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Buprofezin

Proposed Interim Registration Review Decision
Case Number 7462

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Approved by: _____

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I. INTRODUCTION

This document is the Environmental Protection Agency's (the EPA or the agency) Proposed Interim Registration Review Decision (PID) for buprofezin (PC Code 275100, case 7462), and is being issued pursuant to 40 CFR sections 155.56 and 155.58. A registration review decision is the agency's determination whether a pesticide continues to meet, or does not meet, the standard for registration in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The agency may issue, when it determines it to be appropriate, an interim registration review decision before completing a registration review. Among other things, the interim registration review decision may require new risk mitigation measures, impose interim risk mitigation measures, identify data or information required to complete the review, and include schedules for submitting the required data, conducting the new risk assessment and completing the registration review. Additional information on buprofezin, can be found in the EPA's public docket (EPA-HQ-OPP-2012-0373) at www.regulations.gov.

FIFRA, as amended by the Food Quality Protection Act (FQPA) of 1996, mandates the continuous review of existing pesticides. All pesticides distributed or sold in the United States must be registered by the EPA based on scientific data showing that they will not cause unreasonable risks to human health or to the environment when used as directed on product labeling. The registration review program is intended to make sure that, as the ability to assess and reduce risk evolves and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, the agency periodically re-evaluates pesticides to make sure that as these changes occur, products in the marketplace can continue to be used safely. Information on this program is provided at http://www.epa.gov/pesticide-reevaluation. In 2006, the agency implemented the registration review program pursuant to FIFRA section 3(g) and will review each registered pesticide every 15 years to determine whether it continues to meet the FIFRA standard for registration.

The EPA is issuing a PID for buprofezin so that it can (1) move forward with aspects of the registration review that are complete and (2) implement interim risk mitigation (see Appendices A and B). The agency is currently working with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (together, the Services) to develop methodologies for conducting national threatened and endangered (listed) species assessments for pesticides in accordance with the Endangered Species Act (ESA) Section 7. Therefore, although the EPA has not yet fully evaluated risks to listed species, the agency will complete its listed species assessment and any necessary consultation with the Services for buprofezin prior to completing the buprofezin registration review. Likewise, the agency will complete endocrine screening for buprofezin, pursuant to the Federal Food, Drug, and Cosmetic Act (FFDCA) section 408(p), before completing registration review. Last, the EPA will determine whether pollinator exposure and effects data are necessary to make a final registration review decision for buprofezin and issue a data call-in (DCI) to obtain any such data prior to completing the buprofezin registration review. See Appendices C and D, respectively, for additional information on the endangered species assessment and the endocrine screening for the buprofezin registration review.

Buprofezin (2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thidiazinan-4-one), a chitin biosynthesis inhibitor, is a foliar insecticide classified by Insecticide Resistance Action Committee (IRAC) as a Group 16 chemical. As an insect growth regulator (IGR), buprofezin may be applied as broadcast foliar applications to control homopteran pests such as cicadas, whiteflies, mealybugs, leafhoppers, plant hoppers, and scales. Products containing buprofezin are registered for use on cotton and ornamental plants, as well as a variety of food/feed crops including pistachios, grapes, berries, stone fruit, pome fruit, tropical fruit, citrus, vegetables, and coffee. No buprofezin-containing products are registered for homeowner use and there are no buprofezin-containing products registered for application to residential areas by commercial applicators. The first product containing buprofezin was registered in 2000, and buprofezin was not subject to reregistration.

This document is organized in five sections: the *Introduction*, which includes this summary and a summary of public comments and the EPA's responses; *Use and Usage*, which describes how and why buprofezin is used and summarizes data on its use; *Scientific Assessments*, which summarizes the EPA's risk and benefits assessments, updates or revisions to previous risk assessments, and provides broader context with a discussion of risk characterization; the *Proposed Interim Registration Review Decision*, which describes the mitigation measures proposed to address risks of concern and the regulatory rationale for the EPA's proposed interim registration review decision; and, lastly, the *Next Steps and Timeline* for completion of this registration review.

A. Summary of Buprofezin Registration Review

Pursuant to 40 CFR section 155.50, the EPA formally initiated registration review for buprofezin with the opening of the registration review docket for the case. The following summary highlights the docket opening and other significant milestones that have occurred thus far during the registration review of buprofezin.

- July 2012 – The *Buprofezin Preliminary Work Plan* (PWP*), BEAD Chemical Profile, Buprofezin Human Health Scoping Document*, and *Environmental Fate and Effects Problem Formulation* were posted to the docket for a 60-day public comment period.

- December 2012 –The *Buprofezin Final Work Plan* (FWP) and *Response to Buprofezin Preliminary Work Plan Comments* were published. Public comments were received during the 60-day comment period for the buprofezin PWP. The FWP identified data gaps which were inadvertently omitted from the data needs section of the PWP. The *Buprofezin Human Health Scoping Document in Support of Registration Review – Addendum* was also published.

- April 2013 – A Generic Data Call-In (GDCI) for buprofezin was issued for data needed to conduct the registration review risk assessments. All data required by the GDCI have been submitted and evaluated by the agency.

- December 2017 – The agency announced the availability of the *Buprofezin Human Health Draft Risk Assessment for Registration Review* and the *Preliminary Ecological Risk Assessment for the Registration Review of Buprofezin* for a 90-day public comment period. During the comment period, 13 comments were received from 12 sources. These comments and the agency's responses are summarized below. The comments did not change the risk assessments or registration review timeline for buprofezin.

- December 2018 – The agency is announcing the availability of the PID in the docket for buprofezin, for a 60-day public comment period. Along with the PID, the following documents are also posted to the buprofezin docket:
    - *Benefits Information for Registration Review Proposed Interim Decision (PID)*
    - *Revised Occupational Post-Application Risk Estimates Incorporating New DFR Data to Support Registration Review*
    - *Buprofezin* and *Chitin Synthesis Inhibitors (Buprofezin and Cyromazine): Screening Analysis of Toxicological Profiles to consider Whether a Candidate Common Mechanism Group Can Be Established*
    - *Buprofezin: EFED Response to Comments Submitted to the Docket on the Preliminary Interim Ecological Risk Assessment*
    - *Buprofezin: Response to Comments on the Human Health Draft Risk Assessment for Registration Review*.

B. Summary of Public Comments on the Draft Risk Assessments and Agency Responses

The public comment period for the buprofezin draft risk assessments opened on December 15, 2017 and closed on March 15, 2018. Comments were submitted by: National Cotton Council (NCC), the United States Department of Agriculture (USDA), Northwest Horticultural Council (NHC), National Agricultural Aviation Association (NAAA), California Fresh Fruit Association (CFFA), IR-4 Project, University of Georgia, University of Hawaii, Nichino America, Inc. (NAI or Nichino), the Almond Alliance of California, the Center for Biological Diversity, and the general public. Substantive comments, comments of a broader regulatory nature, and the agency's responses to those comments are summarized below. The agency thanks all commenters for their comments and has considered them in developing this Proposed Interim Registration Review Decision. The EPA's full responses may be found in *Buprofezin: EFED Response to Comments Submitted to the Docket on the Preliminary Interim Ecological Risk Assessment, Buprofezin: Response to Comments on the Human Health Draft Risk Assessment for Registration Review*, and the *Benefits Information for Registration Review Proposed Interim Decision (PID)*.

Comments Submitted by the National Cotton Council in EPA-HQ-OPP-2012-0373-0033 and EPA-HQ-OPP-0373-0045

Comment: The NCC described buprofezin as a critical tool for whitefly control in cotton. NCC noted that the human health and ecological risk assessments identified risks of concern and encouraged refinement of the risk assessments. Regarding the ecological risk assessment, NCC

noted that LOC exceedances were found for some taxa from chronic exposure and again endorsed refinements.

EPA Response: The EPA thanks NCC for their comments and information provided regarding the use of buprofezin in the cotton industry. The agency understands that buprofezin is a valuable insecticide to the cotton industry and has worked with Nichino during the development of this proposed interim decision to refine occupational post-application risks of concern.

Comments Submitted by USDA in EPA-HQ-OPP-2012-0373-0034

Comment: USDA stated that buprofezin is an important component of integrated pest management (IPM) programs in various crops for the control of whiteflies, mealybugs, scale, leafhoppers, psyllids and planthoppers. USDA asserted that scale insects, in particular, are receiving attention from pest managers in fruit trees and nut crops due to many IPM programs shifting from broad-spectrum organophosphate (OP) and carbamate insecticides to more selective insecticides that do not provide control of scale. The comments also included input on buprofezin usage, pollinator risks and references on residues in pollen, and buprofezin's role in integrated pest and resistance management. Due to the importance of buprofezin use for managing pests, USDA requests that the EPA work with the registrant to identify areas where the occupational risk assessment might be further refined.

EPA Response: The agency thanks the USDA for their comments and has reviewed additional dislodgeable foliar residue (DFR) data to refine occupational post-application risks of concern. As noted in the ecological risk assessment, the extent of potential risks to pollinators (*e.g.*, honey bees) are uncertain due to the lack of toxicity data capturing exposure at the sensitive (larval) life stage. If the EPA receives such a study, this, along with any USDA information that can be incorporated, will be considered in a future assessment of risks to pollinators.

Comments Submitted by Northwest Horticultural Council in EPA-HQ-OPP-2012-0373-0035 and EPA-HQ-OPP-2012-0373-0039

Comment: The NHC cited buprofezin as an important tool for growers in Washington, Oregon, and Idaho for use on fruit trees such as apples, pears, and cherries. The NHC conferred the benefits of buprofezin from having a different mode of action and that it is used in rotation with other insecticides to prevent resistance. The comments also described pests, such as pear psylla and grape mealybug, and the specific damage induced by these pests.

EPA Response: The agency thanks the NHC for their comments and has considered the information provided in the development of buprofezin's proposed interim registration review decision.

Comments Submitted by National Agricultural Aviation Association in EPA-HQ-OPP-2012-0373-0036

Comment: The NAAA expressed concerns with several aspects of the Tier 1 model in AgDRIFT, including assumption of droplet size, spray boom height and swath displacement definition. NAAA contested that the model does not reflect modern agricultural aircraft practices for aerial application, and discussed additional aspects used by aerial applicators to reduce spray drift.

EPA Response: The EPA appreciates the additional information on such agricultural aircraft and continues to work with industry to update and improve modeling methods to better reflect these practices. It is noted, however, that modeling is based on label instructions, and in the absence of specific application requirements, default assumptions are used. Additionally, the risk assessment provided outputs for risks associated with ground and aerial applications, which were considered in the development of this PID.

Comments Submitted by California Fresh Fruit Association in EPA-HQ-OPP-2012-0373-0037

Comment: Comments from CFFA illustrated the effect of San Jose scale on fruit trees, and the benefit of utilizing buprofezin with annual oil sprays to control this pest. CFFA also provided use information and expressed concerns about overestimating aquatic risks of concern determined in the agency's ecological risk assessment.

EPA Response: EPA appreciates CFFA's comments and took the information that was provided into consideration in developing this PID.

Comments Submitted by IR-4 in EPA-HQ-OPP-2012-0373-0038

Comment: Comments from IR-4 focused on buprofezin's importance as an IGR specific to the nymphal stages of various pests. The comments note that buprofezin's unique mode of action has made it an important tool in IPM programs. IR-4's comments also provided values for registration assistance, trials, and specialty crop commodities.

EPA Response: The agency recognizes that buprofezin is a useful insect management tool and acknowledges that buprofezin is registered to treat pests across a wide range of uses. These comments were considered in the development of the PID for buprofezin.

Comments Submitted by University of Georgia in EPA-HQ-OPP-2012-0373-0040

Comment: The University of Georgia's (UGA) comments covered the importance of buprofezin to insect management in vegetables produced in the fall. Specifically, UGA referenced the use of buprofezin during historically high pest pressure from the sweet potato whitefly in 2017. UGA noted that buprofezin's unique mode of action makes it a beneficial tool for growers.

EPA Response: The EPA thanks the University of Georgia for the information provided in their comments and considered these data and perspectives when developing this PID.

Comments Submitted by University of Hawaii in EPA-HQ-OPP-2012-0373-0041

Comment: Comments from the University of Hawaii, submitted on behalf of the Western Integrated Pest Management Center, discussed the limited number of products available for use on specialty tropical crops to control pests listed on labels for products containing buprofezin. These pests include scales, whiteflies, mealybugs, and leafhoppers. The University of Hawaii also notes the benefits of buprofezin's 12-hour restricted-entry interval (REI).

EPA Response: The agency thanks the University of Hawaii for their comments. This PID takes the benefits of the registered uses of buprofezin into consideration.

Comments Submitted by the Center for Biological Diversity (CBD) in EPA-HQ-OPP-2012-0373-0042

Comment: CBD's comments focused on the agency's duty to consult with the Services on the registration review of buprofezin in accordance with the Endangered Species Act (ESA). The CBD comments mentioned various aspects of the risk assessment process, specifically use of the best available data, including all necessary data and studies, particularly to develop listed species risk assessments, and evaluation of effects on listed species and their designated critical habitat regarding the rigor of the agency's preliminary determination regarding the effects of buprofezin on listed species and their designated critical habitat for the buprofezin registration review. In addition, CBD expressed concern about effects on pollinators and other beneficial insects, effects on human health or environmental safety concerning endocrine disruption, and any additive, cumulative or synergistic effects of the use of the pesticide.

