Summary of EPA Registration Review of Neonicotinoids

For consideration by the Massachusetts Pesticide Board Subcommittee

Massachusetts Department of Agricultural Resources
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1. Introduction and Background

The purpose of this document is to summarize information from EPA's latest updates on the registration review of the neonicotinoids. EPA's comprehensive review has generated a large number of documents and information on these pesticides. To facilitate the review of the relevant information for the special review of neonicotinoids by the Massachusetts Pesticide Board Subcommittee, MDAR staff has compiled the most relevant information in this document. It also provides links to the individual documents and dockets to facilitate access to the additional information.

The IEc literature review[1] included summaries of EPA's preliminary pollinator risks assessment for the various neonicotinoids.[2] Since the completion of the IEc review in December 2019, additional information on EPA's registration review has become available. In January 2020, EPA released the proposed interim decision documents (PIDs)[3] for the various neonicotinoids for public comment. The PIDs include updated information on risk assessments and proposed mitigation measures. Along with PIDs, several additional supporting documents were made available, including final bee risk assessments, updated aquatic risk assessments, responses to public comments [4], updated open literature reviews, benefits assessments, and proposed risk mitigation measures.

These updated risk assessment documents and PIDs provide information that is relevant to the special review of neonicotinoids by the Subcommittee. Therefore, a summary of and reference to information relevant to the Subcommittee's special review of neonicotinoids is provided in this document.

The IEc literature review concludes that neonicotinoid exposure *can* adversely affect a range of pollinator species relevant to the Commonwealth of Massachusetts. This conclusion is consistent with EPA's risk characterizations of various neonicotinoid uses to pollinators. EPA's comprehensive risk assessments provide information that can complement the IEc literature review, particularly relative to aspects related to the probability and severity of risks to pollinators in MA. EPA assessed risks for a variety of use patterns and crops that can inform the evaluation of use patterns and crops that are relevant to MA. Furthermore, EPA proposed mitigation measures which may assist with the

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[1] Industrial Economics, Incorporated (IEc), December 2019. Pesticide Literature Compilation and Results; Memorandum and Framework.

[2] Douglass and White, 2017 (Acetamiprid); Farruggia and Boharty, 2017 (Dinotefuran); Housenger et al., 2016 (Imidacloprid); and Wagman et al., 2017 (Clothianidin and Thiamethoxam)

[3] Proposed Interim Decision (PID) on Neonicotinoids, U.S. EPA, 2020. Access at: https://www.epa.gov/pollinator-protection/epa-actions-protect-pollinators

[4] Appendix C: Responses from EPA to comments from the Massachusetts Attorney General.

Subcommittee's task to evaluate whether additional restrictions are needed to ensure pollinator protection in MA.

As noted above, the IEc literature review included summaries of EPA's preliminary pollinator risk assessments for the neonicotinoids. A general description of EPA risk assessment approach was described in the memorandum, and the framework provides notes on and key conclusions from these preliminary assessments. The IEc review acknowledges that these were large documents and IEc provides a clarification on the approach with the review of these complex documents. For further information, the reader was referred to the full text documents.

Relative to the Subcommittee's special review, the information provided in EPA's comprehensive risk assessments can provide further insight and information that can assist the Subcommittee with the evaluation of neonicotinoids risks to pollinators in MA. It is therefore relevant and useful to consider the updated information from EPA in the context of this special review of neonicotinoids in MA. To facilitate the Subcommittee's review and consideration of the most relevant information, MDAR staff generated this summary of the most relevant EPA information and documents.

Relative to the neonicotinoids addressed here, it should be noted that thiacloprid, a pyridylmethylamine neonicotinoid, is not included in this review. The registration of this neonicotinoid is being cancelled and EPA stopped registration review in 2014.

