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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

Date: June 3, 2019

SUBJECT: **Buprofezin.** Human Health Risk Assessment for Proposed New Uses on Figs and Greenhouse-Grown Peppers and the Establishment of Permanent Tolerances in/on Fig and Tolerance Conversions to Leafy Greens, Subgroup 4-16A, Except Head Lettuce and Radicchio; *Brassica*, Leafy Greens, Subgroup 4-16B; Vegetable, *Brassica*, Head and Stem, Group 5-16; Leaf Petiole Vegetable Subgroup 22B; Celtuce; Florence Fennel; Kohlrabi; and Tolerance Expansions to All Members of Fruit, Citrus Group 10-10; Fruit, Stone, Group 12-12; Nut, Tree, Group 14-12; Tropical and Subtropical, Small Fruit, Edible Peel, Subgroup 23A; Tropical and Subtropical, Small Fruit, Inedible Peel, Subgroup 24A; Cottonseed Subgroup 20C; and Fruit, Small, Vine Climbing, Except Fuzzy Kiwifruit, Subgroup 13-07F.

PC Code: 275100
Decision No.: 537589

Petition No.: 7E8654
Risk Assessment Type: Single Chemical Aggregate
TXR No.: Not Applicable
MRID No.: Not Applicable

DP Barcode: D446327
Registration Nos.: 71711-16 (Technical Product), 71711-20, and 71711-21
Regulatory Action: Section 3 Registration
Case No.: 7462
CAS No.: 69327-76-0 (old); 953030-84-7 (new)
40 CFR: §180.511

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The Registration Division (RD) of the Office of Pesticide Programs (OPP) has requested that the Health Effects Division (HED) evaluate the hazard data and conduct dietary (food and drinking water), residential, aggregate, and occupational exposure assessments to estimate the risks to human health that may result from the proposed new uses of buprofezin on fig and greenhouse grown pepper and multiple crop group conversions/expansions. This memorandum serves as HED's human health risk assessment and is provided in the abbreviated format. The hazard characterization and endpoint selection were provided by Minerva Mercado; the residue chemistry assessment was provided by Janet Camp; the dietary assessment was provided by Thurston Morton; the occupational and residential exposure (ORE) assessment was provided by Brian Van Deusen; and the risk assessment was provided by Bonnie Cropp-Kohlligian.

Since the last human health risk assessment for buprofezin conducted in 2017 in support of registration review (i.e., The Buprofezin Draft Risk Assessment (DRA); D431562, B. Cropp-Kohlligian et al., 9/27/2017), the following changes/updates have been incorporated into this risk assessment for buprofezin.

1) HED reviewed a number of comments on the DRA and provided a response to those comments (D447127, B. Cropp-Kohlligian et al., 8/07/2018). HED has incorporated this new information into this risk assessment.
2) HED completed its review of the chitin synthesis inhibitors (buprofezin and cyromazine) (D446787, H. Pope-Varsalona et al., 4/19/2018). The conclusions from this review are incorporated into the cumulative risk assessment.
3) The ORE risk assessment was updated for this risk assessment. HED received dislodgeable foliar residue (DFR) data which were reviewed after the DRA and used to revise the occupational post-application risk assessment (D448121, B. Van Deusen, 8/13/2018). These data have been incorporated into the ORE risk assessment.
4) The dietary assessments for buprofezin and buprofezin-derived aniline were updated for this risk assessment.

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1.0 EXECUTIVE SUMMARY

Buprofezin (2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thidiazinan-4-one) is an insect growth regulator effective against the nymphal stages of whitefly, scales, psylla, meal-bugs, plant-hoppers, and leafhoppers. Buprofezin works by inhibiting chitin biosynthesis, suppressing oviposition of adults, and reducing viability of eggs. It is applied as broadcast foliar applications on a variety of food/feed crops and ornamentals. It may also be used in greenhouses, lath and shade houses, and nurseries. Formulated products include soluble concentrates, dry flowables, and wettable powders in water-soluble packets. It is applied using ground or aerial equipment. Equipment for occupational use includes aerial, airblast equipment, ground boom sprayer, handheld spray equipment, and foggers. All registered labels require occupational handlers to wear baseline attire (long sleeved shirt, long pants, shoes, and socks), and waterproof and/or chemical resistant gloves. For certain activities/products, additional personal protective equipment (PPE) is required, such as coveralls and/or protective eyewear. The restricted entry interval (REI) on all registered labels is 12 hours. There are no buprofezin-containing products registered for homeowner use and no products registered for application to residential areas.

Currently, buprofezin is in the process of undergoing registration review and HED has completed a buprofezin draft risk assessment (DRA; D431562, B. Cropp-Kohlligian et al., 9/27/2017) which is the most recent risk assessment for buprofezin, a response to comments on the DRA (D447127, B. Cropp-Kohlligian et al., 8/7/2018), a review of the chitin synthesis inhibitors (buprofezin and cyromazine) (D446787, H. Pope-Varsalona et al., 4/19/2018), and a revised occupational post-application risk assessment (D448121, B. Van Deusen, 8/13/2018) that incorporate dislodgeable foliar residue (DFR) data submitted subsequent to the DRA (D445664, B. Van Deusen, 4/11/2018 and D446830, B. Van Deusen, 8/8/2018). This assessment incorporates all of the relevant findings and determinations from these previous reviews. There have been no new buprofezin data submitted to HED since these reviews except the new fig and greenhouse-grown pepper field trial data (MRIDs 50466601 and 50466602) submitted to support this petition.

Proposed Uses

Under petition 7E8654, Interregional Project No. 4 (hereafter referred to as IR-4 or the petitioner), on behalf of the Agricultural Experiment Stations of California and on behalf of the Agricultural Experiment Stations of North Carolina, Tennessee, Oklahoma, and Florida, is proposing a new foliar use of buprofezin on fig and greenhouse-grown pepper, respectively. In addition, IR-4 is proposing the crop group conversions to (i) Leafy greens subgroup 4-16A, except head lettuce and radicchio, (ii) *Brassica*, leafy greens, subgroup 4-16B, (iii) Vegetable, *Brassica*, head and stem, group 5-16, (iv) Leaf petiole vegetable subgroup 22B, (v) Celtuce, (vi) Fennel, Florence, (vii) Kohlrabi; and (2) crop group expansions to all members of (i) Tropical and subtropical, small fruit, edible peel, subgroup 23A, (ii) Tropical and subtropical, small fruit, inedible peel, subgroup 24A, (iii) Cottonseed subgroup 20C, (iv) Fruit, citrus, group 10-10, (v) Fruit, stone, group 12-12, (vi) Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F, (vii) Nut, tree, group 14-12.

Hazard Identification

No new toxicity and/or metabolism data have been received since the most recent risk assessment. The toxicology database for buprofezin is adequate for evaluating and characterizing buprofezin toxicity. The primary organs of buprofezin toxicity are the liver and the thyroid (increased organ weight, and microscopic lesions). Increased incidence of follicular cell hyperplasia and hypertrophy of the thyroid were observed in subchronic and chronic rat studies. A rat dermal toxicity study showed inflammatory infiltrate of the liver and skin effects (increase in acanthosis and hyperkeratosis) in females. Following inhalation exposure of rats, the adrenal gland was the target of buprofezin toxicity (i.e., increased weight and microscopic findings of minimal hypertrophy of the cortex). Developmental and reproductive toxicity studies did not present evidence to suggest offspring were more sensitive to buprofezin exposure. However, evidence of enhanced offspring sensitivity was observed in a comparative thyroid toxicity assay (CTA) study. In the CTA study, pups exhibited decreased body weight during early lactation and increased thyroid stimulating hormone (TSH) levels at a dose that was not maternally toxic. Buprofezin was classified by HED's Cancer Assessment Review Committee (CARC) as having "Suggestive Evidence of Carcinogenicity, but not sufficient to assess human carcinogenic potential" in 1999 based on liver tumors in female mice. Buprofezin exhibits low acute toxicity (Toxicity Category III for acute oral toxicity and Toxicity Category IV for acute dermal and inhalation toxicity, and eye and skin irritation). It is not a dermal sensitizer.

Dose Response Assessment

There have been no changes to the selected endpoints since the most recent risk assessment. An acute dietary point of departure (POD) of 200 mg/kg/day (No Observed Adverse Effect Level (NOAEL)) was selected for females 13-49 years of age from a developmental study in rats based on incomplete ossification and reduced fetal weight. An acute dietary POD for the general population was not selected because the effects observed in the animal studies that could be attributed to a single day exposure were not applicable to the general population. Chronic dietary (all populations), incidental oral (short-term), dermal (short- and intermediate-term durations), and inhalation (short- and intermediate-term durations) PODs of 10.0 mg/kg/day were selected from the offspring Lowest Observed Adverse Effect Level (LOAEL) in the CTA study (based on decreased body weight and increased thyroid stimulating hormone (TSH) levels in pups). The offspring endpoint from the CTA study was selected for these scenarios because it matches the anticipated duration of exposure, it accounts for known offspring sensitivity, and it is the most protective POD in the toxicity database. Since the pup susceptibility seen in the CTA study was the result of repeated exposure, the CTA study would not be appropriate for assessing acute dietary exposure and risk. In the absence of a dermal absorption study for buprofezin, HED has estimated a dermal absorption factor of 10% for dermal assessments based on the comparison of the LOAELs in a 90-day rat oral subchronic study (68.6 mg/kg/day) and a 24-day dermal subchronic study (1000 mg/kg/day). Because oral, dermal, and inhalation toxicity endpoints are the same, these routes of exposure may be combined.

A total uncertainty factor of 100x (10x for interspecies extrapolation (UF_A) and 10x for intraspecies variation (UF_H)) is applied for the acute dietary assessment. Since there is a clear NOAEL from the developmental study and there is no residual uncertainty related to the

incomplete ossification and reduced fetal weight observed in the study used for the acute POD selection, the FQPA SF is reduced to 1x. The acute population adjusted dose (aPAD) is equivalent to the aRfD.

A total uncertainty factor of 300x (3x for interspecies extrapolation (UF_A), 10x for intraspecies variation (UF_H), and 10x FQPA SF for LOAEL to NOAEL extrapolation (UF_L)) was applied for the chronic dietary, incidental oral, dermal, and inhalation assessments which were based on the CTA study. Given that the POD derived from the CTA study is an offspring LOAEL, the FQPA SF of 10x is retained for the lack of a NOAEL in the selected CTA study. The interspecies extrapolation was reduced to 3x because adult rats are known to be more sensitive to this form of thyroid toxicity than humans.[1] While the POD from the CTA study is based on thyroid disruption in rat pups not adults, in the case of buprofezin, this uncertainty in the rat pup pharmacokinetics is already captured in the 10x FQPA SF/UF_L that accounts for the uncertainty in the offspring sensitivity due to the lack of a NOAEL. Therefore, reducing the UF_A to 3x is appropriate for all exposure scenarios that were assessed using the offspring POD from the CTA study.
The chronic population adjusted dose (cPAD) is equivalent to the cRfD.

Anticipated Exposure Pathways

Dietary (food and drinking water) exposures are expected based on proposed and existing uses of buprofezin. There are no buprofezin-containing products registered for homeowner use and no buprofezin-containing products registered for application to residential areas by commercial applicators. However, there is the potential for non-occupational bystander spray drift exposures following applications to adjacent agricultural fields. Incidental oral and dermal exposures from non-occupational spray drift are expected to be short-term (1 to 30 days) in duration. Occupational exposures are also expected from use of buprofezin. For agricultural occupational handlers and post-application workers, dermal and inhalation exposures are expected to be both short- (1 to 30 days) and/or intermediate-term (1 to 6 months) in duration.

Dietary Exposure (Food and Drinking Water) and Risk Assessment for Buprofezin

Screening level acute and partially refined chronic dietary exposure (food and drinking water) and risk assessments for buprofezin and its metabolites with similar toxicity show exposure estimates are below HED's level of concern (<100% of the acute population adjusted dose (aPAD) or chronic PAD (cPAD)) for the general population and all population subgroups. The acute dietary exposure (food and drinking water) and risk assessment at the 95th percentile of exposure for females 13-49 years old was 4.8% of the aPAD. The chronic dietary exposure (food and drinking water) and risk estimate for the most highly exposed population (children 1 to 2 years old) was 51% of the cPAD.

1 Interim Guidance: Thyroid Disrupting Pesticides: Use of Rat Thyroid Data and Application of Uncertainty Factors for RfD Derivation; Prepared and Reviewed by the Hazard Science Policy Council (V. Dellarco, W. Burnam, K. Baetcke, L. Scarano, R. Kent, Jess Rowland, and Karen Whitby dated 11/01/2015

Dietary Exposure (Cooked Food Only) and Risk Assessment for Buprofezin-derived Aniline

Aniline may be formed in food from buprofezin and its aniline-containing metabolites as a result of cooking but is toxicologically different from buprofezin and its other metabolites. EPA's Integrated Risk Information System (IRIS) classified aniline as a B2-probable human carcinogen with an oral cancer slope factor of $5.7x10^{-3}$ $(mg/kg/day)^{-1}$ which is considered very conservative for cancer assessment of aniline. IRIS did not identify any other oral endpoint.

Based on the available database, the maximum conversion of buprofezin residues to aniline is 18.9% due to high temperature hydrolysis conditions simulating pasteurization, brewing, baking, boiling, and sterilization. Other than cooked foods, there are no other potential exposures to buprofezin-derived aniline. While aniline exposures from sources other than buprofezin are possible, these exposures cannot be reliably estimated.

A highly refined cancer dietary exposure (cooked food forms only) and risk assessment for buprofezin-derived aniline residues, including those derived from aniline-containing metabolites of buprofezin, was previously conducted using (1) buprofezin monitoring data for raw/uncooked agricultural commodities (RACs) provided by the United States Department of Agriculture Pesticide Data Program (PDP) to estimate average residues of buprofezin, (2) average buprofezin percent crop treated (PCT) data provided by the Biological and Economic Analysis Division (BEAD), and (3) the maximum conversion factor for buprofezin-derived aniline of 18.9%. Only cooked food forms were included in the dietary analysis. The highly refined estimated exposure of the highest exposed adult population (adults 20-49 years old) to buprofezin-derived aniline results in an upper bound cancer risk estimate of 3×10^{-7}. Details of this assessment are provided only in Appendix H and are not discussed elsewhere in this document.

Residential Exposure and Risk Assessment

There are no buprofezin-containing products registered for homeowner use and no products registered for application to residential areas. Hence, a residential exposure and risk assessment was not conducted for buprofezin.

Non-Occupational Spray Drift Exposure and Risk Assessment

A quantitative non-occupational spray drift assessment was previously conducted for buprofezin as part of registration review (D439400, B. Van Deusen, 9/27/2017). The spray drift assessment, which includes crop groups and subgroups that are proposed under this petition, resulted in combined dermal and incidental oral risks of concern at the field edge for children 1 to <2 years old. Adult dermal risk estimates were not of concern at the field edge.

Aggregate Exposure and Risk Assessment

There are no residential uses of buprofezin; therefore, the aggregate risk assessment is equivalent to the acute and chronic dietary (food and drinking water) exposure and risk assessments. The acute and chronic dietary risk assessments are below HED's level of concern (<100% PAD).

Occupational Handler Exposure and Risk Assessment

Occupational handler dermal and inhalation exposure and risk estimates were calculated for the proposed new fig and greenhouse-grown pepper uses of buprofezin (D450358, B. Van Deusen, 6/03/2019). The occupational handler dermal and inhalation exposure and risk estimates for the crop group conversions/expansions were previously assessed for the registration review for buprofezin (D439400, B. Van Deusen, 9/27/2017). The occupational handler exposure and risk estimates indicate that there are combined dermal and inhalation risk estimates of concern (MOEs<300) for multiple exposure scenarios assuming the use of baseline attire and/or label required PPE (all registered labels require baseline attire plus waterproof or chemical resistant gloves). For the scenarios that result in risk estimates of concern at baseline attire or label required PPE, additional PPE and/or engineering controls (ECs) were assessed. With the additional PPE and or engineering controls, there were six remaining scenarios of concern.

Five scenarios of concern apply to both the proposed new fig and greenhouse-grown pepper uses as well as the proposed crop group conversions/expansions. These include:

- mixing/loading DF formulation for aerial application to orchards/vineyards, and
- mixing/loading/applying liquid and DF formulations via mechanically pressurized handgun equipment to orchard/vineyard and greenhouse use sites.

A sixth scenario of concern applies only to the proposed crop group conversions/expansions. This includes:

- mixing/loading/applying liquid formulations via mechanically pressurized handgun equipment to typical field crops.

Occupational Post-Application Exposure and Risk Assessment

Proposed new fig and greenhouse-grown pepper uses: Using buprofezin-specific dislodgeable foliar residue (DFR) data, the occupational post-application dermal MOEs are not of concern (i.e., MOEs ≥ 300, ranging from 310 to 4,300) for the proposed new and greenhouse-grown pepper uses on the day of product application (D450358, B. Van Deusen, 6/03/2019).

Proposed crop group conversions/expansion: The occupational post-application exposure and risk estimates for the crop group conversions/expansions were previously assessed for the registration review for buprofezin (D439400, B. Van Deusen, 9/27/2017) and later updated with chemical-specific dislodgeable foliar residue data (D448121, B. Van Deusen, 8/13/2018). Dermal MOEs of concern (i.e., MOEs < 300) were identified for the registered uses on cotton, grape, olive, and stone fruit on the day of product application and, therefore, apply to all registered uses for Crop Subgroup 20C, Crop Subgroup 13-07F, Crop Subgroup 23A, and Crop Group 12-12. The 12-hour REI listed on the proposed labels may not be adequately protective for workers engaged in post-application activities following buprofezin usage since dermal post-application MOEs are of concern for up to 8 days after product application.

A quantitative occupational post-application inhalation exposure assessment was not performed. 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 buprofezin.

Use of Human Studies

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 Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); the Outdoor Residential Exposure Task Force (ORETF) database; the Agricultural Handler Exposure Task Force (AHETF) database; and the Agricultural Reentry Task Force (ARTF) database 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[2].

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,"

2 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

(https://www.epa.gov/laws-regulations/summary-executive-order-12898-federal-actions-address-environmental-justice).

2.0 HED CONCLUSIONS

HED has examined the residue chemistry database for buprofezin. Pending the recommended revisions to section F of the petition (see section 2.2.4 Revisions to Petitioned-For Tolerances) and revisions to section B of the petition and the end-use product labels (see section 2.3 Label Recommendations), there are no residue chemistry issues that would preclude granting the requested new uses of buprofezin on fig and greenhouse-grown peppers and establishment of a new tolerance for residues of buprofezin [2-[(1,1-dimethylethyl)imino]tetrahydro-3(1-methylethyl)-5-phenyl-4*H*-1,3,5-thiadiazin-4-one] in/on fig and the proposed conversions and expansions of buprofezin. The currently established tolerance in/on vegetable, fruiting, group 8-10 is adequate to cover the proposed maximum use rate on greenhouse-grown peppers which is the same as the currently registered maximum use rate on field-grown pepper.

HED notes that there are several occupational handler exposure scenarios for the proposed new fig and greenhouse-grown pepper uses which are of concern at the currently registered levels of attire or PPE and may require additional PPE or ECs to mitigate risks.

HED also notes there are several occupational handler and post-application exposure scenarios which are of concern for the proposed crop group conversions/expansions as previously identified during registration review (D431562, B. Cropp-Kohlligian et al., 9/27/2017) and the revised occupational post-application risk estimates incorporating new DFR data to support registration review for buprofezin (D448121, B. Van Deusen, 8/13/2018). Additional PPE or ECs, as well as a revision to the REI statement may be required to address these risk estimates.

2.1 Data Deficiencies

The Agency defines ultra-low volume (ULV) uses as <2 gallons spray per acre; <10 gallons spray per acre for orchards (OPPTS 860.1500). There are no buprofezin field trial data available reflecting ULV uses of buprofezin. Unless section B of the petition and the proposed SC and DF labels (EPA Reg. Nos. 71711-20 and 71711-21, respectively) are revised as recommended under section 2.3.1 below, field trial data reflecting <10 GPA for orchard crops is required to support ULV uses of buprofezin on orchard crops.

2.2 Tolerance Considerations

2.2.1 Enforcement Analytical Method

Adequate enforcement methods are available in Pesticide Analytical Manual Volume I (PAM I) and PAM II for enforcement of buprofezin tolerances, including gas chromatography methods with nitrogen phosphorus detection (GC/NPD), and a GC/mass spectrometry (GC/MS) method for confirmation of buprofezin residues in plant and livestock commodities. The GC/MS method used for plant commodities utilizes three ions for identification of buprofezin. The validated

LOQ was 0.05 ppm.

2.2.2 Analytical Reference Standard

An analytical standard for buprofezin from Nihon Nohyaku with a 5/31/21 expiration date is currently available in the EPA National Pesticide Standard Repository (e-mail communication from T. Cole to B. Cropp-Kohlligian dated 2/21/2017). See Appendix E.

2.2.3 Recommended Tolerances

Tolerances established for residues of buprofezin in/on registered crops range from 0.02-80 ppm (40 CFR §180.511). Tolerances with no U.S. registrations have been established for residues of buprofezin in/on rice, grain (1.5 ppm) and tea (20 ppm). Tolerances have also been established for residues of buprofezin as a result of secondary residues in milk (0.01 ppm) and meat (0.05 ppm). The tolerance expression for buprofezin in 40 CFR §180.511 is in accordance with HED's Interim Guidance on Tolerance Expressions (5/27/2009, S. Knizner).

The proposed tolerances for the new uses and the proposed tolerance conversions and expansions are listed in Table 2.2.3.1 of this section, along with the tolerances recommended by HED. For the convenience of RD in preparation of the forthcoming federal register notice, the HED tolerance recommendations are reiterated below in alphabetical order as they would be in the CFR.

The commodities to be added to 40 CFR §180.511(a) are:

Brassica, leafy greens, subgroup 4-16B 60
Celtuce 35
Cottonseed subgroup 20C 0.35
Fennel, Florence, fresh leaves and stalk 35
Fig 0.7
Fruit, citrus, group 10-10 4
Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F 1
Fruit, stone, group 12-12, except nectarine and peach 2
Grape, raisin 2
Kohlrabi 12
Leaf petiole vegetable subgroup 22B 35
Leafy greens subgroup 4-16A 35
Nut, tree, group 14-12 .....0.05
Tropical and subtropical, small fruit, edible peel, subgroup 23A 5
Tropical and subtropical, small fruit, inedible peel, subgroup 24A 0.3
Vegetable, *Brassica*, head and stem, group 5-16 12

Upon establishment of the above tolerances, the commodities to be removed from 40 CFR §180.511(a) are:

Acerola.....0.30
Apricot.....9.0
Brassica, head and stem, subgroup 5A.....12.0
Brassica, leafy greens, subgroup 5B.....60
Cotton, undelinted seed.....0.35
Fruit, citrus, group 10.....2.5
Fruit, stone, group 12, except apricot and peach.....1.9
Grape.....2.5
Lettuce, head.....6.0
Longan.....0.30
Lychee.....0.30
Nut, tree group 14.....0.05
Olive.....3.5
Olive, oil.....4.8
Pistachio.....0.05
Radicchio.....6.0
Spanish lime.....0.30
Turnip, greens.....60
Vegetable, leafy, except Brassica, group 4, except head lettuce and radicchio.....35
Wax jambu.....0.30

Table 2.2.3.1. Tolerance Summary for Buprofezin (40 CFR §180.511(a)).

