ≥ 1,000) at baseline (i.e., no respirator); the MOEs range from 2,600,000 to 78,000,000.

The Agency matches quantitative occupational exposure assessment with appropriate characterization of exposure potential. While HED presents quantitative risk estimates for human flaggers where appropriate, agricultural aviation has changed dramatically over the past two decades. According the 2012 National Agricultural Aviation Association (NAAA) survey of their membership, the use of GPS for swath guidance in agricultural aviation has grown steadily from the mid 1990's. Over the same time period, the use of human flaggers for aerial pesticide applications has decreased steadily from ~15% in the late 1990's to only 1% in the most recent (2012) NAAA survey. The Agency will continue to monitor all available information sources to best assess and characterize the exposure potential for human flaggers in agricultural aerial applications.

HED has no data to assess exposures to pilots using open cockpits. The only data available is for exposure during aerial applications (covering both airplanes and helicopters) of liquid formulations to pilots in enclosed cockpits (data from AHETF) and of granule formulations in

enclosed cockpits (data from PHED). Therefore, risks to pilots are assessed using the engineering control (enclosed cockpits) and baseline attire (long-sleeved shirt, long pants, shoes, and socks); use of the data in this fashion is consistent with the Agency's Worker Protection Standard (WPS) stipulations for engineering controls, which says label-required PPE for applicators can be reduced when using an enclosed cockpit (40 CFR 170.240(d)(6)(iii)) as well as a provision regarding use of gloves for aerial applications (40 CFR 170.240(d)(6)(i)), which says pilots are not required to wear protective gloves for the duration of the application. With this level of protection, there are no risk estimates of concern for applicators.

**Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for NAA.**

| Exposure Scenario | Crop or Target | Inhalation Unit Exposure (µg/lb ai)[1] | Level of PPE or Engineering control[1] | Maximum Application Rate[2] | App Rate Unit[2] | Area Treated or Amount Handled Daily[3] | Area Treated/Amount Handled Unit[3] | Inhalation | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Dose (mg/kg/day)[4] | MOE[5] (LOC = 1,000) |
| **Mixer/Loader** | | | | | | | | | |
| Liquid, Dip (swim vat), Broadcast | Animal (direct), livestock as a surrogate for Dip Treatment of Ornamental Bulbs | 0.219 | No-R | 0.0096 | lb ai/gallon solution | 100 | gallons solution | 0.00000263 | 9,500,000 |
| Liquid, Aerial, Broadcast | Orchard/Vineyard (Olive) | 0.219 | No-R | 0.33 | lb ai/acre | 350 | acres | 0.000316 | 79,000 |
| Liquid, Aerial, Broadcast | Sod | 0.219 | No-R | 0.0013 | lb ai/acre | 350 | acres | 0.00000125 | 20,000,000 |
| Liquid, Airblast, Broadcast | Orchard/Vineyard (Olive) | 0.219 | No-R | 0.33 | lb ai/acre | 40 | acres | 0.0000361 | 690,000 |
| Liquid, Groundboom, Broadcast | Golf course (tees and greens only) | 0.219 | No-R | 0.0074 | lb ai/acre | 5 | acres | 0.000000101 | 250,000,000 |
| Liquid, Groundboom, Broadcast | Landscaping, turf (lawns, athletic fields, parks, etc.) | 0.219 | No-R | 0.0074 | lb ai/acre | 5 | acres | 0.000000101 | 250,000,000 |
| Liquid, Groundboom, Broadcast | Golf course (fairways, tees, greens) | 0.219 | No-R | 0.0074 | lb ai/acre | 40 | acres | 0.00000081 | 31,000,000 |
| Liquid, Groundboom, Broadcast | Sod | 0.219 | No-R | 0.0013 | lb ai/acre | 80 | acres | 0.000000285 | 88,000,000 |
| Liquid, Groundboom, Broadcast | Orchard/Vineyard (Olive) | 0.219 | No-R | 0.33 | lb ai/acre | 40 | acres | 0.0000361 | 690,000 |
| Wettable Powder, Aerial, Broadcast | Orchard/Vineyard (Apple, Pear) | 2.75 | No-R | 0.11 | lb ai/acre | 350 | acres | 0.00133 | 19,000 |
| Wettable Powder, Airblast, Broadcast | Orchard/Vineyard (Apple, Pear) | 2.75 | No-R | 0.11 | lb ai/acre | 40 | acres | 0.000151 | 170,000 |
| Wettable Powder, Groundboom, Broadcast | Orchard/Vineyard (Apple, Pear) | 2.75 | No-R | 0.11 | lb ai/acre | 40 | acres | 0.000151 | 170,000 |
| **Applicator** | | | | | | | | | |
| Spray (all starting formulations), Aerial, Broadcast | Orchard/Vineyard (Olive) | 0.0049 | EC | 0.33 | lb ai/acre | 350 | acres | 0.00000708 | 3,500,000 |
| Spray (all starting formulations), Aerial, Broadcast | Sod | 0.0049 | EC | 0.0013 | lb ai/acre | 350 | acres | 2.79E-08 | 900,000,000 |
| Spray (all starting formulations), Airblast, Broadcast | Orchard/Vineyard (Olive) | 4.71 | No-R | 0.33 | lb ai/acre | 40 | acres | 0.000778 | 32,000 |

**Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for NAA.**

| Exposure Scenario | Crop or Target | Inhalation Unit Exposure (µg/lb ai)[1] | Level of PPE or Engineering control[1] | Maximum Application Rate[2] | App Rate Unit[2] | Area Treated or Amount Handled Daily[3] | Area Treated/Amount Handled Unit[3] | Inhalation | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Dose (mg/kg/day)[4] | MOE[5] (LOC = 1,000) |
| Spray (all starting formulations), Groundboom, Broadcast | Golf course (tees and greens only) | 0.34 | No-R | 0.0074 | lb ai/acre | 5 | acres | 0.000000158 | 160,000,000 |
| Spray (all starting formulations), Groundboom, Broadcast | Landscaping, turf (lawns, athletic fields, parks, etc.) | 0.34 | No-R | 0.0074 | lb ai/acre | 5 | acres | 0.000000158 | 160,000,000 |
| Spray (all starting formulations), Groundboom, Broadcast | Golf course (fairways, tees, greens) | 0.34 | No-R | 0.0074 | lb ai/acre | 40 | acres | 0.00000126 | 20,000,000 |
| Spray (all starting formulations), Groundboom, Broadcast | Sod | 0.34 | No-R | 0.0013 | lb ai/acre | 80 | acres | 0.000000443 | 56,000,000 |
| Spray (all starting formulations), Groundboom, Broadcast | Orchard/Vineyard (Olive) | 0.34 | No-R | 0.33 | lb ai/acre | 40 | acres | 0.0000561 | 450,000 |
| Liquid, Dip (manual), Broadcast | Animal (direct), livestock as a surrogate for Dip Treatment of Ornamental Bulbs | 26.6 | No-R | 0.0096 | lb ai/gallon solution | 100 | gallons solution | 0.000319 | 78,000 |
| **Flagger** | | | | | | | | | |
| Spray (all starting formulations), Aerial, Broadcast | Orchard/Vineyard (Olive) | 0.35 | No-R | 0.33 | lb ai/acre | 350 | acres | 0.000505 | 50,000 |
| Spray (all starting formulations), Aerial, Broadcast | Sod | 0.35 | No-R | 0.0013 | lb ai/acre | 350 | acres | 0.00000199 | 13,000,000 |
| **Mixer/Loader/Applicator** | | | | | | | | | |
| Liquid, Backpack, Ground/soil-directed | Orchard/Vineyard (Olive) | 2.58 | No-R | 0.11 | lb ai/gallon solution | 40 | gallons solution | 0.000143 | 170,000 |
| Liquid, Backpack, Broadcast (foliar) | Landscaping, trees/shrubs/bushes | 69.1 | No-R | 0.11 | lb ai/gallon solution | 40 | gallons solution | 0.0038 | 6,600 |
| Liquid, Backpack, Broadcast (foliar) | Landscaping, plants/flowers | 69.1 | No-R | 0.0013 | lb ai/gallon solution | 40 | gallons solution | 0.0000449 | 560,000 |
| Liquid, Backpack, Broadcast | Landscaping, turf (lawns, athletic fields, parks, etc.) | 69.1 | No-R | 0.000017 | lb ai/gallon solution | 40 | gallons solution | 0.000000588 | 43,000,000 |
| Liquid, Backpack, Spot | Landscaping, turf (lawns, athletic fields, parks, etc.) | 2.58 | No-R | 0.000017 | lb ai/gallon solution | 40 | gallons solution | 0.0000000219 | 1,100,000,000 |

**Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for NAA.**

| Exposure Scenario | Crop or Target | Inhalation Unit Exposure (µg/lb ai)[1] | Level of PPE or Engineering control[1] | Maximum Application Rate[2] | App Rate Unit[2] | Area Treated or Amount Handled Daily[3] | Area Treated/Amount Handled Unit[3] | Inhalation | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Dose (mg/kg/day)[4] | MOE[5] (LOC = 1,000) |
| Liquid, Manually-pressurized Handwand, Broadcast (foliar) | Landscaping, trees/shrubs/bushes | 30 | No-R | 0.11 | lb ai/gallon solution | 40 | gallons solution | 0.00165 | 15,000 |
| Liquid, Manually-pressurized Handwand, Broadcast (foliar) | Landscaping, plants/flowers | 30 | No-R | 0.0013 | lb ai/gallon solution | 40 | gallons solution | 0.0000195 | 1,300,000 |
| Liquid, Manually-pressurized Handwand, Broadcast | Landscaping, turf (lawns, athletic fields, parks, etc.) | 30 | No-R | 0.000017 | lb ai/gallon solution | 40 | gallons solution | 0.000000255 | 98,000,000 |
| Liquid, Mechanically-pressurized Handgun, Broadcast (foliar) | Orchard/Vineyard (Olive) | 8.68 | No-R | 0.11 | lb ai/gallon solution | 1000 | gallons solution | 0.0119 | 2,100 |
| Liquid, Mechanically-pressurized Handgun, Drench/Soil-/Ground-directed | Orchard/Vineyard (Olive) | 8.68 | No-R | 0.11 | lb ai/gallon solution | 1000 | gallons solution | 0.0119 | 2,100 |
| Liquid, Mechanically-pressurized Handgun, Broadcast | Golf course (tees and greens only) | 1.9 | No-R | 0.0074 | lb ai/acre | 5 | acres | 0.000000879 | 28,000,000 |
| Liquid, Mechanically-pressurized Handgun, Broadcast | Golf course (fairways, tees, greens) | 1.9 | No-R | 0.0074 | lb ai/acre | 5 | acres | 0.000000879 | 28,000,000 |
| Liquid, Mechanically-pressurized Handgun, Broadcast (foliar) | Landscaping, trees/shrubs/bushes | 8.68 | No-R | 0.11 | lb ai/gallon solution | 1000 | gallons solution | 0.0119 | 2,100 |
| Liquid, Mechanically-pressurized Handgun, Broadcast | Landscaping, turf (lawns, athletic fields, parks, etc.) | 1.9 | No-R | 0.0074 | lb ai/acre | 5 | acres | 0.000000879 | 28,000,000 |
| Wettable Powder, Backpack, Ground/soil-directed | Orchard/Vineyard (Apple, Pear) | 2.58 | No-R | 0.0011 | lb ai/gallon solution | 40 | gallons solution | 0.00000143 | 17,000,000 |
| Wettable Powder, Mechanically-pressurized Handgun, Broadcast (foliar) | Orchard/Vineyard (Apple, Pear) | 8.68 | No-R | 0.0011 | lb ai/gallon solution | 1000 | gallons solution | 0.000119 | 210,000 |
| Wettable Powder, Mechanically-pressurized Handgun, Drench/Soil-/Ground-directed | Orchard/Vineyard (Apple, Pear) | 3931 | No-R | 0.0011 | lb ai/gallon solution | 1000 | gallons solution | 0.054 | **460** |
| Wettable Powder, Mechanically-pressurized Handgun, Drench/Soil-/Ground-directed | Orchard/Vineyard (Apple, Pear) | 393.1 | PF10 R | 0.0011 | lb ai/gallon solution | 1000 | gallons solution | 0.0054 | 4,600 |

Bolded values = MOEs < 1,000.