EPA Response: The agency has reviewed CBD's comments and plans to address many of the concerns regarding listed species as part of the implementation plan for assessing the risks of pesticides to listed species based on the recommendations of April 2013 National Academy of Sciences (NAS) report. See Endangered Species Assessment in Appendix C of this document for more information. The agency will address concerns specific to buprofezin particularly with regard to pollinators, ESA, and endocrine disruption, in connection with the development of its final registration review decision for this pesticide. See Endocrine Disruptor Screening Program in Appendix D of this document for more information regarding endocrine disruption. The agency is currently developing an agency policy on how to consider claims of synergy being made by registrants in their patents. The agency intends to release this policy for public comment. After the agency has received and considered public comment on the proposed policy, and once that policy has been finalized, the EPA will consider its implications on the EPA's final decision for buprofezin.

Comments Submitted by Nichino America, Inc. in EPA-HQ-OPP-2012-0373-0043

Nichino, the sole registrant for buprofezin, provided comments on both the *Buprofezin Human Health Draft Risk Assessment for Registration Review* and the *Preliminary Ecological Risk Assessment for the Registration Review of Buprofezin*.

Comment: Regarding the human health assessment, the registrant disagreed with the EPA's conclusion that the comparative thyroid toxicity study (CTA) did not establish a no-observed-adverse-effects-level (NOAEL). Nichino also disagreed with the EPA's finding that the repeated dermal dose study did not allow for assessment of the relevant endpoint in the subpopulation of concern. The registrant is of the position that the NOAECs (no observed adverse effects concentrations) from the dermal dose study and repeated dose inhalation study are appropriate for short and intermediate term risk assessment. The comments further state that there is no differentially sensitive population (*i.e.*, offspring are not more susceptible that adults).

In addition to comments regarding identified risks of concern, Nichino requested that tolerances for grapes and raisins be updated to support harmonization with other countries and minimize potential trade barriers.

The registrant also noted in their comments that they submitted dislodgeable foliar residue (DFR) data in greenhouse tomatoes (MRID 50523901) to refine the post-application exposure risk. Nichino provided additional DFR data on grapes and citrus (MRIDs 50573101 and 50573102) following review of MRID 50523901 to further refine post-application margins of exposure.

The registrant also cited benefits of buprofezin's unique mode of action, and listed specific corrections to the CAS number, water solubility, and other physical characteristics of this chemical.

EPA Response: Regarding the buprofezin CTA study (MRID 49615301), conclusions were based on comprehensive and extensive review and analysis by EPA toxicologists and statisticians, which revealed that offspring were more susceptible to buprofezin toxicity than the adult females and fetuses to the effects of buprofezin on the thyroid. Because the inhalation study did not evaluate the effects on the thyroid, the 28-day inhalation study, as suggested by the registrant, would not be appropriate for assessment of the subpopulation of concern.

Chemical-specific dislodgeable foliar residue (DFR) data had not previously been submitted for buprofezin. Therefore, the *Buprofezin Human Health Draft Risk Assessment for Registration Review* used a default assumption that 25% of the application is available for transfer on a day 0 following the application and the residues dissipate at a rate of 10% each following day. Based on the exposure assessment and DFR assumptions, multiple dermal post-application risk estimates were of concern on the day of product application. The DFR data that Nichino submitted fulfilled the EPA's data requirement for dislodgeable foliar residues (875.2100). Following review, a number of post-application margins of exposure that were previously below EPA's level of concern were refined and were no longer considered risks of concern. However, manual activities such as hand-thinning, tying, and training, still indicated potential risks in several uses to occupational handlers for up to 8 days after application. These revised values are available in *Buprofezin: Revised Occupational Post-Application Risk Estimates Incorporating New DFR Data to Support Registration Review*.

The EPA has re-examined the available grape field trial data (MRIDs 46629901 and 47676701) and 1 trial in 2003 (MRID 47159101) reflecting the currently registered use rate for buprofezin on grapes and agrees that the currently established tolerance in/on grape may be lowered to 1.0 ppm to harmonize with the currently established Codex and Canadian MRLs in/on grapes. The EPA also agrees that a separate tolerance will need to be established for residues of buprofezin in/on grape, raisin but not at the proposed level (1.7 ppm). Instead the EPA is considering a tolerance of 2.0 ppm in/on grape, raisin to harmonize with the currently established Codex and Canadian MRLs of 2 ppm in/on dried grapes (currants, raisins, and sultanas) and raisins, respectively.

The agency appreciates the clarification information (*i.e.*, corrections to the CAS number, water solubility, and other physical characteristics of this chemical) provided by Nichino for buprofezin. Based on the submitted data (MRID 49749501) the vapor pressure of technical buprofezin was determined at 25°C to be 5.00×10^{-5} Pa or 3.75×10^{-7} mmHg. This is an

extrapolated value estimated through the use of linear regression on log scale. Future assessments will include this updated information.

Comments Submitted by the Almond Alliance of California in EPA-HQ-OPP-2012-0373-0044

Comment: The Almond Alliance comments described how buprofezin is used by almond growers, applications rates, and the amount of buprofezin used at different times. Comments were also provided on the *Buprofezin Human Health Draft Risk Assessment for Registration Review* and *Preliminary Ecological Risk Assessment for the Registration Review of Buprofezin*. The Almond Alliance questioned the proposal to require a 25-foot buffer in the *Buprofezin Human Health Draft Risk Assessment for Registration Review* as part of spray drift mitigation and expounded on California regulations, application rates, and use patterns as issues for characterizing uncertain risks to non-target organisms, including pollinators.

EPA Response: The agency appreciates the comments and how this additional information may be utilized in interpreting potential ecological risks associated with almond applications, particularly with respect to pollinators. As mentioned in the comments provided by the Almond Alliance, and as recognized by the EPA in the *Preliminary Ecological Risk Assessment for the Registration Review of Buprofezin*, uncertainties are present in assessing potential pollinator risks and may be better informed with additional data (*i.e.*, chronic larval study).

II. USE AND USAGE

Buprofezin (2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thidiazinan-4-one) is a non-systemic, selective, insect growth regulator effective against the nymphal stages of whitefly, scales, psylla, mealybugs, planthoppers, and leafhoppers. Buprofezin works by inhibiting chitin biosynthesis, suppressing oviposition of adults, and reducing viability of eggs. Products containing buprofezin may be formulated as a wettable powder, dry flowable concentrates, water dispersible granules, water-soluble packets, and soluble concentrates. Registered uses for buprofezin products include grapes, citrus, pistachios, strawberries, pears, apples, apricots, peaches, cherries, squash, lettuce, cabbage, cauliflower, broccoli, tomatoes, cotton, and tropical fruits. It may also be used in greenhouses, lath and shade houses, and nurseries. Buprofezin is applied foliarly via broadcast applications utilizing the following equipment for occupational use: aerial, airblast equipment, ground boom sprayer, handheld spray equipment, and foggers. No buprofezin products are registered for non-agricultural uses, residential use, or for application to residential areas. As of September 2018, there are four registrations for end-use products containing buprofezin.

There are approximately 176,000 pounds of buprofezin applied to 219,000 acres annually. Lettuce and pistachios have the highest number of acres treated with buprofezin. Pistachios, pears, and cherries have high usage of buprofezin in terms of pounds applied. Strawberries, pears, and pistachios have the highest percent crop treated (PCT). Most crops have average application rates below 1 lb a.i./acre with the exception of fruit and nut tree crops, like pistachios and pears. The maximum number of applications for most crops does not exceed two, and the average number for most crops is around one per year, with strawberries having the highest

average number of applications. Please see the *Benefits Information for Registration Review Proposed Interim Decision (PID)* for more information.

III. SCIENTIFIC ASSESSMENTS

A. Human Health Risks

A summary of the agency's human health risk assessment is presented below. The agency used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of buprofezin. For additional details on the human health assessment for buprofezin, see the *Buprofezin Human Health Draft Risk Assessment for Registration Review*, which is available in the public docket.

1. Risk Summary and Characterization

Dietary (Food + Water) Risks

Risk estimates were not of concern for the U.S. general population or the most highly exposed population subgroup (level of concern (LOC) > 100%). The unrefined acute dietary exposure and risk assessment at the 95th percentile of exposure for females 13 to 49 years old was 6.2% of the acute population-adjusted dose (aPAD). No acute endpoint was identified for the remaining population subgroups. The partially refined chronic dietary exposure and risk estimate for the most highly exposed population, children 1 to <2 years old, was 52% of the chronic population-adjusted dose (cPAD).

Dietary Cancer Risks

Buprofezin is classified as having "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential." Therefore, no quantification of cancer risk is required. A metabolite of buprofezin, aniline, was classified by the EPA's Integrated Risk Information System (IRIS) as a B2 "probable human carcinogen." There are no potential exposures to buprofezin-derived aniline other than cooked foods. A highly refined cancer dietary (cooked food only) exposure and risk assessment was conducted for buprofezin-derived aniline. While aniline exposures from sources other than buprofezin are possible, these exposures cannot be reliably estimated. For more information, please see the *Buprofezin Human Health Draft Risk Assessment for Registration Review*.

The refined cancer dietary exposure (cooked food forms only) and risk assessment estimated exposure of the highest exposed adult population (adults 20 to 49 years old) to buprofezin-derived aniline at 0.000053 mg/kg/day which resulted in an upper bound cancer risk estimate of 3×10^{-7}. Potential cancer risks are not identified as of concern.

Residential Handler Risks

A residential exposure and risk assessment was not conducted for buprofezin because there are no buprofezin-containing products registered for homeowner use and no products registered for application to residential areas.

Aggregate Risks

Aggregate risk is derived from the combination of both dietary exposures and residential use exposures. Since there are no residential uses of buprofezin, the aggregate risk assessments are equivalent to the acute and chronic dietary exposure and risk assessments, which do not have potential risks of concern.

Non-occupational Spray Drift Exposure Risks

Spray drift may be a source of exposure for individuals adjacent to applications of buprofezin; therefore, a quantitative non-occupational spray drift exposure and risk assessment was conducted for the registered uses of buprofezin.

Dermal and incidental-oral exposures to children 1 to < 2 years old were combined because the toxicity endpoints for these exposure routes were based on the same effects.

There are no risks of concern to adults or children as a result of spray drift from ground spray or airblast applications; all margins of exposure (MOEs) were above the LOC of 300. In addition, aerial applications of buprofezin to orchards and vineyards did not present risks of concern to adults. However, aerial application of buprofezin resulted in risks of concern for children 1 to < 2 years old at a rate of 2 lbs a.i./A with very fine or coarser droplet sizes up to 100 feet from the field edge with combined (dermal + incidental) MOEs ranging from 150 – 280. Fine to medium droplet sizes also resulted in potential risks of concern to children 1 to < 2 years old up to 10 feet from the field edge (MOEs = 220 – 270). Increasing droplet sizes can result in reduced spray drift and reduced exposure. There are no risks of concern at the edge of the field with coarse to very coarse droplet sizes.

Cumulative Risks

The EPA conducted a screening analysis of the chitin synthesis inhibitors, buprofezin and cyromazine, to determine if these active ingredients were candidates for establishing a common mechanism group (CMG). The chitin synthesis inhibitors share a pesticidal mechanism of action (MOA). However, the screening analysis indicated that it was unlikely that these chitin synthesis inhibitors would have a similar MOA in humans. Furthermore, the available toxicity studies show that chitin synthesis inhibitors do not share a common mammalian toxicological profile. Taken together, the weight of evidence does not support a testable hypothesis for a common mechanism of action for the chitin synthesis inhibitors. Therefore, the agency concludes that a candidate CMG cannot be formed and no further cumulative evaluation is necessary for these pesticides. For more information, see *Chitin Synthesis Inhibitors (Buprofezin and Cyromazine): Screening Analysis of Toxicological Profiles to Consider Whether a Candidate Common Mechanism Group Can be Established* in the docket.

Occupational Handler Risks

Dermal and inhalation exposures to occupational handlers were combined because the toxicity endpoints for these exposure routes were based on the same effects. At a minimum, the dry flowable and water-soluble formulation labels require occupational handlers to wear baseline attire (long sleeved shirt, long pants, shoes, and socks), and waterproof gloves. For soluble concentrates, occupational handlers must also wear chemical resistant gloves and protective eyewear. Protective eyewear is required for BUPROFEZIN 40 SC Insect Growth Regulator (EPA Reg. No. 71711-20).