Commodity/ **Correct Commodity Definition**	Proposed/Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
***Brassica*, leafy greens, subgroup 4-16B**	--	60	Crop group conversion from parts of crop group 4, subgroups 5A and 5B to subgroup 4-16B[1, 6]. Commodity definition correction to italicize *Brassica*.
Brassica, leafy greens, subgroup 4-16B	60	--	
Brassica, leafy greens, subgroup 5B	60	Remove	
Turnip, greens	60	Remove	
Celtuce	35	35	Crop group conversion from group 4 to subgroup 22B.
Cottonseed subgroup 20C	0.35	0.35	Expansion of the currently established tolerance at 0.35 ppm on Cotton, undelinted seed to Cottonseed subgroup 20C at 0.35 ppm.
Cotton, undelinted seed	0.35	Remove	
Fennel, Florence, fresh leaves and stalk	--	35	Crop group conversion from group 4 to subgroup 22B. Commodity definition correction.
Fennel, Florence	35	--	
Fig	0.70	0.7	Corrected value to be consistent with OECD rounding class practice; no trailing zeros.
Fruit, citrus, group 10-10	2.5	4	Crop group expansion from 10 to 10-10[1, 2, 3]
Fruit, citrus, group 10	2.5	Remove	
Fruit, stone, group 12-12, except nectarine and peach	--	2	Crop group expansion from 12 to 12-12 and new representative crop for apricot.[1, 4] Note: Section F of the petition did not request removal of established tolerance in/on apricot.
Apricot	9.0	Remove	
Fruit, stone, group 12, except apricot and peach	1.9	Remove	
Fruit, stone, group 12-12, except apricot and peach	2.0	--	

Table 2.2.3.1. Tolerance Summary for Buprofezin (40 CFR §180.511(a)).			
Commodity/ **Correct Commodity Definition**	Proposed/Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments
Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F	2.5	1	Expansion of the currently established tolerance on grape[5].
Grape	2.5	Remove	
Grape, raisin	--	2	
Kohlrabi	12.0	12	Crop group conversion from subgroup 5A to subgroup 22B[1]. Corrected value to be consistent with OECD rounding class practice; no trailing zeros.
Leaf petiole vegetable subgroup 22B	35	35	Crop group conversion from parts of crop group 4 to subgroup 22B[1, 10].
Leafy greens subgroup 4-16A	--	35	Crop group conversion from parts of group 4 to subgroups 4-16A, 4-16B, and 22B, and individual tolerance in/on celtuce and Florence fennel[1, 7]. Note: Section F of the petition did not request removal of established tolerances in/on lettuce, head and radicchio.
Leafy greens subgroup 4-16A, except head lettuce and radicchio	35	--	
Vegetable, leafy, except brassica, group 4, except head lettuce and radicchio	35	Remove	
Lettuce, head	6.0	Remove	
Radicchio	6.0	Remove	
Nut, tree, group 14-12	0.05	0.05	Crop group expansion from 14 to 14-12[1].
Nut, tree group 14	0.05	Remove	
Pistachio	0.05	Remove	
Tropical and subtropical, small fruit, edible peel, subgroup 23A	5.0	5	Expansion of the currently established tolerance at 3.5 ppm on Olive. Tolerance increased from 3.5 ppm to 5 ppm for harmonization purposes with Canada[8]. A separate tolerance in olive oil is no longer needed. Corrected value to be consistent with OECD rounding class practice; no trailing zeros.
Acerola	0.30	Remove	
Olive	3.5	Remove	
Olive, oil	4.8	Remove	
Wax jambu	0.30	Remove	
Tropical and subtropical, small fruit, inedible peel, subgroup 24A	0.30	0.3	Expansion of the currently established tolerance at 0.3 ppm on Lychee, Longan, and Spanish lime to Tropical and subtropical, small fruit, inedible peel, subgroup 24A. Corrected value to be consistent with OECD rounding class practice; no trailing zeros.
Lychee	0.30	Remove	
Longan	0.30	Remove	
Spanish lime	0.30	Remove	
Vegetable, *Brassica*, head and stem, group 5-16	--	12	Crop group conversion from parts of crop subgroup 5A to crop group 5-16[1, 2, 9]. Corrected value to be consistent with OECD rounding class practice; no trailing zeros. Commodity definition correction.
Brassica, head and stem, subgroup 5A	12.0	Remove	
Vegetable, brassica, head and stem, group 5-16	12.0	--	

[1] Consistent with previous recommendations by HED during registration review (D431562, B. Cropp-Kohlligian et al., 9/27/2017). However, commodity definitions recommended during registration review for crop group 5-16 and subgroups 4-16A, 4-16B, and 22B have been updated to reflect current definitions.

[2] The Canadian MRL was determined using U.S. data and OECD calculation procedures, while the established U.S. tolerance was determined with older tolerance calculation procedures, including the NAFTA spreadsheet. For example, orange MOR data (MRID 45694204) were entered into the OECD calculator, which resulted in a 4 ppm tolerance value for orange. The orange tolerance value of 2.5 ppm (D296492, T. Bloem, 12/17/2003, MRID 45694204) was calculated using the spreadsheet method. Since orange is the representative crop for the citrus fruit group, the tolerance level for citrus fruit commodities was increased to harmonize with Canada, which is based on U.S. orange (representative crop for subgroup 10-10A) data.

[3] Tolerance level has been increased to harmonize with Canada MRL for citrus fruit commodities. The Canada MRL is based on

U.S. orange (representative crop for citrus fruit group 10-10) data.

[4] Tolerance level has been increased to harmonize with Canada MRLs for commodities in the cherry subgroup 12-12A and plum subgroup 12-12C, which are based on U.S. cherry (representative crop for subgroup 12-12A) and plum (representative crop for subgroup 12-12C) data.
Peach has a separate tolerance established at 9.0 ppm. A tolerance in/on peach will cover nectarine (§180.1(g)). Peach and nectarine are the only members of the peach subgroup 12-12B.
Crop group conversion has resulted in a change of the representative commodity for apricot from peach (SOP 2000.1, 9/12/2000) to plum. Apricot is covered by the tolerance (2 ppm) of group 12-12, which has been increased from 1.9 ppm to 2 ppm to harmonize with Codex and Canada MRLs for cherry and plum subgroups.

[5] HED previously agreed to lower the currently established tolerance in/on grape from 2.5 ppm to 1.0 ppm to harmonize with the currently established Codex and Canada MRLs in/on grapes, based on a response to comment during registration review (D447127, B. Cropp-Kohlligian et al., 8/7/2018).
Due to crop group expansion and lowering of the currently established tolerance in/on grape (2.5 ppm) to subgroup 13-07F (1 ppm), a separate tolerance in/on grape, raisin is recommended.
A tolerance of 2 ppm is recommended to harmonize with currently established Codex and Canada MRLs of 2 ppm in/on dried grapes and raisins, respectively.

[6] The tolerance is compatible with Canadian MRLs (60 ppm) for broccoli raab, bok choy Chinese cabbages, collards, kales, mustard greens and rape leaves commodities, which are based on U.S. mustard greens (representative crop for subgroup 4-16B) data. Data support maximum use rate of 2 applications at 0.38 lb ai/A with a 1-day PHI.

[7] Currently established tolerances in/on head lettuce and radicchio are covered by crop subgroup 4-16A (35 ppm). The tolerance is compatible with Canadian MRLs (35 ppm) for amaranth, garland chrysanthemum, dandelion leaves, endive, head lettuce, leaf lettuce, radicchio, spinach, Swiss chard commodities, which are based on U.S. leaf lettuce and spinach (representative crops for subgroup 4-16A) data. Data support maximum use rate of 2 applications at 0.38 lb ai/A with a 7-day PHI.

[8] HED previously recommended to increase the currently established tolerance in/on olive from 3.5 ppm to 5.0 ppm for harmonization purposes (D431562, B. Cropp-Kohlligian et al., 9/27/2017). The Canada MRL was determined using U.S. olive data and OECD calculation procedures. The established U.S. tolerance of 3.5 ppm was determined using older tolerance calculation procedures (D340284; D345185, T. Bloem, 1/16/2008). The tolerance value of 5 ppm is compatible with the Codex MRL for Table Olives. MOR data for olives were entered into the OECD calculator, which generated a tolerance of 4 ppm for olives.

[9] The tolerance is compatible with Canadian MRLs (12 ppm) for commodities of broccoli, Brussels sprouts, cabbages, cauliflowers, Chinese mustard cabbages and Napa Chinese cabbage, which are based on U.S. broccoli and cabbage (representative crops for group 5-16) data. Data support a maximum use rate of 2 applications at 0.38 lb ai/A with a 1-day PHI.

[10] The tolerance is compatible with Canadian MRLs (35ppm) for cardoon, celery, Chinese celery, rhubarb commodities, which are based on U.S. celery (representative crop for subgroup 22B) data. Data support a maximum use rate of 2 applications at 0.38 lb ai/A with a 7-day PHI.

2.2.4 Revisions to Petitioned-For Tolerances

The petitioner should submit a revised Section F of the petition with the following revisions:

- All trailing zeroes should be removed from proposed tolerances.
- The commodity definitions should be revised for Florence fennel, crop group 5-16, and crop subgroup 4-16B.
- The petitioned-for tolerance in/on crop group 10-10 should be revised from 2.5 ppm to 4 ppm.
- The petitioned-for tolerance in/on crop subgroup 13-07F should be revised from 2.5 ppm to 1 ppm.
- A tolerance of 2 ppm in/on grape, raisin should be added.
- The petitioned-for tolerance in/on the fruit, stone, group 12-12, except apricot and peach at 2 ppm should be revised to fruit, stone, group 12-12, except nectarine and peach at 2 ppm.
- The petitioned-for tolerance in/on leafy greens subgroup 4-16A, except head lettuce and radicchio at 35 ppm should be revised to leafy greens, subgroup 4-16A at 35 ppm.
- Request removal of the established tolerances in/on apricot; lettuce, head; and radicchio.

See Table 2.2.3.1, above, for an explanation from HED.

2.2.5 International Harmonization

No Codex, Canadian, or Mexican maximum residue limits (MRLs) have been established for residues of buprofezin in/on fig. Mexico adopts U.S. tolerances and/or Codex MRLs for its export purposes.

Codex has established several MRLs for residues of buprofezin in/on some of the remaining raw agricultural commodities (RACs) in this action, including cherries, plums, grapes, almonds, and table olives, which are harmonized with proposed U.S. tolerances. Additionally, Codex has an established MRL on dried grapes (including currants, raisins, and sultanas), which is harmonized with the proposed U.S. tolerance in/on grape, raisin. Codex has also established a more restrictive MRL in/on citrus fruits which is too low to harmonize with U.S. tolerances due to significant differences in good agricultural practices (GAP).

Canada has established numerous MRLs in/on individual crop commodities. With the adoption of the recommended U.S. tolerances, U.S. tolerances will be harmonized with Canadian MRLs with the exception of the Canadian MRLs in/on Chinese broccoli, some leafy greens (arugula, garden cress, upland cress), acerolas and wax jambus, which are too low to harmonize with established U.S. tolerances. This issue is the consequence of proposed crop conversions that were included in this petition but it is assumed that Canada will eventually do likewise and future harmonization with Canada is likely.

The Canadian and Codex MRLs are expressed in terms of buprofezin. The U.S. tolerance expression is harmonized with Canada and Codex. U.S. and international tolerances and MRLs are summarized in Appendix D.

2.3 Label Recommendations

2.3.1 Recommendations from Residue Reviews

Section B of the petition and the proposed SC and DF labels (EPA Reg. Nos. 71711-20 and 71711-21, respectively) must be revised to specify a minimum spray volume of 10 gallons per acre (GPA) for aerial application to orchard crops or produce residue data reflecting ultra-low volume (ULV) data to support these minimum aerial spray volumes. It is of note that the proposed labels do not specify that the proposed uses are actually intended to be ULV. Only the proposed use on greenhouse-grown pepper allows for the use of ULV equipment but based on the minimum GPA is not considered a ULV use as defined by guideline criteria for minimum GPA.

2.3.2 Recommendations from Occupational Assessment

The proposed DF label (EPA Reg. No. 71711-21) does not specify the exact use pattern intended for fogging equipment. Product labels should define whether fogging equipment is only used indoors (i.e., greenhouses), and also provide an application rate specifically for fogging

equipment with a rate in units of lb ai/ft^3, or equivalent units. In lieu of use pattern information and specific application rates for the fogging use pattern, worst case assumptions have been used for risk assessment.

The proposed SC label (EPA Reg. No. 71711-20) contains contradictory language around the use of irrigation application equipment. The label prohibits applications through any type of irrigation system but also gives instructions for chemigation applications to watercress.

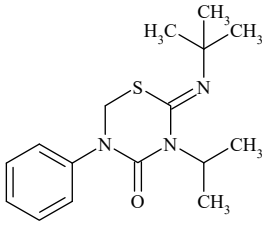
HED notes that there are several occupational handler exposure scenarios for the proposed new fig and greenhouse-grown pepper uses which are of concern at the currently proposed levels of attire or PPE and may require additional PPE or ECs to mitigate risks.

HED also notes there are several occupational handler and post-application exposure scenarios which are of concern for the proposed crop group conversions and expansions as previously identified during registration review (D431562, B. Cropp-Kohlligian et al., 9/27/2017) and in the revised occupational post-application risk estimates incorporating new DFR data to support registration review for buprofezin (D448121, B. Van Deusen, 8/13/2018). Additional PPE or ECs, as well as a revision to the REI statement may be required to address these risk estimates.

3.0 INGREDIENT PROFILE

3.1 Chemical Identity

Table 3.1.1. Buprofezin Nomenclature.

Compound	
Common name	Buprofezin
Company experimental name	BF1
IUPAC name	2-*tert*-butylimino-3-isopropyl-5-phenyl-3,4,5,6-tetrahydro-3*H*-1,3,5-thiadiazin-4-one
CAS name	2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4*H*-1,3,5-thiadiazin-4-one
CAS registry number	69327-76-0 (old) and 953030-84-7 (new)

3.2 Physical/Chemical Characteristics

Technical buprofezin is a white odorless solid with a melting point of 104.2-105.5 °C and a low vapor pressure of 3.75 x 10^{-7} mmHg at 20 °C. Buprofezin is sparingly soluble in water and is soluble in several organic solvents. A detailed description of the physicochemical properties of the technical grade buprofezin is provided in Appendix C.

3.3 Pesticide Use Pattern

Buprofezin (2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thidiazinan-4-one) is an insect growth regulator effective against the nymphal stages of whitefly, scales, psylla, mealybugs, plant-hoppers, and leafhoppers by inhibiting chitin biosynthesis, suppressing oviposition of adults, and reducing viability of eggs.

Buprofezin is currently registered for several agricultural, tree, and orchard crops; such as almonds; avocado; beans (succulent); bell peppers; *Brassica* cole crops and leafy greens subgroup 5B; bushberries; Christmas trees; citrus; coffee; cotton (fiber and non-fiber crop); cucurbits; field and container grown ornamentals; flavoring and spice crops (cress); fruiting vegetables; grapes; ground covers; landscape ornamentals; leafy and stem vegetables; non-bearing fruit and nut trees in nurseries; ornamental plants in greenhouses, lath houses, shade houses, and nurseries; pome fruit; persimmon; stone fruit; strawberries; tea; tree nuts group 14, including pistachio; tropical and subtropical fruit; and turnip greens. There are no residential uses. There are also tolerances without U.S. registration in/on rice grain and tea.

Existing formulated products include a water dispersible granule (WDG, EPA Reg. No. 2749-587) containing up to 70% buprofezin active ingredient (ai), a soluble concentrate (SC, EPA Reg. No. 71711-21) containing up to 40% buprofezin ai, a dry flowable (DF, EPA Reg. No. 71711-21) containing up to 70% buprofezin ai, and wettable powder in a water-soluble packet (WSP, EPA Reg. No. 71711-15) containing up to 70% buprofezin ai. All registered labels require occupational handlers to wear baseline attire (long sleeved shirt, long pants, shoes, and socks), and waterproof and/or chemical resistant gloves. For certain activities/products, additional personal protective equipment (PPE) is required such as, coveralls and/or protective eyewear. There are currently no buprofezin products registered for homeowner use and no products registered for application to residential areas. The restricted entry interval (REI) on all registered labels is 12 hours.
Under the current petition (7E8654), IR-4, on behalf of the Agricultural Experiment Stations of California (fig) and on behalf of the Agricultural Experiment Stations of North Carolina, Tennessee, Oklahoma, and Florida (greenhouse-grown pepper), is proposing new foliar uses of buprofezin on fig and greenhouse-grown pepper for the SC and DF formulations (EPA Reg Nos. 71711-20 and 71711-21, respectively). The proposed maximum use rate on greenhouse-grown pepper is the same as that already registered on field-grown pepper.

Also under this petition and for the SC and DF formulations (EPA Reg Nos. 71711-20 and 71711-21, respectively), IR-4 is also requesting (1) crop group conversions to (i) Leafy greens subgroup 4-16A, except head lettuce and radicchio, (ii) *Brassica*, leafy greens, subgroup 4-16B, (iii) Vegetable, *Brassica*, head and stem, group 5-16, (iv) Leaf petiole vegetable subgroup 22B, (v) Celtuce, (vi) Fennel, Florence, (vii) Kohlrabi; and (2) crop group expansions to all members of (i) Tropical and subtropical, small fruit, edible peel, subgroup 23A, (ii) Tropical and subtropical, small fruit, inedible peel, subgroup 24A, (iii) Cottonseed subgroup 20C, (iv) Fruit, citrus, group 10-10, (v) Fruit, stone, group 12-12, (vi) Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F, (vii) Nut, tree, group 14-12.

The proposed new uses for the ai buprofezin is for two end-use products, Buprofezin 40SC Insect Growth Regulator® (EPA Reg. No. 71711-20; containing 40% buprofezin) and Applaud 70DF Insect Growth Regulator® (EPA Reg No. 71711-21; containing 70% buprofezin). These labels specify a 0-day plant-back interval (PBI) for all crops registered for use, 30-days for cereal crops, and 60-days for all other crops. These labels require occupational applicators and other handlers to wear a long-sleeved shirt, long pants, shoes plus socks, and personal protective equipment (PPE) including chemical- or water-resistant gloves and/or protective eyewear. The proposed labels currently require a 12-hour restricted entry interval (REI). See Table 3.3.1 for a summary of the proposed uses of buprofezin.

Table 3.3.1. Summary of Proposed Directions for Use of Buprofezin.

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Celtuce						
Ground or aerial.	3.6 lb ai/gral Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.77	7	• Allow at least 7 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.
Fennel, Florence, fresh leaves and stalk						
Ground or aerial.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.77	7	• Allow at least 7 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.
Fig						
Ground or aerial.	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	2.0	2 applications per crop cycle	4.0	14	• Allow at least 14 days between applications. • For ground application, use a minimum of 15 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.

Table 3.3.1. Summary of Proposed Directions for Use of Buprofezin.						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Ground or aerial.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	2.0	2 applications per crop cycle	4.0	14	• Allow at least 14 days between applications. • For ground application, use a minimum of 15 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.
Fruit, citrus, group 10-10						
Ground or aerial.	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	1.5-2.0	2 applications per growing season	4.0	3	• Allow at least 60 days between applications. • For ground application, use a minimum of 750 gallons of water per acre. In Florida and Texas only, use a minimum of 250 gallons of water per acre for ground application. • For aerial application, use a minimum of 5 gallons of water per acre.
Fruit, stone, group 12-12						
Ground	3.6 lb ai/gal Buprofezin 40SC [71711-20]	1.5	2 applications per growing season	3.0	14	• Allow at least 14 days between applications. • For ground application, use a minimum of 50 gallons of water per acre. • Not for use in California.
Ground or aerial.	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	1.5	2 applications per growing season	3.0	14	• Allow at least 14 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.

Table 3.3.1. Summary of Proposed Directions for Use of Buprofezin.						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Greenhouse-grown pepper						
Ground	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	0.26-0.40	2 applications per growing cycle	0.8	1	• Allow at least 5 days between applications. • Apply on 2 acres minimum with 20 gallons of water per acre. • Applications may be made with high volume, low volume or ultra low volume (thermal and nonthermal foggers, misters, etc.) ground equipment only
Ground	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.76	1	
Cottonseed subgroup 20C						
Ground or aerial.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.35	2 applications per crop cycle	0.70	14	• For ground application, use 10 to 50 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.
Kohlrabi						
Ground or aerial.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.77	1	• Allow at least 7 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.

Table 3.3.1. Summary of Proposed Directions for Use of Buprofezin.						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Brassica, leafy greens, subgroup 4-16B						
Ground or aerial or chemigation.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.77	1	• Allow at least 7 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre. • Not for use on watercress in California. • Chemigation for use on watercress only.
Leafy greens subgroup 4-16A						
Ground or aerial.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.77	7	• Allow at least 7 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.
Nut, tree, group 14-12						
Ground or aerial.	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	1.5-2.0	1 application per rowing season	2.0	60	• For ground application, use a minimum of 100 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.
Vegetable, head and stem, *Brassica*, group 5-16						
Ground or aerial.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.77	1	• Allow at least 7 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.

Table 3.3.1. Summary of Proposed Directions for Use of Buprofezin.						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Leaf petiole vegetable subgroup 22B						
Ground or aerial.	3.6 lb ai/gal Buprofezin 40SC [71711-20]	0.25-0.38	2 applications per crop cycle	0.77	7	• Allow at least 7 days between applications. • For ground application, use a minimum of 20 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre.
Tropical and subtropical, small fruit, edible peel, subgroup 23A						
Ground or aerial.	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	1.5-2.0	2 applications per growing season	4.0	21	• Apply by ground using 110-500 gallons per acre spray volume. • For aerial application, use a minimum of 5 gallons of water per acre. • Allow at least 50 days between applications.
Tropical and subtropical, small fruit, inedible peel, subgroup 24A						
Ground or aerial.	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	1.5	2 applications per growing season	3.0	21	• Apply by ground using a minimum of 75 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre. • Allow at least 14 days between applications.
Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F						
Ground or aerial.	0.7 lb ai/lb product Applaud® 70 DF [71711-21]	0.40-0.53	2 applications per growing season	1.05	7	• Apply by ground using a minimum of 50 gallons of water per acre. • For aerial application, use a minimum of 5 gallons of water per acre. • Allow at least 14 days between applications.
		1.05 (CA and AZ only)	1 application per growing season		30	

3.4 Anticipated Exposure Pathways

Dietary (food and drinking water) exposures are expected based on proposed and existing uses of buprofezin. There are no buprofezin-containing products registered for homeowner use and no buprofezin-containing products proposed or registered for application to residential areas by commercial applicators. Incidental oral and dermal exposures from non-occupational spray drift following agricultural applications are expected to be short-term (1 to 30 days) in duration. For agricultural occupational handlers and post-application workers, dermal and inhalation exposures are expected to be both short- (1 to 30 days) and/or intermediate-term (1 to 6 months) in duration.