1 Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data); Level of mitigation: No-R = No Respirator; PF10 R = PF10 Respirator; EC = Engineering Control.

2 Based on registered labels (See Table F.1. in Appendix F).

3 Exposure Science Advisory Council Policy #9.1.

4 Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre) × Area Treated Daily (A/day) ÷ BW (80 kg).
5 Inhalation MOE = Inhalation NOAEL (25 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). Short- and Intermediate-term level of concern = 1,000.

**Table 11.1.2. Occupational Handler Inhalation MOEs for Registered Seed Treatment Uses of NAA.**

| Exposure Scenario | Application Type | Crop / Target Category | Application Rate | Units[1] | Amount Of Seed Treated[2] | Units | Inhalation Unit Exposures (ug/lb ai)[3] | Inhalation Dose (mg/kg-day)[4] | Inhalation MOE[5] (LOC = 1,000) |
|---|---|---|---|---|---|---|---|---|---|
| Worker Activity | | | Value[1] | | Value | | No-R | No-R | No-R |
| Loader/Applicator | Commercial Seed Treatment | Potato, russet | 0.00000028 | lb ai/lb seed | 800000 | lb/day | 0.34 | 0.000000953 | 26,000,000 |
| Loader/Applicator | Commercial Seed Treatment | Potato, non-russet | 0.0000002 | lb ai/lb seed | 800000 | lb/day | 0.34 | 0.00000068 | 37,000,000 |
| Sewer | Commercial Seed Treatment | Potato, russet | 0.00000028 | lb ai/lb seed | 800000 | lb/day | 0.23 | 0.000000644 | 39,000,000 |
| Sewer | Commercial Seed Treatment | Potato, non-russet | 0.0000002 | lb ai/lb seed | 800000 | lb/day | 0.23 | 0.00000046 | 54,000,000 |
| Bagger | Commercial Seed Treatment | Potato, russet | 0.00000028 | lb ai/lb seed | 800000 | lb/day | 0.16 | 0.000000448 | 56,000,000 |
| Bagger | Commercial Seed Treatment | Potato, non-russet | 0.0000002 | lb ai/lb seed | 800000 | lb/day | 0.16 | 0.00000032 | 78,000,000 |
| Multiple Activities | Commercial Seed Treatment | Potato, russet | 0.00000028 | lb ai/lb seed | 800000 | lb/day | 1.6 | 0.00000448 | 5,600,000 |
| Multiple Activities | Commercial Seed Treatment | Potato, non-russet | 0.0000002 | lb ai/lb seed | 800000 | lb/day | 1.6 | 0.0000032 | 7,800,000 |
| Planters | Commercial Seed Treatment | Potato, russet | 0.00000028 | lb ai/lb seed | 425000 | lb/day | 3.4 | 0.00000506 | 4,900,000 |

**Table 11.1.2. Occupational Handler Inhalation MOEs for Registered Seed Treatment Uses of NAA.**

| Exposure Scenario | Application Type | Crop / Target Category | Application Rate | Units[1] | Amount Of Seed Treated[2] | Units | Inhalation Unit Exposures (ug/lb ai)[3] | Inhalation Dose (mg/kg-day)[4] | Inhalation MOE[5] (LOC = 1,000) |
|---|---|---|---|---|---|---|---|---|---|
| Worker Activity | | | Value[1] | | Value | | No-R | No-R | No-R |
| Planters | Commercial Seed Treatment | Potato, non-russet | 0.0000002 | lb ai/lb seed | 425000 | lb/day | 3.4 | 0.00000361 | 6,900,000 |
| On Farm Mixer/Loader/Applicator | On Farm Seed Treatment | Potato, russet | 0.00000028 | lb ai/lb seed | 425000 | lb/day | 6.4 | 0.00000953 | 2,600,000 |
| On Farm Mixer/Loader/Applicator | On Farm Seed Treatment | Potato, non-russet | 0.0000002 | lb ai/lb seed | 425000 | lb/day | 6.4 | 0.0000068 | 3,700,000 |
| On Farm Loader/Planter | On Farm Seed Treatment | Potato, russet | 0.00000028 | lb ai/lb seed | 425000 | lb/day | 3.4 | 0.00000506 | 4,900,000 |
| On Farm Loader/Planter | On Farm Seed Treatment | Potato, non-russet | 0.0000002 | lb ai/lb seed | 425000 | lb/day | 3.4 | 0.00000361 | 6,900,000 |

1 Based on registered labels (see Table F.1. in Appendix F).
2 HED default for lb seed treated/planted per day from HED Exposure Science Advisory Council Policy 15.2.
3 Unit Exposures from HED Exposure Science Advisory Council Policy 14: Standard Operating Procedures for Seed Treatment.
4 Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/lb seed) × Amount Treated or Planted (lb seed/day ÷ BW (80 kg).
5 Inhalation MOE = Inhalation NOAEL (25 mg/kg/day) ÷ Inhalation Dose (mg/kg/day). LOC = 1,000.

## 11.2 Occupational Post-application Exposure/Risk Estimates

Occupational post-application dermal exposure was not assessed for NAA since a dermal POD was not selected.

Dislodgeable Foliar Residue (DFR): In accordance with the updated Part 158 data requirements (2007), one or more DFR studies are required when a pesticide has residential or occupational uses that could result in post-application dermal exposure. Since there is no hazard via the dermal route of exposure, a non-cancer dermal post-application risk assessment was not performed for NAA. Therefore, DFR studies are not needed for NAA at this time. If the PODs change, the need for DFR studies may be reevaluated in the future to refine the post-application assessment.

### 11.2.1 Occupational Post-application Inhalation Exposure/Risk Estimates

There are multiple potential sources of post-application inhalation exposure to individuals performing post-application activities in previously treated fields. These potential sources include volatilization of pesticides and resuspension of dusts and/or particulates that contain pesticides. The Agency sought expert advice and input on issues related to volatilization of pesticides from its Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP) in December 2009, and received the SAP's final report on March 2, 2010 (http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2009-0687-0037). The Agency has evaluated the SAP report and has developed a Volatilization Screening Tool and a subsequent Volatilization Screening Analysis (https://www.regulations.gov/#!docketDetail;D=EPA-HQ-OPP-2014-0219). During Registration Review, the Agency will utilize this analysis to determine if data (i.e., flux studies, route-specific inhalation toxicological studies) or further analysis is required for NAA.

In addition, the Agency is continuing to evaluate the available post-application inhalation exposure data generated by the Agricultural Reentry Task Force. Given these two efforts, the Agency will continue to identify the need for and, subsequently, the way to incorporate occupational post-application inhalation exposure into the Agency's risk assessments.

Furthermore, inhalation exposure during dusty mechanical activities such as shaking and mechanical harvesting is another potential source of post-application inhalation exposure. However, the airblast applicator scenario is believed to represent a reasonable worst case surrogate estimate of post-application inhalation exposure during these dusty mechanical harvesting activities. The non-cancer inhalation risk estimate for commercial airblast application is not of concern (i.e., MOE > 1000).

The Worker Protection Standard for Agricultural Pesticides contains requirements for protecting workers from inhalation exposures during and after greenhouse applications through the use of ventilation requirements.[40 CFR 170.110, (3) (Restrictions associated with pesticide applications)]

A post-application inhalation exposure assessment is not required for seed treatment uses as exposure is expected to be negligible. Seed treatment assessments provide quantitative inhalation exposure assessments for seed treaters and secondary handlers (i.e., planters). It is expected that these exposure estimates would be protective of any potential low-level post-application inhalation exposure that could result from these types of applications.

Restricted Entry Interval

NAA has low acute toxicity via the oral, inhalation and dermal routes of exposure (Toxicity Category III or IV). NAA is not a skin irritant (Toxicity Category IV) or a dermal sensitizer. However, eye irritation was severe in animals exposed to naphthaleneacetic acid and NAA sodium salt products (Toxicity Category I), while exposure to NAA ethyl ester and NAA acetamide led to mild, transient irritation (Toxicity Category IV). Under 40 CFR 156.208 (c) (2), ai's classified as Acute I for eye irritation are assigned a 48-hour REI. Therefore, the [156 subpart K] Worker Protection Statement interim REI of 48 hours is adequate to protect agricultural workers from post-application exposures to NAA. HED would recommend a REI of 48 hours for products containing the naphthaleneacetic acid and NAA sodium salt products. The currently registered labels have REIs of 12, 24, or 48 hours.

## 12.0 Incident and Epidemiological Data Review

1-Naphthaleneacetic Acid (NAA) incidents were previously reviewed in 2014 (E. Evans and S. Recore, 23-JUL-2014, D421705). At that time, no NAA incident cases were reported to either Incident Data System (IDS) or NIOSH Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides and further investigation was not warranted.

In the current five-year IDS analysis from January 1, 2014 to October 23, 2019, there were no incidents reported that involved the active ingredient NAA. In aggregate IDS for the five years from January 1, 2014 to October 23, 2019, there was one incident reported involving NAA (056001). This incident was classified as minor severity. A query of SENSOR-Pesticides 1998-2015 identified 24 cases involving NAA.

The Agricultural Health Study (AHS) is a federally-funded study that evaluates associations between pesticide exposures and cancer and other health outcomes and represents a collaborative effort between the US National Cancer Institute (NCI), National Institute of Environmental Health Sciences (NIEHS), CDC's National Institute of Occupational Safety and Health (NIOSH), and the US EPA. NAA is not included in the AHS, and therefore this study does not provide information for this report.

Based on the continued low frequency of NAA incidents reported to both IDS and SENSOR-Pesticides, there does not appear to be a concern at this time. The Agency will continue to monitor the incident data and if a concern is triggered, additional analysis will be conducted. For additional information on the information found in the databases, see the memo *"**1-Naphthaleneacetic acid (NAA)**: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment"* (S. Recore, 25-NOV-2019, D455115).

## 13.0 References

**Table 13.0. References.**

| Author | Barcode | Date | Title |
|---|---|---|---|
| B. Cropp-Kohlligian et.al. | D445386 | 03-DEC-2018 | Naphthalene Acetates. Human Health Risk Assessment for Proposed Amended Uses of Naphthaleneacetic Acid, Potassium Salt (PC Code 056003) on Mandarins (Tangerines, Tangelos, Tangors, and Clementines) and Oranges and a New End-Use Product Registration. |
| Austin Wray et al. | D423654, D423656 | 18-NOV-2015 | Naphthalene Acetates: Human Health Risk Assessment for a Proposed New Use on Pomegranate. |
| T. Morton | D426996 | 18-NOV-2015 | Naphthalene Acetates- Chronic Dietary and Drinking Water Exposure and Risk Assessment for Section 3 New Use of Naphthalene Acetic Acid-ester on Pomegranate |
| Z. Ruge | D454904 | 05-NOV-2019 | Naphthaleneacetic Acid and Its Sodium, Potassium, and Ammonium Salts, Ethyl Ester, and Acetamide: Drinking Water Assessment (DWA) for Registration Review |
| B. Cropp-Kohlligian | D448272 | 28-NOV-2018 | Naphthaleneacetic Acid, Potassium Salt (NAA-K). New Product Registration with Amended Uses on Mandarins (Tangerines, Tangelos, Tangors, and Clementines) and Orange. Summary of Analytical Chemistry and Residue Data. |
| G. Otakie | D217162 | 06-NOV-2003 | Naphthaleneacetic Acid, Salts, Ester and Acetarnide (056001, 056002, 056003, 056004, 056007, and 056008); Various Naphthaleneacetic Acid Studies/DER's (See List Below). DP Barcodes # (See List Below). Case 0379. MRID Nos.(See List Below). |
| G. Otakie | D293239 | 18-NOV-2003 | 1-Naphthaleneacetic Acid (NAA), Its Salts, Ester, and Acetarnide. RED - Reregistration Eligibility Decision: Product Chemistry Considerations |
| A. Habtemichael | D455451 | 16-DEC-2019 | Naphthalene Acetates- Summary of Waiver Request for Olive Oil Storage Stability Data. |
| M. Hawkins | D454588 | 16-DEC-2019 | 1-Naphthaleneacetic Acid, Its Salts, Ester, and Acetamide (NAA). Occupational and Residential Exposure Assessment for Registration Review. |
| S. Recore | D455115 | 25-NOV-2019 | 1-Naphthaleneacetic acid (NAA): Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment |

# APPENDICIES

## Appendix A. Toxicology Profile and Executive Summaries

### A.1 Toxicology Data Requirements

The requirements (40 CFR 158.500) for naphthalene acetate food use are in Table 1. Use of the new guideline numbers does not imply that the new (1998) guideline protocols were used.

| Study | | Technical | |
|---|---|---|---|
| | | Required | Satisfied |
| 870.1100 | Acute Oral Toxicity | yes | yes |
| 870.1200 | Acute Dermal Toxicity | yes | yes |
| 870.1300 | Acute Inhalation Toxicity | yes | yes |
| 870.2400 | Primary Eye Irritation | yes | yes |
| 870.2500 | Primary Dermal Irritation | yes | yes |
| 870.2600 | Dermal Sensitization | yes | yes |
| 870.3100 | Oral Subchronic (rodent) | yes | yes |
| 870.3150 | Oral Subchronic (nonrodent) | yes | yes |
| 870.3200 | 21-Day Dermal | yes | yes |
| 870.3250 | 90-Day Dermal | no | - |
| 870.3465 | 90-Day Inhalation | yes | no[1] |
| 870.3700a | Developmental Toxicity (rodent) | yes | yes |
| 870.3700b | Developmental Toxicity (nonrodent) | yes | yes |
| 870.3800 | Reproduction | yes | yes |
| 870.4100a | Chronic Toxicity (rodent) | yes | yes |
| 870.4100b | Chronic Toxicity (nonrodent) | yes | yes |
| 870.4200a | Oncogenicity (rat) | yes | yes |
| 870.4200b | Oncogenicity (mouse) | yes | yes |
| 870.4300 | Chronic/Oncogenicity | yes | yes |
| 870.5100 | Mutagenicity—Gene Mutation - bacterial | yes | yes |
| 870.5300 | Mutagenicity—Gene Mutation - mammalian | yes | yes |
| 870.5xxx | Mutagenicity—Structural Chromosomal Aberrations | yes | yes |
| 870.5xxx | Mutagenicity—Other Genotoxic Effects | yes | yes |
| 870.6100a | Acute Delayed Neurotoxicity (hen) | no | - |
| 870.6100b | 90-Day Neurotoxicity (hen) | no | - |
| 870.6200a | Acute Neurotoxicity Screening Battery (rat) | yes | waived[1] |
| 870.6200b | 90-Day Neurotoxicity Screening Battery (rat) | yes | waived[1] |
| 870.6300 | Develop. Neurotoxicity | no | - |
| 870.7485 | General Metabolism | yes | yes |
| 870.7600 | Dermal Penetration | no | NA |
| 870.7800 | Immunotoxicity | yes | waived[1] |

[1]HED HASPOC (K. Rury, 16-OCT-2012, TXR 0056465; J. Leshin, 21-MAY-2014, TXR 0056968)

## A.2 Toxicity Profiles

Note: Only guideline studies for NAA acetamide, NAA, NAA sodium salt, and NAA ethyl ester are included in the toxicity profile table.

**Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates**

| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
|---|---|---|---|---|
| Acute - Oral | **MRID 43495901** (1994)<br>$LD_{50}$ > 5050 mg/kg<br>**Category IV** | **MRID 00103128** (1982)<br>$LD_{50}$ (95% C.I.) = 2520 mg/kg (2100-3021)<br>**Category III** | **MRID 00108829** (1982)<br>$LD_{50}$ (95% C.I.) =<br>(M) 1.35 g/kg (1.12–1.64)<br>(F) 0.933 g/kg (0.631-1.38)<br>**Category III** | **MRID 43494101** (1994)<br>$LD_{50}$ (95% C.I.) = 2186 (1907-2506) mg/kg<br>**Category III** |
| Acute - Dermal | **MRID 43495902** (1994)<br>$LD_{50}$ > 2020 mg/kg<br>**Category III** | **MRID 00103129** (1982)<br>$LD_{50}$ > 2000 mg/kg<br>**Category III** | **MRID 00108829** (1982)<br>$LD_{50}$ > 2000 mg/kg<br>**Category III** | **MRID 43494102** (1994)<br>$LD_{50}$ > 2020 mg/kg<br>**Category III** |
| Acute - Inhalation | **MRID 43495903** (1994)<br>$LC_{50}$ > 2.17 mg/L<br>**Category IV** | **MRID 00128256** (1983)<br>$LC_{50}$ > 0.45 mg/L<br>**Category III** | | **MRID 43494103** (1994)<br>$LC_{50}$ > 2.13 mg/L<br>**Category IV** |
| Eye Irritation | **MRID 00103051** (1982)<br>corrosive **Category I**<br><br>**MRID 43495904** (1994)<br>minimally irritating<br>**Category IV** | **MRID 00103127** (1982)<br>corrosive<br>**Category I** | **MRID 00108829** (1982)<br>corrosive<br>**Category I** | **MRID 43494104** (1994)<br>minimally irritating<br>**Category IV** |