The current restricted entry interval (REI) on all registered labels is 12 hours. The occupational handler risk estimates indicate that certain occupational exposure scenarios result in potential risk estimates of concern (MOE < LOC of 300) even with the maximum level of PPE or engineering controls (EC). These scenarios include:

- Mixing/loading dry flowables for aerial applications to orchards/vineyards (total (dermal + inhalation) MOE with EC = 260).
- Mixing/loading water soluble packets for aerial applications to orchards/vineyards (total MOE = 260).
- Mixing/loading/applying dry flowables or soluble concentrates for fogging orchards and vineyards with an inhalation MOE of 260.
- Mixing/loading/applying soluble concentrates and water-soluble packets for mechanically pressurized handgun (MPH) to treat orchards/vineyards, and typical field crops (Dermal MOEs = 68 – 270).
- Mixing/loading/applying dry flowables for MPH applications to orchards/vineyards, Christmas Tree farms, greenhouse ornamentals/vegetables, nursery ornamentals, and landscaping trees/shrubs/bushes (Dermal MOEs = 68 – 170).

Occupational handler risk estimates also indicated potential risks of concern for multiple scenarios assessed assuming the use of baseline attire and/or label required PPE:

- Mixing/loading/applying dry flowables via backpack to Christmas Tree farms, nursery ornamentals, landscaping trees/shrubs/bushes/plants/flowers
  - Combined MOEs with double layer and gloves = 320 (double layer PPE to be worn as coveralls over long pants and long-sleeved shirts with gloves). With baseline PPE, the MOE is 190.
- Applicator spray (all starting formulations) via airblast to orchards/vineyards
  - Combined MOE with single layer PPE with gloves plus chemical resistant hat (CRH) = 330; use of baseline PPE results in an MOE of 52.
- Mixers/loaders for soluble concentrates for aerial application to orchards/vineyards
  - Combined MOEs with double layer and gloves = 320; the MOE is 250 with baseline PPE.

The occupational exposures with risks of concern from aerial application involves mixers and loaders to orchards and vineyards. Aerial applications to orchards/vineyards are not common

(see *Buprofezin Benefits Information for Registration Review Proposed Interim Decision*). Therefore, the potential risks to occupational handlers from mixing and loading dry flowable or water-soluble packets for aerial application, is likely less than calculated. Applying engineering controls for occupational workers mixing and loading dry flowable formulations or double-layer PPE with gloves for occupational handlers mixing and loading soluble concentrates would further reduce potential risks. Use of engineering controls for mixing and loading dry flowables or water-soluble packets increases MOEs to 260. The MOEs for soluble concentrates rise to 320 with additional PPE (i.e., double layer plus gloves).

Treatment of several uses via backpack resulted in potential risks of concern. Combined MOEs from backpack application for the uses with risks of concern (Christmas Tree farms, nursery ornamentals, landscaping trees/shrubs/plants/flowers/bushes) were below the LOC of 300 with an MOE of 96 with baseline attire and 190 with baseline attire and gloves. Use of gloves and coveralls over baseline attire increases MOEs to 320. In addition, the registrant, Nichino, has stated that the company is unaware of backpack or mechanically-pressurized handgun applications outside of some greenhouse uses (see Summary of Correspondence, correspondence from Nichino, August 20, 2018).

Application via mechanically-pressurized handgun (MPH) resulted in risks of concern with coveralls and gloves when treating orchards/vineyards and typical field crops with soluble concentrate or water-soluble packets (MOEs = 68 – 270). Potential risks of concern were also identified when applying dry flowable formulations to all assessed uses, even with the use of coveralls and gloves (MOEs = 68-170).

Airblast applications to orchards and vineyards using current label required PPE resulted in an MOE of concern (MOE = 48). By their nature, airblast sprayers distribute pesticide products using high air pressure and strong air currents that can provide a broad area of application. The MOE is no longer of concern with use of a chemical resistant hat and gloves or with use of an enclosed cab (MOE= 330).

Risks to occupational handlers utilizing fogging equipment and stationary fogging applications were assessed. No potential risks of concern were found with the use of stationary fogging applications. For application with fogging equipment, MOEs for mixers and loaders only were above the LOC. However, MOEs for applicators, mixers, and loaders treating orchards and vineyards were 260 with a PF10 respirator for the dry flowable and soluble concentrate formulations. There is currently no data available to assess dermal risks to applicator from fogging applications and it is not clear if occupational handlers are typically present during fogging applications. The registrant, Nichino, has stated that fogging equipment is not used in orchards and vineyards; rather it is used in greenhouses (correspondence from Nichino, August 20, 2018). Additional PPE and specific application instructions would reduce exposure to occupational handlers.

Occupational Post-Application Risks

The term, post-application exposure, or re-entry exposure, is used to describe exposures that occur when individuals are present in an environment that has been currently treated with a

pesticide. Occupational post-application dermal exposure risk estimates were initially assessed at Day 0 for registered uses of buprofezin using default assumptions and maximum application rates. Initial estimates indicated re-entry risks of concern for a number of uses and activities with some MOEs not reaching the LOC until 19 days after treatment. Following issuance of the *Buprofezin Human Health Draft Risk Assessment for Registration Review*, Nichino provided dislodgeable foliar residue (DFR) data as a means of refining the potential risks associated with post-application activities (MRIDs 50523901, 50573101, and 50573102) and to satisfy the data requirement, guideline 875.2100, foliar dislodgeable residue dissipation. The DFR studies provided are as follows:

- MRID 50523901: Dissipation of Dislodgeable Foliar Residues of Buprofezin Following Applications to Tomatoes in Greenhouses
- MRID 50573101: Dislodgeable Foliar Residue Decline Study on Grapes in Northern and Southern Europe in 2015
- MRID 50573102: Dislodgeable Foliar Residue Decline Study on Citrus in Southern Europe

As a result, the post-application exposure assessment was revised (D448121, *Buprofezin: Revised Occupational Post-Application Risk Estimates Incorporating New DFR Data to Support Registration Review*). The revised MOES resulted in an increase of MOEs for several uses and activities that were previously considered risks of concern (MOE < LOC). MOEs below the LOC at the current re-entry interval (REI) of 12 hours still remain for the following uses and activities:

Crop/Site	**Activities**	**MOE in exceedance of the LOC (Current REI = 12 hours)**	**MOE values for different REI Days**
Pome fruit, crop group 10-11 (Apple)	Thinning fruit	160	Day 4 (260) Day 5 (290) Day 6 (330)
Cotton	Harvesting, mechanical, tramper	240	Day 1 (270) Day 2 (300)
Grape (raisin, table, juice, wine) @ 1.05 lb a.i./A (Higher rate for CA and AZ)	Tying/training; harvesting, hand; leaf pulling	130	Day 5 (270) Day 6 (310)
Grape (raisin, table, juice, wine) @ 0.53 lb a.i./A (Maximum rate outside of CA and AZ)	Tying/training; harvesting, hand; leaf pulling	260	Day 1 (300)
Stone fruits (Crop group 12) (Nectarine)	Thinning fruit	160	Day 4 (260) Day 5 (290) Day 6 (330)

Nursery ornamentals	Irrigation (hand set)	280	Day 1 (330)
Olive	Thinning fruit	120	Day 7 (280) Day 8 (320)
Pears and Asian Pears	Thinning fruit	120	Day 7 (270) Day 8 (320)

There is potential for dermal post-application exposure to buprofezin from pome fruit, stone fruit, grapes, cotton, olives, pears and Asian pears, and nursery ornamental uses. Based on the current exposure assessment, short term dermal post-application risk estimates were of potential concern for activities for up to 8 days after application. The scenarios that present potential risks of concern pertain to activities conducted manually. For example, thinning fruit by hand results of risks of concern for pome fruit, stone fruit, pears and Asian pears, and olives. However, chemical and mechanical thinning of fruit does not result in risks of concern as occupational workers will have limited direct contact with foliar residues during these processes. Extending the REIs to Day 6 for pome fruit (apples), grapes (raisin, table, juice, wine for CA and AZ), and nectarines (stone fruit), and to Day 8 for olives, pears, and Asian pears for hand-thinning activities only will increase the MOE above the LOC of 300. For cotton, revising the REI from 12 to 24 hours brings to MOE above the LOC (330 on Day 1).

2. Human Incidents and Epidemiology

The EPA completed a review of existing incidents data for buprofezin in the Incident Data System (IDS) and the Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health (CDC/NIOSH) Sentinel Event Notification System for Occupational Risk-Pesticides (SENSOR) databases. From January 1, 2012 to March 16, 2017, there were no reported incidents in the Incident Data Systems. A query of the SENSOR-Pesticides database from 2000 – 2013 identified three cases involving buprofezin. All three cases were low in severity and involved exposure to multiple active ingredients and pesticide products. Two of these cases were occupational and one was non-occupational.

Based on the low frequency and severity of buprofezin incidents reported to both IDS and SENSOR-Pesticides, there does not appear to be a concern at this time. The agency will continue to monitor the incident information. Additional analyses will be conducted if ongoing human incident monitoring indicates a concern.

3. Tolerances

Tolerances for residues of buprofezin in/on registered crops are published in 40 CFR §180.511. Tolerances with no U.S. registrations have been established for residues of buprofezin in/on rice, grain and tea. Tolerances have also been established for residues of buprofezin as a result of secondary residues in milk and meat. Under Registration Review, the EPA is proposing a number of tolerance conversions/revisions to update crop group definitions. These revisions include increased tolerances for residues of buprofezin in/on banana, citrus fruit, coffee, cucurbit vegetable, low growing berry subgroup 13-07G, olive, stone fruit (except peach and nectarine),

and tea for the sole purpose of harmonization with Codex and/or Canadian maximum residue limits (MRLs).

In response to comments from Nichino, the EPA agrees with the registrant that the currently established tolerance in/on grape may be lowered from 2.5 ppm to 1.0 ppm to harmonize with the currently established Codex and Canadian MRLs in/on grapes and that a separate tolerance will need to be established for residues of buprofezin in/on grapes. The EPA is proposing a tolerance of 2.0 ppm in/on grape, raisin to harmonize with the currently established Codex and Canadian MRLs of 2 ppm in/on dried grapes (currants, raisins, and sultanas) and raisins, respectively. The following tolerances will be updated as part of registration review.

Table 1. Buprofezin, 40 CFR §180.511: Summary of Proposed Tolerance Actions

Commodity	Established Tolerance (ppm)	Proposed Recommended Tolerance (ppm)	Comments
Apricot	9.0	Remove	Crop group conversion/revision 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 (2.0 ppm) of Crop Group 12-12 (Stone Fruits Group), which has been increased from 1.9 ppm to 2.0 ppm to harmonize with Codex and Canada MRLs for Cherry and Plum Subgroups.
Banana	0.20	0.30	*Banana* Tolerance level has been increased to harmonize with Codex MRL and Canada MRL for banana commodities. The Canada MRL for banana commodities is based on U.S. banana data[2]**.**
Berry, low growing, subgroup 13-07G	2.5	3.0	*Berry, low growing, subgroup 13-07G* Tolerance level has been increased to harmonize with Canada MRL for subgroup13-07G commodities. The Canada MRL is based on U.S. strawberry (representative crop for subgroup 13-07G) data[2].
Birida	0.30	0.30	*Biriba* "Birida" spelling should be corrected to "Biri**b**a."
Brassica, head and stem, subgroup 5A	12	Remove	Crop group conversion/revision[1]
Brassica, leafy greens, subgroup 5B	60	Remove	Crop group conversion/revision[1]
Celtuce	--	35	*Celtuce*[1] Crop group conversion/revision from group 4 to subgroup 22A. HED is recommending that tolerance level and use rate be consistent with subgroup 22B.
Coffee, green bean	0.35	0.40	*Coffee, green bean* Tolerance level has been increased to harmonize with Codex MRL for coffee beans commodities.