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," (https://www.epa.gov/laws-regulations/summary-executive-order-12898-federal-actions-address-environmental-justice). 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 USDA under the National Health and Nutrition Survey/What We Eat in America (NHANES/WWEIA) and 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. 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

No new toxicity and/or metabolism data have been received since the last risk assessment. This assessment reflects the most recent assessment (D431562, B. Cropp-Kohlligian et al., 9/27/2017). The toxicology database for buprofezin is adequate for evaluating and characterizing buprofezin toxicity and selecting endpoints for purposes of this risk assessment. Based on a weight of evidence (WOE) approach, HED recommends that an acute neurotoxicity study is not required at this time and may be waived (TXR 0055414, A. Khasawinah, 1/19/2011). The

following studies are supportive of this evaluation:

- Acute: Oral, dermal, inhalation, eye irritation, dermal irritation, and skin sensitization
- Subchronic: 90-day oral toxicity (rat, dog, mouse), 24-day dermal toxicity (rabbit), and a 28-day inhalation toxicity (rats)
- Developmental toxicity: prenatal toxicity (rat, rabbit)
- Reproduction: 2-generation reproduction (rat)
- Chronic: combined oral chronic toxicity/carcinogenicity (rat), carcinogenicity (mouse), chronic oral toxicity (dog)
- Neurotoxicity: Subchronic neurotoxicity (rat)
- Mutagenicity battery
- Metabolism (rat)
- Immunotoxicity (rat)
- Comparative thyroid toxicity assay (CTA) (rat)

4.2 Absorption, Distribution, Metabolism and Excretion

The absorption, distribution, metabolism, and excretion of ^{14}C-buprofezin were studied in rats. The rat metabolism study indicated that 95% of the administered dose was excreted in urine and feces within 72 hours (feces - 79.1%; urine - 12.9%). In the feces, about 45% of the administered dose was recovered as parent compound, with the remainder as several metabolites. Biliary excretion accounted for 32-39 % of the administered dose during 24 hours of post dosing. Maximum concentrations in blood following a single oral dose occurred at 9 hours. ^{14}C-buprofezin was detected in tissues and organs after 168 hours of administration with highest concentrations in the liver, thyroid and red blood cells and these represented less than 0.2% of the administered radioactivity.

Metabolites in feces consisted primarily of unchanged parent (45.4%) with lesser amounts of BF27 (2-tert-butylimino-5-(4-hydroxy-3-methoxyphenyl)-3-isopropyl-1,3,5-thiadiazinan-4-one; 7.2% of dose) and BF28 (2-[3-isopropyl-3-[methylsulfonylmethyl(phenyl)carbamoyl] ureido]-2-methylpropionic acid; 4.6% of dose). Hydrolysis of the extracted fecal fiber resulted in minor amounts (< 0.1% each) of BF9 (3-isopropyl-5-phenyl-1,3,5-thiadiazinan-2,4-dione), BF10 (2-tertbutylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one-1-oxide), BF12(1-isopropyl-3-phenylurea), and BF13 (1-(4-hydroxyphenyl)-3-isopropylurea). In urine, 12.9% of the administered dose was recovered. Polar conjugates released by sulfatase hydrolysis consisted of BF13 (0.5% of dose), BF23 (N-(4-hydroxyphenyl) acetamide; 2.5% of dose), and BF28 (0.3% of dose). A total of 60.7% of the administered dose was identified and no unknown metabolite or fiber bound residue exceeded 3.7% of the dose.

4.2.1 Dermal Absorption

There are no dermal absorption studies available with buprofezin. HED has estimated a dermal absorption factor of 10% based on the comparison of the LOAEL in a 90-day rat oral subchronic

study (68.6 mg/kg/day) and a 24-day dermal subchronic study (1000 mg/kg/day) (TXR 0051342, P.V. Shah, 10/19/2002).

4.3 Toxicological Effects

The primary organs of buprofezin toxicity are the liver and the thyroid. In subchronic toxicity studies in rats, increased microscopic lesions in liver and thyroid, increased liver weights, and increased thyroid weight in males were seen. In chronic studies in the rat, an increased incidence of follicular cell hyperplasia and hypertrophy in the thyroid of males were reported. In chronic studies in the dog, increased relative liver weights were reported in females. Effects observed in a 24-day dermal toxicity study in rats included inflammatory infiltrate of the liver and an increase in acanthosis and hyperkeratosis of the skin in females. Following inhalation exposure of rats, the adrenal gland was the target of buprofezin toxicity (i.e., increased weight and microscopic findings of minimal hypertrophy of the cortex).

The developmental toxicity study in the rat showed reduced ossification and reduced pup weight at maternally toxic doses (death, decreased pregnancy rates, increased resorption rates). No developmental toxicity was observed in the rabbit at or below maternally toxic dose levels. The reproductive toxicity study showed decreased pup body weights at dose levels where liver effects (increased relative and/or absolute liver weights) and decreased body weight gains were observed in the parental generations. In contrast, evidence of post-natal offspring sensitivity was observed in the CTA study. Rat pups experienced decreased body weight during early lactation and increased TSH levels at a dose that did not elicit toxicity in the dams. Higher doses were required to elicit maternal toxicity which included increased serum TSH concentration, decreased serum T4 levels and histopathological findings in the thyroid (increased follicular cell height and follicular cell hypertrophy). Pre-natal sensitivity was not evident in the CTA study as fetal toxicity (increased thyroid weight in males and increased TSH levels in males and females) was observed only at maternally toxic doses.

EPA's Cancer Assessment Review Committee (CARC) classified buprofezin as "Suggestive Evidence of Carcinogenicity, but not sufficient to assess human carcinogenic potential" based on liver tumors in female mice only in accordance with the July 1999 Agency's Draft guidelines for Cancer Risk Assessment (TXR 0014045, S. Diwan, 3/16/2000). Buprofezin was negative in *in vitro* and *in vivo* genotoxicity assays. The CARC noted findings from the published literature indicate that buprofezin causes cell transformation and induces micronuclei *in vitro,* but determined that, in the absence of a positive response in an *in vivo* micronucleus assay, buprofezin may have aneugenic potential which is not expressed *in vivo*.

Buprofezin has low acute toxicity. It is Toxicity Category III for acute oral toxicity and Toxicity Category IV for acute dermal toxicity, acute inhalation toxicity, eye irritation, and dermal irritation. It is not a dermal sensitizer.

The complete toxicity profile for buprofezin is provided in Appendix A.

4.4 Safety Factor for Infants and Children (FQPA Safety Factor)[3]

The toxicology database for buprofezin is sufficient for FQPA assessment. Developmental toxicity studies in rats and rabbits and reproduction studies in rats provided no indication of increased susceptibility of rats or rabbits following *in utero* exposure or of rats following pre/postnatal exposure to buprofezin. However, a CTA study demonstrated offspring susceptibility, but not fetal susceptibility to buprofezin oral (gavage) administration. Points of departure (PODs) for risk assessment that are derived from this CTA study are based on the most sensitive endpoint of concern. For exposure scenarios using a NOAEL as POD, the FQPA SF which was previously retained due to data deficiency may be reduced to 1x. However, for assessments that use the CTA study to derive a POD, a FQPA SF of 10x is retained to account for the lack of a NOAEL.

4.4.1 Completeness of the Toxicology Database

The toxicity database for buprofezin is adequate to evaluate risks to infants and children. The database includes developmental toxicity studies in the rat and rabbit, multi- and single-generation reproduction studies in the rat, and a CTA.

4.4.2 Evidence of Neurotoxicity

There was no evidence of neurotoxicity in the toxicity database.

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

There was no evidence in developmental and reproductive toxicity studies of quantitative or qualitative sensitivity in the young; however, the CTA study demonstrated enhanced sensitivity in pups but not fetuses relative to maternal animals. A NOAEL could not be established for rat pups in the CTA study and, as a result, the 10x FQPA SF was retained to account for the uncertainty in the offspring sensitivity introduced by the lack of a NOAEL.

4.4.4 Residual Uncertainty in the Exposure Database

There are no residual uncertainties in the exposure database. The dietary risk assessment is conservative and will not underestimate dietary exposure to buprofezin. There are no residential

3 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).

uses of buprofezin, but non-occupational exposure (oral and dermal) from spray drift is anticipated.

4.5 Toxicity Endpoint and Point of Departure

4.5.1 Dose-Response Assessment

Toxicity endpoints and points of departure (PODs) for dietary (food and water), occupational, and residential exposure scenarios were previously selected as part of registration review (D431562, B. Cropp-Kohlligian et al., 9/27/2017) and are summarized below. There was no change in endpoints for the current action. A detailed description of the studies used as a basis for the selected endpoints is presented in Appendix A.

Acute Dietary

An acute POD for the general population was not selected due to the lack of acute toxicity in the available studies. An acute POD of 200 mg/kg (NOAEL) was selected for females age 13-49 years from a developmental toxicity study in rats based on incomplete ossification and reduced fetal weight at 800 mg/kg/day. This acute dietary POD should be viewed as a conservative estimate of acute toxicity as reduced fetal weight and decreased ossification are not considered to be acute effects based on current practices in HED. Thyroid effects in the CTA are related to repeated exposure to buprofezin and, therefore, are not appropriate for this acute endpoint. The acute exposure scenarios are not likely to result in toxicologically significant changes in thyroid hormonal levels because there is a normal daily fluctuation in thyroid levels which may be indistinguishable from any single dose effects on hormone levels. An uncertainty factor (UF) of 100x (10x to account for interspecies extrapolation and 10x for intraspecies variation) was applied to the NOAEL to obtain an acute reference dose (aRfD) of 2.0 mg/kg. FQPA SF for the acute dietary assessment has been reduced to 1x, as explained in Section 4.4 above. The acute population adjusted dose (aPAD) is equivalent to the aRfD.

Chronic Dietary

A chronic dietary POD of 10.0 mg/kg/day was selected for all populations based on the LOAEL from the CTA study. The CTA study is appropriate for selecting a chronic POD for all populations since it evaluated the most sensitive endpoints of toxicity (thyroid and thyroid hormones) in adults, fetuses, and offspring, and the study duration and route of administration are relevant to a chronic dietary exposure. In the CTA study, offspring toxicity was seen at 10.0 mg/kg/day based on significant decreased pup body weight (↓8-13% in males during lactation days (LD) 4-10 and ↓8-9% in females during LD 4-7) compared to controls and increased TSH levels on LD 4 and LD 21 pups (↑23-34% in males). These pup effects were observed in the absence of maternal toxicity. A NOAEL was not established in the CTA study. The 10x FQPA SF (for extrapolating a LOAEL to a NOAEL), a 10x for intraspecies variation, and a 3x for interspecies extrapolation was applied to the POD to obtain a chronic reference dose (cRfD) of 0.033 mg/kg/day. The cRfD and cPAD were identical. Generally, the interspecies uncertainty factor can be reduced to 3x when the POD is based on disruption of thyroid hormone regulation

in rats because adult rats are known to be more sensitive to this form of thyroid toxicity than humans due to differences in pharmacodynamics (PD)[4] . However, the POD from the CTA is based on thyroid disruption in rat pups, not adults, and the relationship between the observed PD for chemical induced thyroid hormone disruption in rat pups and the predicted response in infants and children is not as well understood. Yet, in the case of buprofezin, this uncertainty in the rat pup PD is already captured in the 10x FQPA SF/UF_L that accounts for the uncertainty in the offspring sensitivity due to the lack of an established NOAEL. Therefore, reducing the UF_A to 3x is appropriate for all exposure scenarios that were assessed using the offspring POD from the CTA study. The retained 3x portion of the interspecies factor addresses pharmacokinetic differences between rats and humans and could not be further refined with the available data.

Short-Term Incidental Oral

Although there are no residential uses for buprofezin, incidental oral exposures may be encountered due to potential non-occupational exposure from spray drift from agricultural applications. The CTA study provides an appropriate endpoint (10.0 mg/kg/day with a total UF of 300x) for assessing risk from incidental oral exposures (short-term duration).

Short- and Intermediate-Term Dermal

For assessing risk from dermal exposures the POD of 10 mg/kg/day from the CTA study was selected, with an MOE of 300 based on a 10x FQPA SF (for extrapolating a LOAEL to a NOAEL), a 10x for intraspecies variation, and a 3x for interspecies extrapolation. Since an oral POD is used, the estimated dermal absorption factor of 10% is applied.

Inhalation (all Durations)

Although a route specific inhalation study is available, that study did not evaluate the pup susceptibility seen in the CTA study. Therefore, to assess inhalation exposures, it is more appropriate to use the POD of 10 mg/kg/day from the CTA study with an MOE of 300 based on a 10x FQPA SF (for extrapolating a LOAEL to a NOAEL), a 10x for intraspecies variation, and a 3x for interspecies extrapolation. This POD is appropriate to assess risks from occupational and non-occupational (bystander) exposures to buprofezin. Toxicity by the inhalation route is considered to be equivalent to the toxicity by the oral route of exposure.

Body Weight

Since the dermal and inhalation PODs are based on developmental and/or fetal effects, the body weight appropriate for dermal and inhalation assessments is 69 kg.

4 Interim Guidance: Thyroid Disrupting Pesticides: Use of Rat Thyroid Data and Application of Uncertainty Factors for RfD Derivation; Prepared and Reviewed by the Hazard Science Policy Council (V. Dellarco, W. Burnam, K. Baetcke, L. Scarano, R. Kent, Jess Rowland, and Karen Whitby dated 11/01/2015

4.5.2 Recommendations for Combining Exposure Routes

When there are potential residential exposures to the pesticide, aggregate risk assessment must consider exposures from three major sources: oral, dermal and inhalation exposures. Oral, dermal, and inhalation exposures may be combined because toxicity endpoints for these exposure routes are the same.

4.5.3 Classification of Carcinogenic Potential

In assessing the carcinogenic potential of buprofezin, HED's Cancer Assessment Review Committee evaluated a 2-year combined chronic toxicity/carcinogenicity study in Sprague-Dawley rats and a 24-month carcinogenicity study in ICR-Cr mice. Based on the increased incidence of liver tumors in female mice only, no evidence of carcinogenicity in rats, and no evidence of genotoxicity in submitted guideline studies using *in vitro* and *in vivo* genotoxicity assays, under the Agency's Draft guidelines for Cancer Risk Assessment (July, 1999) the CARC (TXR 0014045, S. Diwan, 3/16/2000) classified buprofezin as having "Suggestive Evidence of Carcinogenicity, but not sufficient to assess human carcinogenic potential." No quantification of cancer risk is required. The CARC noted that although buprofezin was negative in *in vitro* and *in vivo* genotoxicity assays, the findings from the published literature indicate that it causes cell transformation and induces micronuclei *in vitro*; however, in the absence of a positive response in an *in vivo* micronucleus assay, the CARC concluded that buprofezin may have aneugenic potential which is not expressed *in vivo*.

4.5.4 Summary of Points of Departure Used in Risk Assessment

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

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

Exposure/ Scenario	Point of Departure	Uncertainty/ FQPA Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General Population)	An acute RfD for the general population including infants and children was not selected because the effects observed in the animal studies that could be attributed to a single day exposure were not applicable to the general population.			
Acute Dietary (Females 13-49 years)	NOAEL = 200 mg/kg	UF_A= 10x UF_H=10x FQPA SF= 1x	Acute RfD = 2.0 mg/kg/day aPAD = 2.0 mg/kg	Developmental Toxicity Study - Rat (MRID 42873813) Developmental LOAEL = 800 mg/kg/day based on reduced ossification & decreased fetal body weight.

Table 4.5.4.1. Summary of Toxicological Doses and Endpoints for Buprofezin for Use in Dietary and Non-Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty/ FQPA Safety Factors**	**RfD, PAD, LOC for Risk Assessment**	**Study and Toxicological Effects**
Chronic Dietary (All Populations)	LOAEL = 10 mg/kg/day	UF_A = 3x UF_H = 10x FQPA SF = UF_L = 10x	Chronic RfD = 0.033 mg/kg/day cPAD = 0.033 mg/kg/day	Comparative Thyroid Toxicity Analysis (CTA) Study-rats (MRID 49615301) Offspring LOAEL = 10.0 mg/kg/day based on significantly decreased pup body weight (↓8-13% in males during LD 4-10 and ↓8-9% in females during LD 4-7) compared to controls and increased TSH levels on LD 4 and LD 21 (↑23-34% in males).
Incidental Oral (all durations)	LOAEL = 10 mg/kg/day	UF_A = 3x UF_H = 10x FQPA SF = UF_L = 10x	Residential LOC for MOE = 300	Comparative Thyroid Toxicity Analysis (CTA) Study-rats (MRID 49615301) See above
Dermal Short (1-30 days) and Intermediate (1-6 months) Term	LOAEL= 10 mg/kg/day DAF = 10%	UF_A = 3x UF_H = 10x FQPA SF = UF_L = 10x	LOC for MOE = 300	Comparative Thyroid Toxicity Analysis (CTA) Study-rats (MRID 49615301) See above
Inhalation (all durations)	Non-occupational inhalation exposure was not assessed for buprofezin; therefore, an inhalation POD was not selected.			
Cancer (all routes)	"Suggestive Evidence of Carcinogenicity, but not sufficient to assess human carcinogenic potential" (TXR 0014045, S. Diwan, 3/16/2000). The cRfD is considered protective of the cancer effects.			

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_L = use of a LOAEL to extrapolate to a NOAEL. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. N/A = not applicable. DAF = dermal absorption factor (see Section 4.2.1)

Table 4.5.4.2. Summary of Toxicological Doses and Endpoints for Buprofezin for Use in Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal Short (1-30 days) and Intermediate (1-6 months) Term	LOAEL = 10 mg/kg/day DAF = 10%	UF_A = 3x UF_H = 10x UF_L = 10x	Occupational LOC for MOE = 300	Comparative Thyroid Toxicity Analysis (CTA) Study-rats (MRID 49615301) See above
Inhalation Short (1-30 days) and Intermediate (1-6 months) Term	LOAEL = 10 mg/kg/day	UF_A = 3x UF_H = 10x UF_L = 10x	Occupational LOC for MOE = 300	Comparative Thyroid Toxicity Analysis (CTA) Study-rats (MRID 49615301) See above
Cancer (all routes)	"Suggestive Evidence of Carcinogenicity, but not sufficient to assess human carcinogenic potential (TXR 0014045, S. Diwan, 3/16/2000). The cRfD is considered protective of the cancer effects.			

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_L = use of a LOAEL to extrapolate to a NOAEL. MOE = margin of exposure. LOC = level of concern. N/A = not applicable. DAF = dermal absorption factor (see Section 4.2.1)

5.0 DIETARY AND DRINKING WATER EXPOSURE AND RISK ASSESSMENT

5.1 Metabolite/Degradate Residue Profile

Structures and names of buprofezin metabolites/degradates discussed below are provided in Appendix B.

5.1.1 Summary of Plant Metabolism Studies

The qualitative nature of buprofezin residues in plants is understood based on the available lettuce, cotton, tomato, lemon and rice metabolism studies. Buprofezin is metabolized via hydroxylation of the tert-butyl group to form an intermediate metabolite identified as free metabolite BF4 (free metabolite BF4 was not isolated) which conjugates or degrades fairly rapidly via oxidation and cleavage to form metabolite BF9 and opening of the thiadiazine ring to form metabolite BF12. In minor routes, buprofezin may undergo opening of the thiadiazine ring to form metabolite BF25, which may undergo oxidation to form metabolite BF11; or free metabolite BF4 may undergo opening of the thiadiazine ring and further oxidation to form metabolite BF26. Collectively, the available metabolism data indicate that with relatively short PHIs (≤ 7-days) the major residue in/on fruits and vegetables is buprofezin; however, with longer PHIs (> 7-days) metabolite BF4 Conjugate (maximum residues may be estimated from the lemon metabolism study as the sum of its hydrolysis products which include BF9, BF12, BF26, and an unknown/unidentified hydrolysis product) is also a significant residue. Most of the residues remain in/on crop surfaces but are not readily removed with simple rinsing with water. Residues that penetrate the surface may remain in the peel and over time will consist of significant levels of metabolite BF4 Conjugate. Under typical processing conditions, the BF4 metabolite (free or conjugated) may be hydrolyzed to form significant residues of the metabolites BF9 and BF12 and a grape processing study indicated the potential for residues of metabolites BF9 and/or BF12 to concentrate in processed commodities to a greater degree than buprofezin.

In addition to determining that buprofezin is the residue of concern for tolerance setting and risk assessment in crops, HED has concluded that: (1) the residues of concern for risk assessment in grape juice are buprofezin and BF12; (2) residues of BF9 and BF12 should be monitored in all future processing studies and field trials; and (3) residues of metabolite BF4 Conjugate should be estimated for risk assessment purposes in/on crops with extended application to harvest intervals (PHIs > 7 days). Residues of metabolite BF4 Conjugate was not determined in many of the field trial and processing studies but maximum residues of metabolite BF4 Conjugate can be estimated based on the available lemon metabolism data as the sum of its hydrolysis products which include BF9, BF12, BF26, and an unknown/unidentified hydrolysis product. The buprofezin risk assessment team determined that the buprofezin:BF4 Conjugate residue ratio

from the lemon metabolism study (1.8x) should be used to estimate anticipated residues of metabolite BF4 Conjugate in/on crops and should be applied to crops with PHIs > 7 days.

5.1.2 Comparison of Metabolic Pathways

Buprofezin is the primary residue in plants, ruminants, poultry, and rats. Plant metabolism studies also identified the metabolites BF4 Conjugate, BF9, BF12, and BF26 as potentially significant residues. In milk and ruminant tissues, metabolites BF23 and BF2, respectively, were also significant metabolites. In rats, only feces and urine were investigated; 95% of the administered compound is recovered in the feces and urine within 72 hours, and that 45% is recovered in feces as the parent compound, with the remainder as several metabolites, including BF27 (7.2% of dose) and BF28, BF9, BF10, BF12, and BF13. Smaller amounts of buprofezin and metabolites were recovered in urine.

5.1.3 Environmental Fate and Transport

Buprofezin may get into surface water via spray drift, in solution in runoff water, or attached to soil particles eroded during runoff events. If it reaches acidic water (pH≤5), buprofezin is expected to slowly hydrolyze. In neutral or alkaline water (pH≥7), buprofezin will likely remain bound to sediment or suspended particles (due to its high soil/water partitioning coefficients) and could persist for several months if the water is deep, static, and/or cloudy. However, buprofezin persistence may be reduced significantly by photolysis if the water is shallow and clear. Based on the Henry's Law constant, buprofezin loss to air is expected to be minor. Although moderately persistent in soils, the use rates and the mobility/leaching data indicated that buprofezin will have low propensity to leach into ground water.

5.1.4 Residues of Concern Summary and Rationale

The qualitative nature of buprofezin residues in plants is understood based on the available lettuce, cotton, tomato, lemon and rice metabolism studies. Residues of concern for tolerance enforcement include only buprofezin. Residues of concern for risk assessment include buprofezin and the BF4 Conjugate. Residues of BF4 Conjugate should be estimated for risk assessment purposes in/on crops with longer pre-harvest intervals (PHI > 7-days) using the buprofezin:BF4 Conjugate residue ratio from the lemon metabolism study (1.8x) and the buprofezin anticipated residue estimate.

Adequate ruminant and poultry metabolism studies are available for buprofezin. The tolerance expression for milk and ruminant tissues includes only buprofezin; for purposes of risk assessment, the residues of concern in milk are buprofezin and BF23; for purposes of risk assessment, the residues of concern in ruminant tissues are buprofezin and BF2. There is no reasonable expectation of finite residues in poultry commodities at the present time.