The outline of summarized information from PIDs for neonicotinoids presented below is:

- 2 Risk Summaries
    - Terrestrial Invertebrates: Imidacloprid, Clothianidin, Thiamethoxam, Dinotefuran
    - Off-field Risk
    - Risks for Exposure through poultry litter
    - Risk Estimates on a Colony-Level
- 3 Refined Risk Characterization
    - Terrestrial Invertebrates: Imidacloprid, Clothianidin, Thiamethoxam, Dinotefuran
- 4 Risks to Other Non-Target Organisms
    - Aquatic risks, Aquatic Invertebrates
    - Mammals
    - Birds
- 5 Proposed Interim Registration Review Decisions
    - Imidacloprid, Clothianidin &Thiamethoxam, and Dinotefuran
- 6 Risk Summary and Proposed Mitigation for Acetamiprid
- 7 Summary of Proposed Actions and Label Changes
- 8 Schedule for EPA Registration Review of Neonicotinoids + Links to Dockets
- Appendices

2. Risk Summaries and Characterizations from Proposed Interim Decisions for the Neonicotinoids

EPA identified ecological risks of concern, particularly to pollinators and aquatic invertebrates. The summaries presented below focus on pollinators (terrestrial invertebrates. Risk to aquatic invertebrates will also be briefly summarized. Risks to avian and mammalian species, and other non-target organisms is not summarized here, but information is available in EPA's PIDs and supporting documents.

Clothianidin, Dinotefuran, Imidacloprid and Thiamethoxam are in the N-nitroguanidine group of neonicotinoids. EPA issued the PIDs for the four N-nitroguanidine neonicotinoid pesticides concurrently to ensure consistency across the class. The summary presented below (sections 2 through 5) combine the information from the PIDs for the individual N-nitroguanidine neonicotinoids. A summary of information for ***Acetameprid***, a chloropyridinyl neonicotinoid, is presented separately in section 6.

2.1. Terrestrial Invertebrates Risk Estimates: Imidacloprid, Clothianidin & Thiamethoxam, and Dinotefuran

This section incorporates information provided in the *Preliminary Pollinator Assessment to Support the Registration Reviews of Imidacloprid, Dinotefuran, Clothianidin and Thiamethoxam* as well as the more recent *Final Bee Risk Assessment to Support the Registration Reviews* of these four neonicotinoids. The initial preliminary pollinator assessments published in 2016-2017evaluated the potential risk associated with the registered agricultural uses of these neonicotinoids to bees alone. The preliminary assessments utilized available data at the time. This included a robust registration review required dataset to help characterize the acute and chronic toxicity of neonicotinoids to adult and larval honeybees at the Tier I (individual bee effects) level.

The final bee risk assessments update the preliminary pollinator assessments and incorporate additional information submitted to the EPA since the previous assessments. This new assessments also include additional residue study data, which provide information on residues of neonicotinoids in nectar, pollen, and other plant matrices for registered crop uses; as well as a residue bridging strategy to extrapolate residue data among crops, chemicals, and plant matrices to address lack of residue data for certain crops between the neonicotinoids where appropriate. This additional information includes higher tiered (Tier II and III) data. Tier II data included both semi-field tunnel (rate-response) and feeding (dose-response) studies to help better evaluate potential colony-level effects, and tier III data evaluated colony-level effects which represented a more real-world scenario, however was associated with more uncertainty.

In both the preliminary and final assessments, a plethora of available *open literature* data were also reviewed in addition to the required data. For additional information on how EPA use information from open literature studies, see Appendix D.

The agency is concerned about potential risks from neonicotinoid use to all pollinators. During testing, honeybees (*Apis mellifera*) were used as a surrogate for other species of bees (e.g. bumblebees, solitary bees). Risks to these other non-Apis bees are evaluated qualitatively based on available information. As the pollinator risk assessment framework used by the EPA indicates, honeybees are intended to be reasonable surrogates for other bee species, and conclusions from the weight of evidence for the honeybee can be used to help inform about potential risks to other non-Apis species. An exception is noted based on the differences in attractiveness of crops to different bee species.

Among the four neonicotinoids (imidacloprid, clothianidin, thiamethoxam, and dinotefuran), robust data sets of pollen and nectar residue data are available for foliar and/or soil applications to the following bee-attractive crops and crop groups: cotton, cucurbits, citrus, stone fruit, pome fruit, tree nuts, berries/small fruits, and ornamentals. Surrogate residue data from the other neonicotinoids were used to represent uses on crops where limited or no residue data were available. Generally, the imidacloprid risk assessment found that foliar or soil applications of imidacloprid to honeybee attractive crops that are not harvested prior to bloom result in the potential for colony-level risks of concern. Risks associated with pre-bloom applications are generally greater than those associated with post-bloom applications.