Table 1. Buprofezin, 40 CFR §180.511: Summary of Proposed Tolerance Actions			
Commodity	Established Tolerance (ppm)	Proposed Recommended Tolerance (ppm)	Comments
Fennel, Florence, fresh leaves and stalk	--	35	*Fennel, Florence, fresh leaves and stalk*[1] Crop group conversion/revision from group 4 to subgroup 22A. HED is recommending that tolerance level and use rate be consistent with subgroup 22B.
Fruit, citrus, group 10	2.5	4.0	*Fruit, citrus, group 10-10* Crop group conversion from 10 to 10-10. 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[2].
Fruit, stone, group 12, except apricot and peach	1.9	2.0	*Fruit, stone, group 12-12, except nectarine and peach* Crop group conversion from 12 to 12-12. -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[2]. -Apricot is now covered by the tolerance (2.0 ppm) of Crop Group 12-12. -Nectarine and peach (both/only members of the peach subgroup 12-12B) have separate tolerances established at 9.0 ppm.
Grape	2.5	1.0	In response to registrant comment, the currently established tolerance in/on grape may be lowered from 2.5 ppm to 1.0 ppm to harmonize with the currently established Codex and Canadian MRLs in/on grapes. Establish a separate tolerance for grapes, raisin to harmonize with Codex and Canada MRLs in/on dried grapes (=currants, raisins and sultanas) and raisins, respectively.
Grape, raisin	2.5	2.0	
Kohlrabi	--	12	*Kohlrabi*[1] Crop group conversion/revision from subgroup 5A to subgroup 22A. HED is recommending that tolerance level and use rate be consistent with group 5-16.
Leafy greens, subgroup 4-16A	--	35	*Leafy greens, subgroup 4-16A*[1] Crop group conversion from parts of group 4 to subgroup 4-16A. 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-

Table 1. Buprofezin, 40 CFR §180.511: Summary of Proposed Tolerance Actions			
Commodity	Established Tolerance (ppm)	Proposed Recommended Tolerance (ppm)	Comments
			16A) data. Data support maximum use rate of 2 applications at 0.38 lb a.i./A with a 7-day PHI.
Leafy greens, *Brassica*, subgroup 4-16 B	--	60	*Leafy greens, Brassica, subgroup 4-16 B*[1] Crop group conversion from parts of crop group 4, subgroups 5A and 5B (major part) to subgroup 4-16B. 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 a.i./A with a 1-day PHI.
Lettuce, head	6.0	Remove	Covered by crop subgroup 4-16A (35 ppm). Also, tolerance level will be harmonized with Canadian MRL (35 ppm) in/on head lettuce.
Nut, tree group 14	0.05	0.05	*Nut, tree, group 14-12* Crop group conversion from 14 to 14-12.
Olive	3.5	5.0	*Olive* Tolerance level has been increased to harmonize with Canada MRL for olive commodities. The Canada MRL is based on U.S. olive data[2]. The tolerance value of 5 ppm is compatible with Codex MRL for Table Olives. (Note: The MOR data were inputted to the OECD calculator, which generated 4.0 ppm tolerance for buprofezin on olives.)
Olive, oil	4.8	Remove	Covered by olive tolerance (5.0 ppm).
Pistachio	0.05	Remove	Covered by the tolerance (0.05 ppm) of Crop Group 14-12, Tree Nuts.
Radicchio	6.0	Remove	Covered by crop subgroup 4-16A (35 ppm). Also, tolerance level will be harmonized with Canadian MRL (35 ppm) in/on radicchio.
Tea[3]	20	30	Tea[3] Tolerance level has been increased to harmonize with Canada MRL for tea (dried leaves).
Turnip, greens	60	Remove	Covered by the tolerance (60 ppm) of Crop Subgroup 4-16B, *Brassica* leafy greens.
Vegetable, head and stem, *Brassica*, group 5-16	--	12	*Vegetable, head and stem, Brassica, group 5-16*[1] Crop group conversion from parts of crop subgroup 5A to crop group 5-16. 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[2]. Data support a maximum use rate of 2 applications at 0.38 lb a.i./A with a 1-day PHI.

Table 1. Buprofezin, 40 CFR §180.511: Summary of Proposed Tolerance Actions			
Commodity	Established Tolerance (ppm)	Proposed Recommended Tolerance (ppm)	Comments
Vegetables, cucurbit, group 9	0.50	0.70	*Vegetable, cucurbit, group 9* Tolerance level has been increased to harmonize with Codex MRLs for fruiting vegetables, cucurbits commodities. The tolerance of 0.7 ppm is compatible with Canada MRLs for cucurbit vegetable commodities.
Vegetable, leaf petiole, subgroup 22B	--	35	*Vegetable, leaf petiole, subgroup 22B*[1] Crop group conversion from parts of crop group 4 to subgroup 22B. 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 a.i./A with a 7-day PHI.
Vegetable, leafy, except Brassica, group 4, except head lettuce and radicchio	35	Remove	Crop group conversion/revision[1]

1 These recommended conversions of existing tolerances in/on crop subgroup 5A, crop subgroup 5B, and crop group 4 to crop group 5-16 (vegetable, brassica, head and stem), crop subgroup 4-16A (leafy greens), crop subgroup 4-16B (leafy greens, *Brassica*), crop subgroup 22B (vegetable, leaf petiole), celtuce, Florence fennel, and kohlrabi are consistent with the document entitled "Attachment - Crop Group Conversion Plan for Existing Tolerances as a Result of Creation of New Crop Groups under Phase IV (4-16, 5-16, and 22)," dated 11/3/2015 with the following exceptions: recommending the removal of existing tolerances in/on head lettuce (6.0 ppm) and radicchio (6.0 ppm) which are members of crop subgroup 4-16A (leafy greens) for harmonization with Canadian MRLs in/on these commodities and (2) removal of the exception for head lettuce and radicchio from the new leafy greens, subgroup 4-16A (35 ppm) tolerance. EPA is proposing requiring labeled use directions for celtuce and Florence fennel be consistent with crop subgroup 22B and that labeled use directions for kohlrabi be consistent with crop group 5-16.

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 in the OECD calculator, which resulted in a **4.0 ppm** tolerance value for orange. The orange tolerance value of 2.5 ppm (D296492, 12/17/2003, T. Bloem, 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 There are no U.S. registrations.

4. Human Health Data Needs

The registrant submitted dislodgeable foliar residue data to facilitate exposure assessment refinements. This fulfilled remaining data requirements under 40 CFR; therefore, there are no additional human health data needed for buprofezin at this time.

B. Ecological Risks

A summary of the agency's ecological risk assessment is presented below. The EPA used the most current science policies and risk assessment methodologies to prepare a risk assessment in support of the registration review of buprofezin. For additional details on the ecological assessment for buprofezin, see the *Preliminary Ecological Risk Assessment for the Registration Review of Buprofezin*, which is available in the public docket.

The EPA is currently working with its federal partners and other stakeholders to implement an interim approach for assessing potential risk to listed species and their designated critical habitats. Once the scientific methods necessary to complete risk assessments for listed species and their designated critical habitats are finalized, the agency will complete its endangered species assessment for buprofezin. See Appendix C for more details. As such, potential risks for non-listed species only are described below.

1. Risk Summary and Characterization

Terrestrial Risks

Mammals

There are no acute risks of concern for mammals; acute risk quotient (RQ) values range from <0.01 to 0.18 (LOC = 0.5). Using upper-bound estimated environmental concentration (EEC) values resulted in a chronic dietary-based RQ range of 0.08 to 6.9 and a dose-based range of 0.3 to 57.3 and are above the LOC (1). Using mean EEC values, chronic dietary-based RQs ranged from to 0.04 to 2.4; chronic dose-based RQs ranged from 0.2 to 20.3. The highest RQs were calculated from uses with the higher labeled application rates (*e.g.*, coffee and fruit trees) for mammals across all dietary items and mammal sizes; the highest exposure is to small mammals feeding on short grass.

RQs listed above are based on the NOAEC value of 100 mg/kg-diet from the study; when considering the LOAEC (lowest observed adverse effects concentration) of 1000 mg/kg-diet, the RQs are reduced by 10-fold. The endpoint for the LOAEC was based on significantly decreased pup weights (12%) at 5 weeks into the 2-generation rat reproduction study. No treatment related mortality was observed at this concentration and by the end of the study (26 weeks), reduced pup weight was 4% lower than controls, but no longer statistically significant. Greatest RQ exceedances were for fruits, including citrus, pome, stone, tropical and minor crops, and for coffee.

When assessing the potential for risk off-site (from the edge of the treated field) from exposure to residues on non-target plants, using the upper bound Kenaga values and the NOAEC, the off-site risks to mammals ranged up to 262 feet from the edge of the field for aerial applications. However, when using the LOAEC, the distance off-site is predicted to be no more than 23 feet from the edge of field.

In addition to the study used for RQ calculations, other mammalian studies were reviewed for effects in the range of concentrations of the NOAEC and LOAEC. Other studies generally had NOAEC values in the range of the LOAEC from this study. Given the lack of effects observed in other studies, the wide dose-spacing between the NOAEC and the LOAEC, the lack of mortality as well as the noted recovery for the reduced pup weight observed in the study, as well as the predicted distance from the edge of field when using the LOAEC, risks to mammals from use of buprofezin are anticipated to be relatively low.

Birds, Reptiles, and Terrestrial-Phase Amphibians

Acute toxicity studies for birds did not yield definitive acute toxicity endpoints; therefore, no acute risk quotients could be determined for birds, reptiles, terrestrial-phase amphibians, and the species for which they are surrogates. Risks are not anticipated based on highest acute test concentrations being greater than peak EECs.

Potential chronic risks of concern were identified for birds with dietary-based RQs from 0.02 – 1.37 (LOC = 1.0). RQs exceeded the LOC for uses with higher application rates, including on most fruit trees with the highest RQs for pears and coffee. Chronic dietary RQs based on mean EEC values ranged from 0.01 to 0.49 and are below the LOC. The most sensitive chronic endpoints (LOAEC) were based on avian reproductive effects, including eggshell thickness (5% decrease) and 14-day chick weights (10% decrease) at 2000 mg/kg-diet; no mortality or effects on survival were observed in the study. Then considering the LOAEC value, RQs are below the LOC, therefore, risks to birds are expected to be low.

Invertebrates (honeybees)

Acute and chronic adult honey bee studies for buprofezin resulted in non-definitive endpoints with the LD_{50} determined to be greater than 88 μg a.i./bee. Using these non-definitive values as a screen, RQs are predicted to not exceed the LOC. However, buprofezin's toxic mechanism of action, as a chitin biosynthesis inhibitor, is likely to be much greater to eggs of exposed adults and later larval stages of development when chitin formation occurs. While the extent of potential risk to pollinators (*e.g.*, honey bees), relative to predicted exposure concentrations, could not be assessed due to the lack of a chronic honey bee larval toxicity study, open literature studies demonstrate adverse reproductive effects to other bees (bumble) and other terrestrial invertebrates. Buprofezin has a number of uses, including those in highly attractive crop groups for bees (almonds, citrus and various fruit trees), that could lead to exposures during sensitive life stages, depending on timing of application. Being an insect growth regulator, risks are expected to terrestrial invertebrates.

Additional data may be necessary to fully evaluate risks to non-target terrestrial invertebrates, especially pollinators. Although the EPA identified the need for certain data to evaluate potential effects to pollinators when initially scoping the registration review for buprofezin, the problem formulation and registration review DCI for buprofezin, were both issued prior to the EPA's

issuance of the June 2014 *Guidance for Assessing Pesticide Risks to Bees*[1]. This 2014 guidance lists additional pollinator studies that were not included in the buprofezin registration review DCI. Therefore, the EPA is currently determining whether additional pollinator data are needed for buprofezin. If the agency determines that additional pollinator exposure and effects data are necessary to help make a final registration review decision for buprofezin, then the EPA will issue a DCI to obtain these data. The pollinator studies that could be required for buprofezin are listed in Table 2 below.

Table 2. Potential Pollinator Data Requirements for Buprofezin

Guideline #	Study
Tier 1	
850.3020	Acute contact toxicity study with adult honey bees
850.3030	Honey bee toxicity of residues on foliage
Non-Guideline (OECD 213)	Honey bee adult acute oral toxicity
Non-Guideline (OECD 237)	Honey bee larvae acute oral toxicity
Non-Guideline	Honey bee adult chronic oral toxicity
Non-Guideline	Honey bee larvae chronic oral toxicity
Tier 2†	
Non-Guideline	Field trial of residues in pollen and nectar
Non-Guideline (OECD 75) †	Semi-field testing for pollinators
Tier 3	
850.3040†	Full-Field testing for pollinators

† The need for higher tier tests for pollinators will be determined based upon the results of lower tiered tests and/or other lines of evidence and the need for a refined pollinator risk assessment.

Terrestrial Plants

There were no LOC exceedances identified for terrestrial plants. The NOAEC and EC_{25} are greater than the maximum seasonal application rate (4 lbs a.i./A for citrus and coffee). Risk to terrestrial plants are considered to be low.

Aquatic Risks

Freshwater Fish and Aquatic-Phase Amphibians

The limited solubility of buprofezin in water prevented the determination of definitive acute endpoints; therefore, acute RQs for freshwater and estuarine/marine fish could not be calculated. A conservative risk screen indicated that the highest acute test concentration tested was greater than peak predicted EECs. Acute risks are not anticipated for freshwater and estuarine/marine fish (or aquatic-phase amphibian for which freshwater fish are surrogates).

Chronic RQs for freshwater fish and the species which they represent ranged from 0.15 to 2.17 exceeding the LOC of 1.0 for stone fruit, citrus, coffee, pome fruit, and tropical fruit. For estuarine/marine fish, RQs ranged from 0.22 – 3.14 with LOC exceedances for the same uses as

[1] http://www2.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf

for freshwater fish as well as for grapes. Since the freshwater fish life cycle study was noted to have issues with high variability and did not establish a NOAEC value, the chronic estuarine/marine fish study is considered to be more reliable than the freshwater results.

For chronic effects to fish, the NOAEC (sheepshead minnow) was based on a 3% change in mean length by the end of the study. For the most sensitive endpoints in this study, all statistically significant observed effects on growth that occurred within the range of corresponding EECs were associated with a 5% or less change in length as compared to controls. More significant effects, such as an 11% decrease in female weight and 25% increase in time until eggs hatched, were reported at higher concentrations outside the range of relevant predicted EECs. Overall, risks to freshwater and estuarine/marine fish are considered low.

Freshwater and Estuarine/marine Invertebrates

Acute toxicity testing demonstrates that buprofezin is not acutely toxic to aquatic invertebrates at the solubility limit. Given that acute endpoints for saltwater invertebrates are non-definitive and that the predicted environmental concentrations are below the highest test concentrations, acute risks are considered low.