Table 5.1.4.1. Summary of Buprofezin Residues of Concern.[1]		
Matrix	**Residues of Concern**	
	For Risk Assessment	**For Tolerance Expression**
Crops with ≤7-day PHI[2]	Buprofezin	Buprofezin
Crops with >7-day PHI[2]	Buprofezin and BF4 Conjugate	
Grape juice	Buprofezin, BF4 Conjugate, and BF12	
Processed Commodities	Based on the results of the grape processing study which indicate that BF9 and/or BF12 residues may concentrate to a greater degree than parent, default processing factors in DEEM should not be reduced based on buprofezin data alone.	
Rotational crops[3]	Buprofezin, BF9, and BF12	
Ruminant tissue	Buprofezin and BF2	
Milk	Buprofezin and BF23	
Poultry and eggs	Due to the limited residues in egg and tissue samples collected from the poultry metabolism study, the MARC determined that a conclusion pertaining to the residues of concern in egg and poultry was not possible.	
Water	Buprofezin	Not Applicable

1 D264546, T. Bloem, 4/20/2000; D273214, T. Bloem, 3/13/2001; TXR 0052261, T. Bloem, 12/10/2003.
2 Table updated with risk assessment team decision concerning circumstances under which the BF4 Conjugate should be considered a residue of concern for the risk assessment and is based on updated information.
3 Residues of concern in rotational crops are buprofezin, BF9 and BF12. However, there are no rotational crop tolerances.

5.2 Food Residue Profile

Adequate plant and ruminant metabolism data, magnitude of the residue data (i.e., field trial, processing, and cattle feeding studies), and storage stability data are available to support the proposed uses of buprofezin. Data indicate that residues of buprofezin are fat soluble and will partition into milk fat. Due to the low radioactivity in eggs and tissue samples collected from the poultry metabolism study, the nature of the residue in poultry could not be determined; however, these data are adequate to demonstrate that there is no expectation of finite residues of buprofezin in egg and poultry tissue commodities from currently registered uses of buprofezin. Based on adequate confined rotational crop data, a 30-day plant-back interval (PBI) is appropriate for non-labeled leafy vegetable and cereal crops and a 60-day PBI is appropriate for non-labeled root/tuber vegetable and all other crops.

Adequate fig and greenhouse-grown pepper field trial data reflecting the proposed maximum use rates of buprofezin on these commodities were submitted with this petition. Adequate fig processing data were submitted with this petition indicting that buprofezin residues of concern do not concentrate in dried fig and a separate tolerance for residues of buprofezin in/on dried figs is not needed. Using the Organization for Economic Cooperation and Development (OECD) tolerance calculation procedures, the recommended tolerance for residues of buprofezin in/on fig would be 0.7 ppm, which is the same as the petitioned-for tolerance. The greenhouse-grown pepper field trial data demonstrate that the currently established tolerance in/on vegetable, fruiting, group 8-10 is adequate to cover the proposed use of buprofezin on greenhouse-grown peppers.

Adequate field trial data are available to support the proposed/recommended crop group conversions to (i) Leafy greens subgroup 4-16A, (ii) *Brassica*, leafy greens, subgroup 4-16B, (iii) Vegetable, *Brassica*, head and stem, group 5-16, (iv) Leaf petiole vegetable subgroup 22B, (v) Celtuce; (vi) Fennel, Florence, and (vii) Kohlrabi.

Adequate field trial and processing data are available to support the proposed/recommended crop group expansions to all members of (i) Tropical and subtropical, small fruit, edible peel, subgroup 23A, (ii) Tropical and subtropical, small fruit, inedible peel, subgroup 24A, (iii) Cottonseed subgroup 20C, (iv) Fruit, citrus, group 10-10, (v) Fruit, stone, group 12-12, (vi) Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F, and (vii) Nut, tree, group 14-12. HED notes that there are no data available reflecting minimum spray volume of <2 gallons per acre (GPA) or <10 GPA for orchard crops to support ultra-low volume (ULV) uses of buprofezin.

5.3 Water Residue Profile

Drinking water residues were incorporated directly into the acute and chronic dietary analyses ("water, direct, all sources" and "water, indirect, all sources") and were previously provided by the Environmental Fate and Effects Division (EFED; D437195, J. Hetrick, 12/19/2016) in support of registration review. EFED has confirmed that these estimates are adequate for the current petition (email 7/11/2018 from R. Louie-Juzwiak). The drinking water assessment for buprofezin was completed using current models (Pesticide Root Zone Model version 5 and Variable Volume Water Model (PRZM5/VVWM) and PRZM GroundWater (PRZM-GW)) and guidance. Parent buprofezin was the only residue considered in the drinking water assessment. In past drinking water assessments, the highest EDWCs for buprofezin were associated with use on coffee. A reanalysis of the surface water modeling using current models and guidance indicates that buprofezin use on coffee still yields the highest EDWCs.

The EDWCs for buprofezin in surface source water are not expected to exceed 78.8 µg/L for the 1 in 10-year daily peak, 19 µg/L for the 1 in 10-year annual average, and 12 µg/L for the 30-year annual average. There was no breakthrough of buprofezin into ground water during a 100-year simulation using the PRZM-GW model. Buprofezin, therefore, is not expected to be detected in shallow ground water. Additionally, there was no monitoring data to provide an assessment of buprofezin concentrations in ambient surface or ground water.

As recommended by EFED, the EDWCs used in the dietary risk assessment for the 1 in 10-year daily peak, 1 in 10-year annual average, and 30-year annual average were 78.8 µg/L, 19 µg/L and 12 µg/L, respectively.

5.4 Dietary and Drinking Water Exposure and Risk

Screening level acute and partially refined chronic dietary and drinking water exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model with the Food Commodity Intake Database (DEEM-FCID™). Dietary risk assessment incorporates both

exposure and toxicity of a given pesticide. For acute and chronic dietary assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the reference dose (RfD) divided by the additional Safety Factor, if applied. For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD.

5.4.1 Acute Dietary and Drinking Water Analysis

A screening level acute dietary analysis was conducted for this assessment assuming 100% crop treated for all commodities. Total residues of concern in crop commodities (i.e., buprofezin and the BF4 Conjugate which is not detectable by data-collection methods but which may be estimated from metabolism data) were based on tolerance level residues of buprofezin and available metabolism/magnitude of the data to estimate other residues of concern. The residues of concern in/on crops with a preharvest interval (PHI) of ≤7 days is buprofezin and in/on crops with a PHI >7 days are buprofezin and the BF4 Conjugate. BF4 Conjugate residues were estimated, where needed, by multiplying the buprofezin residue level by 1.8x. Given the potential for BF9 and BF12 to concentrate to a greater degree than buprofezin in processed commodities, DEEM default processing factors were retained for all commodities, except for tomato paste and puree, which were reduced based on empirical data. Based on the submitted lemon metabolism data, which indicated that residues of concern are primarily found in/on the peel, the maximum theoretical concentration factor for peel was used to estimate residues of concern in citrus peel. Total residues of concern in meat (i.e., buprofezin and BF2) and milk (i.e., buprofezin and BF23) were based on the feeding study data which were used to establish meat and milk tolerances. Based on the submitted data, which indicated a 5x concentration of residues into milk cream and fat and a Log K_{ow} of 4.31, a default 25x concentration factor was applied for milk fat. The acute analysis also incorporated the 1 in 10-year peak surface drinking water estimate resulting from application of buprofezin to coffee. The resulting acute exposure estimate for females 13-49 years old is not of concern to HED (4.8% acute population adjustment dose (aPAD)). No acute endpoint was identified for the remaining population subgroups.

Table 5.4.1.1. Summary of Acute Dietary Exposure and Risk for Buprofezin.

Population Subgroup	aPAD (mg/kg/day)	Acute (95th Percentile)	
		Exposure (mg/kg/day)	%aPAD
Females 13-49 years old	2.0	0.096350	4.8

5.4.2 Chronic Dietary and Drinking Water Analysis

A partially refined chronic dietary analysis was conducted for this assessment using average percent crop treated estimates when available. Total residues of concern in crop commodities (i.e., buprofezin and the BF4 Conjugate which is not detectable by data-collection methods but which may be estimated from metabolism data) were based on tolerance level residues of buprofezin and available metabolism/magnitude of the data to estimate other residues of concern. The residues of concern in/on crops with a preharvest interval (PHI) of ≤7 days is buprofezin and in/on crops with

a PHI >7 days are buprofezin and the BF4 Conjugate. BF4 Conjugate residues were estimated, where needed, by multiplying the buprofezin residue level by 1.8x. Given the potential for BF9 and BF12 to concentrate to a greater degree than buprofezin in processed commodities, DEEM default processing factors were retained for all commodities, except for tomato paste and puree, which were reduced based on empirical data. Based on the submitted lemon metabolism data, which indicated that residues of concern are primarily found in/on the peel, the maximum theoretical concentration factor for peel was applied to residues in citrus peel. Total residues of concern in meat (i.e., buprofezin and BF2) and milk (i.e., buprofezin and BF23) were based on the feeding study data which were used to establish meat and milk tolerances. Based on the submitted data, which indicated a 5x concentration of residues into milk cream and fat and a Log K_{ow} of 4.31, a default 25x concentration factor was applied for milk fat. The chronic analysis also incorporated the 1 in 10-year average surface drinking water estimate resulting from application of buprofezin to coffee. The resulting chronic exposure estimates indicate no risks of concern for the general population or other population subgroups. The chronic risk exposure estimate for children 1-2 years old, the most highly exposed population, was 51% of the cPAD.

The chronic exposure assessment is conservative and is likely to overestimate risks based on a number of factors including, use of 100% crop treated assumptions for a number of crops for which data were unavailable, use of a conservative factor to account for the BF4 Conjugate, use of default processing factors, and use of drinking water exposure estimates for application of buprofezin to coffee, which is grown in limited areas in the U.S. (e.g., Puerto Rico, Hawaii).

Table 5.4.2.1. Summary of Chronic Dietary and Drinking Water Exposure and Risk for Buprofezin.

Population Subgroup	cPAD (mg/kg/day)	Chronic	
		Exposure (mg/kg/day)	%cPAD
General U.S. Population	0.033	0.006822	21
All Infants (< 1 year old)		0.011049	34
Children 1-2 years old		0.016698	**51**
Children 3-5 years old		0.012318	37
Children 6-12 years old		0.006927	21
Youth 13-19 years old		0.004344	13
Adults 20-49 years old		0.005740	17
Adults 50+ years old		0.007245	22
Females 13-49 years old		0.005696	17

5.4.3 Percent Crop Treated Used in Dietary Assessment

The Biological and Economic Analysis Division (BEAD) provided a screening level usage analysis (SLUA) report for buprofezin dated 8/11/2016. The acute dietary exposure analyses assumed 100% CT. Average % CT data was used for the following crops to refine the chronic dietary exposure analyses: almond 1%, apple 2.5%, apricot 10%, broccoli 5%, Brussels sprout 2.5%, cabbage 5%, cantaloupe 5%, cauliflower 10%, cherry 2.5%, cotton 1%, grapefruit 5%, grape 5%, lemon 2.5%, lettuce 10%, nectarine 5%, olive 2.5%, orange 2.5%, peach 5%, pear 10%, pepper 2.5%, pistachio 10%, plum/prune 5%, pomegranate 15%, pumpkin 1%, spinach 1%, squash 1%, strawberry 15%, tomato 1%, walnut 1%, and watermelon 2.5%. [Note: These average % CT data were also used to refine the cancer dietary exposure analysis for buprofezin-derived aniline, discussed in Appendix H.]

6.0 RESIDENTIAL EXPOSURE AND RISK ASSESSMENT

There are no proposed or existing residential uses for buprofezin; therefore, a residential exposure assessment has not been conducted.

7.0 AGGREGATE EXPOSURE AND RISK ASSESSMENT

In accordance with the FQPA, when there are potential residential exposures to a pesticide, aggregate risk assessment must consider exposures from three major routes: oral, dermal, and inhalation. There are three sources for these types of exposures: food, drinking water, and residential uses. 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. There are no residential uses of buprofezin; therefore, the aggregate risk assessment is equivalent to the acute and chronic dietary (food and drinking water) exposure and risk assessments. The acute and chronic dietary risk assessments for the U.S. population and all population subgroups are not of concern (<100% PAD).

7.1 Acute Aggregate Risk

The acute aggregate risk assessment combines exposures to buprofezin in food and drinking water only. The acute dietary (food and drinking water) exposure and risk assessment at the 95th percentile of exposure for females 13-49 years old is not of concern to HED (4.8% acute population adjustment dose (aPAD)). No acute endpoint was identified for the remaining population subgroups.

7.2 Chronic Aggregate Risk

The chronic aggregate risk assessment combines exposures to buprofezin in food and drinking water only. The chronic dietary (food and drinking water) exposure and risk assessment is not of concern to HED for the general population or other population subgroups. The chronic exposure and risk estimate for children 1-2 years old, the most highly exposed population, was 51% of the cPAD.

8.0 NON-OCCUPATIONAL SPRAY DRIFT EXPOSURE AND RISK ASSESSMENT

Spray drift is a potential source of exposure to those nearby pesticide applications. This is particularly the case with aerial application, but, to a lesser extent, spray drift can also be a potential source of exposure from the ground application methods (e.g., groundboom and airblast) employed for buprofezin. The Agency has been working with the Spray Drift Task Force (a task force composed of various registrants which was developed as a result of a Data Call-In issued by EPA), EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices (see the Agency's Spray

Drift website for more information). [5] The Agency has also developed a policy on how to appropriately consider spray drift as a potential source of exposure in risk assessments for pesticides. The potential for spray drift was quantitatively evaluated for buprofezin during the registration review process. The approach is outlined in the revised (2012) *Standard Operating Procedures For Residential Risk Assessment (SOPs) - Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift.* This document outlines the quantification of indirect non-occupational exposure to drift. The non-occupational spray drift assessment for adults and children 1 to < 2 years old resulted in recommended distances from the edge of field ranging from 0 feet up to 25 feet. Please refer to the occupational and residential exposure assessment for registration review for buprofezin (D439400, B. Van Deusen, 9/27/2017) for full non-occupational spray drift risk estimates and algorithms for the existing uses of buprofezin.

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-2009-0687-0037). 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 buprofezin.

10.0 CUMULATIVE RISK

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)[6] and conducting cumulative risk assessments (CRA)[7]. The agency has utilized this framework for buprofezin and determined that the available toxicological data suggests

5 Available: http://www.epa.gov/reducing-pesticide-drift
6 *Guidance For Identifying Pesticide Chemicals and Other Substances that have a Common Mechanism of Toxicity* (USEPA, 1999)
7 *Guidance on Cumulative Risk Assessment of Pesticide Chemicals That Have a Common Mechanism of Toxicity* (USEPA, 2002)

buprofezin does not share a similar toxicological profile with other pesticides. Thus, no further cumulative evaluation is necessary for buprofezin (D446787, H. Pope-Varsalona et al., 4/19/2018).

11.0 OCCUPATIONAL EXPOSURE/RISK CHARACTERIZATION

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 proposed uses of buprofezin. The quantitative exposure/risk assessment for the proposed new use on fig and greenhouse-grown pepper (D450358, B. Van Deusen, 6/03/2019) developed for occupational handlers is based on the scenarios identified in Table 11.1.1 and are discussed in some detail below. The proposed crop group conversions and expansions, in addition to other registered uses and formulations, were previously assessed in the Occupational and Residential Exposure Assessment for registration review for buprofezin (D439400, B. Van Deusen, 9/27/2017) and the results of that assessment are re-iterated in Table F.1.

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 maximum single application rate is identified on the proposed label and summarized in Table 3.3.1.

Unit Exposures: 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 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[8]", 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[9].

8 Available: https://www.epa.gov/sites/production/files/2016-11/documents/handler-exposure-table-2016.pdf
9 Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

Area Treated or Amount Handled: The inputs for area treated and amount handled were based on information in HED ExpoSAC Standard Operating Procedure (SOP) No. 9.1. For the greenhouse uses on buprofezin, HED's assumption for the volume treated by stationary foggers in commercial/agricultural buildings is 1,000,000 ft^3. Since the label rate was given in lb ai/A, the volume treated was converted to an area treated assuming a ceiling height of 7 feet resulting in a worst-case area treated of 142,857 ft^2. Based on this information and ExpoSAC Policy 9.1, the area treated or amount handled in a day was assumed to be:

- 350 acres for mixing/loading/applying during aerial applications to figs;
- 40 acres for mixing/loading/applying airblast and groundboom applications to figs;
- 60 acres for mixing/loading/applying during groundboom applications to greenhouse-grown peppers;
- 350 acres for flagging activities during aerial applications to figs;
- 1,000 gallons for mixing/loading/applying during mechanically pressurized handgun applications to figs and greenhouse-grown peppers;
- 40 gallons for mixing/loading/applying during manually pressurized handgun and backpack applications to figs and greenhouse-grown peppers; and,
- 1,000,000 cubic feet (142,857 ft^2) for mixing/loading/applying during fogging applications to greenhouse-grown peppers.

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 buprofezin, handler exposure is expected to be short- or intermediate-term based on information on the proposed labels (i.e., 2 applications per year and RTI's of 5 or 14 days). For both short- and intermediate-term durations, the PODs selected are the same; therefore, risk estimates are considered protective of both durations.

Long-term exposures are not typically assessed for greenhouse uses due to the cultural practices in greenhouses. While it may be possible for greenhouse uses to result in longer exposure durations due to growing crops year round, the occupational exposures are likely a series of short- or intermediate-term exposures, rather than a continuous long-term exposure duration.

Mitigation/Personal Protective Equipment: Estimates of dermal and inhalation exposure were calculated for various levels of PPE. For this assessment baseline attire is defined as a long-sleeved shirt, long pants, and shoes plus socks. The label-required PPE for the DF formulation are baseline attire plus waterproof gloves. The label-required PPE for the SC formulation is baseline attire plus chemical resistant (such as nitrile or butyl) gloves and protective eyewear.

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 the ORE document that supports this risk assessment (D450358, B. Van Deusen, 6/03/2019).

Combining Exposures/Risk Estimates
Dermal and inhalation risk estimates were combined in this assessment, since the toxicological effects for these exposure routes were the same. Dermal and inhalation risk estimates were combined using the following formula:

Total MOE = Point of Departure (mg/kg/day) ÷ Combined dermal + inhalation dose (mg/kg/day)

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates
Occupational handler dermal and inhalation exposure and risk estimates were calculated for the proposed new uses of buprofezin on fig and greenhouse-grown pepper (D450358, B. Van Deusen, 6/03/2019) and multiple crop group conversions/expansions (D439400, B. Van Deusen, 9/27/2017). A summary of occupational handler risk estimates for the proposed new fig and greenhouse-grown pepper uses is provided in Table 11.1.1. A summary of occupational handler risk estimates for the proposed crop group conversions and expansions is provided in Table F.1.

The occupational handler exposure and risk estimates indicate that there are combined dermal and inhalation risk estimates of concern (MOEs<300) for multiple scenarios assessed assuming the use of baseline attire and/or label required PPE (all registered labels require baseline attire plus waterproof or chemical resistant gloves). For the scenarios that result in risk estimates of concern at baseline attire or label required PPE, additional PPE and/or engineering controls were assessed. With the additional PPE and or engineering controls, there were six remaining scenarios of concern.

Five scenarios of concern, listed below, apply to both the proposed new fig and greenhouse-grown pepper uses as well as the proposed crop group conversions/expansions:

- mixing/loading DF formulation for aerial application to orchards/vineyards, and
- mixing/loading/applying liquid and DF formulations via mechanically pressurized handgun equipment to orchard/vineyard and greenhouse use sites.

The sixth scenario of concern, listed below, only applies to the proposed crop group conversions/ expansions:

- mixing/loading/applying liquid formulations via mechanically pressurized handgun equipment to typical field crops.

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 to pilots in enclosed cockpits. Therefore, risks to pilots are assessed using the engineering control (enclosed cockpits) and baseline attire (long-sleeve shirt, long pants, shoes, and socks); per the Agency's Worker Protection Standard stipulations for engineering controls, 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 Buprofezin.										
Exposure Scenario	**Crop or Target**	**Dermal Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control**	**Inhalation Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control**	**Maximum Application Rate[2]**	**Area Treated or Amount Handled Daily[3]**	**Dermal**		**Inhalation**		**Total**
						Dose (mg/kg/ day)[4]	**MOE[5] (LOC = 300)**	**Dose (mg/kg/ day)[6]**	**MOE[7] (LOC= 300)**	**MOE[8] (LOC= 300)**
Mixer/Loader										
Dry Flowable, Aerial, Broadcast	Orchard/Vineyard	51.6 SL/G	8.96 No-R	2 lb ai/acre	350 acres	0.0523	**190**	0.0909	**110**	**SL/G No-R 70**
		41.2 DL/G	0.896 PF10-R	2 lb ai/acre	350 acres	0.0417	**240**	0.0104	1,100	**DL/G PF10 R 200**
		12.5 EC	2.6 EC	2 lb ai/acre	350 acres	0.0127	790	0.0264	380	**EC 260**
Dry Flowable, Airblast, Broadcast	Orchard/Vineyard	51.6 SL/G	8.96 No-R	2 lb ai/acre	40 acres	0.00599	1,700	0.0104	960	SL/G No-R 610
Dry Flowable, Groundboom, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	227 SL/No G	8.96 No-R	0.4 lb ai/acre	60 acres	0.0079	1,300	0.00312	3,200	920
Dry Flowable, Groundboom, Broadcast	Orchard/Vineyard	51.6 SL/G	8.96 No-R	2 lb ai/acre	40 acres	0.00599	1,700	0.0104	960	SL/G No-R 610
Dry Flowable, Stationary/Automatic Fogger/Mister (with re-entry restriction), Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	227 SL/No G	8.96 No-R	0.00000132 lb ai/ft3	1000000 ft3	0.000435	23,000	0.000171	58,000	16,000
Liquid, Aerial, Broadcast	Orchard/Vineyard	37.6 SL/G	0.219 No-R	2 lb ai/acre	350 acres	0.0381	**260**	0.00222	4,500	**SL/G No-R 250**
		29.1 DL/G	0.219 No-R	2 lb ai/acre	350 acres	0.0296	340	0.00222	4,500	**DL/G No-R 320**
Liquid, Airblast, Broadcast	Orchard/Vineyard	220 SL/No G	0.219 No-R	2 lb ai/acre	40 acres	0.0255	390	0.000254	39,000	390
Liquid, Groundboom, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	220 SL/No G	0.219 No-R	0.38 lb ai/acre	60 acres	0.00728	1400	0.0000723	140000	1,400
Liquid, Groundboom, Broadcast	Orchard/Vineyard	220 SL/No G	0.219 No-R	2 lb ai/acre	40 acres	0.0255	390	0.000254	39000	390

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.										
Exposure Scenario	**Crop or Target**	**Dermal Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control**	**Inhalation Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control**	**Maximum Application Rate[2]**	**Area Treated or Amount Handled Daily[3]**	**Dermal**		**Inhalation**		**Total**
						Dose (mg/kg/ day)[4]	**MOE[5] (LOC = 300)**	**Dose (mg/kg/ day)[6]**	**MOE[7] (LOC= 300)**	**MOE[8] (LOC= 300)**
Liquid, Stationary/Automatic Fogger/Mister (with re-entry restriction), Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	220 SL/No G	0.219 No-R	0.00000125 lb ai/ft3	1000000 ft3	0.000399	25000	0.00000397	2500000	25,000
Applicator										
Spray (all starting formulations), Aerial, Broadcast	Orchard/Vineyard	2.08 EC	0.0049 EC	2 lb ai/acre	350 acres	0.00212	4700	0.0000497	200000	**EC 4600**
Spray (all starting formulations), Airblast, Broadcast	Orchard/Vineyard	1590 SL/ G	4.71 No-R	2 lb ai/acre	40 acres	0.184	54	0.00546	1800	**SL/G No-R 52**
		215 SL/G/CRH	4.71 No-R			0.0249	400	0.00546	1800	**SL/G/CRH No-R 330**
		14.6 EC	0.068 EC			0.0017	5900	0.0000788	130000	**EC 5600**
Spray (all starting formulations), Groundboom, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	78.6 SL/No G	0.34 No-R	0.4 lb ai/acre	60 acres	0.00274	3600	0.000118	85000	3500
Spray (all starting formulations), Groundboom, Broadcast	Orchard/Vineyard	78.6 SL/No G	0.34 No-R	2 lb ai/acre	40 acres	0.00912	1100	0.000394	25000	1100
Flagger										
Spray (all starting formulations), Aerial, Broadcast	Orchard/Vineyard	11 SL/No G	0.35 No-R	2 lb ai/acre	350 acres	0.0112	890	0.00355	2800	680
Mixer/Loader/Applicator										
Dry Flowable, Stationary/Automatic Fogger/Mister (without re-entry restriction), Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	No Data SL/No G	891.6 PF10 R	0.00000132 lb ai/ft3	1000000 ft3	No Data	No Data	0.0171	580	No Data