| **Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates** | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| Dermal Irritation | **MRID 00103220** (1982)<br>Non-irritating<br>**Category IV** | **MRID 00103127** (1982)<br>Non-irritating<br>**Category IV** | **MRID 00108829 (**1982)<br>Non-irritating<br>**Category IV** | **MRID 00103053/ 00103218** (1982)<br>Non-irritating<br>**Category IV** |
| Sensitization | **MRID 43495905** (1994)<br>Not a skin sensitizer.<br>No positive control but study still<br>**Acceptable/Guideline** | **MRID 00153217** (1984)<br>Not a skin sensitizer | | **MRID 43494105** (1994)<br>Not a skin sensitizer.<br>No positive control but study still<br>**Acceptable/Guideline** |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| Subchronic - Rat | **MRID 43896001** (1995) **Acceptable/Guideline** 0, 250, 1,000, or 4,000 ppm (0, 19.1, 73.8, or 292.1 mg/kg/day for males and 0, 20.4, 81.5, or 313.5 mg/kg/day for females) in the diet for 90 days<br><br>**LOAEL = 292.1 mg/kg/day** based on decreased body weight and weight gain & food consumption, and increased relative liver weights with adaptive histopathological changes in both sexes.<br><br>**NOAEL = 73.8 mg/kg/day** | **MRID 00043624** (1979) **Acceptable/Guideline** 0, 50, 150, or 300 mg/kg/day to SD rats (20/sex/dose) in diet for 13 weeks<br><br>**LOAEL = 300 mg/kg/day** based on decreased body weight in both sexes and enlarged liver weights in females.<br><br>**NOAEL = 150 mg/kg/day** | **MRID 42932601** (1993) **Acceptable/Guideline** 0, 200, 2000, or 8000 ppm (13.9, 136.6, and 564.9 for males and 15.2, 149.3, and 583.4 mg/kg/day for females) in the diet for 13 weeks<br><br>**LOAEL = 136.6 mg/kg/day for males and 149.3 mg/kg/day for females** based on decreased hematocrit and hemoglobin, increased liver weights and vacuolation of the periportal hepatocytes along with hypertrophy of the cells of the adrenal cortex zona glomerulosa.<br><br>**NOAEL = 13.9 mg/kg/day for males and 15.2 mg/kg/day for females** | **MRID 43896002** (1995) **Acceptable/Guideline** 0, 400, 2000 or 8000 ppm (Average doses at study end were 19-25; 92-123; and 388 - 519 mg/kg/day for males-females) in the diet for 13 weeks<br><br>**LOAEL= 594 mg/kg/day** based on lower body weight and weight gain, and food consumption. Males and females at this dose also exhibited increased total bilirubin (19-21% higher) in conjunction with reduced RBC counts, hemoglobin, and hematocrits.<br><br>**NOAEL= 144 mg/kg/day** |
| 10-day range finding - rat | | **MRID 00043623** (1976) **Acceptable/Non-Guideline** 0, 250, 1000 or 4000 mg/kg bw/day by gavage for 10 days (3 | | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| | | rats/sex/dose).<br><br>Death of all high dose rats, one female in the mid dose and none in the low dose. Dose related depression in body weight gain and food consumption. Discoloration of lungs, liver and kidneys, distended bladder (high dose), blood and gas in the GI tract.<br><br>**MTD = 250 mg/kg/day** | | |
| Subchronic - Dog | **MRID 43895901** (1995) **Acceptable/Guideline** 0, 30, 100, or 300 mg/kg/day via capsule for 13 weeks.<br><br>**LOAEL = 300 mg/kg/day** based on increased platelet count, decreased red cell parameters, and increased mean corpuscular volume which correlate with histopathological changes observed in the liver, spleen, and bone marrow in both sexes.<br><br>**NOAEL = 100 mg/kg/day** | **MRID 00136446** (1979) **Acceptable/Guideline** 0, 50, 150, or 300 mg/kg/day via gelatin capsule for **6 months**<br><br>**LOAEL = 50 mg/kg/day**, the lowest dose tested, based on hepatic liver changes (pericholangistis)<br><br>**NOAEL = not derived in this study.** | **MRID 42983801** (1993) **Acceptable/Guideline** 0, 25, 150, or 450 mg/kg/day via capsule for 13 weeks<br><br>**LOAEL =150 mg/kg/day** based on lesions of the GI tract and hypocellularity of the bone marrow<br><br>**NOAEL = 25 mg/kg/day** | **MRID 43914901** (1995) **Acceptable/Guideline** 0, 40, 125, or 400 mg/kg/day via gelatin capsules for 13 weeks.<br><br>**LOAEL= 400 mg/kg/day** based on soft/liquid feces and depressed body weight gains of male and female dogs. Blood parameters (RBC, hemoglobin, hematocrit and mean platelet volume) were all depressed in the male |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| | | | | dogs at this level.<br><br>**NOAEL = 125 mg/kg/day** |
| 21-day - Dermal | **MRID 43581001** (1995)<br>**Acceptable/Guideline**<br>0, 100, 300, or 1000 mg/kg for 6-6.5 hours/day, 5 days/week, for 3 weeks.<br><br>**LOAEL = was not established**<br><br>**NOAEL = 1000 mg/kg bw/day (the highest dose tested)** | | **MRID 43134701** (1994)<br>**Acceptable/Guideline**<br>0, 100, 300, or 1000 mg/kg for 6-6.5 hours/day, 5 days/week, for 3 weeks.<br><br>**Systemic LOAEL was not established**<br><br>**Systemic NOAEL = 1000 mg/kg/day**<br><br>**Dermal LOAEL = 1000 mg/kg/day** based on microscopic changes in the skin<br><br>**Dermal NOAEL = 300 mg/kg/day** | **MRID 43581002** (1995)<br>**Acceptable/Guideline**<br>0, 100, 300, or 1000 mg/kg for 6-6.5 hours/day, 5 days/week, for 3 weeks.<br><br>**Systemic LOAEL was not established**<br><br>**Systemic NOAEL =1000 mg/kg/day**<br><br>**Dermal LOAEL = 100 mg/kg/day** based on the epidermal hyperplasia and hyperkeratosis, sebaceous gland hyperplasia, and dermal inflammation in the treated skin.<br><br>**Dermal NOAEL < 100 mg/kg/day** |
| 28-day inhalation | Not available | | | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| Developmental Rat | | **MRID 00042765** (1977) **Acceptable/Guideline** 0, 10, 50 or 250 mg/kg/day via gastric intubation to pregnant rats (24/group) from days 6 through 15 of gestation<br><br>**Maternal LOAEL = 250 mg/kg/day** based on decreased body weight gain during the compound administration<br><br>**Maternal NOAEL = 50 mg/kg/day**<br><br>**Developmental LOAEL >250 mg/k/day**<br><br>**Developmental NOAEL = 250 mg/kg/day** | **MRID 46685803** (2004) **Acceptable/Guideline** 0, 15, 50 or 150 mg/kg bw/day via gavage to 24 female SD rats/dose from days 5 through 21 (inclusive) of gestation.<br><br>**Maternal NOAEL = 150 mg/kg bw/day (HDT)** Note: A statistically significant but not biologically significant decreases of maternal body weight (<10%) throughout the treatment period was observed.<br><br>**Developmental LOAEL = 150 mg/kg/day** based on slightly decreased fetal weight (4-8%) and minor skeletal changes (centrum 5 not ossified, cervical arch 7 cartilage fused to arch 6 cartilage, shortened 7$^{th}$ cervical rib)<br><br>**Developmental NOAEL = 50 mg/kg/day** | |
| Developmental - Rabbit | | **MRID 00137821, 00137822** (1983) | **MRID 46685801** (2003) **Acceptable/Guideline** | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| | | **Acceptable/Guideline** 0, 37.5, 75 or 150 mg/kg/day via oral gavage from days 6 through 27 of gestation<br><br>**Maternal LOAEL = 150 mg/kg/day** based on day based on lethality<br><br>**Maternal NOAEL = 75 mg/kg/day**<br><br>**Developmental LOAEL = >150 mg/kg/day**<br><br>**Developmental NOAEL = 150 mg/kg/day (HDT)** | 0, 30, 100 or 300 mg/kg bw/day in water via gavage from days 5 through 29 (inclusive) of gestation maternal<br><br>**Maternal LOAEL= 300 mg/kg/day** based on reduced body weight and food consumption, clinical signs (few/no feces) and stomach irritation (red/black spots/areas in the glandular mucosa of the stomach).<br><br>**Maternal NOAEL = 100 mg/kg/day**<br><br>**Developmental LOAEL = 300 mg/kg/day** based on an increase in the overall incidences of fetuses with minor skeletal defects and variants (dumbbell ossification of the 7$^{th}$ thoracic centrum, extra thoracolumbar ribs and 27 pre-pelvic vertebrae) and a decrease in ossification of the manus.<br><br>**Developmental NOAEL =** 100 mg/kg/day | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| Reproduction | | | **MRID 43796301** (1995)<br>**Acceptable/Guideline**<br>0, 100, 1000 or 3000 ppm (0, 7, 69, and 210 mg/kg/day for males and 0, 8, 81, and 239 mg/kg/day for females) via diet<br><br>**Systemic and repro./develop LOAEL = 210 mg/kg/day for males and 239 mg/kg/day for females** based upon reduced body weight and food consumption in parental animals and reduced litter survival, and pup weight throughout lactation in both generations of offspring.<br><br>**Systemic and repro./develop NOAEL = 69 mg/kg/day for males and 81 mg/kg/day for females** | |
| Chronic/Oncogenicity - Rat | | | **MRID 44157501** (1996)<br>**Acceptable/Guideline**<br>0, 100, 1000, or 5000 ppm (0, 4.4, 43.8, and 224.5 mg/kg/day for males and 0, 5.6, 55.8, and 303.6 | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| | | | mg/kg/day for females) via diet to Crl:CD® BR rats<br><br>**LOAEL = 224.5 mg/kg/day for males and 303.6 mg/kg/day for females** based on an increased incidence of stomach (mucosal gland dilation) and lung lesions (focal alveolar macrophages) in both sexes, and on lowered bw gain and food efficiency in females<br><br>**NOAEL= 43.8 mg/kg/day for males and 55.8 mg/kg/day for females**<br><br>*Increased incidence ($p \leq 0.01$) of uterine endometrial stromal polyps in high-dose females (2/60, 1/60, 3/60, 13/60 at 0, 100, 1000, 5000 ppm, respectively). | |
| Chronic - Mouse | **NCI study (Innes *et al* 1969)**<br>**Acceptable/Non-Guideline**<br>NAA acetamide was tested at one dose (MTD according to the published article) as part of a testing | | **MRID 46685802** (2004)<br>**Acceptable/Guideline**<br>0, 100, 500, or 2500 ppm [0, 10.8, 53.3, 276.0 / 0, 14.3, 70.9, 348.7 mg/kg bw/day M/F, respectively] via diet to CD-1 Alpk mice for at least 80 weeks | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| | program of 120 chemicals. Only the preliminary results were published. The test materials were administered to two hybrid strains of mice: C57BL/6 x C3H/Anf and C57BL/6 x AKR (18/sex/hybrid strain). The mice were administered NAA acetamide at one week of age by stomach intubation at 464 mg/kg/day until weaning at 4 weeks of age and administered the NAA acetamide in the diet at 1298 ppm for approx. 18 months.<br><br>*Gross and histopath examination of the mice at the end of the feeding period did not reveal a significant increase in tumors over the controls. | | **LOAEL = 276 mg/kg/day for males and 348.7 mg/kg/day for females** based on ↓body weight, food consumption, ↑liver and kidney weights in both sexes and epididymis in males, ↓brain weights in males, hepato-cellular vacuolation in males, adenomas of the liver and lung in males, ↑in the incidence of multiple tumors in females<br><br>**NOAEL = 53.3 mg/kg/day for males and 70.9 mg/kg/day for females**<br><br>*There was no treatment related increase in tumor incidence when compared to controls. Dosing was considered adequate based on the effects observed on the top dose (2500 ppm/kg/day). | |
| Chronic - Dog | | | **MRID 43744201** (1995) **Acceptable/Guideline** 0, 15, 75, or 225 mg/kg/day via gelatin capsule for 52 weeks | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| | | | **LOAEL= 75 mg/kg/day in males and 225 mg/kg/day in females** based on emesis, capsular regurgitation incidences, gross and histopathologic changes in stomachs, and sinusoidal histiocytosis in livers.<br><br>**NOAEL= 15 mg/kg/day in males and 75 mg/kg/day in females.** | |
| Gene mutation-bacterial | **MRID 43581006** (1996)<br>**Acceptable/Guideline**<br>*Salmonella*<br>Five doses 100-5000 ug/plate. No mutagenic effect with or without S9 activation | **MRID 00042761** (1978)<br>**Acceptable/Guideline**<br>*Escherichia coli polA*.<br>Strains W3110 and p3478 at 1, 2 or mg/ml. Not mutagenic.<br><br>**MRID 00042762** (1978)<br>**Acceptable/Guideline**<br>*Salmonella.*<br>At 0.5-5000 ug/plate. Not mutagenic | | **MRID 43581004**<br>**Acceptable/Guideline**<br>*Salmonella*<br>Five doses 33-5000 ug/plate. No mutagenic effect with or without S9 activation |
| Gene mutation - mammalian: mouse lymphoma cells | **MRID 43580202** (1995)<br>**Acceptable/Guideline**<br>-S9: not mutagenic<br>+S9 mutagenic at 100 ug/mL and above | | | **MRID 43580201** (1994)<br>**Acceptable/Guideline**<br>-S9: not mutagenic<br>+S9 mutagenic at 300 ug/mL and above |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| Erythrocyte micronuleus mice | **MRID 43581005** (1994) **Acceptable/Guideline** IP injections 250, 500 or 1000 mg/kg to 5 mice/sex. Lethargy and death at high dose. Did not induce a clastogenic or aneurogenic effect. | **MRID 00042763** (1979) **Acceptable/Guideline** IP injections 60 or 125 mg/kg to 4 mice/sex. No overt symptoms at high dose. Negative. | | **MRID 43581003** (1994) **Acceptable/Guideline** IP injections 305, 610, or 1220 mg/kg to 5 mice/sex. Lethargy and death (48%) at high dose. Did not induce a clastogenic or aneurogenic effect |
| Mitotic gene conversion: *Saccharomyces cervisiae* | | **MRID 00042758, 00042759, 00042760** (1978) NAA was tested at $10^{-2}$, $10^{-3}$, $10^{-4}$, $10^{-5}$, $10^{-6}$ M.. NAA was not mutagenic in this test system. **Unacceptable**. No purity, not run at toxic dose, no S9 activation | | |
| Rodent dominant lethal assay | | **MRID 00042764** (1979) **Acceptable/Guideline** Oral doses of 125, 250, or 500 mg/kg/day to 10 male rats/dose for 5 days. NAA did not produce dominant lethal effects as measured by pre implantation and post implantation losses | | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| Metabolism | **Dixon *et al.*1977. NAA $^{14}$C as Na salt**. 60-100% of the AD was excreted in the urine by the end of 48 hours. **The glucuronic acid conjugate (GAC)**: major urinary metabolite in man, rhesus monkey, marmoset, rabbit, rat, and fruit bat. In the cat, no **GAC** was detected; but taurine and glycine conjugates. The **glycine** conjugate was a major urinary metabolite (>20%) in the cat, squirrel and bushbaby monkey and a minor metabolite in rabbit, rat, capuchia and marmoset monkey. **1-NAA glutamine** conjugate was formed only in the cynomolgus, squirrel and capuchin monkeys and marmoset in amounts not exceeding 3% of the AD. **1-NAA taurine** was excreted by all species except the rabbit, rat and the fruit bat. It was a major excretion product (>6%) in the squirrel and capuchin monkeys, the marmoset and the cat. When female rats were given ip doses of 5-500 mg/kg, bile duct cannulation showed that 10-44% of the radioactivity was present in the bile 3 hours after injection. While 0.6-32% was present in the urine. At the higher doses urinary GAC predominated whereas at the lower doses the glycine conjugates predominated. In the bile the GAC was the major metabolite (>80% of the bile radioactivity) and the glycine conjugate was a minor metabolite (<4% of the bile radioactivity). There was no analysis of the fecal radioactivity.<br><br>**Lethco and Brouwer, 1966. Carboxy -$^{14}$C-1- NAA as NA salt** in male rats. Within 3 days, 71-90% of the AD was excreted in the urine. At the lower doses (0.1-100 mg/kg) most of the radioactivity was excreted during the first 24 hours, while at the higher dose (250 mg/kg), excretion was highest on the second day. Fecal excretion was 3-10% at the 0.1-1.0 mg/kg doses and 14-21% of the AD at the 100 and 250 mg/kg doses. After the third day, no radioactivity was detected in the feces or urine at any dose. 70-93% of the urinary radioactivity was **NAA glycine conjugate** and **NAA GAC**. The GAC predominated at the two high doses and the glycine conjugate predominated at the lower dose. Minor amounts of NAA and two other minor unidentified metabolites were detected in the urine. Bile cannulation experiments demonstrated biliary metabolism and excretion of the test material. At the high dose a maximum of 29% of the AD was recovered at 6 hours, while a maximum of 54% was recovered at the low dose at 2 hours. At the low dose, the NAA glycine conjugate was the major urinary metabolite and the NAA GAC was a minor metabolite, while in the bile the preponderance of these two metabolites was reversed. Unchanged NAA was detected in the bile but not in the urine at both doses. At the high dose the NAA GAC was the major metabolite in both urine and bile while the glycine conjugate was a minor metabolite.<br><br>**MRID 43961701 (1996), Acceptable/Guideline**. Rats (5/sex) were given a single 1 or 100 mg/kg bw oral dose of [$^{14}$C] ring labeled -1-naphthaleneacetic acid, ethyl ester, or a 14-day repeated dose (1 mg/kg/day) of unlabeled material followed by a single dose of the labeled material. Overall recovery of AD was 98.6-101.8%. NAA ethyl ester was readily absorbed and excreted within 36 - 48 hours following all exposure regimens (urinary excretion: 67.6-85.3% of the AD at the low dose and 61.8-78% of the AD at the high dose). Fecal excretion was 12.3-35.2% of the AD. Tissue radioactivity was very low. The major pathway of metabolism involved ester cleavage followed by glycine and glucuronide conjugation at the low and low repeat doses. At the high dose, glucuronide conjugation | | | |

| Table A.2 Acute, Subchronic and Chronic Toxic Profile – Naphthalene Acetates | | | | |
|---|---|---|---|---|
| Study | PC 056001: Acetamide | PC 056002: NAA | PC 056007: Na salt | PC 056008: Ethyl ester |
| | appeared to play a more important role following ester cleavage. Parent compound was detected at low concentrations (0.5-4.7% of administered) only in feces.<br><br>**MRID 43963301 (1996), Acceptable/Guideline**. Rats (5/sex) were given either a single 1 or 100 mg/kg bw oral dose, or a 14-day repeated dose (1 mg/kg/day) using **[$^{14}$C] ring labeled -1-naphthaleneacetamide (NAAD).** Overall recovery of the AD was 97.2-101%. NAAD was readily absorbed and excreted within 36 hours (urinary excretion: 70.8-74.1% of the AD at the low dose, single or multiple, 66.2-69.5% of the AD excreted in urine at the high dose). Fecal excretion was 21.6-26.2% of the AD. Tissue radioactivity was very low (<0.5% of the AD). Metabolism involved amide cleavage followed by glycine conjugation (13.7-47.3% of the AD) glucuronide conjugation (4.5-7.0% of the AD at the low dose and 12.8-18.1% of the AD at the high dose in the urine). For feces, the major metabolite detected was the dihydrodiol of naphthaleneacetamide (3.6-11.3% of the AD). Parent compound was detected at low concentrations (0.7-1.9% of administered) only in feces. | | | |