No chronic RQs exceeded the levels of concern for freshwater invertebrates; chronic RQs ranged from 0.03 – 0.32 (LOC = 1). Therefore, chronic risk to freshwater invertebrates from exposure to buprofezin is not expected.

Based on the NOAEC, chronic RQs exceeded the LOC of 1 for saltwater invertebrates for the highest application rates (*i.e.*, pome and stone fruit uses) with RQs ranging up to 1.33. The chronic endpoint was based on a 5% decrease in male body length. The observed effects at the LOAEC of 30 μg a.i./L are higher than the highest 21-day EEC of 25.2 mg a.i./L associated with pome fruit use, suggesting that potential risk may be lower than estimated. RQs for benthic invertebrates ranged from 0.01 to 0.99 with no use sites exceeding the LOC.

Aquatic Vascular and Non-Vascular Plants

RQs did not exceed the LOC for aquatic plants. Therefore, risks to aquatic plants are considered low.

2. Ecological Incidents

The search reflects reported incidents since its registration and includes any reports in the database as of May 2017, including a review of the agency's Incident Data System (IDS). All four of the reported incidents involved effects to honey bees following the reported application of a buprofezin-containing product. The four reported incidents were classified as "possible," but is difficult to discern as multiple pesticides, Protocol® and Tourismo®, with multiple active ingredients were applied to almond trees during bloom while bees were foraging. It is also possible that these reports represent the same incident based on the timing and description of the incidents. Based on available data, there does not seem to be a concern identified with available reported incidents at this time, and reporting will continue to be monitored. For additional

information, please see the *Preliminary Ecological Risk Assessment for the Registration Review of Buprofezin.*

3. Ecological and Environmental Fate Data Needs

There are no data gaps for the environmental fate studies. The adult contact, adult dietary, and acute larval studies do not capture the most likely and anticipated sensitive life stage given the mode of action for buprofezin: inhibition of chitin formation. These effects would likely be observed in a chronic honey bee larval toxicity study. With only limited data available to assess the potential toxicity of buprofezin to bees, the risk to terrestrial invertebrates is considered uncertain. The EPA will consider issuing a DCI to obtain pollinator data as a separate action.

C. Benefits Assessment

Buprofezin controls insects by interrupting the growth and development of the larval stages by inhibiting chitin biosynthesis. It also suppresses oviposition of adult insects and reduces the viability of insect eggs. As the only chitin-inhibiting insecticide, and the only insecticide listed in IRAC group 16, buprofezin offers a valuable tool for integrated pest management (IPM) programs and resistance management programs.

Buprofezin offers control of multiple homopteran pests (cicada, whitefly, aphids, scale and psylla) which are some of the most commonly found pests across agricultural production. Some production systems benefit from the selective spectrum of activity offered by buprofezin. In certain production systems, such as for tropical fruits (banana, coffee, pomegranate), growers may rely on biological controls to suppress pest populations most of the year, however in critical periods of production an insecticide application may be needed. The spectrum of activity offered by buprofezin allows for its use to control unwanted insect pests at these key periods in production, while not destroying the naturally occurring populations of predatory and parasitic beneficial insects present in the field.

The initial use of insect growth regulators, such as buprofezin, in the mid-1990's allowed for successful resistance management programs in crops where insecticide resistance (*e.g.*, OPs, carbamates, and pyrethroids) had become a problem (*e.g.*, whiteflies in cotton and pear psylla in pears). Buprofezin is a key control option and rotational partner for growers managing sweet potato whiteflies in cotton. Since the introduction of B-biotype whitefly in the 1980's and more recently the Q-biotype whitefly, growers have been continually battling to maintain the efficacy of all available alternatives to manage these ongoing case studies on insecticidal resistance. Pear psylla are commonly associated with huge yield losses in pear production caused by both their damage and their effect on the harvestability of the crop. Pear psylla can require intensive management and reduced susceptibility to multiple classes of insecticides has been documented.

Buprofezin offers high benefits to certain crops such as cotton, grapes, pears, and pistachios for control of key pests within those production systems. In grapes, buprofezin is typically used to target mealybugs. Although susceptibility to mealybugs is variable by grape variety, all species of mealybugs can transmit grape viruses such as leafroll and corky bark, which can result in vine dieback and yield loss. Additionally, buprofezin is the top control option for Gill's mealybugs in

pistachios. This pest can directly damage pistachios by reducing nut size, and potentially cracking the hull of the nut leading to dried nuts. Compounding the issue dried nut hulls promote other pests by providing over wintering habitat (*e.g.*, navel orangeworm). Banana, citrus, coffee, pomegranate, and olive growers use buprofezin to manage scales and psyllids, which are key pests in these systems.

IV. PROPOSED INTERIM REGISTRATION REVIEW DECISION

A. Proposed Risk Mitigation and Regulatory Rationale

The agency has reviewed the uses, risks, and benefits of buprofezin. As discussed in Section III of this document, the EPA identified potential risks from non-occupational spray drift and potential risks to occupational handlers and to several of the ecological taxa assessed.

As discussed in Section III.A of this PID, non-occupational spray drift risks of concern resulted from aerial and ground applications. The EPA is proposing spray drift mitigation, including droplet size, to mitigate these risks. These measures are expected to mitigate some ecological risks of concern as well. Occupational risks of concern were identified with use of backpack sprayers, mechanically-pressurized handguns, fogging equipment, and for mixers and loaders for aerial application(s). The EPA is proposing additional PPE for certain scenarios and restricting selected application methods and uses. To mitigate post-application risks of concern identified in the human health risk assessment, the EPA is extending the REI for select activities and use sites.

The agency has discussed the proposed label changes with the registrant, Nichino. Nichino is in agreement with most of the proposed changes and provided additional information to help characterize the potential risks. Nichino stated that the water-soluble packet formulation is currently not commercialized; therefore, the registrant has agreed to remove aerial application and MPH application methods from that label. The registrant also agreed to remove fogging equipment application methods on orchard/vineyard uses and to remove the application of soluble concentrates to orchards/vineyards via MPH. Regarding proposed mitigation for REIs, Nichino was in favor of limiting the extension of REIs for selected activities for certain uses. Through this proposed interim decision, the agency is seeking comments on all of the proposed mitigation and information to help characterize and/or refine the potential risks identified.

1. Increased Droplet Size for Aerial Application

Potential non-occupational spray drift risks were identified for children from aerial applications of buprofezin to orchards and vineyards. The agency is proposing to require coarse or coarser droplet sizes for aerial applications as spray drift mitigation to address these concerns. Aerial applications of buprofezin to orchards or vineyards are not common, so low impacts are expected for these proposed changes.

2. Application Method Restrictions

To address risks of concern to mixers, loaders, and applicators resulting from specific applications methods, the EPA is proposing the following mitigation measures:

- Prohibit aerial application of water soluble packet (WSP) formulations to orchards/vineyards;
- Prohibit mechanically-pressurized handgun (MPH) application of soluble concentrates and WSP formulations for application to orchards/vineyards and typical field crops.
- Prohibit fogging applications for water-soluble packets and dry flowable formulations; and
- Limit fogging application of soluble concentrate to greenhouse uses only (tomatoes and nursery ornamentals).

Per correspondence with the registrant, WSP formulations are currently not commercialized and they have agreed to remove several application methods from the WSP formulations including aerial application to orchards and vineyards and mechanically-pressurized handguns. As such, the agency is proposing to prohibit aerial application of WSP formulations to orchard/vineyards. Since, aerial applications of buprofezin to orchards and vineyards are not common, and the WSP formulation is not commercialized so no impacts are expected from prohibiting these uses.

The use of MPHs is common for spot or perimeter treatments, but they are generally regarded as not suitable for general field use due to efficiency issues such as time and labor costs and issues with ensuring complete coverage relative to other types of application equipment (*i.e.,* boom sprayer or airblast). The agency data on spot treatments suggests that there have not been any buprofezin spot treatments in recent years. Nichino has also stated that handheld application methods (*i.e.,* backpack sprayer and MPH) are not applicable to its uses. However, they requested that these application methods be retained for some formulations as their supplemental distributor markets to greenhouse growers who typically use handheld application methods. Given the current understanding of these uses, the agency is proposing to prohibit mechanically-pressurized handgun (MPH) application of soluble concentrates and WSP formulations for application to orchards/vineyards and typical field crops. The agency expects limited impacts on growers from the prohibition of buprofezin applications by MPHs of certain formulations in orchards, vineyards and typical field crops.

The agency does not have quantitative data on how often fogging applications, MPHs, or backpacks are used to apply buprofezin. Fogging is typically used in greenhouse production for post-harvest applications. Fogging is not a recommended application method for orchard, vineyards or field production scenarios, as it works most favorably when performed in enclosed spaces. Moreover, issues with drift and canopy penetration in the outdoor environment make fogging a prohibitive application method for orchards, vineyards and field crops alike. As such, the agency is proposing to limit fogging application of soluble concentrate to greenhouse uses only (tomatoes and nursery ornamentals) and to prohibit fogging applications for water-soluble packets and dry flowable formulations. For these reasons, the limitations and prohibitions on fogging applications are not expected to impact growers.

3. Personal Protective Equipment

The EPA is proposing requiring additional personal protective equipment for several uses and application methods to reduce dermal and inhalation exposure to occupational handlers while mixing, loading, and/or applying buprofezin.

There is currently no data available to assess dermal risks to applicators from fogging applications. Results of acute dermal toxicity studies (MRID 46213301 indicate that buprofezin is classified as Toxicity Category IV for dermal toxicity. However, since the risks from this application method are uncertain, the agency is proposing to limit applications by fogging equipment to greenhouse uses only with additional PPE will also mitigate exposure to occupational handlers. The EPA is also proposing limiting backpack sprayer applications to greenhouse uses only with additional PPE. Use of additional PPE for mixers and loaders for aerial application of soluble concentrates for orchards and vineyards as well as additional PPE for applicators during airblast applications will increase MOEs for these methods to levels above the LOC.

MOEs for handlers applying dry flowable formulations via backpack sprayers were below the LOC of 300. Use of coveralls and gloves increased MOEs to 320. No major impacts are expected from restricting backpack application of dry flowable formulation to greenhouses only with additional use of PPE, double layer (coveralls) and chemical-resistant gloves.

No risks of concern were found with application of soluble concentrates with baseline PPE. MOEs for the application of dry flowables with MPHs ranged from 68 to 170 with double layer PPE (coveralls) and gloves. Application of soluble concentrate formulations to orchards/ vineyards via MPH resulted in MOEs of 68 with double layer PPE and gloves. Airblast applications to orchards and vineyards resulted in dermal MOEs of 49 – 54 with baseline and double layer PPE. Use of gloves and chemical resistant hat (headgear) with baseline PPE increased MOEs to 400 and engineering controls (enclosed cab) resulted in MOEs of 5,900. The water-soluble packet formulation is currently not commercialized, according to the registrant.

To address potential combined risks to occupational handlers, the agency is proposing the following:

- Occupational handlers applying buprofezin via fogging equipment must wear, in addition to baseline attire, double layer (coveralls), an elastomeric half-mask respirator, and chemical-resistant gloves.

- Restrict backpack application of dry flowable formulation to greenhouses only with additional use of PPE, double layer (coveralls) and chemical-resistant gloves.

- Occupational handlers applying buprofezin via airblast equipment must wear, in addition to baseline attire, chemical resistant gloves and a chemical resistant hat or apply buprofezin using an enclosed cab.

- Occupational handlers must wear chemical resistant gloves and a double layer of PPE (coveralls over long pants and long-sleeved shirts) during the following scenarios:

    - Mixing, loading, applying soluble concentrate formulations for mechanically-pressurized handgun applications (for use in greenhouses only);

    - Mixing, loading, applying dry flowable formulations by backpack application (for use in greenhouses only); and

    - Mixing and loading soluble concentrates for aerial application.

The EPA is proposing use of engineering controls for occupational workers mixing and loading dry flowable formulations for aerial application to orchards and vineyards to reduce potential risk to workers associated with these tasks (MOE = 260). The agency has determined that the benefits of buprofezin use for pears is high and aerial application is still a needed application method.

For risks to handlers resulting from fogging applications of soluble concentrates, the agency is proposing mitigation for label consistency and to reduce inhalation risks identified with these application methods. In addition, the EPA is proposing that fogging equipment applications (handheld and portable equipment) be limited to greenhouse uses only. Current labels do not require a respirator for any registered products containing buprofezin. Inhalation MOEs without a respirator during fogging equipment applications are 39. The EPA is proposing the use of an elastomeric half mask respirator which will increase inhalation MOEs to 390 for fogging equipment applications of soluble concentrates in greenhouses.

To mitigate potential inhalation risk to occupational handlers, the agency is proposing requiring a respirator and, for pesticides covered by the Worker Protection Standard[2] (WPS), the associated fit test, training, and medical evaluation for the following:

- Mixing, loading, and applying soluble concentrates for fogging equipment applications (for use in greenhouses only).