Table 11.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.										
Exposure Scenario	**Crop or Target**	**Dermal Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control**	**Inhalation Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control**	**Maximum Application Rate[2]**	**Area Treated or Amount Handled Daily[3]**	**Dermal**		**Inhalation**		**Total**
						Dose (mg/kg/ day)[4]	**MOE[5] (LOC = 300)**	**Dose (mg/kg/ day)[6]**	**MOE[7] (LOC= 300)**	**MOE[8] (LOC= 300)**
Liquid, Stationary/Automatic Fogger/Mister (without re-entry restriction), Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	No Data SL/No G	891.6 PF10 R	0.00000125 lb ai/ft3	1000000 ft3	No Data	No Data	0.0161	620	No Data
Dry Flowable, Backpack, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	13200 SL/No G	140 No-R	0.02 lb ai/gallon solution	40 gallons solution	0.0154	650	0.00162	6,200	590
Dry Flowable, Handheld/Portable Fogger/Mister, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	No Data SL/No G	891.6 PF10 R	0.00000132 lb ai/ft3	1000000 ft3	No Data	No Data	0.0171	580	No Data
Dry Flowable, Manually-pressurized Handwand, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	430 SL/G	30 No-R	0.02 lb ai/gallon solution	40 gallons solution	0.000499	20000	0.000348	29,000	SL/G No-R 12,000
Dry Flowable, Mechanically-pressurized Handgun, Broadcast (foliar)	Orchard/Vineyard	1360 DL/G	8.68 No-R	0.133 lb ai/gallon solution	1000 gallons solution	0.262	**38**	0.0167	600	**DL/G No-R 36**
Dry Flowable, Mechanically-pressurized Handgun, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	1600 DL/G	120 No-R	0.02 lb ai/gallon solution	1000 gallons solution	0.0464	**220**	0.0348	290	**DL/G No R 130**
			12 PF10 R			0.0464	**220**	0.00348	2,900	**DL/G PF10 R 200**
Liquid, Backpack, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	13200 SL/No G	140 No-R	0.019 lb ai/gallon solution	40 gallons solution	0.0145	690	0.00154	6500	620
Liquid, Handheld/Portable Fogger/Mister, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	No Data SL/No G	891.6 PF10 R	0.00000125 lb ai/ft3	1000000 ft3	No Data	No Data	0.0161	620	No Data
Liquid, Manually-pressurized Handwand, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	430 SL/G	30 No-R	0.019 lb ai/gallon solution	40 gallons solution	0.000474	21,000	0.00033	30,000	SL/G No-R 12,000

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

Exposure Scenario	Crop or Target	Dermal Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control	Inhalation Unit Exposure (µg/lb ai)[1] / Level of PPE or Engineering control	Maximum Application Rate[2]	Area Treated or Amount Handled Daily[3]	Dermal		Inhalation		Total
						Dose (mg/kg/day)[4]	MOE[5] (LOC = 300)	Dose (mg/kg/day)[6]	MOE[7] (LOC= 300)	MOE[8] (LOC= 300)
Liquid, Mechanically-pressurized Handgun, Broadcast (foliar)	Orchard/Vineyard	1360 DL/G	8.68 No-R	0.133 lb ai/gallon solution	1000 gallons solution	0.262	**38**	0.0167	600	**DL/G No-R 36**
Liquid, Mechanically-pressurized Handgun, Broadcast	Greenhouse (ornamentals, roses, cut flowers, container stock, vegetables)	1600 DL/G	120 No-R	0.019 lb ai/gallon solution	1000 gallons solution	0.0441	**230**	0.033	300	**DL/G No-R 130**

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: Baseline, PPE, Eng. Controls (EC), SL=Single Layer, DL=Double Layer, G=Gloves, CRH=Chemical-Resistant Hat, R=Respirator.
2 Based on proposed labels (Reg. Nos. 71711-20 & 71711-21). See Table 3.3.1.
3 Exposure Science Advisory Council Policy #9.1.
4 Dermal Dose = Dermal Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled (A or gal/day) × DAF (10%) ÷ BW (69 kg).
5 Dermal MOE = Dermal LOAEL (10 mg/kg/day) ÷ Dermal Dose (mg/kg/day).
6 Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled (A or gal/day) ÷ BW (69 kg).
7 Inhalation MOE = Inhalation LOAEL (10 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).
8 Total MOE = 1 ÷ (1/Dermal MOE + 1/Inhalation MOE).

11.2 Occupational Post-Application Exposure/Risk Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

Short- and intermediate-term exposure to occupational workers performing post-application activities in previously treated areas is expected based on the anticipated use patterns and proposed labeling.

The quantitative exposure/risk assessment for the proposed new uses on fig and greenhouse-grown pepper (D450358, B. Van Deusen, 6/03/2019) developed for occupational post-application workers is based on the scenarios identified in Table 11.2.2.3 and are discussed in some detail below. The proposed crop group conversions and expansions, in addition to other registered uses and formulations, were previously assessed in the revised occupational post-application risk estimates incorporating new DFR data to support registration review for buprofezin (D448121, B. Van Deusen, 8/13/2018) and the results of that assessment are re-iterated in Table G.1.

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 buprofezin.

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.

The Worker Protection Standard for Agricultural Pesticides contains requirements for protecting

workers from inhalation exposure during and after greenhouse applications through the use of ventilation requirements. [40 CFR 170.110, (3) (Restrictions associated with pesticide applications.)]

11.2.2 Occupational Post-Application Dermal Exposure/Risk Estimates

Occupational Post-application Dermal Exposure Data and Assumptions

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

Exposure Duration: HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. For buprofezin, based on the proposed uses, short- and intermediate-term exposures are expected. However, the POD for dermal exposures is the same for both durations; therefore, the occupational post-application exposures assessed are applicable to both short- and intermediate-term exposures.

Transfer Coefficients: It is the policy of HED to use the best available data to assess post-application exposure. Sources of generic post-application data, used as surrogate data in the absence of chemical-specific data, are derived from ARTF exposure monitoring studies, and, as proprietary data, are subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting post-application exposure that are used in this assessment, known as "transfer coefficients", are presented in the ExpoSAC Policy 3[10]" which, along with additional information about the ARTF data, can be found at the Agency website[11]. A summary of the anticipated post-application activities and associated transfer coefficients for the proposed new fig and greenhouse-grown pepper use sites are included in Table 11.2.2.3.

As described in ExpoSAC Policy 3, transfer coefficients are generally foliar-based and are not established for contact with residues on bark or branches that might result from contact with soil/thatch during windrowing and sweeping following applications to almonds or dormant hand pruning (minimum foliage density) for orchard crops and nut trees (i.e., figs). These post-application activities are therefore not assessed; however, exposures are not expected to be greater than others that are assessed, and any assigned crop-specific REIs should be protective of worker risks for these activities.

Application Rate: The maximum single application rate is identified on the proposed label and summarized in Table 3.3.1.
Exposure Time: The average occupational workday is assumed to be 8 hours.

Dislodgeable Foliar Residues: In accordance with the updated Part 158 data requirements

10 Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data
11 Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

(2007), one or more DFR studies are required when a pesticide has residential or occupational uses that could result in post-application dermal exposure. Of the DFR studies submitted and previously reviewed, the studies on citrus and greenhouse tomatoes have been incorporated into this exposure assessment (MRID 50573102, D446830, B. Van Deusen, 8/08/2018; MRID 50523901, D445664, B. Van Deusen, 4/11/2018) because they most closely reflect the characteristics of the proposed new use crops. The data and the results of the pseudo-first order statistical analysis are summarized below in Tables 11.2.2.1 and 11.2.2.2. Full study summaries and analysis can be found in the ORE document that supports this risk assessment (D450358, B. Van Deusen, 6/03/2019).

Table 11.2.2.1. Review of Dissipation of Dislodgeable Foliar Residues of Buprofezin on Citrus Foliage (MRID 50573102).

Statistic	Italy	Spain (Algemesi)	Spain (Catadau)
Application Rate (lb ai/A)	0.895	0.855	0.877
Measured Average Day 0 Residue ($\mu g/cm^2$)	1.4604	0.1778	0.2946
Predicted Day 0 Residue ($\mu g/cm^2$)	**0.897**	0.079	0.201
Slope	-0.122	-0.120	-0.121
Half-Life (days)	5.7	5.8	5.7
R^2	0.955	0.8235	0.9143

Table 11.2.2.2. Review of Dissipation of Dislodgeable Foliar Residues of Buprofezin on Tomato Foliage (MRID 50523901).

Statistic	California
Application Rate (lb ai/A)	0.393 lb ai/A
Measured Average Day 0 Residue ($\mu g/cm^2$)	0.6913
Predicted Day 0 Residue ($\mu g/cm^2$)	**1.06**
Slope	-0.169
Half-Life (days)	4.1
R^2	0.8748

Occupational Post-Application Non-Cancer Dermal Exposure and Risk Estimate Equations

The algorithms used to estimate non-cancer exposure and dose for occupational post-application workers can be found in the ORE document that supports this risk assessment (D450358, B. Van Deusen, 6/03/2019).

Occupational Post-Application Non-Cancer Dermal Risk Estimates

Proposed new fig and greenhouse-grown pepper uses: Using buprofezin-specific DFR data, the occupational post-application MOEs are not of concern (i.e., MOEs ≥ 300, ranging from 310 to 4,300) for the proposed new fig and greenhouse-grown pepper uses on the day of application (D450358, B. Van Deusen, 6/03/2019). Post-application risk estimates for the proposed new fig and greenhouse-grown pepper activities are presented in Table 11.2.2.3.

Proposed crop group conversions/expansion: The occupational post-application exposure and risk estimates for the crop group conversions/expansions were previously assessed for the registration review for buprofezin (D439400, B. Van Deusen, 9/27/2017) and later updated with

chemical-specific dislodgeable foliar residue data (D448121, B. Van Deusen, 8/13/2018). Dermal MOEs of concern (i.e., MOEs < 300) were identified for the registered uses on cotton, grape, olive, and stone fruit on the day of product application and, therefore, apply to all registered uses for Crop Subgroup 20C, Crop Subgroup 13-07F, Crop Subgroup 23A, and Crop Group 12-12. The 12-hour REI listed on the proposed labels may not be adequately protective for workers engaged in post-application activities following buprofezin usage since dermal post-application MOEs are of concern for up to 8 days after product application. Post-application risk estimates for the proposed crop group conversions and expansions are presented in Table G.1.

Table 11.2.2.3. Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Buprofezin on Day 0

Crop/Site	Activities	Transfer Coefficient (cm^2/hr)	DFR	Application Rate (lb ai/A)[1]	Dermal Dose (mg/kg/day)[2]	MOE (LOC=300)[3]
Short- and Intermediate-Term						
Fig	Harvesting, hand; pollination	1400	2.0	2.0	0.033	310
	Scouting; Pruning, hand	580			0.013	740
	Transplanting	230			0.005	1,900
	Orchard maintenance; Weeding, hand	100			0.002	4,300
Greenhouse tomatoes	Harvesting, hand; pinching; pollination; pruning, hand; scouting; turning; tying/training; weeding, hand; propagating	1200	1.08	0.40	0.015	670
	Transplanting; irrigation (hand watering)	230			0.003	3,500

1 DFR Data Source: Fig: Citrus DFR data MRID 50573102, D446830: Day 0 residue: 0.897 ug/cm^2, study application rate = 0.895 lb ai/A; and, Greenhouse Pepper: Greenhouse Tomato DFR data MRID 50523901, D445664: Day 0 residue: 1.06 ug/cm^2, study application rate = 0.393 lb ai/A.
2 Application Rate = Identified in Table 3.3.1.
3 Daily Dermal Dose = [DFR (µg/cm^2) × Transfer Coefficient × 0.001 mg/µg × 8 hrs/day × dermal absorption (10%)] ÷ BW (69 kg).
4 MOE = POD (10 mg/kg/day) / Daily Dermal Dose.

Restricted Entry Interval

Buprofezin is classified as Toxicity Category III for acute oral toxicity and Toxicity Category IV for acute dermal and inhalation toxicity, as well as eye and skin irritation. It is not a dermal sensitizer. Under 40 CFR §156.208 (c) (2), ai's classified as Acute III or IV for acute dermal, eye irritation, and primary skin irritation are assigned a 12-hour REI. Therefore, the [156 subpart K] Worker Protection Statement interim REI of 12 hours is adequate to protect agricultural workers from post-application exposures to buprofezin based on the proposed new fig and greenhouse-grown pepper uses. However, some post-application activities related to the crop group conversions/expansions resulted in risk estimates of concern on day 0 (12 hours following application) as detailed in the revised occupational post-application risk assessment (D448121, B. Van Deusen, 8/13/2018). Risk estimates of concern were related to thinning, harvesting, tying/training, and leaf pulling activities for multiple crops; therefore, HED is recommending that the REI be revised on the label to address those concerns.

12.0 REFERENCES

Buprofezin Revised Human Health Risk Assessment for Proposed Use of Buprofezin on Tree Nut Crop Group 14 including Pistachio, Brassica Leafy Greens Subgroup 5B, Turnip Greens, Tea, and Persimmon & Expanded Uses on Fruiting Vegetables, Succulent Beans, Citrus Fruit, and Pome Fruit. – B. Cropp-Kohlligian, D394902/D396296, 8/23/2012.

Drinking Water Assessment for Registration Review of Buprofezin – J. Hetrick, D437195, 12/19/2016.

Buprofezin: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment – S. Recore and E. Evans, D438750, 8/09/2017.

Evaluation of Potential Aniline Formation from Buprofezin in Drinking Water. – J. Hetrick, D442267, 8/28/2017.

Buprofezin. Occupational and Residential Exposure Assessment for Registration Review. – B. Van Deusen, D439400, 9/27/2017.

Buprofezin. Human Health Draft Risk Assessment for Registration Review. – B. Cropp-Kohlligian et al., D431562, 9/27/2017

Chitin Synthesis Inhibitors (Buprofezin and Cyromazine): Screening Analysis of Toxicological Profiles to Consider Whether a Candidate Common Mechanism Group Can Be Established. – H. Pope-Varsalona et al., D446787, 4/19/2018

Buprofezin. Determination of Dislodgeable Foliar Residues on Tomato Foliage Treated with Buprofezin (MRID No. 50523901). – B. Van Deusen, D445664, 4/11/2018.

Buprofezin. Response to Comments on the Human Health Draft Risk Assessment for Registration Review. – B. Cropp-Kohlligian et al., D447127, 8/07/2018

Buprofezin. Determination of Dislodgeable Foliar Residues on Citrus and Grape Foliage Treated with Buprofezin (MRID Nos. 50573101 & 50573102). – B. Van Deusen, D446830, 8/08/2018.

Buprofezin: Revised Occupational Post-Application Risk Estimates Incorporating New DFR Data to Support Registration Review. – B. Van Deusen, D448121, 8/13/2018.

Buprofezin – Acute, Chronic, and Cancer (Aniline) Dietary Risk Assessments for the New Use on Figs and Greenhouse Peppers; Conversions to: Leafy greens, subgroup 4-16A, except head lettuce and radicchio; Brassica, leafy greens, subgroup 4-16B; Vegetable, brassica, head and stem, group 5-16; Leaf petiole vegetable subgroup 22B; Celtuce; Florence Fennel; Fruit, citrus group 10-10; Fruit, stone, group 12-12, except apricot and peach; and Nut, tree, group 14-12; and Expansions to Tropical and subtropical, small fruit, edible peel, subgroup 23A; Tropical and

subtropical, small fruit, inedible peel, subgroup 24A; Cottonseed subgroup 20C; and Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F. – T. Morton, D449526, 6/03/2019.

Buprofezin. Occupational and Residential Exposure Assessment for Proposed New use on Figs and Greenhouse Peppers. – B. Van Deusen, D450358, 6/03/2019.

Buprofezin. Proposed New Uses on Figs and Greenhouse-Grown Peppers and the Establishment of Permanent Tolerances in/on Fig and Tolerance Conversions to Leafy Greens Subgroup 4-16A, Except Head Lettuce and Radicchio; *Brassica*, Leafy Greens, Subgroup 4-16B; Vegetable, *Brassica*, Head and Stem, Group 5-16; Leaf Petiole Vegetable Subgroup 22B; Celtuce; Florence Fennel; Kohlrabi; and Tolerance Expansions to All Members of Fruit, Citrus Group 10-10; Fruit, Stone, Group 12-12; Nut, Tree, Group 14-12; Tropical and Subtropical, Small Fruit, Edible Peel, Subgroup 23A; Tropical and Subtropical, Small Fruit, Inedible Peel, Subgroup 24A; Cottonseed Subgroup 20C; and Fruit, Small, Vine Climbing, Except Fuzzy Kiwifruit, Subgroup 13-07F. Summary of Analytical Chemistry and Residue Data. Summary of Analytical Chemistry and Residue Data. – J. Camp, D451162, 6/03/2019.

APPENDIX A. Toxicology Data Summary

A.1 Guideline Data Requirements

Table A.1.1. Guideline Data Requirements for Buprofezin

Test	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	yes
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
870.5375 Mutagenicity—Structural Chromosomal Aberrations	yes	yes
870.5900 Mutagenicity—Other Genotoxic Effects	yes	yes
870.6100a Acute Delayed Neurotox. (hen)	no	-
870.6100b 90-Day Neurotoxicity (hen)	no	-
870.6200a Acute Neurotox. Screening Battery (rat)	yes	yes[1]
870.6200b 90-Day Neuro. Screening Battery (rat)	yes	yes
870.6300 Develop. Neuro	no	--
870.7485 General Metabolism	yes	yes
870.7600 Dermal Penetration	--	--
870.7800 Immunotoxicity	yes	yes
Non-guideline Comparative Thyroid Toxicity	yes	yes

[1]Recommended to be waived (TXR 0055414, A. Khasawinah, 1/19/2011)

A.2 Toxicity Profiles

Table A.2.1. Acute Toxicity Profile Buprofezin [PC 275100]				
Guideline No./Study Type	**MRID No.**	**TXR No.**	**Results**	**Toxicity Category**
870.1100 Acute oral toxicity	42873806	0011358	LD_{50} = 1635 mg/kg (M) LD_{50} = 2015 mg/kg (F)	III
870.1200 Acute dermal toxicity	46213301	5003505	LD_{50} > 5000 mg/kg	IV
870.1300 Acute inhalation toxicity	42873808	0011358 5003504[1]	LC_{50} > 4.7 mg/L	IV
870.2400 Acute eye irritation	46213302	5003505	Minimal	IV
870.2500 Acute dermal irritation	46213303	5003505	Slight	IV
870.2600 Skin sensitization	46213304	5003505	Negative	NA

[1] MRID was upgraded from Unacceptable to Acceptable in TXR 5003504 (D292012, J. Redden, 1/13/2004)

Table A.2.2. Subchronic, Chronic and Other Toxicity Profile for Buprofezin and Metabolite BF26		
Guideline No. Study Type	**MRID No. (year) Classification Dose Levels**	**Results TXR No.**
870.3050 28-day oral toxicity rodents (rat)	49175903 (2008) **Acceptable/Guideline** gavage at dose levels of 0, 3, 15, or 75 mg/kg bw/day	**NOAEL** = 75 mg/kg/day **LOAEL** > 75 mg/kg/day (highest dose tested) 0057599
870.3100 90-day oral toxicity rodents (rat)	42935201 (1986) **Acceptable/Guideline**	**NOAEL** = 13.0 mg/kg/day males; 16.3 mg/kg/day females **LOAEL** = 68.6 mg/kg/day males; 81.8 mg/kg/day females; based on increased relative thyroid weight (males), increased liver weights (both sexes), increased microscopic lesions in liver and thyroid (both sexes) 0011358
870.3150 Oral Subchronic in non-rodents (dog)	42873809 (1985) **Acceptable/Guideline** 0, 2, 10, 50, 300 mg/kg/day	**NOAEL** = 10 mg/kg/day **LOAEL** = 50 mg/kg/day based on increased serum alkaline phosphatase activity, increased thyroid weight (males), increased liver weight and homogeneous hepatocytoplasm decreased bodyweight gain, subdued mood and distended abdomen
870.3200 24-day dermal toxicity (rat)	44394024 (1995) **Acceptable/non-guideline** Non-guideline because it used 5 animals/sex/dose instead of 10 animals/sex/dose	**Systemic NOAEL** = 300 mg/kg/day **Systemic LOAEL**: 1000 mg/kg/day based on increased focal necrosis with an inflammatory infiltrate in liver (females only) **Dermal NOAEL**: 300 mg/kg/day **Dermal LOAEL**: 1000 mg/kg/day based on increased

Table A.2.2. Subchronic, Chronic and Other Toxicity Profile for Buprofezin and Metabolite BF26		
Guideline No. Study Type	**MRID No. (year) Classification Dose Levels**	**Results TXR No.**
		acanthosis and hyperkeratosis in skin (females only) 0050318
870.3465 28-Day Inhalation	49614701 (2015) **Acceptable/guideline** 0, 23, 112, or 509 mg/m^3	**LOAEC** = 509 mg/m^3 based on a treatment-related effect on the adrenal gland (increased weight and microscopic findings of minimal hypertrophy of the cortex). **NOAEL** = 112 mg/m^3 0057225
870.3700a Developmental Toxicity in rodents (rat)	42873813 (1987) **Acceptable/guideline**	**Maternal NOAEL** = 200 mg/kg/day **Developmental NOAEL** = 200 mg/kg/day **Maternal LOAEL =** 800 mg/kg/day based on mortality, decreased pregnancy rates, increased resorption rates **Developmental LOAEL**= 800 mg/kg/day based on reduced ossification, reduced fetal weight, fetal edema. 0011358
870.3700b Developmental Toxicity in non-rodents (rabbit)	42873812 (1986) **Acceptable/guideline**	**Maternal NOAEL =** 50 mg/kg/day **Maternal LOAEL** = 250 mg/kg/day based on decreased food consumption, decreased body weights. **Developmental NOAEL** = 250 mg/kg/day **Developmental LOAEL** was not established 0011567
870.3800 Reproduction and fertility effects in rats	42873814, 44394027 (1997) **Acceptable/guideline**	**Parental NOAEL** = 7.89 mg/kg/day **Parental LOAEL**= 81.47 mg/kg/day based on decreased body weight gain and on organ weight changes **Reproductive/Developmental NOAEL =** 7.89 mg/kg/day **Reproductive/Developmental LOAEL** = 81.47 mg/kg/day based on decreased pup weight. 0011567
870.4100 Chronic toxicity in dogs	42873810 (1994) **Acceptable/guideline** 0, 2, 20, or 200 mg/kg/day for 107 weeks buprofezin >99% purity	**NOAEL** = 2 mg/kg/day **LOAEL** = 20 mg/kg/day based on increased bile duct hyperplasia and increased serum alkaline phosphatase activity in both sexes, increased relative and absolute liver weights and decreased liver function in females. 0050318
870.4300 Chronic toxicity/ carcinogenicity in rodents (rat)	42935202, 44394025 (1997) **Acceptable/guideline**	**NOAEL** = 1.0 mg/kg/day **LOAEL** = 8.7 mg/kg/day based on increased incidence of follicular cell hyperplasia and hypertrophy in thyroid in males. **No evidence of carcinogenicity** 0050318