## A.3 Literature Search for NAA

Date and Time of Search: 07/23/2019; 11:42 am
Search Details:
("1-Naphthaleneacetic acid") AND (rat OR mouse OR dog OR rabbit OR monkey OR mammal)

Citations Identified in PubMed*: 28
SWIFT-Review**Tags:
Number of Swift Articles: 20 for Animal
Number of Swift Articles: 14 for Human
Number of Swift Articles: 0 for No Tag

Date and Time of Search: 07/23/2019; 11:30 am
Search Details:
(("1-Naphthaleneacetamide") AND (rat OR mouse OR dog OR rabbit OR monkey OR mammal))

Citations Identified in PubMed*: 2
SWIFT-Review**Tags:
Number of Swift Articles: 0 for Animal
Number of Swift Articles: 0 for Human
Number of Swift Articles: 0 for No Tag

Other searches of note:
056001 - 1-Naphthaleneacetamide PubMed hits: 2
056002 - 1-Naphthaleneacetic acid PubMed hits: 28
056003 - Potassium 1-naphthaleneacetate PubMed hits: 0
056004 - Ammonium 1-naphthaleneacetate PubMed hits: 0
056007 - Sodium 1-naphthaleneacetate PubMed hits: 0
056008 - Ethyl 1-naphthaleneacetate PubMed hits: 0

All studies identified in the PubMed search were screened when the citation list was ≤100. Screening of larger citations lists (>100 citations) was conducted after prioritization in SWIFT-Review and focused on studies identified with the "Animal" and/or "Human" tag.

Conclusion of Literature Search: Following title/abstract and/or full text screening, no studies were identified as containing potentially relevant information (either quantitative or qualitative) for the NAA human health registration review risk assessment.

*PubMed is a freely available search engine that provides access to life science and biomedical references predominantly using the MEDLINE database.
**SWIFT-Review is a freely available software tool created by Sciome LLC that assists with literature prioritization. SWIFT-Review was used to prioritize studies identified in the PubMed search based on the model of interest in the study (e.g. human, animal, *in vitro*, etc.).
Studies could have resulted in multiple tags which would account for citations identified in PubMed not matching the number of tagged citations.

## Appendix B. Physical/Chemical Properties

| Table B.1. Physicochemical Properties of the Naphthalene Acetates | | |
|---|---|---|
| **Parameter** | **Value** | **Reference** |
| **Active Ingredient** | **NAA acetamide** | |
| Melting point/range | 182-184 °C | Farm Chemicals Handbook |
| pH of 1% aqueous suspension | 5.1 | Product CSF |
| Density or specific gravity | 0.221 g/cm$^3$ | Product CSF |
| Water solubility (20 °C) | not available | |
| Solvent solubility (20 °C) | not available | |
| Vapor pressure at 20 °C | not available | |
| Dissociation constant (pK$_a$) | not available | |
| Octanol/water partition coefficient (K$_{ow}$) | not available | |
| UV/vis absorption spectrum | not available | |
| **Active ingredient** | **NAA** | |
| Melting point/range | 130 °C | Farm Chemicals Handbook |
| pH of 1% aqueous suspension | 3.45 | RD B. Kitchens, 15-MAY-2000, D265117 |
| Density or specific gravity | 0.45 g/mL | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| Water solubility (26 °C) | 0.042 g/100 mL | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| Solvent solubility (26 °C) | xylene 5.5 g/100 mL<br>$CCl_4$ 1.06 g/100 mL<br>freely soluble in acetone, ether, and chloroform | CB Nos. 3468 and 3469, 6/3/88, F. Suhre<br><br>Farm Chemicals Handbook |
| Vapor pressure at 20 °C | 0.3 mm Hg at 26 °C | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| Dissociation constant (pK$_a$) | 3.16 x 10$^{-4}$ | CB Nos. 3970 and 3971, 7/5/88, F. Suhre |
| Octanol/water partition coefficient (K$_{ow}$) | not applicable; polar compound | |
| UV/vis absorption spectrum | not available | |
| **Active ingredient** | **NAA sodium salt** | |
| Melting point/range | >300 °C | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| pH of 1% aqueous suspension | 9.1 | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| Density or specific gravity | 0.46 g/mL | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| Water solubility (26 °C) | 340 g/100 mL | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| Solvent solubility (26 °C) | insoluble in nonpolar solvents | CB Nos. 3468 and 3469, 6/3/88, F. Suhre |
| Vapor pressure at 20 °C | not available | |
| Dissociation constant (pK$_a$) | 3.16 x 10$^{-4}$ | CB Nos. 3970 and 3971, 7/5/88, F. Suhre |
| Octanol/water partition coefficient (K$_{ow}$) | not applicable; polar compound | |
| UV/vis absorption spectrum | not available | |

| Table B.1. Physicochemical Properties of the Naphthalene Acetates | | |
|---|---|---|
| **Parameter** | **Value** | **Reference** |
| **Active ingredient** | **NAA ethyl ester** | |
| Boiling point/range | >150 °C | Old un-reviewed Union Carbide data |
| pH of 1% aqueous suspension | not available | |
| Density or specific gravity | 1.11 at 20 °C | Old un-reviewed Union Carbide data |
| Water solubility (26 °C) | insoluble | Old un-reviewed Union Carbide data |
| Solvent solubility | soluble in xylene, toluene, ethanol, acetone, and methyl ethyl ketone | Old un-reviewed Union Carbide data |
| Vapor pressure at 20 °C | not available | |
| Dissociation constant ($pK_a$) | not available | |
| Octanol/water partition coefficient ($K_{ow}$) | not available | |
| UV/vis absorption spectrum | not available | |

## Appendix C. Summary of Occupational and Residential Non-cancer Algorithms

Residential Non-cancer Post-application Algorithms

Post-application Hand-to-Mouth Exposure Algorithm– Physical Activities on Turf
Exposure from hand-to-mouth activity is calculated as follows (based on the algorithm utilized in the SHEDS-Multimedia model):

$$E = [HR * (F_M * SA_H) * (ET * N\_Replen) * (1- (1- SE)^{(Freq\_HtM/N-Replen)})]$$

where:

E = exposure (mg/day);
HR = hand residue loading (mg/cm$^2$);
FM = fraction hand surface area mouthed / event (fraction/event);
SAH = typical surface area of one hand (cm$^2$);
ET = exposure time (hr/day);
N_Replen = number of replenishment intervals per hour (intervals/hour);
SE = saliva extraction factor (i.e., mouthing removal efficiency); and
Freq_HtM = number of hand-to-mouth contacts events per hour (events/hour).

and

$$HR = \frac{Fai_{hands} * DE}{SA_H * 2}$$

where:

HR = hand residue loading (mg/cm$^2$);
$Fai_{hands}$ = fraction ai on hands compared to total surface residue from dermal transfer coefficient study (unitless);
DE = dermal exposure (mg); and
$SA_H$ = typical surface area of one hand (cm$^2$).

Dose, normalized to body weight, is calculated as:

$$D = \frac{E}{BW}$$

where:

| | |
|---|---|
| D | = dose (mg/kg-day); |
| E | = exposure (mg/day); and |
| BW | = body weight (kg). |

| Table C-1: Turf (Physical Activities) – Inputs for Residential Post-application Hand-to-Mouth Exposure | | | |
|---|---|---|---|
| **Algorithm Notation** | **Exposure Factor (units)** | | **Point Estimate(s)** |
| $Fai_{hands}$ | Fraction of ai on hands from dermal transfer coefficient study (unitless) | Liquid formulations | 0.06 |
| | | Granular formulations | 0.027 |
| DE | Dermal exposure (mg) | | Calculated |
| $SA_H$ | Typical surface area of one hand ($cm^2$), children 1 < 2 years old | | 150 |
| AR | Application rate (mass active ingredient per unit area) | | **See Table F.1.** |
| HR | Residue available on the hands ($mg/cm^2$) | | Calculated via (DE * $Fai_{hands}$)/$SA_H$ |
| $F_M$ | Fraction hand surface area mouthed (fraction/event) | | 0.127 |
| N_Replen | Replenishment intervals per hour (intervals/hr) | | 4 |
| ET | Exposure time (hrs/day) | | 1.5 |
| SE | Saliva extraction factor (unitless) | | 0.48 |
| Freq_HtM | Hand-to-mouth events per hour (events/hr) | | 13.9 |
| BW | Body Weight (kg) | Children 1 < 2 years old | 11 |

Post-application Object-to-Mouth Exposure Algorithm– Physical Activities on Turf

Exposure from object-to-mouth activity is calculated as follows (based on the algorithm utilized in SHEDS-Multimedia):

$$E = [OR^* CF1 * SAMo * (ET * N\_Replen) * (1- (1- SEo)^{(Freq\_OtM/N\_Replen)})]$$

where:

E = exposure (mg/day);
OR = chemical residue loading on the object on day "t" ($ug/cm^2$);
CF1 = weight unit conversion factor (0.001 mg/µg);
SAMo = area of the object surface that is mouthed ($cm^2$/event);
ET = exposure time (hr/day);
N_Replen = number of replenishment intervals per hour (intervals/hour);
SEo = saliva extraction factor (i.e., mouthing removal efficiency); and
Freq_OtM = number of object-to-mouth contact events per hour (events/hour).

and

$$OR = AR * Fo * CF2 * CF3$$

where:

OR = chemical residue loading on the object (µg/cm$^2$);
AR = application rate (lbs ai/ft$^2$ or lb ai/acre);
Fo = fraction of residue available on the object (unitless);
CF2 = weight unit conversion factor (4.54 x 10$^8$ µg/lb); and
CF3 = area unit conversion factor (1.08 x 10$^{-3}$ ft$^2$/cm$^2$ or 2.47 x 10$^{-8}$ acre/cm$^2$).

Dose, normalized to body weight, is calculated as:

$$D = \frac{E}{BW}$$

where:

| | | |
|---|---|---|
| D | = | dose (mg/kg-day); |
| E | = | exposure (mg/day); and |
| BW | = | body weight (kg). |

**Table C-2: Turf (Physical Activities) – Inputs for Residential Post-application Object-to-Mouth Exposure**

| Algorithm Notation | Exposure Factor (units) | | Point Estimate(s) |
|---|---|---|---|
| AR | Application rate (to turf) (mass active ingredient per unit area) | | **See Table F.1.** |
| Fo | Fraction of AR as OR following application [1] | | 0.01 (liquids) 0.02 (solids) |
| SAM$_O$ | Surface area of object mouthed (cm$^2$/event) | | 10 |
| N_Replen | Replenishment intervals per hour (intervals/hour) | | 4 |
| SE$_O$ | Saliva extraction factor (fraction) | | 0.48 |
| ET | Exposure time (hours per day) | | 1.5 |
| Freq_OtM | Object-to-mouth events per hour (events/hr) | | 8.8 |
| BW | Body Weight (kg) | Children 1 < 2 years old | 11 |

[1] This SOP assumes that all of the residue on the turf could be transferred to the object (e.g., object residue is equal to turf transferable residue).

Post-application Incidental Soil Ingestion Exposure Algorithm– Physical Activities on Turf
Exposure from incidental soil ingestion is calculated as follows:

$$E = SRt * SIgR * CF1$$

where:
E = exposure (mg/day);
SRt = soil residue on day "t" (µg/g);
SIgR = ingestion rate of soil (mg/day); and
CF1 = weight unit conversion factor (1 x 10$^{-6}$ g/µg).

and

$$SRt = AR * FS * (1\text{-}F_D)^t * CF2 * CF3 * CF4$$

where:

$SR_t$ = soil residue on day "t" (µg/g);
AR = application rate (lbs ai/$ft^2$ or lb ai/acre);
FS = fraction of ai available in uppermost cm of soil (fraction/cm);
$F_D$ = fraction of residue that dissipates daily (unitless);
T = post-application day on which exposure is being assessed;
CF2 = weight unit conversion factor (4.54 x $10^8$ µg/lb);
CF3 = area unit conversion factor (1.08 x $10^{-3}$ $ft^2/cm^2$ or 2.47 x $10^{-8}$ acre/$cm^2$); and
CF4 = soil volume to weight unit conversion factor (0.67 $cm^3$/g soil).