The EPA has recently required fit testing, training, and medical evaluations[3] for all handlers who are required to wear respirators and whose work falls within the scope of the WPS.[4] If a buprofezin handler currently does not have a respirator, an additional cost will be incurred by the handler or the handler's employer, which includes the cost of the respirator plus, for WPS-covered products, the cost for a respirator fit test, training, and medical exam.

[2] 40 CFR 170

[3] Fit testing, training, and medical evaluations must be conducted according to OSHA regulations 29 CFR 1910.134, 29 CFR 1910.134(k)(1)(i) through(vi), and 29 CFR 1910.134, respectively.

[4] 40 CFR 170 (see also Appendix A of chapter 10 of the Label Review Manual, https://www.epa.gov/pesticide-registration/label-review-manual)

Respirator costs are extremely variable depending upon the protection level desired, disposability, comfort, and the kinds of vapors and particulates being filtered. Based on available information that the EPA has, the average cost of a disposable particulate filtering face-piece respirator) is about $5 and an elastomeric half mask respirator is $35, with their replacement cartridges averaging around $19[5]. Given this information, the average cost of a particulate filtering facepiece respirator is assumed to be lower than the average cost of an elastomeric half mask respirator. The estimated cost of a respirator fit test, training and medical exam is about $180 annually.[6] The impact of the proposed respirator requirement is likely to be substantially lower for a buprofezin handler who is already using a respirator because the handler or handler's employer uses other chemicals requiring a respirator in the production system or as part of the business (*i.e.*, the handler or employer will only incur the cost of purchasing filters for the respirator on a more frequent basis). Respirator fit tests are currently required by the Occupational Safety and Health Administration (OSHA) for other occupational settings to ensure proper protection.[7]

The EPA acknowledges that requiring a respirator and the associated fit testing, training, and medical evaluation places a burden on handlers or employers. However, the proper fit and use of respirators is essential to accomplish the protections respirators are intended to provide. In estimating the inhalation risks, and the risk reduction associated with different respirators, the EPA's human health risk assessments assume National Institute for Occupational Safety and Health (NIOSH) protection factors (*i.e.*, respirators are used according to OSHA's standards). If the respirator does not fit properly, use of buprofezin may cause unreasonable adverse effects on the pesticide handler.

4. Crop Group and Use Pattern Clarifications

In light of the proposed tolerance revisions and differences in use rates and patterns, the EPA is proposing to amend the use sites on labels to conform to the updated crops, crop subgroups, and crop groups listed in Section III.A.3. For crop group 5-16 and crop subgroups 4-16A, 4-16B, and 22B, data support a maximum use rate of 2 applications at 0.38 lb a.i./A with PHIs of 1-day, 7-days, 1-day, and 7-days, respectively. Further, the EPA is proposing to amend labels to ensure that labeled use rates and patterns for celtuce and Florence fennel are consistent with those for crop subgroup 22B (2 applications at 0.38 lb a.i./A with a 7-day PHI) and labeled use rates and patterns for kohlrabi are consistent with those for crop group 5-16 (2 applications at 0.38 lb a.i./A with a 1-day PHI).

Two of the registered labels (EPA Reg. Nos. 71711-15 and 71711-21) do not specify the exact use pattern intended for fogging equipment. The EPA is proposing that product labels include clarifying language that indicates that fogging equipment is restricted to greenhouse applications

[5] Gempler's. 2016. Commercial-Grade Outdoor Work Gear Online Catalogue. Accessed online on August 26, 2016, at http://www.gemplers.com/respirators

[6] Economic Analysis of the Agricultural Worker Protection Standard Revisions. Biological and Economic Analysis Division, Office of Pesticide Programs, U.S. EPA. 2015. p. 205. Available at www.regulations.gov, docket number EPA-HQ-OPP-2011-0184-2522

[7] 29 CFR § 1910.134

only, and also provide an application rate specifically for fogging equipment with a rate in units of lb a.i./ft^3, or equivalent units.

Since the potential risks to applicators from fogging applications are uncertain, the EPA is proposing the following label language to reduce exposure to workers: "To avoid contact with the treated area, begin by spraying area of greenhouse furthest from the entrance/exit walking backwards as the fog/spray is applied. Finish application at the entrance/exit of the greenhouse."

5. Re-entry Interval

Short-term dermal occupational post-application risk estimates were of concern for apple (pome fruit), nectarine (stone fruit), grapes, cotton, nursery ornamentals, olives, and pears for up to eight days. The current label prescribes a restricted entry interval (REI) of 12 hours. MOEs for hand-thinning fruit for apples and nectarines did not reach the agency's LOC until six days following application (MOE = 330). MOEs for hand thinning olives, pears and Asian pears did not reach the LOC until Day 8. Nichino indicated that the majority of thinning is done by chemical or mechanical means. Therefore, to reduce worker exposure to buprofezin residues, the EPA is proposing to extend the REI for apples (pome fruit) and nectarines (stone fruit) until Day 6 and until Day 8 olives, pears, and Asian pears for hand-thinning activities only.

For pears, pome fruit, and stone fruit, the impacts are expected to be low from an increase in the REI due to a wide window, usually a few weeks, during which thinning typically occurs in these fruits. However, if a grower wanted to engage in scouting to see if the application was effective, then they may have to wait longer than desired. The agency does not have enough data to determine what the impacts would be for olives from the increase in REIs. The largest impacts on growers from the expansion of the REI from 12 hours to 6 or 8 days will come from the posting requirements that accompany any REI that is over 48 hours. The requirement to post and remove signage around the perimeter of the treated field will result in direct increases in time and labor costs associated with these activities, and will likely decrease the ease of use buprofezin currently offers to growers.

Hand-set irrigation for nursery ornamentals resulted in MOEs of 280 on Day 0; MOEs were 330 at one day post-application. Although Nichino has stated that hand-setting irrigation is not applicable due to the "permanent structures" used for irrigation, modification or manipulation of irrigation components following application cannot be precluded. The EPA is proposing extending the REI for hand-set irrigation of nursery ornamentals from 12 hours to 24 hours to address these potential risks of concern.

For ornamentals the increases in REI from 12 hours to 24 hours is expected to have minimal impacts. Although there is a wide range of potential activities that may need to be carried out in a given ornamental production system, as long as plants are properly irrigated the agency expects limited impacts from an additional 12-hour delay in those activities from current label restrictions.

For grapes where buprofezin is applied at a rate of 1.05 lbs a.i./A in California and Arizona, MOEs for tying/training, hand-harvesting, and leaf pulling resulted in initial MOEs of 130 with

MOEs of 310 on Day 6. For grapes where buprofezin is applied at a rate of 0.53 lbs a.i./A, MOEs reached 300 on Day 1. According to the *Buprofezin Benefits Information for Registration Review Proposed Interim* Decision, nearly all applications for grapes are conducted at 0.53 lbs a.i./A or lower. The PHI of 7 days (30 days in California and Arizona) is protective of occupational handlers for hand-harvesting activities. Therefore, the EPA is proposing an REI of 6 days for tying/training of vines and hand-pulling leaves in grapes for the higher rate applied in California and Arizona (1.05 lbs a.i./A) and an REI of 24 hours for tying/training and leaf pulling for the lower rate of 0.53 lbs a.i./A.

An increase in REI could have impacts for some grape growers, mainly in two ways. Impacts could occur when certain activities such as hand thinning, leaf-pulling and vine training need to be carried out at a crop stage that overlaps with the timing for buprofezin applications. Data shows that buprofezin usage may coincide with thinning activities in grapes, the agency is uncertain what impact the expanded REI may have as some growers may thin using a chemical thinning agent, while others may thin by hand. There is also uncertainty as to the frequency for which chemical thinning must be followed up by hand thinning in grape production. Given the timing at which thinning may occur (over the course of 1-2 months) the expanded REI for grapes to 6 days is expected to have minimal impacts arising from delays in carrying out other infield activities. The greatest impacts on growers from the expansion of the REI from 12 hours to 6 days will come from the posting requirements that accompanies any REI that is over 48 hours. The requirement to post and remove signage around the perimeter of the treated field will result in direct increases in time and labor costs for these activities to take place and will likely decrease the ease of use buprofezin currently offers to growers.

In addition, extending the REI to 6 days for tying/training vines and hand-pulling leaves for grapes increase MOEs to above the LOC of 300. The current post-harvest interval (PHI) for grapes in California and Arizona is 30 days. This is protective of occupational workers harvesting grapes by hand following buprofezin application as the PHI is greater than the REI.

The PHI for cotton is 14 days. The MOEs for cotton reach 300 two days following application for harvesting (mechanically, tramper); therefore, the PHI is considered protective of occupational workers mechanically harvesting cotton with a mechanical tramper. Hand-setting irrigation in nursery ornamentals resulted in post-application MOEs of 280. Hand-setting irrigation is typically used for greenhouse and nursery operations and is not typically used for field crops.

6. Spray Drift Reduction

The EPA is proposing label changes to reduce off-target spray drift and establish a baseline level of protection against spray drift that is consistent across all buprofezin products. Reducing spray drift will reduce the extent of environmental exposure and risk to non-target plants and animals. Although the agency is not making a complete endangered species finding at this time, these label changes are expected to reduce the extent of exposure and may reduce risk to listed species whose range and/or critical habitat co-occur with the use of buprofezin.

The agency is proposing the following spray drift mitigation language to be included on all buprofezin product labels for products applied by liquid spray application. The proposed spray

drift language is intended to be mandatory, enforceable statements and supersede any existing language already on product labels (either advisory or mandatory) covering the same topics. The agency is providing recommendations which allow buprofezin registrants to standardize all advisory language on buprofezin product labels. Registrants must ensure that any existing advisory language left on labels does not contradict or modify the new mandatory spray drift statements proposed in this proposed interim decision once effective.

- For aerial applications, the distance of the outer most nozzles on the boom must not exceed 75% of the length of the wingspan or 90% of the rotor diameter. To further reduce drift, use one half of the length of the wingspan or rotor diameter at the edge of the field.
- Applicators must only spray when wind speed is 10 miles per hour or less.
- Applicators must not spray during temperature inversions.
- For aerial applications, the release height must be no higher than 10 feet from the top of the crop canopy or ground, unless a greater application height is required for pilot safety.
- For ground boom applications, apply with the release height no more than 4 feet above the ground or crop canopy. For all other ground applications, the release must be no more than 4 feet from the target vegetation.
- For aerial application, applicators must use one-half swath displacement upwind at the downwind edged of the field.
- For ground and aerial applications, select nozzle and pressure that deliver Coarse or coarser droplets as indicated in nozzle manufacturer's catalogues and in accordance with American Society of Agricultural & Biological Engineers Standard 572.1.
- For airblast applications, nozzles directed out of the orchard must be turned off in the outer row.
- For airblast applications, applications must be directed into the canopy foliage.

The agency does not know how efficacy may be impacted when droplet size increases are required for various insecticides. This is a concern where there is a dense canopy (*e.g.,* cotton) and finer droplets are required to penetrate the canopy where the target pests reside (*e.g.,* whiteflies). The dependency of one route of exposure versus another is variable by target pest and in some cases the target stage of development of that pest. These restrictions may also impact pre-mix or tank mix partners with less systemic chemical profiles or chemical adjuvants which may be rendered ineffective when applied at a larger droplet size. The droplet size restrictions proposed to reduce exposure must be balanced with the agency's effort to combat the evolution of insecticidal resistance.

The EPA expects limited impacts from most of the proposed mandatory spray drift language such as release heights, nozzle directions, etc. However, the requirement of a minimum spray droplet size of medium or coarser for ground applications is an area of uncertainty regarding potential impacts. The agency is uncertain how droplet size may impact efficacy or resistance management. The agency, therefore, encourages comments on any potential impacts to growers of requiring a minimum droplet size of coarse or coarser for ground applications.

In addition to including the following spray drift restrictions on buprofezin labels, all references to volumetric mean diameter (VMD) information for spray droplets are proposed to be removed

from all buprofezin labels where such information currently appears. The proposed new language above, which cites ASABE S572.1, eliminates the need for VMD information.

7. Insecticide Resistance Management

Pesticide resistance may occur when genetic or behavioral changes enable a portion of plant pest populations (such as bacteria, fungi, insects or other organisms) to tolerate or survive what would otherwise be lethal doses of a pesticide. The surviving pest populations increase with continued exposure to a no longer effective pesticide. Resistance to pesticides by plant pest appears to be increasing in the U.S. and worldwide. Managing the evolution of pesticide resistance in plant pests is an important part of sustainable pest management and an integral part of IPM programs, to assist crop producers to manage plant pests effectively.

The development of pesticide resistance is influenced by a number of factors. One important factor that fosters pesticide resistance is the repeated use of pesticides with the same mode of action on the same pest population. Repeated use of a pesticide with a single mode of action kills sensitive pests but allows pests in the population that are tolerant of the pesticide to increase in numbers. These individuals will generally be unaffected by the repeated pesticide applications and may ultimately make-up a substantial portion of the pest population. Thus, an important proactive pesticide resistance-management strategy is to rotate pesticides with different modes of action to increase the likelihood of controlling target pests in any given location or area. This approach may delay and/or prevent the development of resistance to a particular mode of action without resorting to increased rates and frequency of application and may prolong the useful life of pesticides. The EPA is proposing resistance-management labeling, as listed in Appendix B, for products containing the insecticide, buprofezin, in order to provide pesticide users with easy access to important information to help maintain the effectiveness of useful pesticides. Additional information on the EPA's guidance for resistance management can be found at the following website: https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year.