Table A.2.2. Subchronic, Chronic and Other Toxicity Profile for Buprofezin and Metabolite BF26		
Guideline No. Study Type	**MRID No. (year) Classification Dose Levels**	**Results TXR No.**
870.4200 Carcinogenicity study in mice	42873811 (1992) **Acceptable/guideline**	**NOAEL** = 1.82 / 17.9 mg/kg/d (males/females) **LOAEL** = 17.40 / 191.0 mg/kg/d (males/females) based on increased absolute liver weights in males and females, increased hepatocellular adenomas + carcinomas in females 0050318
870.5100 Mutagenicity: gene mutation Salmonella	42873815 (1988) **Acceptable/guideline**	Not mutagenic, with or without activation tested up to cytotoxic levels 0011358
870.5100 Mutagenicity: gene mutation Salmonella	49175902 (2004) **Acceptable/guideline** **Test chemical: Buprofezin Plant Metabolite BF26**	Not mutagenic, with or without activation tested up to cytotoxic levels 0057556
870-5300 Mutagenicity: gene mutation mouse lymphoma	42873816 (1988) **Acceptable/guideline**	Not mutagenic, with or without activation tested up to cytotoxic levels 0011358
870.5300 Mutagenicity: in vitro human cytogenetic assay	42873818 (1988) **Acceptable/guideline**	Negative for chromosomal aberrations tested up to cytotoxic levels 0011358
870.5300 Mutagenicity: mouse micronucleus assay	42873817 (1983) **Acceptable/guideline**	Negative for micronucleus induction in bone marrow cells of males and females tested up to cytotoxic levels 0011358
870.5300 Mutagenicity: Unscheduled DNA synthesis	42873819 (1988) **Acceptable/guideline**	Negative for DNA repair tested up to cytotoxic levels 0011358
870.7485 Metabolism	42873820, 44394029 (1999) **Acceptable/guideline**	The absorption, distribution, metabolism, and excretion of buprofezin were studied in rats. The rat metabolism study indicated that 95% of the administered dose was excreted in urine and feces within 72 hours (feces - 79.1%; urine - 12.9%). In the feces, about 45% of the radioactivity was recovered as parent compound, with the remainder as several metabolites. Biliary excretion of radioactivity accounted for 32-39 % of the administered dose during 24 hours of post dosing. Maximum concentrations in blood following single oral dosing of radiolabeled ^{14}C-buprofezin occurred at 9 hours. ^{14}C-buprofezin radioactivity was detected in tissues and organs after 168

Table A.2.2. Subchronic, Chronic and Other Toxicity Profile for Buprofezin and Metabolite BF26		
Guideline No. Study Type	**MRID No. (year) Classification Dose Levels**	**Results TXR No.**
		hours of administration with highest concentrations in the liver, thyroid and red blood cells. Metabolites in feces consisted primarily of unchanged parent (BF1; 45.4%) with lesser amounts of BF27 (2-tert-butylimino-5-(4-hydroxy-3-methoxyphenyl)-3-isopropyl-1,3,5-thiadiazinan-4-one; 7.2% of dose) and BF28 (2-[3-isopropyl-3-[methylsulfonylmethyl(phenyl)carbamoyl] ureido]-2-methylpropionic acid; 4.6% of dose). Hydrolysis of the extracted fecal fiber resulted in minor amounts (< 0.1% each) of BF9 (3-isopropyl-5-phenyl-1,3,5-thiadiazinan-2,4-dione), BF10 (2-tertbutylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one-1-oxide), BF12(1-isopropyl-3-phenylurea), and BF13 (1-(4-hydroxyphenyl)-3-isopropylurea). In urine, 12.9% of the administered dose was recovered. Polar conjugates released by sulfatase hydrolysis consisted of BF13 (0.5% of dose), BF23 (N-(4-hydroxyphenyl) acetamide; 2.5% of dose), and BF28 (0.3% of dose). A total of 60.7% of the administered dose was identified and no unknown metabolite or fiber bound residue exceeded 3.7% of the dose. 0057560
870.6200 Subchronic neurotoxicity	48083902 (2005) **Acceptable/guideline**	**LOAEL** > 5000 ppm, no neurotoxicity was observed **NOAEL** = 5000 ppm (358.1/433.0 mg/kg/day in males/females, the highest dose tested) 0055414
870.7800 Immunotoxicity Sprague-Dawley Crl:CD(SD) rats	48440101 (2011**)** **Acceptable/guideline** 10 rats/sex/dose in the diet at 0, 200, 1000, or 5000 ppm (♂0, 15.8, 78.1, or 343 mkd ♀0, 15.4, 79, or 346 mkd**)**	Not immunotoxic at doses tested. 0056054
Non-Guideline Comparative Thyroid Toxicity Analysis (CTA) Study-rats	49615301 (2015) 49615302 (2015) 49738501 (2013) 0, 10, 80 or 160 mg/kg/day A: Pregnant dams GD 6-20 B: Pregnant dams GD 0-LD6 C: Non-pregnant dams dosed 21 days before evaluation. B pups dosed PND 7-21 **Acceptable/non-guideline**	**Adult LOAEL =** 80 mg/kg bw/day in pregnant and nonpregnant dams based on increased serum TSH concentration (↑41-49%), decreased serum T4 levels in pregnant rats (↓15%) but not in the non-pregnant rats and histopathological findings in the thyroid (increased follicular cell height and follicular cell hypertrophy). The liver (hepatocellular hypertrophy considered adverse for the lack of liver enzyme measurements). **Adult NOAEL** = 10 mg/kg bw/day. **Fetal LOAEL =** is 80 mg/kg/day based on increased thyroid weight in males (↑36%) and increased TSH levels in males (↑31%) and females (↑71%).

Table A.2.2. Subchronic, Chronic and Other Toxicity Profile for Buprofezin and Metabolite BF26		
Guideline No. Study Type	**MRID No. (year) Classification Dose Levels**	**Results TXR No.**
		Fetal NOAEL = is 10 mg/kg/day. **Offspring LOAEL =** 10 mg/kg/day based on significantly decreased pup body weight (↓8-13% in males during LD 4-10 and ↓8-9% in females during LD 4-7) compared to controls and increased TSH levels on LD 4 and LD 21 (↑23-34% in males). **Offspring NOAEL was not defined in this study.** It is noted that this offspring LOAEL may be conservative considering that in the 2- gen study (MRID 42873814), the LOAEL for offspring toxicity was 85 mg/kg/day with a NOAEL of 8.5 mg/kg/day. However, the methods of compound administration were different (dietary vs. gavage) and may contribute to the dose at which effects are observed in these studies. A positive control study (MRID 49738501) performed in this laboratory using 6-propyl-2-thiouracil (PTU) administered to dams by gavage from GD 6-LD 21 (pups were not directly dosed) demonstrated anti-thyroid effects in dams and their pups using methods equivalent with the current study. 0057225

APPENDIX B. Chemical Names and Structures of Metabolites

Table B.1. Chemical Names and Structures of Buprofezin Metabolites.

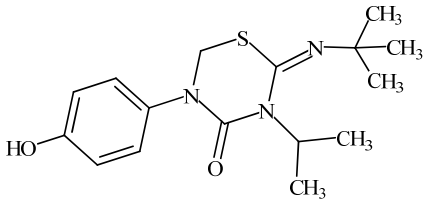
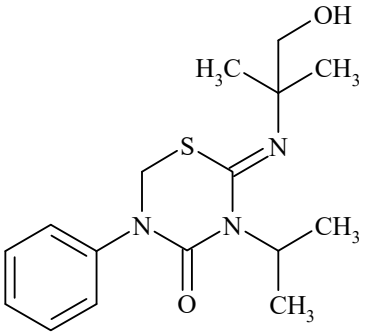
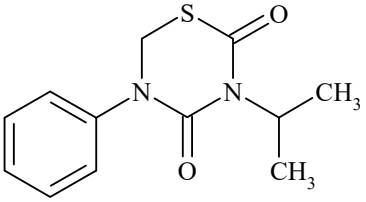
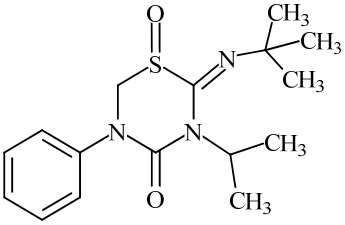
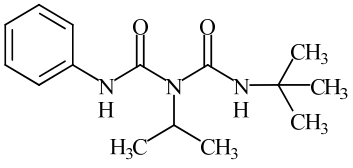
Common name; Company code	Chemical name	Chemical structure
BF2	2-tert-butylimino-5-(4-hydroxyphenyl)-3-isopropyl-1,3,5-thiadiazinan-4-one	
BF4	2-(2-hydroxy-1,1-dimethylethylimino)-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one	
BF9	3-isopropyl-5-phenyl-1,3,5-thiadiazinan-2,4-dione	
BF10	2-*tert*-butylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one-1-oxide	
BF11	1-*tert*-butyl-3-isopropyl-5-phenylbiuret	

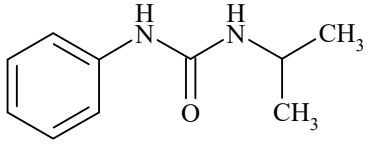
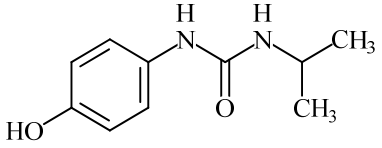
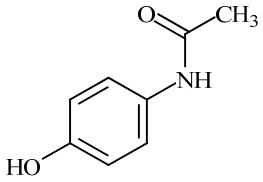
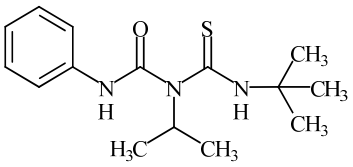
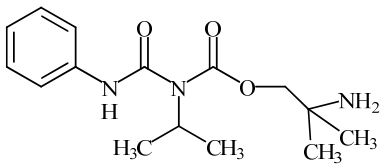
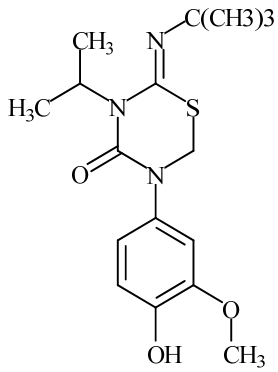
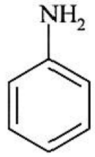
Table B.1. Chemical Names and Structures of Buprofezin Metabolites.		
Common name; Company code	Chemical name	Chemical structure
BF12	1-isopropyl-3-phenylurea	
BF13	1-(4-hydroxyphenyl)-3-isopropylurea	
BF23	N-(4-hydroxyphenyl) acetamide	
BF25	1-*tert*-buty-3-isopropyl-5-phenyl-2-thiobiuret	
BF26	2-amino-2-methylpropyl-2-methylethyl-4-phenyl-allophanate	
BF27	2-*tert*-butylimino-5-(4-hydroxy-3-methoxyphenyl)-3-isopropyl-1,3,5-thiadiazinan-4-one	

Table B.1. Chemical Names and Structures of Buprofezin Metabolites.		
Common name; Company code	Chemical name	Chemical structure
BF28	2-[3-isopropyl-3-[methylsulfonylmethyl(phenyl)carbamoyl] ureido]-2-methylpropionic acid	
Aniline (high temperature hydrolysis product)	phenylamine, benzenamine, aminobenzene	

APPENDIX C. Physical/Chemical Properties of Buprofezin

Table C.1. Physicochemical Properties of the Technical Grade Buprofezin.[1]		
Parameter	Value	Reference
Molecular Weight	305.4	D280879, B. Kitchens, 6/06/2002 D430571, H. Mukhoty, 2/11/2016
Melting point/range	104-106 °C	
pH	Not dispersible with water	
Density	1.18 g/cm^3 at 21 °C	
Water solubility (25 ºC)	0.382 mg/L	
Solvent solubility (25 ºC)	240 g/L in acetone 220 g/L in ethyl acetate 320 g/L in toluene 20 g/L in methanol 520 g/L in chloroform 20 g/L in n-hexane	
Dissociation constant, pK_a	Does not dissociate	
Octanol/water partition coefficient	log P_{ow} = 4.31 at 20 °C	
UV/visible absorption spectrum	Not available	
Vapor pressure (25 ºC)	3.75 x 10^{-7} mmHg	

1 Data from Buprofezin Technical (EPA Reg. No. 71711-16, 99.1% buprofezin).

APPENDIX D. International Residue Limit Status Sheet

Table D.1. Summary of US and International Tolerances and Maximum Residue Limits.

Residue Definition:

US	Canada	Mexico [2]	Codex
40 CFR §180.511: Tolerances are established for residues of buprofezin, including its metabolites and degradates in or on the commodities. Compliance with the tolerance levels specified is to be determined by measuring only the buprofezin, 2-[(1,1-dimethylethyl)imino]tetrahydro-3(1-methylethyl)-5-phenyl-4 H-1,3,5-thiadiazin-4-one, in the commodity.	2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1, 3, 5-thiadiazin-4-one.		For compliance with the MRL and for estimation of dietary intake for plant and animal commodities: buprofezin. The residue is not fat soluble.

Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US[2]	Canada	Mexico[2]	Codex
Brassica, leafy greens, subgroup 4-16B	60	12 Chinese broccoli 35 Arugula, Garden cress, Upland cress 60 Broccoli raab, Bok choy, Chinese cabbages, Collards, Kales, Mizuna, Mustard greens, Rape leaves		
Celtuce	35	35 Celtuce		
Cottonseed subgroup 20C	0.35	0.35 Undelinted cotton seeds		
Fennel, Florence, fresh leaves and stalks	35	35 Fresh Florence fennel leaves and stalks		
Fig	0.7			
Fruit, citrus, group 10-10	4	4 Oranges, Tachibana oranges, Trifoliate oranges, Tangerines, Mediterranean mandarins, Satsuma mandarins, Calamondins, Citrus citrons, Citrus hybrids, Tangelos, Tangors		1 Group of Citrus fruit (includes all commodities in this group)
Fruit, stone, group 12-12, except nectarine and peach	2	2 Sweet cherries, Tart cherries, Cherry plums, Apricots, Fresh prune plums, Chickasaw plums, Damson plums, Japanese plums, Plumcots, Fresh prune plums		2 Subgroup of Cherries (includes all commodities in this subgroup) 2 Subgroup of Plums (including fresh Prunes)

Table D.1. Summary of US and International Tolerances and Maximum Residue Limits.				
Residue Definition:				
US		Canada	Mexico [2]	Codex
40 CFR §180.511: Tolerances are established for residues of buprofezin, including its metabolites and degradates in or on the commodities. Compliance with the tolerance levels specified is to be determined by measuring only the buprofezin, 2-[(1,1-dimethylethyl)imino]tetrahydro-3(1-methylethyl)-5-phenyl-4 H-1,3,5-thiadiazin-4-one, in the commodity.		2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1, 3, 5-thiadiazin-4-one.		For compliance with the MRL and for estimation of dietary intake for plant and animal commodities: buprofezin. The residue is not fat soluble.
Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US[2]	Canada	Mexico[2]	Codex
Fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F	1	1 Grapes		1 Grapes
Grape, raisin	2	2 Raisins		2 Dried grapes (currants, raisins and sultanas)
Kohlrabi	12	12 Kohlrabies		
Leaf petiole vegetable subgroup 22B	35	35 Cardoon, Celery, Chinese celery, Rhubarb		
Leafy greens subgroup 4-16A	35	35 Amaranth, Fresh chervil leaves, Garland chrysanthemum, Corn salad, Dandelion leaves, Dock, Endives, Head lettuce, Leaf lettuce, Orach, Fresh parsley leaves, Garden purslane, Winter purslane, Radicchio, Spinach, New Zealand spinach, Malabar spinach, Swiss chard		
Nut, tree, group 14-12	0.05	0.05 Almond nuts, Beechnuts, Brazil nuts, Butternuts, Cashew nuts, Chestnuts, Chinquapin nuts, Hazelnuts, Hickory nuts, Macadamia nuts, Pecan nuts, Pistachio nuts, Black walnuts, English walnuts		0.05 Almonds

Table D.1. Summary of US and International Tolerances and Maximum Residue Limits.				
Residue Definition:				
US		Canada	Mexico [2]	Codex
40 CFR §180.511: Tolerances are established for residues of buprofezin, including its metabolites and degradates in or on the commodities. Compliance with the tolerance levels specified is to be determined by measuring only the buprofezin, 2-[(1,1-dimethylethyl)imino]tetrahydro-3(1-methylethyl)-5-phenyl-4 H-1,3,5-thiadiazin-4-one, in the commodity.		2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1, 3, 5-thiadiazin-4-one.		For compliance with the MRL and for estimation of dietary intake for plant and animal commodities: buprofezin. The residue is not fat soluble.
Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US[2]	Canada	Mexico[2]	Codex
Tropical and subtropical, small fruit, edible peel, subgroup 23A	5	5 Olives 0.3 Acerolas, Wax jambus		5 Table olives
Tropical and subtropical, small fruit, inedible peel, subgroup 24A	0.3	0.3 Lychees, Longans, Spanish limes		
Vegetable, *Brassica*, head and stem, group 5-16	12	12 Broccoli, Brussels sprouts, Cabbages, Napa Chinese cabbages, Cauliflowers		
Completed: J. Camp; 12/12/2018				

[1] Includes only commodities of interest for this action.
[2] Tolerance values are HED recommendations and not those proposed by the applicant.
[3] Mexico adopts US tolerances for its export purposes.

APPENDIX E. Submission of Analytical Standards

An analytical reference standard for buprofezin from Nihon Nohyaku is currently available in the EPA National Pesticide Standards Repository (NPSR) and has an expiration date 5/31/21 (email communication between T. Cole and B. Cropp-Kohlligian, 2/21/2017). The registrant is required to maintain reasonable amounts of the reference standards in the NPSR as long as tolerances remain published in 40 CFR §180.475. When necessary, new reference standards, or updated certificates of analysis (COAs), should be sent to the Analytical Chemistry Branch (ACB), which is located at Fort Meade, MD. It should be sent to the attention of either Theresa Cole or Thuy Nguyen at the address listed below, along with a letter of transmittal. **Please note that the full 9-digit ZIP Code is required, or the mail will be returned to the registrant.**

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

The letter of transmittal should include the assay of the standard, name of the analytical method used, a statement of principal impurities, purification procedures employed, storage requirements, and special precautions for safe handling. Replacement of standards, or updated COAs, may be required periodically if supplies are exhausted, if the standards expire, or if decomposition occurs during storage. Material Safety Data Sheets (MSDSs) must accompany all analytical standards as specified by the Occupational Safety and Health Administration (OSHA) in 29 CFR §1910.1200.

APPENDIX F. Occupational Handler Non-Cancer Exposure and Risk Estimates

Note: This table is taken verbatim from the ORE assessment for registration review document (D439400, B. Van Deusen, 9/27/2017) and is provided here as a summary of results for crop conversions and expansions that are proposed under this petition (i.e., crop group conversions to (i) leafy greens subgroup 4-16A, except head lettuce and radicchio, (ii) Brassica, leafy greens, subgroup 4-16B, (iii) vegetable, Brassica, head and stem, group 5-16, (iv) leaf petiole vegetable subgroup 22B, (v) celtuce, (vi) fennel, Florence, (vii) kohlrabi; and (2) crop group expansions to all members of (i) tropical and subtropical, small fruit, edible peel, subgroup 23A, (ii) tropical and subtropical, small fruit, inedible peel, subgroup 24A, (iii) cottonseed subgroup 20C, (iv) fruit, citrus, group 10-10, (v) fruit, stone, group 12-12, (vi) fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F, (vii) nut, tree, group 14-12). It also includes information for some crops and formulations that are not relevant to this petition.