Dose, normalized to body weight, are calculated as:

$$D = \frac{E}{BW}$$

where:

| | | |
|---|---|---|
| D | = | dose (mg/kg-day); |
| E | = | exposure (mg/day); and |
| BW | = | body weight (kg). |

**Table C-3: Turf (Physical Activities) – Inputs for Residential Post-application Incidental Soil Ingestion Exposure**

| Algorithm Notation | Exposure Factor (units) | | Point Estimate(s) |
|---|---|---|---|
| AR | Application rate (mass active ingredient per unit area) | | **See Table F.1.** |
| FS | Fraction of AR available in uppermost 1 cm of soil (unitless) | | 1 |
| $F_D$ | Daily residue dissipation (fraction) | | 0.1 |
| SIgR | Soil ingestion rate (mg/day) | | 50 |
| BW | Body weight (kg) | Children 1 < 2 years old | 11 |

Occupational Non-cancer Handler Algorithms

Potential daily exposures for occupational handlers are calculated using the following formulas:

$$E=UE * AR * A * 0.001\ mg/ug$$

where:

| | | |
|---|---|---|
| E | = | exposure (mg ai/day), |
| UE | = | unit exposure (µg ai/lb ai), |
| AR | = | maximum application rate according to registered label (lb ai A or lb ai/gal), and |

A = area treated or amount handled (e.g., A/day, gal/day).

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

where:

ADD = average daily dose absorbed in a given scenario (mg ai/kg/day),
E = exposure (mg ai/day),
AF = absorption factor (dermal and/or inhalation), and
BW = body weight (kg).

*Margin of Exposure:* Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers are compared to the appropriate POD (i.e., NOAEL) to assess the risk to occupational handlers for each exposure route. All MOE values are calculated using the following formula:

$$MOE = \frac{POD}{ADD}$$

where:

MOE = margin of exposure: value used by HED to represent risk estimates (unitless),
POD = point of departure (mg/kg/day), and
ADD = average daily dose absorbed in a given scenario (mg ai/kg/day).

## Appendix D. Summary of Spray Drift Algorithms

Modified TTR Equation to Account for Spray Drift

The equation presented below, should be used to evaluate potential risks from spray drift. This equation is similar to the standard TTR equation, except that an additional term has been included (DF or Drift Fraction) that provides an adjustment for the amount of drift that moves into and deposits in a non-target area, such as a lawn. This equation applies to situations where TTR data are not available.

$$TTR = AR * DF * F * (1-D)^t * CF2 * CF3$$

where:

| | | |
|---|---|---|
| TTR | = | turf transferable residue ($\mu g/cm^2$) |
| DF | = | drift fraction of spray drift that deposits on lawns (unitless) |
| AR | = | application rate (lbs ai/$ft^2$ or lb ai/acre) |
| F | = | fraction of ai as transferable residue following application (unitless) |
| D | = | fraction of residue that dissipates daily (unitless) |
| T | = | post-application day on which exposure is being assessed (Day 0 in this SOP) |
| CF2 | = | weight unit conversion factor ($4.54 \times 10^8$ µg/lb) |
| CF3 | = | area unit conversion factor ($1.08 \times 10^{-3}$ $ft^2/cm^2$ or $2.47 \times 10^{-8}$ acre/$cm^2$) |

If chemical specific TTR data are available, the residue on Day 0 is used after it is adjusted based on the ratio of the applicable application rate for risk assessment (i.e., based on the crop of concern) and the application rate for the TTR study followed by an additional adjustment for the drift fraction factor as illustrated above.

Drift Fraction Values

The spray drift fraction (DF) values for selected aerial, groundboom, and airblast application scenarios, based on average deposition values at each distance of interest, are shown in the tables below (Tables D-1, -2, -3).

**Table D-1. Average Drift Fractions for a 50' Wide Lawn Starting at Various Distances Downwind From a Field Treated Using Aerial Equipment.**

| Droplet Size+ | Distance Downwind From Treated Field (feet) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 10 | 25 | 50 | 75 | 100 | 125 | 150 | 200 | 250 | 300 |
| ***Fine to Medium**** | ***0.257*** | ***0.209*** | ***0.169*** | ***0.129*** | ***0.098*** | ***0.076*** | ***0.063*** | ***0.054*** | ***0.041*** | ***0.034*** | ***0.028*** |
| Medium to Coarse* | 0.211 | 0.156 | 0.115 | 0.082 | 0.058 | 0.044 | 0.035 | 0.029 | 0.021 | 0.016 | 0.013 |
| Coarse to Very Coarse* | 0.183 | 0.124 | 0.082 | 0.053 | 0.037 | 0.028 | 0.022 | 0.018 | 0.013 | 0.010 | 0.008 |
| Very Fine to Fine* | 0.373 | 0.340 | 0.305 | 0.262 | 0.226 | 0.197 | 0.175 | 0.155 | 0.127 | 0.108 | 0.095 |
| AT401, M, 10 mph, 34% SD | 0.234 | 0.183 | 0.142 | 0.105 | 0.078 | 0.060 | 0.049 | 0.042 | 0.032 | 0.026 | 0.021 |
| WASP, M, 10 mph, 34% SD | 0.218 | 0.171 | 0.129 | 0.086 | 0.063 | 0.049 | 0.040 | 0.034 | 0.026 | 0.021 | 0.018 |
| AT401, C, 10 mph, 25% SD | 0.198 | 0.141 | 0.099 | 0.067 | 0.047 | 0.036 | 0.029 | 0.024 | 0.017 | 0.013 | 0.011 |
| WASP, C, 10 mph, 25% SD | 0.171 | 0.121 | 0.084 | 0.053 | 0.038 | 0.028 | 0.023 | 0.018 | 0.013 | 0.010 | 0.009 |

**Table D-1. Average Drift Fractions for a 50' Wide Lawn Starting at Various Distances Downwind From a Field Treated Using Aerial Equipment.**

| Droplet Size+ | Distance Downwind From Treated Field (feet) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 10 | 25 | 50 | 75 | 100 | 125 | 150 | 200 | 250 | 300 |
| AT401, VC, 10 mph, 20% SD | 0.175 | 0.115 | 0.072 | 0.044 | 0.031 | 0.023 | 0.018 | 0.014 | 0.010 | 0.008 | 0.006 |
| WASP, VC, 10 mph, 20% SD | 0.138 | 0.088 | 0.057 | 0.036 | 0.025 | 0.019 | 0.014 | 0.012 | 0.008 | 0.007 | 0.006 |

*Information is based on the Tier 1 option in the AgDrift model. The fine to medium spray quality is used in this SOP as the basis for the screening level assessment. These are all based on fixed wing aircraft.
+For further options the AT401 is the representative fixed wing aircraft and the Wasp is the representative helicopter. SD = swath displacement. SD values for non-Tier I options computed using AgDrift automated adjustment option.

**Spray Quality Summaries:** Fine to Medium (F2M): $D_{v0.5}$ = 255 µM; Medium (M): $D_{v0.5}$ = 294 µM; Medium to Coarse (M2C): $D_{v0.5}$ = 341 µM; Coarse (C) $D_{v0.5}$ = 385 µM; Coarse to Very Coarse (C2VC): $D_{v0.5}$ = 439

**Table D-2. Average Drift Fractions for a 50' Wide Lawn Starting at Various Distances Downwind From a Field Treated Using Ground Equipment.**

| Boom Height | Droplet Size | Distance Downwind From Treated Field (feet) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 10 | 25 | 50 | 75 | 100 | 125 | 150 | 200 | 250 | 300 |
| ***High*** | ***Very Fine to Fine*** | ***0.187*** | ***0.093*** | ***0.056*** | ***0.035*** | ***0.025*** | ***0.020*** | ***0.017*** | ***0.014*** | ***0.011*** | ***0.008*** | ***0.007*** |
| Low | Very Fine to Fine | 0.085 | 0.032 | 0.020 | 0.013 | 0.010 | 0.008 | 0.007 | 0.006 | 0.005 | 0.004 | 0.003 |
| High | Fine to Medium/Coarse | 0.049 | 0.019 | 0.013 | 0.009 | 0.007 | 0.006 | 0.005 | 0.005 | 0.004 | 0.003 | 0.003 |
| Low | Fine to Medium/Coarse | 0.033 | 0.012 | 0.008 | 0.006 | 0.005 | 0.004 | 0.003 | 0.003 | 0.002 | 0.002 | 0.002 |

Low Boom 0.508 m (20 in), High Boom 1.27 m (50 in)
Fine to Medium/Coarse (F2M/C): Avg. Droplet size ($D_{v0.5}$) = 341 µM

**Table D-3. Average Drift Fractions for a 50' Wide Lawn Starting at Various Distances Downwind From a Field Treated Using Orchard Blast Equipment.**

| Crop Canopy | Distance Downwind From Treated Field (feet) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 10 | 25 | 50 | 75 | 100 | 125 | 150 | 200 | 250 | 300 |
| ***Sparse*** | ***0.1435*** | ***0.0834*** | ***0.0443*** | ***0.0200*** | ***0.0110*** | ***0.0068*** | ***0.0045*** | ***0.0032*** | ***0.0018*** | ***0.0011*** | ***0.0008*** |
| Normal | 0.0030 | 0.0020 | 0.0013 | 0.0009 | 0.0006 | 0.0005 | 0.0004 | 0.0003 | 0.0003 | 0.0002 | 0.0002 |
| Dense | 0.0422 | 0.0279 | 0.0175 | 0.0100 | 0.0067 | 0.0049 | 0.0039 | 0.0032 | 0.0023 | 0.0018 | 0.0015 |
| Vineyard | 0.0080 | 0.0041 | 0.0022 | 0.0012 | 0.0008 | 0.0006 | 0.0005 | 0.0004 | 0.0003 | 0.0002 | 0.0002 |

Sparse (Young, Dormant): This composite orchard combines small grapefruit and dormant apple orchards. Normal (Stone and Pome Fruit, Vineyard): This composite orchard combines grape and orchards.
Dense (Citrus, Tall Trees): This composite orchard combines almond, orange, grapefruit, small grapefruit (mist blower) and pecan orchards.
Vineyard: This composite curve combines grape air blast sprayer applications and may not apply to other application equipment.
Note: AgDrift also contains an "Orchard" scenario which is a composite of results from all tree canopy types.

Post-application Dermal Exposure Algorithm—Physical Activities on Turf

Exposure resulting from contacting previously treated turf while performing physical activities is calculated as shown below:

$$E = TTR_t \times CF1 \times TC \times ET$$

where:

| | | |
|---|---|---|
| E | = | exposure (mg/day); |
| $TTR_t$ | = | turf transferable residue on day t (µg/cm$^2$); |
| CF1 | = | weight unit conversion factor (0.001 mg/µg); |
| TC | = | transfer coefficient (cm$^2$/hr); and |
| ET | = | exposure time (hr/day). |

Dermal absorbed doses are calculated as:

$$D = \frac{E \times AF}{BW}$$

where:

| | | |
|---|---|---|
| D | = | dose (mg/kg-day); |
| E | = | exposure (mg/day); |
| AF | = | absorption factor (dermal); and |
| BW | = | body weight (kg). |

**Table D-4. Turf (Physical Activities) – Recommended Point Estimates for Post-Application Dermal Exposure Factors**

| Algorithm Notation | Exposure Factor (units) | | | Point Estimate(s) |
|---|---|---|---|---|
| AR | Application rate (mass active ingredient per unit area) | | | See Table F.1. |
| F | Fraction of AR as TTR following application (if chemical-specific data are unavailable) | | L/WP/WDG | 0.01 |
| | | | Granules | 0.002 |
| $F_D$ | Daily residue dissipation (if chemical-specific data are unavailable) (fraction) | | L/WP/WDG | 0.1 |
| | | | Granules | 0.1 |
| TC | Transfer Coefficient (cm$^2$/hr) | L/WP/WDG | Adults | 180,000 |
| | | | Children 1 < 2 years old | 49,000 |
| | | Granules | Adults | 200,000 |
| | | | Children 1 < 2 years old | 54,000 |
| ET | Exposure Time (hours per day) | | Adults | 1.5 |
| | | | Children 1 < 2 years old | 1.5 |
| BW | Body Weight (kg) | | Adults | 69 |
| | | | Children 1 < 2 years old | 11 |

Post-application Hand-to-Mouth Exposure Algorithm—Physical Activities on Turf

Exposure from hand-to-mouth activity is calculated as follows (based on the algorithm utilized in the SHEDS-Multimedia model):

$$E = [HR * (F_M * SA_H) * (ET * N\_Replen) * (1- (1- SE)^{(Freq\_HtM/N-Replen)})]$$

where:

E = exposure (mg/day);

HR = hand residue loading (mg/cm$^2$);
FM = fraction hand surface area mouthed / event (fraction/event);
SAH = typical surface area of one hand (cm$^2$);
ET = exposure time (hr/day);
N_Replen = number of replenishment intervals per hour (intervals/hour);
SE = saliva extraction factor (i.e., mouthing removal efficiency); and
Freq_HtM = number of hand-to-mouth contact events per hour (events/hour).

and

$$HR = \frac{Fai_{hands} * DE}{SA_H * 2}$$

where:

HR = hand residue loading (mg/cm$^2$);
$Fai_{hands}$ = fraction ai on hands compared to total surface residue from dermal transfer coefficient study (unitless);
DE = dermal exposure (mg); and
$SA_H$ = typical surface area of one hand (cm$^2$).