B. Tolerance Actions

The buprofezin tolerance expressions established in 40 CFR §180.511 will be updated to incorporate newly revised crop group definitions and to harmonize with Canadian MRLs. Refer to Section III.A.3 for details.

C. Proposed Interim Registration Review Decision

In accordance with 40 CFR sections 155.56 and 155.58, the agency is issuing this Proposed Interim Registration Review Decision. Except for the Endocrine Disruptor Screening Program (EDSP), the Endangered Species Act (ESA), and pollinator components of this case, the agency has made the following Proposed Interim Registration Review Decision: (1) no additional data are required at this time; and (2) changes to the affected registrations or their labeling are needed at this time, as described in Sections IV. A. and Appendices A and B.

In this proposed interim registration review decision, the EPA is making no human health or environmental safety findings associated with the EDSP screening of buprofezin, nor is it

making a complete endangered species finding or a complete assessment of effects to pollinators. Although the agency is not making a complete endangered species finding at this time, the proposed mitigation described in this document is expected to reduce the extent of environmental exposure and may reduce risk to listed species whose range and/or critical habitat co-occur with the use of buprofezin. The agency's final registration review decision for buprofezin will be dependent upon the result of the agency's ESA assessment and any needed Section 7 consultation with the Services, an EDSP FFDCA section 408(p) determination, and an assessment of non-target exposure to pollinators (bees).

D. Data Requirements

No additional data are anticipated to be needed to be called-in for this chemical at this time. The EPA will consider requiring submission of the pollinator data as a separate action.

V. NEXT STEPS AND TIMELINE

A. Proposed Interim Registration Review Decision

A Federal Register Notice will announce the availability of this proposed interim registration review decision for buprofezin and will allow a 60-day comment period on the proposed interim decision. If there are no significant comments or additional information submitted to the docket during the comment period that leads the agency to change its proposed interim decision, the EPA may issue an interim registration review decision for buprofezin. However, a final decision for buprofezin may be issued without the agency having previously issued an interim decision. A final decision on the buprofezin registration review case will occur after: (1) an EDSP FFDCA section 408(p) determination, (2) an endangered species determination under the ESA and any needed Section 7 consultation with the Services, and (3) an assessment of non-target exposure to pollinators.

B. Implementation of Mitigation Measures

Once the Interim Registration Review Decision is issued, the buprofezin registrants must submit amended labels that include the label changes described in Appendix B. The revised labels must be submitted to the agency for review within 60 days following issuance of the Interim Registration Review Decision.

Appendix A: Summary of Proposed Actions for Buprofezin

Registration Review Case#: 7462 PC Code: 275100 Chemical Type: Insecticide Mechanism of Action/Chemical Family: Chitin biosynthesis inhibitor					
Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions
Bystander, Infants and Children (1 to <2 years old; non-occupational spray drift exposure)	Residues and soil	Dermal Ingestion	Acute	Acute Toxicity	Require coarse or coarser droplet sizes and 10-foot buffer if using medium droplet size. Limit application when wind speed is 10 mph or less.
Occupational handlers (mixers/loaders/applicators): Using MPH for WSP, SC, and DF formulations	Residues	Dermal Inhalation	Acute	Acute Toxicity	Prohibit application of the soluble concentrate formulation for application to orchards/vineyards and typical field crops and water-soluble packets via mechanically- pressurized handgun. Prohibit application of dry flowable formulations with mechanically-pressurized handgun.
Occupational handlers (mixers/loaders/applicators): Fogging equipment applications of dry flowables and soluble concentrates to orchards and vineyards.	Residues	Dermal Inhalation	Acute	Acute Toxicity	Propose restricting fogging application of soluble concentrate to only greenhouse and requiring applicators to wear double layer PPE (coveralls), gloves, and an elastomeric half-mask respirator. Propose additional instructions to minimize exposure (i.e., application towards exits).

					Prohibit fogging application of dry flowable and WSP formulations.
Occupational handlers (mixers/loaders): For aerial application to orchards/vineyards for all formulations)	Residues	Dermal Inhalation	Acute	Acute Toxicity	Propose requiring engineering controls (enclosed system) for dry flowable formulations. Propose double layer PPE and gloves for soluble concentrate formulations. Propose prohibiting aerial application of WSP formulation in orchards/vineyards.
Occupational handlers (mixers/loaders/applicators): Backpack applications of dry flowables on: Christmas tree farms, nursery ornamentals, landscaping	Residues	Dermal Inhalation	Acute	Acute Toxicity	Propose limit backpack applications to greenhouse use only and requiring double layer of PPE and gloves. Propose prohibiting backpack applications of soluble concentrate.
Occupational handlers (mixers/loaders/applicators): Airblast applications at 2.0 lbs a.i./A to orchards and vineyards	Residues	Dermal Inhalation	Acute	Acute Toxicity	Propose requiring use of engineering controls (enclosed cab), or gloves and a chemical resistant hat.
Occupational post application (thinning fruit): Olives, Pears and Asian Pears	Residues	Dermal	Acute	Acute Toxicity	Increase re-entry interval from 12 hours to 8 days for hand thinning.
Occupational post application (thinning fruit): Pome fruit, stone fruit	Residues	Dermal	Acute	Acute Toxicity	Increase re-entry interval from 12 hours to 6 days for hand thinning.
Occupational post application (tying/training; harvesting, hand; leaf pulling): Grapes (raisin, table, juice, wine)	Residues	Dermal	Acute	Acute Toxicity	Increase re-entry interval from 12 hours to 24 hours for lower rate of 0.53 lb a.i./A for the maximum rate outside of California and Arizona. Increase REI

					to 6 days for higher rate of 1.05 lb a.i./A in California and Arizona.
Occupational post application (hand-set irrigation): Nursery ornamentals	Residues	Dermal	Acute	Acute Toxicity	Increase re-entry interval from 12 hours to 24 hours for hand-set irrigation.
Mammals	Residue	Ingestion	Chronic	Chronic Toxicity	Require spray drift reduction measures.
Birds	Residue	Ingestion	Chronic	Chronic Toxicity Reproductive Toxicity	
Estuarine/marine invertebrates	Water	Ingestion Dermal absorption	Chronic	Chronic Toxicity	
Freshwater and estuarine/marine fish	Water	Ingestion Dermal absorption	Chronic	Chronic Toxicity	
Terrestrial Invertebrates	Residue	Ingestion Contact	Acute Chronic	Acute Toxicity Chronic Toxicity (due to mode of action for buprofezin possible growth or survival effects)	

Appendix B: Proposed Labeling Changes for Buprofezin Products

<table>
<tr><th>Description</th><th>Proposed Label Language for Buprofezin Products</th><th>Placement on Label</th></tr>
<tr><td></td><td>End Use Products</td><td></td></tr>
<tr><td>Mode/Mechanism of Action Group Number</td><td>• Include the name of the ACTIVE INGREDIENT in the first column
• Include the word “GROUP” in the second column
• Include the MODE OF ACTION CODE in the third column
• Include the type of pesticide (i.e., HERBICIDE or FUNGICIDE or INSECTICIDE) in the fourth column

Example:
<table><tr><td>BUPROFEZIN</td><td>GROUP</td><td>16</td><td>INSECTICIDE</td></tr></table></td><td>Front Panel, upper right quadrant.
All text should be black, bold face and all caps on a white background, except the mode of action code, which should be white, bold face and all caps on a black background; all text and columns should be surrounded by a black rectangle.</td></tr>
<tr><td>Additional PPE-Required for all products that allow applications with airblast.
Registrants should only add PPE for the uses allowed on current labels.</td><td>“Applicators applying this product by airblast application must apply using an enclosed cab or must wear:
• Chemical-resistant gloves
• Chemical-resistant headgear, if overhead exposure”</td><td>In the Personal Protective Equipment (PPE) within the Precautionary Statements</td></tr>
<tr><td>Additional PPE-Required for all products that allow applications with backpack sprayer and mechanically-pressurized handgun.</td><td>“Applicators applying this product with a backpack sprayer must wear:
• Coveralls worn over long-sleeved shirt and long pants
• Chemical-resistant gloves
• Chemical-resistant footwear plus socks”</td><td>In the Personal Protective Equipment (PPE) within the Precautionary Statements</td></tr>
</table>

Description	Proposed Label Language for Buprofezin Products	Placement on Label
Registrants should only add PPE for the uses allowed on current labels.		
Additional PPE-Required for all products that allow aerial applications. Registrants should only add PPE for the uses allowed on current labels.	For dry flowable formulations applied to orchards and vineyards: "Mixers and loaders must use engineering controls for mixing and loading" For soluble concentrate formulations aerially applied to orchards and vineyards: "Mixers and loaders for aerial applications must wear: • Coveralls worn over long-sleeved shirt and long pants • Chemical-resistant gloves • Chemical-resistant footwear plus socks"	(PPE) within the Precautionary Statements
Additional PPE-Required for all products that allow greenhouse fogging applications Registrants should only add PPE for the uses allowed on current labels.	For soluble concentrate formulations applied by fogging to orchards and vineyards: "Mixers and loaders for fogging applications must wear: • Coveralls worn over long-sleeved shirt and long pants • Chemical-resistant gloves • Chemical-resistant footwear plus socks" "Applicators applying this product with a fogging equipment must wear: a minimum of a NIOSH-approved particulate filtering facepiece respirator with any N*, R or P filter; OR a NIOSH-approved elastomeric particulate respirator with any N*, R or P filter; OR a NIOSH-approved powered air purifying respirator with HE filters." *Drop the "N" option if there is oil in the product's formulation and/or the product is labeled for mixing with oil-containing products. [**Note to registrant:** For respiratory protection from organic vapor **and** particulates (or aerosols), use the following language:] "a minimum of a NIOSH-approved elastomeric half mask respirator with organic vapor (OV) cartridges and combination N*, R, or P filters; OR a NIOSH-approved gas mask with OV canisters; OR a NIOSH-approved powered air purifying respirator with OV cartridges and combination HE filters." [**Note to registrant:** For products requiring protection for organic vapor only, use the following language:] "a minimum of a NIOSH-approved elastomeric half mask respirator with organic vapor (OV) cartridges; OR a NIOSH-approved full-face respirator with OV cartridges; OR a gas mask with OV canisters; OR a powered air purifying respirator with OV cartridges."	In the Personal Protective Equipment (PPE) within the Precautionary Statements

Description	Proposed Label Language for Buprofezin Products	Placement on Label
	*Drop the "N" option if there is oil in the product's formulation and/or the product is labeled for mixing with oil-containing products.	
Limit of fogging application to greenhouse use only for soluble concentrate and dry flowable formulations.	For soluble concentrate and dry flowable formulations: "Fogging applications are restricted to greenhouse use only."	General Information
Additional Required Labelling Action. Applies to all products delivered via fogging applications.	Provide application rates specifically for fogging equipment with a rate in units of lbs a.i./ft^3, or equivalent units.	General Information
For all products allowing fogging applications	"To avoid contact with the treated area, begin by spraying area of greenhouse furthest from the entrance/exit walking backwards as the fog/spray is applied. Finish application at the entrance/exit of the greenhouse."	Directions for Use
Removal of application by mechanically-pressurized handgun for only WSP and dry flowable formulations	For water soluble packet and dry flowable formulations: "Do not apply this product using mechanically-pressurized handgun, backpack sprayer, or with fogging equipment."	General Information
Restriction of application by mechanically-pressurized handgun only for soluble concentrate formulations	For soluble concentrate formulations: "Do not apply this product to orchards/vineyards and typical field crops."	General Information
Removal of backpack	For water soluble packet formulations: "Do not apply this product by backpack or aerial application."	General Information

Description	Proposed Label Language for Buprofezin Products	Placement on Label
application and aerial application for only WSP		
Additional Required Labelling Action. Applies to all products delivered via liquid spray applications.	Remove information about volumetric mean diameter from all labels where such information currently appears.	Directions for Use
Enforceable Spray Drift Management Language for all products delivered via liquid spray application and allow aerial application	**"SPRAY DRIFT** **Aerial Applications**: • Do not release spray at a height greater than 10 ft above the ground or vegetative canopy, unless a greater application height is necessary for pilot safety. • Applicators are required to use a Medium or coarser droplet size (ASABE S572.1). • Applicators must use ½ swath displacement upwind at the downwind edge of the field. • Do not apply when wind speeds exceed 10 miles per hour at the application site. • The boom length must not exceed 75% of the wingspan for airplanes or 90% of the rotor blade diameter for helicopters. • Do not apply during temperature inversions."	Directions for Use, in a box titled "Spray Drift" under the heading "Aerial Applications"
Enforceable Spray Drift Management Language for products that allow airblast applications	**"SPRAY DRIFT** **Airblast applications:** • Sprays must be directed into the canopy. • Do not apply when wind speeds exceed 10 miles per hour at the application site. • User must turn off outward pointing nozzles at row ends and when spraying outer rows. • Do not apply during temperature inversions."	Directions for Use, in a box titled "Spray Drift" under the heading "Airblast Applications"
Enforceable Spray Drift Management Language for products that are applied as liquids and allow ground boom applications	**"SPRAY DRIFT** **Ground Boom Applications:** • User must only apply with the release height recommended by the manufacturer, but no more than 4 feet above the ground or crop canopy. • Applicators are required to use a medium or coarser droplet size (ASABE S572.1). • Do not apply when wind speeds exceed 10 miles per hour at the application site. • Do not apply during temperature inversions."	Directions for Use, in a box titled "Spray Drift" under the heading "Ground Boom Applications"
Enforceable Spray Drift Management Language for	**"SPRAY DRIFT** **Boomless Ground Applications:** • Applicators are required to use a medium or coarser droplet size (ASABE S572.1) for all applications.	Directions for Use, in a box titled "Spray Drift" under the heading