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2]	Inhalation Unit Exposure (µg/lb ai)[2]	Maximum Application Rate[4]	Area Treated or Amount Handled Daily[5]	Dermal		Inhalation		Total
		Level of PPE or Engineering Control[3]	Level of PPE or Engineering Control[3]			Dose (mg/kg/day)[6]	MOE (LOC=300)[7]	Dose (mg/kg/day)[8]	MOE (LOC=300)[9]	MOE (LOC=300)[10]
Mixer/Loader										
Dry Flowables for Aerial Applications	Nursery Ornamentals	227	8.96	0.61 lb ai/A	60 Acres	0.012	830	0.00475	2,100	590
		Baseline	Baseline							
	Orchard/ Vineyard	12.5	2.6	2.0 lb ai/A	350 Acres	0.0127	790	0.0264	380	**EC 260**
		EC	EC							
Dry Flowables for Airblast Applications	Nursery Ornamentals	227	8.96	0.61 lb ai/A	20 Acres	0.00401	2,500	0.00158	6,300	1,800
		Baseline	Baseline							
	Orchard/ Vineyard	51.6	8.96	2.0 lb ai/A	40 Acres	0.00599	1,700	0.0104	960	SL/G 610
		SL/G	Baseline							
Dry Flowables for Groundboom Applications	Field-grown Ornamentals	227	8.96	0.61 lb ai/A	40 Acres	0.00803	1,200	0.00317	3,200	870
		Baseline	Baseline							
	Nursery Ornamentals	227	8.96	0.61 lb ai/A	60 Acres	0.012	830	0.00475	2,100	590
		Baseline	Baseline							
	Greenhouse Ornamentals/ Vegetables	227	8.96	0.61 lb ai/A	60 Acres	0.012	830	0.00475	2,100	590
		Baseline	Baseline							
	Orchard/Vineyard	51.6	8.96	2.0 lb ai/A	40 Acres	0.00599	1,700	0.0104	960	SL/G

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.										
Exposure Scenario	**Crop or Target[1]**	**Dermal Unit Exposure (µg/lb ai)[2]**	**Inhalation Unit Exposure (µg/lb ai)[2]**	**Maximum Application Rate[4]**	**Area Treated or Amount Handled Daily[5]**	**Dermal**		**Inhalation**		**Total**
		Level of PPE or Engineering Control[3]	**Level of PPE or Engineering Control[3]**			**Dose (mg/kg/day)[6]**	**MOE (LOC=300)[7]**	**Dose (mg/kg/day)[8]**	**MOE (LOC=300)[9]**	**MOE (LOC=300)[10]**
		SL/G	Baseline							610
Dry Flowables for Stationary Fogger Applications	Greenhouse Ornamentals/ Vegetables	227	8.96	0.000014 lb ai/ft^2	142,857 ft^2	0.000658	15,000	0.000259	39,000	11,000
		Baseline	Baseline							
Soluble Concentrates for Aerial Applications	Nursery Ornamentals	220	0.219	0.6 lb ai/A	60 Acres	0.0115	870	0.000114	88,000	860
		Baseline	Baseline							
	Orchard/Vineyard	29.1	0.219	2.0 lb ai/A	350 Acres	0.0296	340	0.00222	4,500	**DL/G No-R 320**
		DL/G	Baseline							
	Field crop/ Typical	37.6	0.219	0.38 lb ai/A	350 Acres	0.00725	1,400	0.000422	24,000	SL/G No-R 1,300
		SL/G	Baseline							
	Field crop/ High Acreage	37.6	0.219	0.38 lb ai/A	1200 Acres	0.0248	400	0.00145	6,900	SL/G No-R 380
		SL/G	Baseline							
Soluble Concentrates for Airblast Applications	Nursery Ornamentals	220	0.219	0.6 lb ai/A	20 Acres	0.00383	2,600	0.0000381	260,000	2,600
		Baseline	Baseline							
	Orchard/Vineyard	220	0.219	2.0 lb ai/A	40 Acres	0.0255	390	0.000254	39,000	390
		Baseline	Baseline							
Soluble Concentrates for Groundboom Applications	Field-grown Ornamentals	220	0.219	0.6 lb ai/A	40 Acres	0.00765	1,300	0.0000762	130,000	1,300
		Baseline	Baseline							
	Nursery Ornamentals	220	0.219	0.6 lb ai/A	60 Acres	0.0115	870	0.000114	88,000	860
		Baseline	Baseline							
	Greenhouse Ornamentals/ Vegetables	220	0.219	0.6 lb ai/A	60 Acres	0.0115	870	0.000114	88,000	860
		Baseline	Baseline							

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.										
Exposure Scenario	**Crop or Target[1]**	**Dermal Unit Exposure (µg/lb ai)[2]**	**Inhalation Unit Exposure (µg/lb ai)[2]**	**Maximum Application Rate[4]**	**Area Treated or Amount Handled Daily[5]**	**Dermal**		**Inhalation**		**Total**
		Level of PPE or Engineering Control[3]	**Level of PPE or Engineering Control[3]**			**Dose (mg/kg/day)[6]**	**MOE (LOC=300)[7]**	**Dose (mg/kg/day)[8]**	**MOE (LOC=300)[9]**	**MOE (LOC=300)[10]**
	Orchard/Vineyard	220	0.219	2.0 lb ai/A	40 Acres	0.0255	390	0.000254	39,000	390
		Baseline	Baseline							
	Field crop/ Typical	220	0.219	0.38 lb ai/A	80 Acres	0.0097	1,000	0.0000965	100,000	990
		Baseline	Baseline							
	Field crop/ High Acreage	220	0.219	0.38 lb ai/A	200 Acres	0.0242	410	0.000241	41,000	410
		Baseline	Baseline							
Soluble Concentrates for Stationary Fogger Applications	Greenhouse Ornamentals/ Vegetables	220	0.219	0.000014 lb ai/ft^2	142,857 ft^2	0.000638	16,000	0.00000635	1,600,000	16,000
		Baseline	Baseline							
Water-Soluble Packets for Aerial Applications	Nursery Ornamentals	12.5	2.6	0.6 lb ai/A	60 Acres	0.000652	15,000	0.00136	7,400	EC 5,000
		EC	EC							
	Orchard/ Vineyard	12.5	2.6	2.0 lb ai/A	350 Acres	0.0127	790	0.0264	380	**EC 260**
		EC	EC							
	Field crop/ Typical	12.5	2.6	0.38 lb ai/A	350 Acres	0.00241	4,100	0.00501	2,000	EC 1,300
		EC	EC							
	Field crop/ High Acreage	12.5	2.6	0.35 lb ai/A	1200 Acres	0.00761	1,300	0.0158	630	EC 420
		EC	EC							
Water-Soluble Packets for Airblast Applications	Nursery Ornamentals	12.5	2.6	0.6 lb ai/A	20 Acres	0.000217	46,000	0.000452	22,000	EC 15,000
		EC	EC							
	Orchard/ Vineyard	12.5	2.6	2.0 lb ai/A	40 Acres	0.00145	6,900	0.00301	3,300	EC 2,200
		EC	EC							
Water-Soluble Packets for	Field-grown Ornamentals	12.5	2.6	0.6 lb ai/A	40 Acres	0.000435	23,000	0.000904	11,000	EC 7,400
		EC	EC							

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2]	Inhalation Unit Exposure (µg/lb ai)[2]	Maximum Application Rate[4]	Area Treated or Amount Handled Daily[5]	Dermal		Inhalation		Total
		Level of PPE or Engineering Control[3]	Level of PPE or Engineering Control[3]			Dose (mg/kg/day)[6]	MOE (LOC=300)[7]	Dose (mg/kg/day)[8]	MOE (LOC=300)[9]	MOE (LOC=300)[10]
Groundboom Applications	Nursery Ornamentals	12.5	2.6	0.6 lb ai/A	60 Acres	0.000652	15,000	0.00136	7,400	EC 5,000
		EC	EC							
	Greenhouse Ornamentals/ Vegetables	12.5	2.6	0.6 lb ai/A	60 Acres	0.000652	15,000	0.00136	7,400	EC 5,000
		EC	EC							
	Orchard/ Vineyard	12.5	2.6	2.0 lb ai/A	40 Acres	0.00145	6,900	0.00301	3,300	EC 2,200
		EC	EC							
	Field crop/ Typical	12.5	2.6	0.38 lb ai/A	80 Acres	0.000551	18,000	0.00114	8,800	EC 5,900
		EC	EC							
	Field crop/ High Acreage	12.5	2.6	0.35 lb ai/A	200 Acres	0.00127	7,900	0.00264	3,800	EC 2,600
		EC	EC							
Water-Soluble Packets for Stationary Fogger Applications	Greenhouse Ornamentals/ Vegetables	12.5	2.6	0.000014 lb ai/ft^2	142,857 ft^2	0.0000362	280,000	0.0000754	130,000	EC 89,000
		EC	EC							
Applicator										
Spray via Aerial Applications	Nursery Ornamentals	2.08	0.0049	0.61 lb ai/A	60 Acres	0.00011	91,000	0.00000259	3,900,000	EC 89,000
		EC	EC							
	Orchard/ Vineyard	2.08	0.0049	2.0 lb ai/A	350 Acres	0.00212	4,700	0.0000497	200,000	EC 4,600
		EC	EC							
	Field crop/ Typical	2.08	0.0049	0.38 lb ai/A	350 Acres	0.000401	25,000	0.00000945	1,100,000	EC 24,000
		EC	EC							
	Field crop/ High Acreage	2.08	0.0049	0.38 lb ai/A	1200 Acres	0.00137	7,300	0.0000323	310,000	EC 7,100
		EC	EC							

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.										
Exposure Scenario	**Crop or Target[1]**	**Dermal Unit Exposure (µg/lb ai)[2]**	**Inhalation Unit Exposure (µg/lb ai)[2]**	**Maximum Application Rate[4]**	**Area Treated or Amount Handled Daily[5]**	**Dermal**		**Inhalation**		**Total**
		Level of PPE or Engineering Control[3]	**Level of PPE or Engineering Control[3]**			**Dose (mg/kg/day)[6]**	**MOE (LOC=300)[7]**	**Dose (mg/kg/day)[8]**	**MOE (LOC=300)[9]**	**MOE (LOC=300)[10]**
Spray via Airblast Applications	Nursery Ornamentals	1,770	4.71	0.61 lb ai/A	20 Acres	0.0313	320	0.000833	12,000	310
		Baseline	Baseline							
	Orchard/ Vineyard	215	4.71	2.0 lb ai/A	40 Acres	0.0249	400	0.00546	1,800	**SL/G/CRH No-R 330**
		SL/G/CRH	Baseline							
Spray via Groundboom Applications	Field-grown Ornamentals	78.6	0.34	0.61 lb ai/A	40 Acres	0.00278	3,600	0.00012	83,000	3,500
		Baseline	Baseline							
	Nursery Ornamentals	78.6	0.34	0.61 lb ai/A	60 Acres	0.00417	2,400	0.00018	56,000	2,300
		Baseline	Baseline							
	Greenhouse Ornamentals/ Vegetables	78.6	0.34	0.61 lb ai/A	60 Acres	0.00417	2,400	0.00018	56,000	2,300
		Baseline	Baseline							
	Orchard/ Vineyard	78.6	0.34	2.0 lb ai/A	40 Acres	0.00912	1,100	0.000394	25,000	1,100
		Baseline	Baseline							
	Field crop/ Typical	78.6	0.34	0.38 lb ai/A	80 Acres	0.00346	2,900	0.000149	67,000	2,800
		Baseline	Baseline							
	Field crop/ High Acreage	78.6	0.34	0.38 lb ai/A	200 Acres	0.00865	1,200	0.000374	27,000	1,100
		Baseline	Baseline							
Flagger										
Spray via Aerial Applications	Nursery Ornamentals	11	0.35	0.61 lb ai/A	60 Acres	0.000584	17,000	0.000186	54,000	13,000
		Baseline	Baseline							
	Orchard/ Vineyard	11	0.35	2.0 lb ai/A	350 Acres	0.0112	890	0.00355	2,800	680
		Baseline	Baseline							
	Field crop/ Typical	11	0.35	0.38 lb ai/A	350 Acres	0.00212	4,700	0.000675	15,000	3,600

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.										
Exposure Scenario	**Crop or Target[1]**	**Dermal Unit Exposure (µg/lb ai)[2]**	**Inhalation Unit Exposure (µg/lb ai)[2]**	**Maximum Application Rate[4]**	**Area Treated or Amount Handled Daily[5]**	**Dermal**		**Inhalation**		**Total**
		Level of PPE or Engineering Control[3]	**Level of PPE or Engineering Control[3]**			**Dose (mg/kg/day)[6]**	**MOE (LOC=300)[7]**	**Dose (mg/kg/day)[8]**	**MOE (LOC=300)[9]**	**MOE (LOC=300)[10]**
		Baseline	Baseline							
	Field crop/ High Acreage	11	0.35	0.38 lb ai/A	1,200 Acres	0.00728	1,400	0.00232	4,300	1,100
		Baseline	Baseline							
Mixer/Loader/Applicator										
Dry Flowables for Backpack Applications	Greenhouse Ornamentals/ Vegetables	13,200	140	0.0305 lb ai/ gallon	40 Gallons	0.0233	430	0.00248	4,000	390
		Baseline	Baseline							
	Christmas Tree Farm	16,900	69.1	0.0305 lb ai/ gallon	40 Gallons	0.0299	330	0.00122	8,200	**DL/G No-R 320**
		DL/G	Baseline							
	Nursery Ornamentals	16,900	69.1	0.0305 lb ai/ gallon	40 Gallons	0.0299	330	0.00122	8,200	**DL/G No-R 320**
		DL/G	Baseline							
	Landscaping trees/ shrubs/ bushes/ plants/ flowers	16,900	69.1	0.0305 lb ai/ gallon	40 Gallons	0.0299	330	0.00122	8,200	**DL/G No-R 320**
		DL/G	Baseline							
Dry Flowables for Fogging Equipment Applications	Nursery Ornamentals	No Data	1,783	0.0305 lb ai/ gallon	40 Gallons	No Data	No Data	0.0316	320	No Data
		NA	PF5-R							
	Orchard/ Vineyard	No Data	892	0.075 lb ai/ gallon	40 Gallons	No Data	No Data	0.0388	**260**	No Data
		NA	PF10-R							
	Christmas Tree Farm	No Data	1,783	0.0305 lb ai/ gallon	40 Gallons	No Data	No Data	0.0316	320	No Data
		NA	PF5-R							
	Field-grown Ornamentals	No Data	1,783	0.0305 lb ai/ gallon	40 Gallons	No Data	No Data	0.0316	320	No Data
		NA	PF5-R							
	Greenhouse Ornamentals/ Vegetables	No Data	892	0.000014 lb ai/ft^2	142857 ft^2	No Data	No Data	0.0258	390	No Data
		NA	PF10-R							

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2]	Inhalation Unit Exposure (µg/lb ai)[2]	Maximum Application Rate[4]	Area Treated or Amount Handled Daily[5]	Dermal		Inhalation		Total
		Level of PPE or Engineering Control[3]	Level of PPE or Engineering Control[3]			Dose (mg/kg/day)[6]	MOE (LOC=300)[7]	Dose (mg/kg/day)[8]	MOE (LOC=300)[9]	MOE (LOC=300)[10]
Dry Flowables for Manually-pressurized Handwand Applications	Greenhouse Ornamentals/ Vegetables	430	30	0.0305 lb ai/ gallon	40 Gallons	0.000761	13,000	0.00053	19,000	SL/G No-R 7,700
		SL/G	Baseline							
	Christmas Tree Farm	430	30	0.0305 lb ai/ gallon	40 Gallons	0.000761	13,000	0.00053	19,000	SL/G No-R 7,700
		SL/G	Baseline							
	Nursery Ornamentals	430	30	0.0305 lb ai/ gallon	40 Gallons	0.000761	13,000	0.00053	19,000	SL/G No-R 7,700
		SL/G	Baseline							
	Landscaping trees/ shrubs/ bushes	430	30	0.0305 lb ai/ gallon	40 Gallons	0.000761	13,000	0.00053	19,000	SL/G No-R 7,700
		SL/G	Baseline							
	Landscaping plants/ flowers	430	30	0.0305 lb ai/ gallon	40 Gallons	0.000761	13,000	0.00053	19,000	SL/G No-R 7,700
		SL/G	Baseline							
Dry Flowables for Mechanically-pressurized Handgun Applications	Orchard/ Vineyard	1,360	8.68	0.075 lb ai/ gallon	1000 Gallons	0.148	**68**	0.00943	1,100	**DL/G PF10-R 68**
		DL/G	Baseline							
	Greenhouse Ornamentals/ Vegetables	1,600	24	0.0305 lb ai/ gallon	1000 Gallons	0.0707	**140**	0.0106	940	**DL/G PF10-R 130**
		DL/G	PF5-R							
	Christmas Tree Farm	1,360	8.68	0.0305 lb ai/ gallon	1000 Gallons	0.0601	**170**	0.00384	2,600	**DL/G PF5 or PF10-R 170**
		DL/G	Baseline							
	Nursery Ornamentals	1,360	8.68	0.0305 lb ai/ gallon	1000 Gallons	0.0601	**170**	0.00384	2,600	**DL/G PF5 or PF10-R 170**
		DL/G	Baseline							
	Landscaping trees/ shrubs/ bushes	1,360	8.68	0.0305 lb ai/ gallon	1000 Gallons	0.0601	**170**	0.00384	2,600	**DL/G PF5 or PF10-R 170**
		DL/G	Baseline							
Soluble	Greenhouse	13,200	140	0.006 lb ai/ gallon	40 Gallons	0.00459	2,200	0.000487	21,000	2,000

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2]	Inhalation Unit Exposure (µg/lb ai)[2]	Maximum Application Rate[4]	Area Treated or Amount Handled Daily[5]	Dermal		Inhalation		Total
		Level of PPE or Engineering Control[3]	Level of PPE or Engineering Control[3]			Dose (mg/kg/day)[6]	MOE (LOC=300)[7]	Dose (mg/kg/day)[8]	MOE (LOC=300)[9]	MOE (LOC=300)[10]
Concentrates for Backpack Applications	Ornamentals/ Vegetables	Baseline	Baseline							
	Christmas Tree Farm	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480
		Baseline	Baseline							
	Nursery Ornamentals	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480
		Baseline	Baseline							
	Landscaping trees/ shrubs/ bushes	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480
		Baseline	Baseline							
	Landscaping plants/ flowers	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480
		Baseline	Baseline							
Soluble Concentrates for Fogging Equipment Application	Nursery Ornamentals	No Data	8,916	0.006 lb ai/ gallon	40 Gallons	No Data	No Data	0.031	320	No Data
		NA	Baseline							
	Orchard/ Vineyard	No Data	892	0.075 lb ai/ gallon	40 Gallons	No Data	No Data	0.0388	**260**	No Data
		NA	PF10-R							
	Christmas Tree Farm	No Data	8,916	0.006 lb ai/ gallon	40 Gallons	No Data	No Data	0.031	320	No Data
		NA	Baseline							
	Field-grown Ornamentals	No Data	8,916	0.006 lb ai/ gallon	40 Gallons	No Data	No Data	0.031	320	No Data
		NA	Baseline							
	Greenhouse Ornamentals/ Vegetables	No Data	892	0.000014 lb ai/ft^2	142,857 ft^2	No Data	No Data	0.0258	390	No Data
		NA	PF10-R							
Soluble Concentrates for Manually-pressurized	Greenhouse Ornamentals/ Vegetables	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							
	Christmas Tree	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2] Level of PPE or Engineering Control[3]	Inhalation Unit Exposure (µg/lb ai)[2] Level of PPE or Engineering Control[3]	Maximum Application Rate[4]	Area Treated or Amount Handled Daily[5]	Dermal		Inhalation		Total
						Dose (mg/kg/day)[6]	MOE (LOC=300)[7]	Dose (mg/kg/day)[8]	MOE (LOC=300)[9]	MOE (LOC=300)[10]
Handwand Applications	Farm	SL/G	Baseline							39,000
	Nursery Ornamentals	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							
	Landscaping trees/ shrubs/ bushes	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							
	Landscaping plants/ flowers	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							
Soluble Concentrates for Mechanically-pressurized Handgun Applications	Orchard/ Vineyard	1,360	8.68	0.075 lb ai/ gallon	1000 Gallons	0.148	**68**	0.00943	1,100	**DL/G PF10-R 68**
		DL/G	Baseline							
	Greenhouse Ornamentals/ Vegetables	3,500	120	0.006 lb ai/ gallon	1000 Gallons	0.0304	330	0.0104	960	SL/G No-R 310
		Baseline	Baseline							
	Christmas Tree Farm	2,050	8.68	0.006 lb ai/ gallon	1000 Gallons	0.0178	560	0.000755	13,000	SL/G No-R 540
		SL/G	Baseline							
	Nursery Ornamentals	2,050	8.68	0.006 lb ai/ gallon	1000 Gallons	0.0178	560	0.000755	13,000	SL/G No-R 540
		SL/G	Baseline							
	Landscaping trees/ shrubs/ bushes	2,050	8.68	0.006 lb ai/ gallon	1000 Gallons	0.0178	560	0.000755	13,000	SL/G No-R 540
		SL/G	Baseline							
	Field crop/ Typical	1,360	8.68	0.019 lb ai/ gallon	1000 Gallons	0.0374	**270**	0.00239	4,200	**DL/G PF5-R or PF-10-R 270**
		DL/G	Baseline							
Water Soluble Packets for Backpack Applications	Greenhouse Ornamentals/ Vegetables	13,200	140	0.006 lb ai/ gallon	40 Gallons	0.00459	2,200	0.000487	21,000	2,000
		Baseline	Baseline							
	Christmas Tree	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.										
Exposure Scenario	**Crop or Target[1]**	**Dermal Unit Exposure (µg/lb ai)[2]**	**Inhalation Unit Exposure (µg/lb ai)[2]**	**Maximum Application Rate[4]**	**Area Treated or Amount Handled Daily[5]**	**Dermal**		**Inhalation**		**Total**
		Level of PPE or Engineering Control[3]	**Level of PPE or Engineering Control[3]**			**Dose (mg/kg/day)[6]**	**MOE (LOC=300)[7]**	**Dose (mg/kg/day)[8]**	**MOE (LOC=300)[9]**	**MOE (LOC=300)[10]**
	Farm	Baseline	Baseline							
	Nursery Ornamentals	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480
		Baseline	Baseline							
	Landscaping trees/ shrubs/ bushes	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480
		Baseline	Baseline							
	Landscaping plants/ flowers	58,400	69.1	0.006 lb ai/ gallon	40 Gallons	0.0203	490	0.000241	41,000	480
		Baseline	Baseline							
Water Soluble Packets for Fogging Equipment Application	Nursery Ornamentals	No Data	8,916	0.006 lb ai/ gallon	40 Gallons	No Data	No Data	0.031	320	No Data
		NA	Baseline							
	Christmas Tree Farm	No Data	8,916	0.006 lb ai/ gallon	40 Gallons	No Data	No Data	0.031	320	No Data
		NA	Baseline							
	Field-grown Ornamentals	No Data	8,916	0.006 lb ai/ gallon	40 Gallons	No Data	No Data	0.031	320	No Data
		NA	Baseline							
	Greenhouse Ornamentals/ Vegetables	No Data	892	0.000014 lb ai/ft^2	142,857 ft^2	No Data	No Data	0.0258	PF10-R 390	No Data
		NA	PF10-R							
Water Soluble Packets for Manually-pressurized Handwand Applications	Greenhouse Ornamentals/ Vegetables	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							
	Christmas Tree Farm	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							
	Nursery Ornamentals	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							
	Landscaping trees/ shrubs/ bushes	430	30	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
		SL/G	Baseline							

Table F.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Buprofezin.

Exposure Scenario	Crop or Target[1]	Dermal Unit Exposure (µg/lb ai)[2] Level of PPE or Engineering Control[3]	Inhalation Unit Exposure (µg/lb ai)[2] Level of PPE or Engineering Control[3]	Maximum Application Rate[4]	Area Treated or Amount Handled Daily[5]	Dermal		Inhalation		Total
						Dose (mg/kg/day)[6]	MOE (LOC=300)[7]	Dose (mg/kg/day)[8]	MOE (LOC=300)[9]	MOE (LOC=300)[10]
	Landscaping plants/ flowers	430 SL/G	30 Baseline	0.006 lb ai/ gallon	40 Gallons	0.000149	67,000	0.000104	96,000	SL/G No-R 39,000
Water Soluble Packets for Mechanically-pressurized Handgun Applications	Orchard/ Vineyard	1,360 DL/G	8.68 Baseline	0.0211 lb ai/ gallon	1000 Gallons	0.0416	**240**	0.00265	3,800	**DL/G PF5 or PF10-R 240**
	Greenhouse Ornamentals/ Vegetables	3,500 Baseline	120 Baseline	0.006 lb ai/ gallon	1000 Gallons	0.0304	330	0.0104	960	SL/G No-R 310
	Christmas Tree Farm	2,050 SL/G	8.68 Baseline	0.006 lb ai/ gallon	1000 Gallons	0.0217	560	0.000755	13,000	SL/G No-R 540
	Nursery Ornamentals	2,050 SL/G	8.68 Baseline	0.006 lb ai/ gallon	1000 Gallons	0.0217	560	0.000755	13,000	SL/G No-R 540
	Landscaping trees/ shrubs/ bushes	2,050 SL/G	8.68 Baseline	0.006 lb ai/ gallon	1000 Gallons	0.0217	560	0.000755	13,000	SL/G No-R 540
	Field crop/ Typical	1,360 DL/G	8.68 Baseline	0.019 lb ai/ gallon	1000 Gallons	0.0374	**270**	0.00239	4,200	**DL/G PF5-R or PF10-R 270**

1 Registered crops were combined into surrogate groups for the occupational handler assessment. Orchard/Vineyard = Acerola, almonds, atemoya, avocado, banana, biriba, black sapote, canistel, cherimoya, citrus fruits (crop group 10), coffee, custard apple, feijoa, grapes, guava, ilama, jaboticaba, longan, lychee, mamey sapote, mango, olive, papaya, passion fruit, pear and Asian pear, persimmon, pome fruits (crop group 11-10), pomegranates, pulasan, rambutan, sapodilla, soursop, Spanish lime, star apple, starfruit, stone fruits (crop group 12), sugar apple, tree nuts (crop group 14) and pistachios, wax jambu, etc. Field Crop, High Acreage = Beans (succulent), cotton, etc. Field Crop, Typical Acreage = Beans (snap), cucurbit vegetables (crop group 9), fruiting vegetables (crop group 8-10), brassica (cole) leafy vegetables (crop group 5), leafy vegetable (except brassica vegetables – crop group 4), lettuce (head and leaf), low growing berry (crop subgroup 13-07), tomatoes, etc.

2 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: Baseline, PPE, Eng. Controls.

3 SL=single layer, DL=double layer, G=gloves, EC=engineering controls, CRH=chemical resistant hat, R=respirator; SL/G No-R = label required PPE.