Dose, normalized to body weight, is calculated as:

$$D = \frac{E}{BW}$$

where:

D = dose (mg/kg-day);
E = exposure (mg/day); and
BW = body weight (kg).

**Table D-5. Turf (Physical Activities) – Inputs for Residential Post-application Hand-to-Mouth Exposure**

| Algorithm Notation | Exposure Factor (units) | | Point Estimate(s) |
|---|---|---|---|
| $Fai_{hands}$ | Fraction of ai on hands from dermal transfer coefficient study (unitless) | Liquid formulations | 0.06 |
| | | Granular formulations | 0.027 |
| DE | Dermal exposure (mg) | | Calculated |
| $SA_H$ | Typical surface area of one hand (cm$^2$), children 1 < 2 years old | | 150 |
| AR | Application rate (mass active ingredient per unit area) | | 0.5 |
| HR | Residue available on the hands (mg/cm$^2$) | | Calculated via (DE * $Fai_{hands}$)/$SA_H$ |
| $F_M$ | Fraction hand surface area mouthed (fraction/event) | | 0.127 |
| N_Replen | Replenishment intervals per hour (intervals/hr) | | 4 |
| ET | Exposure time (hrs/day) | | 1.5 |
| SE | Saliva extraction factor (unitless) | | 0.48 |
| Freq_HtM | Hand-to-mouth events per hour (events/hr) | | 13.9 |
| BW | Body Weight (kg) | Children 1 < 2 years old | 11 |

## Appendix E. Children (1 to <2 years old) Risk Estimates (MOEs) Related to Indirect Incidental Oral Spray Drift Exposure for NAA.

| Crop/ Rate Group | Spray Type/ Nozzle Configuration | App. Rate (lb ai/A) | Estimated or Adjusted $TTR_t$ (ug/cm2) | At Edge | 10 Feet | 25 Feet | 50 Feet | 75 Feet | 100 Feet | 125 Feet | 150 Feet | 200 Feet | 250 Feet | 300 Feet |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE |
| **Orchard/Vinevard (Olive)** | | | | | | | | | | | | | | |
| Aerial | ***Fine to Medium*** | 0.33 | 0.0366795 | 19,000 | 24,000 | 29,000 | 39,000 | 51,000 | 65,000 | 79,000 | 92,000 | 120,000 | 150,000 | 180,000 |
| | Medium to Coarse | | | 24,000 | 32,000 | 43,000 | 61,000 | 86,000 | 110,000 | 140,000 | 170,000 | 240,000 | 310,000 | 380,000 |
| | Coarse to Very Coarse | | | 27,000 | 40,000 | 61,000 | 94,000 | 130,000 | 180,000 | 230,000 | 280,000 | 380,000 | 500,000 | 620,000 |
| | Very Fine to Fine | | | 13,000 | 15,000 | 16,000 | 19,000 | 22,000 | 25,000 | 28,000 | 32,000 | 39,000 | 46,000 | 52,000 |
| | AT401, M, 10 mph, 37% SD | | | 21,000 | 27,000 | 35,000 | 47,000 | 64,000 | 83,000 | 100,000 | 120,000 | 160,000 | 190,000 | 240,000 |
| | WASP, M, 10 mph, 37% SD | | | 23,000 | 29,000 | 39,000 | 58,000 | 79,000 | 100,000 | 120,000 | 150,000 | 190,000 | 240,000 | 280,000 |
| | AT401, C, 10 mph, 25% SD | | | 25,000 | 35,000 | 50,000 | 74,000 | 110,000 | 140,000 | 170,000 | 210,000 | 290,000 | 380,000 | 450,000 |
| | WASP, C, 10 mph, 25% SD | | | 29,000 | 41,000 | 59,000 | 94,000 | 130,000 | 180,000 | 220,000 | 280,000 | 380,000 | 500,000 | 550,000 |
| | AT401, VC, 10 mph, 20% SD | | | 28,000 | 43,000 | 69,000 | 110,000 | 160,000 | 220,000 | 280,000 | 360,000 | 500,000 | 620,000 | 830,000 |
| | WASP, VC, 10 mph, 20% SD | | | 36,000 | 57,000 | 87,000 | 140,000 | 200,000 | 260,000 | 360,000 | 410,000 | 620,000 | 710,000 | 830,000 |
| Ground-boom | ***High Boom Very fine to Fine*** | | | 27,000 | 53,000 | 89,000 | 140,000 | 200,000 | 250,000 | 290,000 | 360,000 | 450,000 | 620,000 | 710,000 |

| Crop/ Rate Group | Spray Type/ Nozzle Configuration | App. Rate (lb ai/A) | Estimated or Adjusted $TTR_t$ (ug/cm2) | At Edge | 10 Feet | 25 Feet | 50 Feet | 75 Feet | 100 Feet | 125 Feet | 150 Feet | 200 Feet | 250 Feet | 300 Feet |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE | HtM MOE |
| | Low Boom Very fine to Fine | | | 59,000 | 160,000 | 250,000 | 380,000 | 500,000 | 620,000 | 710,000 | 830,000 | 990,000 | 1,200,000 | 1,700,000 |
| | High Boom Fine to Medium/ Coarse | | | 100,000 | 260,000 | 380,000 | 550,000 | 710,000 | 830,000 | 990,000 | 990,000 | 1,200,000 | 1,700,000 | 1,700,000 |
| | Low Boom Fine to Medium/ Coarse | | | 150,000 | 410,000 | 620,000 | 830,000 | 990,000 | 1,200,000 | 1,700,000 | 1,700,000 | 2,500,000 | 2,500,000 | 2,500,000 |
| Airblast | *Sparse* | | | 35,000 | 60,000 | 110,000 | 250,000 | 450,000 | 730,000 | 1,100,000 | 1,600,000 | 2,800,000 | 4,500,000 | 6,200,000 |
| | Normal | | | 1,700,000 | 2,500,000 | 3,800,000 | 5,500,000 | 8,300,000 | 9,900,000 | 12,000,000.0 | 17,000,000.0 | 17,000,000.0 | 25,000,000.0 | 25,000,000.0 |
| | Dense | | | 120,000 | 180,000 | 280,000 | 500,000 | 740,000 | 1,000,000 | 1,300,000 | 1,600,000 | 2,200,000 | 2,800,000 | 3,300,000 |
| | Vineyard | | | 620,000 | 1,200,000 | 2,300,000 | 4,100,000 | 6,200,000 | 8,300,000 | 9,900,000 | 12,000,000 | 17,000,000 | 25,000,000 | 25,000,000 |