Description	Proposed Label Language for Buprofezin Products	Placement on Label
products that are applied as liquids and allow boom-less ground sprayer applications	• Do not apply when wind speeds exceed 10 miles per hour at the application site. • Do not apply during temperature inversions."	"Boom-less Applications"
Advisory Spray Drift Management Language for all products delivered via liquid spray application	**"SPRAY DRIFT ADVISORIES** THE APPLICATOR IS RESPONSIBLE FOR AVOIDING OFF-SITE SPRAY DRIFT. BE AWARE OF NEARBY NON-TARGET SITES AND ENVIRONMENTAL CONDITIONS. **IMPORTANCE OF DROPLET SIZE** An effective way to reduce spray drift is to apply large droplets. Use the largest droplets that provide target pest control. While applying larger droplets will reduce spray drift, the potential for drift will be greater if applications are made improperly or under unfavorable environmental conditions. **Controlling Droplet Size – Ground Boom** *(**note to registrants:** remove if ground boom is prohibited on product labels)* • Volume - Increasing the spray volume so that larger droplets are produced will reduce spray drift. Use the highest practical spray volume for the application. If a greater spray volume is needed, consider using a nozzle with a higher flow rate. • Pressure - Use the lowest spray pressure recommended for the nozzle to produce the target spray volume and droplet size. • Spray Nozzle - Use a spray nozzle that is designed for the intended application. Consider using nozzles designed to reduce drift. **Controlling Droplet Size – Aircraft** *(**note to registrants:** remove if aerial application is prohibited on product labels)* • Adjust Nozzles - Follow nozzle manufacturers' recommendations for setting up nozzles. Generally, to reduce fine droplets, nozzles should be oriented parallel with the airflow in flight. **BOOM HEIGHT – Ground Boom** *(**note to registrants:** remove if ground boom is prohibited on product labels)* For ground equipment, the boom should remain level with the crop and have minimal bounce. **RELEASE HEIGHT - Aircraft** *(**note to registrants:** remove if aerial application is prohibited on product labels)* Higher release heights increase the potential for spray drift. **SHIELDED SPRAYERS** Shielding the boom or individual nozzles can reduce spray drift. Consider using shielded sprayers. Verify that the shields are not interfering with the uniform deposition of the spray on the target area.	Directions for Use, just below the Spray Drift box, under the heading "Spray Drift Advisories"

Description	Proposed Label Language for Buprofezin Products	Placement on Label
	TEMPERATURE AND HUMIDITY When making applications in hot and dry conditions, use larger droplets to reduce effects of evaporation. **TEMPERATURE INVERSIONS** Drift potential is high during a temperature inversion. Temperature inversions are characterized by increasing temperature with altitude and are common on nights with limited cloud cover and light to no wind. The presence of an inversion can be indicated by ground fog or by the movement of smoke from a ground source or an aircraft smoke generator. Smoke that layers and moves laterally in a concentrated cloud (under low wind conditions) indicates an inversion, while smoke that moves upward and rapidly dissipates indicates good vertical air mixing. Avoid applications during temperature inversions. **WIND** Drift potential generally increases with wind speed. AVOID APPLICATIONS DURING GUSTY WIND CONDITIONS. • Applicators need to be familiar with local wind patterns and terrain that could affect spray drift."	
Advisory Spray Drift Management Language for products that are applied as liquids and allow boom-less ground sprayer applications	**"SPRAY DRIFT** **Boom-less Ground Applications:** • Setting nozzles at the lowest effective height will help to reduce the potential for spray drift."	Directions for Use, just below the Spray Drift box, under the heading "Spray Drift Advisories"
Advisory Spray Drift Management Language for all products that allow liquid applications with handheld technologies	**"SPRAY DRIFT** **Handheld Technology Applications:** • Take precautions to minimize spray drift."	Directions for Use, just below the Spray Drift box, under the heading "Spray Drift Advisories"
Adjust re-entry interval for hand thinning of apples (pome fruit) and nectarines (stone fruit)	"Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours with the following exception: Hand-thinning. The REI is 6 days for treated apples (pome fruit) and nectarines (stone fruit) when hand-thinning. PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated such as plants, soil or water is: • Coveralls over long-sleeved shirt and long pants	Agricultural Use Requirements

Description	Proposed Label Language for Buprofezin Products	Placement on Label
	• Chemical resistant (such as nitrile or butyl rubber) gloves ≥ 14 mils • Shoes plus socks."	
Adjust re-entry interval for hand thinning of olives, pears and Asian pears	"Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours with the following exception: Hand-thinning. The REI is 8 days for treated olives, pears and Asian pears when hand-thinning PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated such as plants, soil or water is: • Coveralls over long-sleeved shirt and long pants • Chemical resistant (such as nitrile or butyl rubber) gloves ≥ 14 mils • Shoes plus socks."	Agricultural Use Requirements
Adjust re-entry interval for hand-set irrigation for nursery ornamentals	"Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours with the following exception: Hand-set irrigation. The REI is 24 hours for treated nursery ornamentals when hand-set irrigating. PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated such as plants, soil or water is: • Coveralls over long-sleeved shirt and long pants • Chemical resistant (such as nitrile or butyl rubber) gloves ≥ 14 mils • Shoes plus socks."	Agricultural Use Requirements
Adjust re-entry interval for tying, training and leaf pulling grapes following application with a rate of 0.53 lbs a.i./A	"Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours with the following exception: tying/training, and leaf pulling. The REI is 24 hours for treated grapes when tying/training and leaf pulling." PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated such as plants, soil or water is: • Coveralls over long-sleeved shirt and long pants • Chemical resistant (such as nitrile or butyl rubber) gloves ≥ 14 mils • Shoes plus socks."	Agricultural Use Requirements
Adjust re-entry interval for tying, training and leaf pulling grapes following application with a rate of 1.05 lbs a.i./A in California and Arizona.	"Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of 12 hours with the following exception: tying/training, and leaf pulling. The REI is 6 days for treated grapes when tying/training and leaf pulling." PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated such as plants, soil or water is: • Coveralls over long-sleeved shirt and long pants • Chemical resistant (such as nitrile or butyl rubber) gloves ≥ 14 mils • Shoes plus socks."	Agricultural Use Requirements

Description	Proposed Label Language for Buprofezin Products	Placement on Label
Updated Respirator Language	[**Note to registrant**: If your end-use product only requires protection from particulates only (low volatility), use the following language:] "Wear a minimum of a NIOSH-approved particulate filtering facepiece respirator with any N*, R or P filter; OR a NIOSH-approved elastomeric particulate respirator with any N*, R or P filter; OR a NIOSH-approved powered air purifying respirator with HE filters." *Drop the "N" option if there is oil in the product's formulation and/or the product is labeled for mixing with oil-containing products. [**Note to registrant:** For respiratory protection from organic vapor a**nd** particulates (or aerosols), use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half mask respirator with organic vapor (OV) cartridges and combination N*, R, or P filters; OR a NIOSH-approved gas mask with OV canisters; OR a NIOSH-approved powered air purifying respirator with OV cartridges and combination HE filters." [**Note to registrant:** For products requiring protection for organic vapor only, use the following language:] "Wear a minimum of a NIOSH-approved elastomeric half mask respirator with organic vapor (OV) cartridges; OR a NIOSH-approved full face respirator with OV cartridges; OR a gas mask with OV canisters; OR a powered air purifying respirator with OV cartridges." • *Drop the "N" option if there is oil in the product's formulation and/or the product is labeled for mixing with oil-containing products.	In the Personal Protective Equipment (PPE) within the Precautionary Statements
Resistance-management labeling statements for insecticides/ acaricides	• Include resistance management label language for insecticides/acaricides from PRN 2017-1 (https://www.epa.gov/pesticide-registration/pesticide-registration-notices-year)	Directions for Use, prior to directions for specific crops.
Updated Gloves Statement	If your chemical products contain an outdated gloves statement, specify the appropriate language based on Chapter 10 of the Label Review Manual (LRM). Registrants are no longer allowed to reference category charts	In the Personal Protective Equipment (PPE) within the Precautionary Statements

Appendix C: Endangered Species Assessment

In November 2013, the EPA, along with the Services and the United States Department of Agriculture (USDA), released a summary of their joint Interim Approaches for assessing risks to endangered and threatened (listed) species from pesticides. The Interim Approaches were developed jointly by the agencies in response to the National Academy of Sciences' (NAS) recommendations and reflect a common approach to risk assessment shared by the agencies as a way of addressing scientific differences between the EPA and the Services. The NAS report[8] outlines recommendations on specific scientific and technical issues related to the development of pesticide risk assessments that EPA and the Services must conduct in connection with their obligations under the ESA and FIFRA.

The EPA received considerable public input on the Interim Approaches through stakeholder workshops and from the Pesticide Program Dialogue Committee (PPDC) and State-FIFRA Issues Research and Evaluation Group (SFIREG) meetings. As part of a phased, iterative process for developing the Interim Approaches, the agencies will also consider public comments on the Interim Approaches in connection with the development of upcoming Registration Review decisions. The details of the joint Interim Approaches are contained in the white paper *Interim Approaches for National-Level Pesticide Endangered Species Act (ESA) Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report*[9], dated November 1, 2013.

Given that the agencies are continuing to develop and work toward implementation of the Interim Approaches to assess the potential risks of pesticides to listed species and their designated critical habitat, the ecological risk assessment supporting this Proposed Interim Decision for buprofezin does not contain a complete ESA analysis that includes effects determinations for specific listed species or designated critical habitat. Although the EPA has not yet completed effects determinations for specific species or habitats, for this proposed interim decision the EPA's evaluation assumed, for all taxa of non-target wildlife and plants, that listed species and designated critical habitats may be present in the vicinity of the application of buprofezin. This assessment will allow the EPA to focus its future evaluations on the types of species where the potential for effects exists once the scientific methods being developed by the agencies have been fully vetted. Once the agencies have fully developed and implemented the scientific methodology for evaluating risks for listed species and their designated critical habitats, these methods will be applied to subsequent analyses for buprofezin as part of completing this registration review.

[8] *Assessing Risks to Endangered and Threatened Species from Pesticides.* Available at http://www.nap.edu/catalog.php?record_id=18344

[9] Available at http://www2.epa.gov/endangered-species/assessing-pesticides-under-endangered-species-act#report

Appendix D: Endocrine Disruptor Screening Program

As required by FIFRA and FFDCA, the EPA reviews numerous studies to assess potential adverse outcomes from exposure to chemicals. Collectively, these studies include acute, sub-chronic and chronic toxicity, including assessments of carcinogenicity, neurotoxicity, developmental, reproductive, and general or systemic toxicity. These studies include endpoints which may be susceptible to endocrine influence, including effects on endocrine target organ histopathology, organ weights, estrus cyclicity, sexual maturation, fertility, pregnancy rates, reproductive loss, and sex ratios in offspring. For ecological hazard assessments, the EPA evaluates acute tests and chronic studies that assess growth, developmental and reproductive effects in different taxonomic groups. As part of its most recent registration decision for buprofezin, the EPA reviewed these data and selected the most sensitive endpoints for relevant risk assessment scenarios from the existing hazard database. However, as required by FFDCA section 408(p), buprofezin is subject to the endocrine screening part of the Endocrine Disruptor Screening Program (EDSP).

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

Under FFDCA section 408(p), the agency must screen all pesticide chemicals. Between October 2009 and February 2010, the EPA issued test orders/data call-ins for the first group of 67 chemicals, which contains 58 pesticide active ingredients and 9 inert ingredients. The agency has reviewed all of the assay data received for the List 1 chemicals and the conclusions of those reviews are available in the chemical-specific public dockets. A second list of chemicals identified for EDSP screening was published on June 14, 2013[10] and includes some pesticides scheduled for Registration Review and chemicals found in water. Neither of these lists should be construed as a list of known or likely endocrine disruptors. Buprofezin is not on either list. For further information on the status of the EDSP, the policies and procedures, the lists of chemicals, future lists, the test guidelines and the Tier 1 screening battery, please visit our website.[11]

In this proposed interim decision, the EPA is making no human health or environmental safety findings associated with the EDSP screening of buprofezin. Before completing this registration review, the agency will make an EDSP FFDCA section 408(p) determination.

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