4 Based on registered labels (See Appendix F of the Buprofezin Draft Risk Assessment (DRA); D431562, Bonnie Cropp-Kohlligian et al., 9/27/2017),

5 Exposure Science Advisory Council Policy #9.1 and HED's rate assumption for commercial/agriculture buildings. (See Section 11.1).

6 Dermal Dose = Dermal Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled Daily (A or gal/day) × DAF (10 %) ÷ BW (69 kg).
7 Dermal MOE = Dermal LOAEL (10 mg/kg/day) ÷ Dermal Dose (mg/kg/day).
8 Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled Daily (A or gal/day) ÷ BW (69 kg).
9 Inhalation MOE = Inhalation LOAEL (10 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).
10 Total MOE = LOAEL (10 mg/kg/day) ÷ Dermal Dose + Inhalation Dose.

APPENDIX G. Occupational Post-Application Non-Cancer Dermal Risk Estimates

Note: This table is taken verbatim from the revised occupational post-application risk estimates incorporating new DFR data to support registration review document (D448121, B. Van Deusen, 8/13/2018) and is provided here as a summary of results for crop conversions and expansions that are proposed under this petition (i.e., crop group conversions to (i) leafy greens subgroup 4-16A, except head lettuce and radicchio, (ii) Brassica, leafy greens, subgroup 4-16B, (iii) vegetable, Brassica, head and stem, group 5-16, (iv) leaf petiole vegetable subgroup 22B, (v) celtuce, (vi) fennel, Florence, (vii) kohlrabi; and (2) crop group expansions to all members of (i) tropical and subtropical, small fruit, edible peel, subgroup 23A, (ii) tropical and subtropical, small fruit, inedible peel, subgroup 24A, (iii) cottonseed subgroup 20C, (iv) fruit, citrus, group 10-10, (v) fruit, stone, group 12-12, (vi) fruit, small, vine climbing, except fuzzy kiwifruit, subgroup 13-07F, (vii) nut, tree, group 14-12). It also includes information for some crops and formulations that are not relevant to this petition.

Table G.1. Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Buprofezin on Day 0

Crop/Site	Activities	Transfer Coefficient (cm^2/hr)	Application Rate (lb ai/A)[1]	Dermal Dose (mg/kg/day)[2]	DFR Data Incorporated MOE (LOC=300)
Short- and Intermediate-Term					
Almond	Scouting	580	2.0	0.013	740
	Transplanting	230		0.005	1,900
	Harvesting, mechanical (shaking)	190		0.004	2,300
	Orchard maintenance and poling	100		0.002	4,300
Apple (Pome fruit crop group 11-10)	Thinning fruit	3600	1.5	0.063	**160 (330 Day 6)**
	Harvesting, hand	1400		0.024	410
	Scouting; pruning, hand (full); training	580		0.010	990
	Transplanting	230		0.004	2,500
	Weeding, hand; propping; orchard maintenance	100		0.002	5,700
Avocado[4]	Harvesting, hand	1400	1.5	0.024	410
	Scouting; pruning, hand (full)	580		0.010	990
	Transplanting	230		0.004	2,500
	Orchard maintenance; weeding, hand	100		0.002	5,700
Banana	Harvesting, hand	1400	0.31	0.006	1,700
	Weeding, hand	100		0.0004	24,000
Bean, snap (succulent)	Irrigation (hand set)	1900	0.38	0.010	1,100
	Harvesting, hand	1100		0.006	1,800
	Scouting	210		0.001	9,500
	Weeding, hand	70		0.00035	29,000
Blueberry, lowbush- Low growing berry (Crop subgroup 13-07)	Irrigation (hand set)	1900	0.38	0.010	1,100
	Harvesting, hand (raking-cranberry); scouting	1100		0.006	1,800
	Transplanting	230		0.001	8,700
	Scouting (strawberry)	210		0.001	9,500
	Weeding, hand; pruning, hand (shears-cranberry); canopy management (strawberry)	70		0.00035	29,000
Broccoli (Crop group 5)	Scouting; harvesting, hand; weeding, hand (full)	4200	0.38	0.021	480
	Irrigation (hand set)	1900		0.010	1,100

Table G.1. Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Buprofezin on Day 0					
Crop/Site	**Activities**	**Transfer Coefficient (cm^2/hr)**	**Application Rate (lb ai/A)[1]**	**Dermal Dose (mg/kg/day)[2]**	**DFR Data Incorporated MOE (LOC=300)**
Short- and Intermediate-Term					
	Weeding, hand (min)	1400		0.007	1,400
	Scouting; thinning plants	330		0.002	6,100
	Transplanting	230		0.001	8,700
Christmas Tree Farm	Irrigation (hand set)	1900	0.61	0.013	740
	Harvesting, hand	1400		0.010	1,000
	Scouting; shaping	580		0.004	2,400
	Transplanting	230		0.002	6,100
	Weeding, hand; grading/tagging	100		0.001	14,000
Coffee (blueberry, highbush)	Irrigation (hand set)	1900	1.0	0.025	400
	Harvesting, hand	1400		0.018	540
	Scouting; pruning, hand; weeding, hand; bird control, frost control	640		0.008	1,200
	Transplanting	230		0.003	3,300
Cotton	Harvesting, mechanical, tramper	5050	0.35	0.041	**240 (300 Day 2)**
	Harvesting, mechanical, raker; harvesting, mechanical, picker operator	2400		0.019	510
	Harvesting, mechanical, module builder operator	900		0.007	1,400
	Scouting	210		0.001	10,000
	Weeding, hand	70		0.00032	31,000
Gourd (Crop group 9)	Irrigation (hand set)	1900	0.38	0.010	1,100
	Harvesting, hand; harvesting, mechanically-assisted; training	550		0.003	3,600
	Transplanting	230		0.001	8,700
	Scouting; weeding, hand; pruning, hand; thinning fruit	90		0.00045	22,000
Grape (raisin, table, juice, wine)	Tying/training; harvesting, hand; leaf pulling	5500	1.05 (CA and AZ higher rate)	0.076	**130 (310 Day 6)**
	Irrigation (hand set)	1900		0.026	380
	Scouting; pruning, hand; weeding, hand	640		0.009	1,100
	Transplanting	230		0.003	3,100
Grape (raisin, table, juice, wine)	Tying/training; harvesting, hand; leaf pulling	5500	0.53 (Current Max. Rate Outside of CA and AZ)	0.038	**260 (300 Day 1)**
	Irrigation (hand set)	1900		0.013	750
	Scouting; pruning, hand; weeding, hand	640		0.004	2,200
	Transplanting	230		0.002	6,200
Greenhouse ornamentals	Harvesting, hand; pruning, hand; scouting; container moving; weeding, hand; transplanting; grafting; propagating; pinching; tying/training	230	0.61	0.004	2,300

Table G.1. Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Buprofezin on Day 0					
Crop/Site	**Activities**	**Transfer Coefficient (cm^2/hr)**	**Application Rate (lb ai/A)[1]**	**Dermal Dose (mg/kg/day)[2]**	**DFR Data Incorporated MOE (LOC=300)**
Short- and Intermediate-Term					
Greenhouse tomatoes	Harvesting, hand; pinching; pollination; pruning, hand; scouting; turning; tying/training; weeding, hand; propagating	1200	0.40	0.015	670
	Transplanting; irrigation (hand set)	230		0.003	3,500
Greens, leafy (Crop group 4)	Irrigation (hand set)	1900	0.38	0.010	1,100
	Harvesting, hand	1100		0.006	1,800
	Transplanting	230		0.001	8,700
	Scouting	210		0.001	9,500
	Thinning plants; weeding, hand	70		0.00035	29,000
Lemon – citrus fruits (Crop group 10)	Harvesting, hand	1400	2.0	0.033	310
	Scouting; pruning, hand	580		0.013	740
	Transplanting	230		0.005	1,900
	Orchard maintenance; weeding, hand; baiting/trapping	100		0.002	4,300
Lettuce, leaf	Irrigation (hand set)	1900	0.38	0.010	1,100
	Harvesting, hand	1100		0.006	1,800
	Transplanting	230		0.001	8,700
	Scouting	210		0.001	9,500
	Weeding, hand; thinning plants	70		0.00035	29,000
Nectarine – stone fruits (Crop group 12)	Thinning fruit	3600	1.5	0.063	**160 (330 Day 6)**
	Harvesting, hand	1400		0.024	410
	Scouting; pruning, hand (full); training	580		0.010	990
	Transplanting	230		0.004	2,500
	Orchard maintenance; propping; weeding, hand	100		0.002	5,700
Nursery ornamentals	Irrigation (hand set)	1900	0.61	0.036	**280 (330 Day 1)**
	Harvesting, hand; pruning, hand; scouting; container moving; weeding, hand; transplanting; grafting; propagating; pinching; tying/training	230		0.004	2,300
Okra (Crop Group 8-10)	Irrigation (hand set)	1900	0.38	0.010	1,100
	Harvesting, hand; tying/training	1100		0.006	1,800
	Transplanting	230		0.001	8,700
	Scouting	210		0.001	9,500
	Weeding, hand	70		0.00035	29,000
Olive	Thinning fruit	3600	2.0	0.084	**120 (320 Day 8)**
	Harvesting, hand	1400		0.033	310
	Pruning, hand; scouting	580		0.013	740
	Transplanting	230		0.005	1,900
	Harvesting, mechanical (shaking)	190		0.004	2,300
	Orchard maintenance	100		0.002	4,300
Papaya (representative	Thinning fruit (Mango exclusive)	3600 (Mango exclusive)	0.53	0.022	450

Table G.1. Occupational Post-Application Non-Cancer Exposure and Risk Estimates for Buprofezin on Day 0					
Crop/Site	**Activities**	**Transfer Coefficient (cm^2/hr)**	**Application Rate (lb ai/A)[1]**	**Dermal Dose (mg/kg/day)[2]**	**DFR Data Incorporated MOE (LOC=300)**
Short- and Intermediate-Term					
of black sapote, canistel, mamey sapote, mango, sapodilla, & star apple)	Harvesting, hand	1400		0.009	1,200
	Pruning, hand; scouting	580		0.004	2,800
	Transplanting	230		0.001	7,100
	Orchard maintenance; weeding, hand	100		0.001	16,000
Pears and Asian Pears	Thinning fruit	3600	2.0	0.084	**120 (320 Day 8)**
	Harvesting, hand	1400		0.033	310
	Scouting; pruning, hand (full); training	580		0.013	740
	Transplanting	230		0.005	1,900
	Orchard maintenance; weeding, hand; propping	100		0.002	4,300
Pistachio – tree nuts (Crop group 14)	Harvesting, hand (net)	1400	2.0	0.033	310
	Scouting	580		0.013	740
	Transplanting	230		0.005	1,900
	Harvesting, mechanical (shaking)	190		0.004	2,300
	Orchard maintenance; weeding, hand	100		0.002	4,300
Pomegranate	Harvesting, hand	1400	2.0	0.033	310
	Scouting; pruning, hand	580		0.013	740
	Transplanting	230		0.005	1,900
	Orchard maintenance	100		0.002	4,300
Tomatoes	Irrigation (hand set)	1900	0.38	0.023	440
	Harvesting, hand; tying/training	1100		0.013	760
	Transplanting	230		0.003	3,700
	Scouting	210		0.002	4,000
	Pruning, hand; Weeding, hand	70		0.001	12,000

*Note the following assignments of the DFR data to the assessed crops:
Greenhouse Tomato DFR Data: Greenhouse tomatoes, Greenhouse ornamentals, Nursery Ornamentals, and tomatoes.
Grape DFR Data: Banana, bean: snap, blueberry low & highbush (coffee), broccoli, cotton, gourd, grapes, leafy greens, lettuce, and okra.
Citrus DFR Data: Almond, apple, avocado, Christmas tree farm, lemon, nectarine, olive, papaya, pears, pistachio, and pomegranate.
Also note that the DFR studies do not affect the Cotton mechanical harvesting exposure estimates.

APPENDIX H. Cancer Assessment for Buprofezin-derived Aniline

Nichino America, Inc. previously submitted a hydrolysis study conducted with [UL-^{14}C-phenyl]buprofezin (MRID 50217001; D438906/D441814, T. Morton, 9/27/2017) which indicates that aniline is a potentially significant degradation product of buprofezin under high temperature conditions simulating pasteurization, brewing, baking, boiling, and sterilization. In contrast, the available supporting buprofezin database, which includes other hydrolysis studies reflecting milder conditions and several processing studies which analyzed samples for aniline, indicates that there is no expectation of significant buprofezin-derived aniline formation under any other conditions. Hence, the only potential exposure to buprofezin-derived aniline is in/on cooked food forms. The Environmental Fate and Effects Division (EFED) has confirmed that there is no expectation of buprofezin-derived aniline in drinking water (D442267, J. Hetrick, 8/28/2017). Further, HED has concluded there is no expectation of buprofezin-derived aniline residential or occupational exposures.

There are numerous other potential sources of aniline exposure. Aniline is predominantly used as a chemical intermediate in the polymer, rubber, dye, and agricultural manufacturing industries.[12] The potential for other pesticides which contain the aniline moiety to hydrolyze to aniline cannot be dismissed; however, hydrolysis data for other aniline-containing pesticides have not been identified. Although no domestic aniline monitoring data (i.e., United States Food and Drug Administration (FDA) pesticide residue monitoring program or Total Diet Study, United States Department of Agriculture Pesticide Data Program (USDA PDP), market basket. etc.) have been identified, there are some limited, older, and primarily nondomestic data that suggest the potential for detectable levels of aniline in foods from sources other than buprofezin. These include (1) a German study conducted in 1977[13] and (2) the 1992 *Handbook of phytochemical constituents of GRAS herbs and other economic plants*[14] that reported maximum levels of aniline for a handful of fruits and vegetables; (3) a Canadian study conducted in 1999 that reported levels of aniline in the fat-free fractions of breast milk[15]; and (4) the Canadian Total Diet studies for the year 2001-2007[16]. However, given the lack of reliable current information and data to estimate residues of aniline from sources other than buprofezin, only buprofezin-derived aniline residues have been addressed in this assessment.

12 See https://pubchem.ncbi.nlm.nih.gov/compound/aniline#section=Top
13 Neurath. G.B., M. Duenger, F.G. Pein, D. Ambrosius and O. Schreiber. 1977. Primary and secondary am1nes in the human environment. Food Cosmet. Toxicol. 14: 275-282.
14 Duke, J. A. (1992). Database of Biologically Active Phytochemicals and Their Activity. Boca Raton, Fla: CRC Press. ISBN 9780849336713. 183 pp.
15 DeBruin, L.S., J.B. Pawliszyn and D.P. Josephy. 1999. Detection of monocyclic aromatic amines, possible mammary carcinogens, in human milk. Chem. Res. Toxicol. 12: 78–82.
16 Cao, X-L., Zhu, J., MacDonald, S., Lalonde, K., Dabeka, B., Cisse, M. 2009. Aniline in vegetable and fruit samples from the Canadian total diet study. Food Additives and Contaminants Vol. 26(6): 808–813.

Hazard Characterization

Aniline has been assessed for carcinogenicity for decades with the conclusion regarding cancer differing among countries and regulatory agencies. Cancer studies dating from the 1970s included two studies in rats (Chemical Industry Institute of Toxicology, CIIT, 1982[17] and National Cancer Institute, NCI, 1978[18]) and one study in mice (NCI 1978) conducted at a range of doses. No statistically significant increase in any type of tumor was observed at very high doses in the NCI mouse study. In the two rat studies, consistent findings of splenic tumors in male rats but none in female rats were reported at the high doses. Increases in hemangiosarcomas in multiple organs including spleen, and a significant dose-related trend in incidence of malignant pheochromocytoma were reported in the NCI study in male rats.

In 1987, the International Agency for Research on Cancer (IARC, 1987) classified aniline in Group 3, not classifiable as to its carcinogenicity to humans based on inadequate evidence for carcinogenicity to humans and limited evidence for carcinogenicity to animals.[19]

In 1988, the US EPA National Center for Environmental Assessment (NCEA) classified aniline as Group B2, probable human carcinogen (USEPA 1988) based on hemangiosarcomas in multiple organs including spleen, and a significant dose-related trend in incidence of malignant pheochromocytoma seen in the NCI 1978 study and some supporting genetic toxicological evidence. NCEA calculated an oral cancer slope factor for aniline as $5.7x10^{-3}$ $(mg/kg/day)^{-1}$ using the linearized multistage procedure. The carcinogenicity of aniline is discussed in EPA's Integrated Risk Information System (IRIS, 1988).[20]

In 1994 the Government of Canada (Health and Environment) in its priority Substances List Assessment Report of Aniline prepared under the Canadian Environmental Protection Act, classified aniline as Group III carcinogen ("Possibly Carcinogenic to Humans") based on inadequate information from epidemiological studies to assess the carcinogenicity of aniline in humans, and the limited evidence of carcinogenicity of aniline in laboratory animals exposed to high doses.[21] For compounds classified in Group III, generally a tolerable daily intake (TDI) is derived on the basis of a No-Observed-(Adverse)-Effect-Level [NO(A)EL] or Lowest-Observed-(Adverse)-Effect-Level [LO(A)EL] in humans or animal species and divided by an uncertainty factor, which when considered appropriate, takes into account the limited evidence of carcinogenicity.

17 Chemical Industry Institute of Toxicology. 1982. Final report: 104-week chronic toxicity study in rats: Aniline. Vol. 1. Research Triangle Park (NC) : CITT.
18 National Cancer Institute. 1978. Bioassay of aniline hydrochloride for possible carcinogenicity. U.S. Department of Health, Education and Welfare, National Institutes of Health, Public Health Service. (Carcinogenesis Technical Report Series No. 130).
19 See http://monographs.iarc.fr/ENG/Monographs/suppl7/Suppl7.pdf
20 See https://cfpub.epa.gov/ncea/iris2/chemicalLanding.cfm?substance_nmbr=350
21 See http://www.hc-sc.gc.ca/ewh-semt/alt_formats/hecs-sesc/pdf/pubs/contaminants/psl1-lsp1/aniline/aniline-eng.pdf

In July 2015, European Union (EU) European Medicines Agency (EMA) completed a comprehensive review of mutagenicity, genotoxicity, and carcinogenicity data for aniline, and concluded that the weight of evidence supports a non-genotoxic mode of action for aniline-induced carcinogenicity.[22] EMA also derived a health-based reference value for use in human health risk assessments of 720 µg/day as a lifetime permissible exposure.

In 2015, the European Union (EU) European Food Safety Authority (EFSA) in its peer review of the pesticide risk assessment for the active substance buprofezin determined that aniline is produced through high temperature processing of commodities with buprofezin residues.[23] EFSA considered aniline as a genotoxic carcinogen and, in 2017, decided to restrict the use of buprofezin to non-edible crops only (Official Journal of European Union dated March 1st, 2017) based on presumption of hazard, rather than on a demonstrated risk and did not set a health-based reference value or complete a human health (consumer) risk assessment. Subsequently, the USDA responded[24] to this decision stating that this is in contrast to the EMA assessment which "concluded that the weight of evidence supports a non-genotoxic mode of action for aniline-induced carcinogenicity and set a health-based reference for risk assessment. The EU's concern about aniline was largely based on a 2004 report from the European Chemicals Agency (ECHA) that classified aniline as potentially mutagenic. The EU does not appear to take into account newer data or the comprehensive review by EMA, even though the thirteen-year old ECHA report acknowledged that there was no scientifically plausible proof that the underlying mechanism of aniline carcinogenicity is based on genotoxic activity, and that other mechanisms could be involved in tumor development.[25] In responding to the EU's reservation, the Joint Meeting on Pesticide Residues (JMPR) concluded that there are different sources of aniline, including natural occurrence in food, and that aniline should be considered as a contaminant.[26] Accordingly, the Joint Expert Committee on Food Additives (JECFA) is currently conducting an evaluation to characterize hazard and estimate exposure to aniline in the diet, including exposure from the use of pesticides."

Although the EMA and Health Canada considered aniline to have a non-genotoxic mode of action and considers the reference dose approach to be health protective, the EPA IRIS assessment dates to 1988 and has not been re-evaluated. Therefore, the IRIS oral cancer slope factor of 5.7×10^{-3} $(mg/kg/day)^{-1}$ was used in this assessment and is considered very conservative for cancer assessment for aniline.

22 See http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/08/WC500191489.pdf.
23 See http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2015.4207/epdf
24 See http://ec.europa.eu/growth/tools-databases/tbt/en/search/?tbtaction=search.detail&Country_ID=EU&num=418&dspLang=en&basdatedeb=&basdatefin=&baspays=&basnotifnum=&basnotifnum2=&bastypepays=ANY&baskeywords=buprofezin
25 See https://echa.europa.eu/documents/10162/0abd36ad-53de-4b0f-b258-10cf90f90493
26 See http://www.fao.org/3/a-i5186e.pdf

Buprofezin Hydrolysis to Aniline Study (MRID 50217001) Summary

An hydrolysis study conducted with [UL-^{14}C-phenyl]buprofezin (MRID 50217001) was recently submitted for review (D438906/D441814, T. Morton, 9/27/2017). An aqueous solution of [UL-^{14}C-phenyl]buprofezin (1 mg/L) was incubated for 20 min at 90 ºC at pH 4, 60 min at 100 ºC at pH 5, or for 20 min at 120 ºC at pH 6. Results expressed as percent of total applied radioactivity (TAR) recovered are provided in the table below. The maximum conversion of buprofezin to aniline due to high temperature hydrolysis was 18.9%.

Table H.1. Summary of Buprofezin High Temperature Hydrolysis Study (MRID 50217001)

Compound	pH 4	pH 5	pH 6
	90 ºC	100 ºC	120 ºC
	20 minutes	60 minutes	20 minutes
	pasteurization	brewing/baking/boiling	sterilization
	Percent of Total Applied Radioactivity (TAR) Recovered		
Buprofezin	28.2	30.5	76.0
Aniline	8.7	**18.9**	7.2
BF11	1.4	0.3	3.5
BF12	17.1	31.1	5.3
BF25	42.9	17.8	6.6
Total recovery	102.9	91.3	91.1

Buprofezin-derived Aniline Cancer Exposure (Cooked Food Only) and Risk Assessment

A highly refined cancer dietary exposure and risk assessment for buprofezin-derived aniline residues was conducted for cooked foods only using an oral cancer slope factor of $5.7x10^{-3}$ $(mg/kg/day)^{-1}$ for aniline (D449526, T. Morton, 6/03/2019). Average residues of buprofezin and its aniline-containing metabolites in/on foods prior to cooking were estimated using (1) monitoring data for uncooked raw agricultural commodities (RACs) provided by USDA PDP, where available, (2) an additional factor based on metabolism data (1.8x) to estimate aniline-containing metabolites, where needed, and (3) average buprofezin percent crop treated (PCT) data provided by the Biological and Economic Analysis Division (BEAD), where available. See Section 5.4.3 for PCT data details. A conversion factor of 18.9%, the highest found in the hydrolysis study, was applied to estimate residues of buprofezin-derived aniline which may form in food as a result of cooking. Only cooked food forms were included in the dietary analysis. The highly refined estimated exposure of the highest exposed adult population (adults 20-49 years old) to buprofezin-derived aniline is 0.000053 mg/kg/day which results in an upper bound cancer risk estimate of 3×10^{-7}.

Table H.2. Results of Cancer Dietary Exposure (Cooked Food Only) Analysis for Buprofezin-derived Aniline.		
Population Subgroup	**Exposure (mg/kg/day)**	**Estimated Cancer Risk**
Adults 20-49 years old	0.000053	3×10^{-7}