## Appendix F. Use Summary for NAA

**Table F.1. Summary of Directions for Use of NAA.**

| Crop/Use Site | | Formulation Type | Type of Application | EPA Reg No. | Max. Single App. Rate | Application Equipment | PPE | REI | Use Directions and Limitations |
|---|---|---|---|---|---|---|---|---|---|
| Olive | Orchard/Vineyard | Liquid | Broadcast | 62097-38 | 0.33 lb ai/A; 0.066 lb ai/gallon | Aerial, Ground, Airblast, Hand-Held Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | Do not apply this product through any type of irrigation system. |
| | | Liquid | Directed Spray | 5481-429 | 0.33 lb ai/A (0.08 lb ai/gallon) | Hand-Held Pump-Up Sprayer, Backpack Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 12 hours | The product is applied with hand-held equipment. The product prevents or inhibits vegetative bud development in woody plants after pruning. The product reduces resprouting on bearing and non-bearing apple, olive, pear, avocado, mamey sapote and mango trees and on ornamental olives, crabapples and woody ornamental plants. Do not |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop/Use Site | | Formulation Type | Type of Application | EPA Reg No. | Max. Single App. Rate | Application Equipment | PPE | REI | Use Directions and Limitations |
| | | | | | | | | | apply this product through any type of irrigation system. |
| | | RTU Liquid | Directed Spray | 5481-452 | 0.11 lb ai/gallon | Hand-Held Sprayer, Backpack Sprayer, Low-Pressure Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, protective eyewear. | 12 hours | Prune existing sprouts and treat during the dormant season. Thoroughly cover area where existing sprouts were removed but restrict treatment to the cut surfaces and 2 to 3 inches of the surrounding area. Apply the product with a small hand-held sprayer or backpack sprayer. For large projects, power operated low pressure spray equipment with an attached hand-gun or trunk-directed nozzle can be used. Do not apply this product through any type of irrigation system. |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| Apple | Orchard/ Vineyard | Wettable Powder | Broadcast | 5481-426 | 0.11 lb ai/A (0.0011 lb ai/gallon) | Aerial, Airblast, Ground, Backpack Sprayer, Hand-Held Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | The product is used for thinning apples. Spray the product at petal fall. Do not apply this product through any type of irrigation system. |
| | | Liquid | Directed Spray | 5481-429 | 0.08 lb ai/gallon | Hand-Held Pump-Up Sprayer, Backpack Sprayer, Handgun sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 12 hours | The product is applied with hand-held equipment. The product prevents or inhibits vegetative bud development in woody plants after pruning. The product reduces resprouting on bearing and non-bearing apple, olive, pear, avocado, mamey sapote and mango trees and on ornamental olives, crabapples and woody ornamental plants. Do not apply this product through any type of irrigation system. |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| | | Water Disperable Granule | Broadcast | 62097-37 | 0.11 lb ai/A (0.002 lb ai/gallon) | Aerial, Ground, Airblast, Hand-Held Sprayer, Backpack Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | Plant growth regulator for thinning and control of pre-harvest drop of apples and pears, and for promoting return bloom of apples the following season. Do not apply this product through any type of irrigation system. |
| | | RTU Liquid | Directed Spray | 5481-452 | 0.11 lb ai/gallon | Hand-Held Pump-Up Sprayer, Backpack Sprayer, Low-Pressure Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, protective eyewear. | 12 hours | Prune existing sprouts and treat during the dormant season. Thoroughly cover area where existing sprouts were removed but restrict treatment to the cut surfaces and 2 to 3 inches of the surrounding area. Apply the product with a small hand-held sprayer or backpack sprayer. For large projects, power operated low pressure spray |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| | | | | | | | | | equipment with an attached hand-gun or trunk-directed nozzle can be used. Do not apply this product through any type of irrigation system. |
| Pear | Orchard/ Vineyard | Wettable Powder | Broadcast | 5481-426 | 0.11 lb ai/A (0.0011 lb ai/gallon) | Aerial, Ground, Airblast, Hand-Held Sprayer, Backpack Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | The product is used for thinning pears. Spray the product at petal fall or within 5 to 7 days after petal fall. Do not apply this product through any type of irrigation system. |
| | | Liquid | Directed Spray | 5481-429 | 0.08 lb ai/gallon | Hand-Held Pump-Up Sprayer, Backpack Sprayer, Handgun Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 12 hours | The product is applied with hand-held equipment. The product prevents or inhibits vegetative bud development in woody plants after pruning. The product reduces resprouting on bearing and non-bearing apple, olive, pear, |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop/Use Site | | Formulation Type | Type of Application | EPA Reg No. | Max. Single App. Rate | Application Equipment | PPE | REI | Use Directions and Limitations |
| | | | | | | | | | avocado, mamey sapote and mango trees and on ornamental olives, crabapples and woody ornamental plants. Do not apply this product through any type of irrigation system. |
| | | RTU Liquid | Directed Spray | 5481-452 | 0.11 lb ai/gallon | Hand-Held Pump-Up Sprayer, Backpack Sprayer, Low Pressure Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, protective eyewear. | 12 hours | Prune existing sprouts and treat during the dormant season. Thoroughly cover area where existing sprouts were removed but restrict treatment to the cut surfaces and 2 to 3 inches of the surrounding area. Apply the product with a small hand-held sprayer or backpack sprayer. For large projects, power operated low pressure spray equipment with an attached hand-gun or trunk-directed nozzle can be used. |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| | | | | | | | | | Do not apply this product through any type of irrigation system. |
| | | Water Dispersible Granule | Broadcast | 62097-37 | 0.05 lb ai/A (0.001 lb ai/gallon) | Aerial, Ground, Airblast, Backpack Sprayer, Hand-Held Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | Do not apply this product through any type of irrigation system. |
| Plum | Orchard/ Vineyard | Liquid | Broadcast | 5481-66 | 0.11 lb ai/A (0.001 lb ai/gallon) | Aerial, Airblast, Ground, Backpack Sprayer, Hand-Held Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | Not Specified | Foliar spray of the product will reduce or eliminate undesirable fruit in plum trees. The product is applied either at full bloom or during the period up to 5 days after full bloom. |
| Landscaping (Trees/Shrubs/Bushes/Plants/ Flowers) | | Liquid | Broadcast | 5481-337 | 0.11 lb ai/A | Ground | Long-sleeved shirt and long pants, shoes plus socks, chemical- | 48 hours | The product is applied as a root stimulant formulated to prevent and overcome transplant shock in plants. |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| | | | | | | | resistant gloves. | | |
| | | | Root treatment at time of planting/ Drench | 5481-337 | 0.0013 lb ai/gal | Ground | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | The product is used to prevent transplant shock in plants. |
| Azarole, Crabapple, Loquat, Mayhaw, Medlar, Asian Pear, Quince, Chinese Quince, Japanese Quince, Tejocote and Cultivars, Varieties | Orchard/ Vineyard | Liquid | Broadcast | 5481-541 | 0.11 lb ai/A | Aerial, Airblast, Ground | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | The product is used for thinning, prevention of pre-harvest fruit drop, and for promoting return bloom. Application timing typically ranges from full bloom to 30 days after full bloom. Do not apply this product through any type of irrigation system. |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| and/or Hybrids of These Trees | | Liquid | Directed Spray | 5481-429 | 0.08 lb ai/gallon | Hand-Held Pump-Up Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 12 hours | The product is applied with hand-held equipment. The product prevents or inhibits vegetative bud development in woody plants after pruning. The product reduces resprouting on bearing and non-bearing apple, olive, pear, avocado, mamey sapote and mango trees and on ornamental olives, crabapples and woody ornamental plants. Do not apply this product through any type of irrigation system. |
| Avocado; Mamey Sapote, Mango | Orchard/ Vineyard | Liquid | Directed Spray | 5481-429 | 0.09 lb ai/gallon | Hand-Held Sprayer, Backpack Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 12 hours | The product is applied with hand-held equipment. The product prevents or inhibits vegetative bud development in woody plants after |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop/Use Site | | Formulation Type | Type of Application | EPA Reg No. | Max. Single App. Rate | Application Equipment | PPE | REI | Use Directions and Limitations |
| | | | | | | | | | pruning. The product reduces resprouting on bearing and non-bearing apple, olive, pear, avocado, mamey sapote and mango trees and on ornamental olives, crabapples and woody ornamental plants. Do not apply this product through any type of irrigation system. |
| Landscaping (Trees, Shrubs, Bushes), Landscaping (Plants, Flowers) | | Liquid | Directed Spray | 5481-429 | 0.08 lb ai/gallon | Hand-Held Sprayer, Backpack Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 12 hours | Aerial applications are prohibited. Do not apply this product through any type of irrigation system. |
| | | RTU Liquid | Directed Spray | 5481-452 | 0.11 lb ai/gallon | Hand-Held Sprayer, Backpack Sprayer, Low-Pressure Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant | 12 hours | Prune existing sprouts and treat during the dormant season. Thoroughly cover area where existing sprouts were removed but restrict |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| | | | | | | | gloves, protective eyewear. | | treatment to the cut surfaces and 2 to 3 inches of the surrounding area. Apply the product with a small hand-held sprayer or backpack sprayer. For large projects, power operated low pressure spray equipment with an attached hand-gun or trunk-directed nozzle can be used. Do not apply this product through any type of irrigation system. |
| Pomegranate | Orchard/ Vineyard | Liquid | Directed Spray | 5481-429 | 0.08 lb ai/gallon | Hand-Held Sprayer, Backpack Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 12 hours | The product is applied with hand-held equipment. Do not apply this product through any type of irrigation system. Aerial applications are prohibited. |
| Citrus (Oranges, Tangerines (Mandarins), | Orchard/ Vineyard | Liquid | Broadcast | 5481-414 | 0.11 lb ai/A; 0.0008 lb ai/gallon | Aerial, Ground, Airblast, Backpack Sprayer, | Long-sleeved shirt and long pants, shoes plus | 48 hours | The product is used for fruit elimination. The entire fruiting area of the tree should |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| Tangelos, and Tangors) | | | | | | Hand-Held Sprayer | socks, chemical-resistant gloves. | | receive a thorough coverage of the spray solution. Do not apply this through any type of irrigation system. |
| Citrus (Non-Bearing) | Orchard/ Vineyard | RTU Liquid | Directed Spray | 5481-452 | 0.11 lb ai/gallon | Hand-Held Sprayer, Backpack Sprayer, Low-Pressure Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, protective eyewear. | 12 hours | Apply the product with a small hand-held sprayer or backpack sprayer. For large projects, power operated low pressure spray equipment with an attached hand-gun or trunk-directed nozzle can be used. Do not apply this product through any type of irrigation system. Sprays must be directed into the crop canopy. |
| Nectarine (Non-Bearing) | Orchard/ Vineyard | RTU Liquid | Directed Spray | 5481-452 | 0.11 lb ai/gallon | Hand-Held Sprayer, Backpack Sprayer, Low Pressure Sprayer | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, | 12 hours | Apply the product with a small hand-held sprayer or backpack sprayer. For large projects, power operated low pressure spray equipment with an attached hand-gun |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop/Use Site | | Formulation Type | Type of Application | EPA Reg No. | Max. Single App. Rate | Application Equipment | PPE | REI | Use Directions and Limitations |
| | | | | | | | protective eyewear. | | or trunk-directed nozzle can be used. Do not apply this product through any type of irrigation system. Sprays must be directed into the crop canopy. |
| Sod | | Liquid | Broadcast | 90866-4 | 0.0013 lb ai/A (0.000033 lb ai/gallon) | Ground | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, protective eyewear. | 24 hours | The product is applied to stimulate early and improved root development. The product contains a mixture of and nutrients that aid in successful transplanting and plant growth. Do not apply this product through any type of irrigation system. |
| Landscaping, Turf (Lawns, Athletic Fields, Parks, etc.); Golf Courses | | Liquid | Broadcast | 90866-4 | 0.0074 lb ai/A (0.000017 lb ai/gallon) | Ground | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, | 24 hours | The product is used for turfgrass. Do not apply this product through any type of irrigation system. |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| | | | | | | | protective eyewear. | | |
| Potato, Russet | Commercial and On-Farm Seed Treatment | Liquid | Seed treatment | 5481-580 | 0.00055 lb ai/A seed (0.000028 lb ai/100 lb seed) | Dispersing Equipment | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | All treated seed must be planted. |
| Potato, Non-Russet | Commercial and On-Farm Seed Treatment | Liquid | Seed treatment | 5481-580 | 0.00040 lb ai/A seed (0.000020 lb ai/lb seed) | Dispersing Equipment | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 48 hours | All treated seed must be planted. |
| Greenhouse (Ornamentals, Roses, cut Flowers, Container Stock, Vegetables) | | Liquid | Dip Treatment | 43905-1 | 0.0096 lb ai/gallon | Dip Tank | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves. | 24 hours | This product is for use in Greenhouses, Plant Nurseries, Shade Houses, and Lath Houses. |
| | | RTU – Dip Gel | Dip Treatment | 87394-4 | 0.0011 lb ai/ container | Dip Tank | Long-sleeved shirt and | Not Applicable | Do not use on plants intended for food use. This |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| | | | | | | long pants, protective eyewear, shoes plus socks, chemical-resistant gloves. | | product is for use in Greenhouses, Plant Nurseries, Shade Houses, and Lath Houses. |
| Greenhouse (Ornamentals, Roses, Cut Flowers, Container Stock, Vegetables), Nurseries, Shadehouses, and Lath Houses | Liquid | Root application at time of planting | 87394-3 | 0.000032 lb ai/gallon | Dip Tank | Long-sleeved shirt and long pants, protective eyewear, shoes plus socks, chemical-resistant gloves. | 24 hours | This product is for use in Greenhouses, Plant Nurseries, Shade houses, and Lath houses. |
| | | Drench | 87394-3 | 0.000011 lb ai/gallon | Root Soaking | Long-sleeved shirt and long pants, protective eyewear, shoes plus socks, chemical-resistant gloves. | 24 hours | The product is applied for root stimulation. This product is for use in Greenhouses, Plant Nurseries, Shade houses, and Lath houses. |

| Table F.1. Summary of Directions for Use of NAA. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Crop/Use Site** | **Formulation Type** | **Type of Application** | **EPA Reg No.** | **Max. Single App. Rate** | **Application Equipment** | **PPE** | **REI** | **Use Directions and Limitations** |
| Landscaping (Trees/Shrubs/Bushes/Plants/ Flowers) | Liquid | Root application at time of planting; Drench | 90866-4 | 0.000032 lb ai/gallon | Ground | Long-sleeved shirt and long pants, shoes plus socks, chemical-resistant gloves, protective eyewear. | 24 hours | The product is applied to stimulate early and improved root development. The product contains a mixture of and nutrients that aid in successful transplanting and plant growth. Do not apply this product through any type of irrigation system. |

## Appendix G. International Residue Limits Table

| **Table G.1 - Summary of US and International Tolerances and Maximum Residue Limits for all registered commodities** | | | | |
|---|---|---|---|---|
| *Residue Definition*: | | | | |
| US | | Canada | Mexico[1] | Codex |
| 40 CFR 180.155<br>1-naphthaleneacetic acid | | | | |
| *Commodity* | *Tolerance (ppm) /Maximum Residue Limit (mg/kg)* | | | |
| | US | Canada | Mexico[1] | Codex |
| Avocado | 0.05 | | | |
| Cherry, sweet | 0.1 | | | |
| Fruit, pome, group 11-10 | 0.15 | | | |
| Mango | 0.05 | | | |
| Olive | 0.7 | | | |
| Orange | 0.1 | | | |
| Pineapple[2] | 0.05 | | | |
| Pomegranate | 0.05 | | | |
| Potato | 0.01 | | | |
| Rambutan | 2 | | | |
| Sapote, mamey | 0.05 | | | |
| Tangerine | 0.1 | | | |
| Completed by: A. Habtemichael 28-OCT-2019 using Global MRL | | | | |

[1]Mexico adopts U.S tolerance.
[2]Import tolerance

## Appendix H. Submittal of Analytical Reference Standards

Analytical standards for (NAA salts): NAA acetamide, NAA potassium salt, NAA sodium salt, NAA ammonium salt and NAA ethyl ester are not currently available and should be submitted to National Pesticide Repository (Email communication with G. Verdin, 4/11/2019).

As reminder to the petitioner, supplies of analytical standards must be replenished as requested by the repository. The reference standards should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, to the attention of Theresa Cole at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

**(Note that the mail will be returned if the extended zip code is not used.)**