2.2. Imidacloprid Risk Estimates

Acute risks: Based on the evaluated data, imidacloprid is classified as very highly toxic to adult honeybees with acute oral and acute contact LD50 values of 0.0039 and 0.043 µg a.i/bee, respectively. For larval toxicity, there was no acute oral study available. At the Tier 1 (individual bee) level, acute contact RQs ranged from 2.5 to 31, which exceeds the level-of-concern (LOC) of 0.4. Acute oral exposure to adult honey bees foraging on the treated field based on refined exposure (measured residues) from foliar applications resulted in RQ exceedances up to 32 (orange), soil use RQ exceedances up to 126 (ornamentals), and combined foliar and soil exceedances up to 208 (cotton). The highest acute exceedances were from uses on citrus, pome fruit, ornamentals and turf.

Chronic Risks: For chronic oral toxicity to adult bees, a 10-day study indicated a No Observed Adverse Effect Concentration (NOAEC), at 0.0011 µg a.i/bee/day. The Lowest Observed Adverse Effect Concentration (LOAEC) based on significant effects on food consumption for this study was 0.0018 µg a.i/bee/day. A 21-day chronic toxicity test did not show significant effects up to and including the highest concentration tested, 40 µg a.i/L (equivalent to 0.00183 µg a.i/bee). At the Tier 1 (individual bee) level, chronic adult oral RQ exceedances from on-field foliar use of imidacloprid based on refined exposure (measured residues) are up to 86 (orange), soil use exceedances are up to 224 (ornamental), foliar and seed exceedances are up to 7.7 (cotton) and, foliar and soil exceedances are up to 518 (cotton) (LOC = 1.0). Like with the acute risk exceedances, the highest chronic risk exceedances noted were from uses on citrus, pome fruit, ornamentals and turf.

2.3. Clothianidin and Thiamethoxam Risk Estimates

Acute Risks: Based on the evaluated data, clothianidin and thiamethoxam are classified as highly toxic to adult honeybees with similar acute oral LD50 values (0.0037 µg c.e./bee and 0.0038 µg c.e./bee, respectively) and acute contact LD50 values (0.0275 µg c.e./bee and 0.021 µg c.e./bee, respectively). There are no acceptable definitive acute oral larval toxicity studies available for clothianidin and thiamethoxam. Therefore, acute dose-based RQs were not calculated for larvae. However, there is an acceptable larval chronic toxicity study for thiamethoxam, which was used to derive an acute oral toxicity estimate (> 0.03 µg c.e./larvae; 5% mortality). For clothianidin and thiamethoxam, there are acute contact risks to adult bees exposed to foliar applications (RQ = 52 and 5.1, respectively; LOC = 0.4). Also, for clothianidin and thiamethoxam, there are acute dose-based oral exposure risks from foliar use (RQs = 3,600 and 350, respectively); from soil (RQs ranged 1.2 – 7.0); and from seed treatment use (RQ = 79). The highest acute exceedances for clothianidin are from foliar uses on berries and small fruit, soil uses for cucurbits, and foliar uses for oilseed. For thiamethoxam, the highest acute exceedances are from foliar uses on ornamentals, soil uses for fruiting vegetables, and foliar uses for berries and small fruit.

Chronic Risks: For clothianidin and thiamethoxam, there were chronic oral toxicity exceedances (LOC = 1) for foliar and soil applications. Adult bee chronic RQs ranged from 3,600 – 36,000 for foliar applications, and 13 – 70 for soil applications. There were also chronic oral toxicity exceedances identified for larval bees (RQs ranged 300 to 1,500) from foliar uses of clothianidin and thiamethoxam. For soil uses of clothianidin (non-agricultural), there were chronic exceedances to bee larvae (RQs ranged 2.1 to 2.3). There were also chronic oral exceedances for seed treatment uses for both adult and larval bees (RQ = 810 and 29, respectively). The highest chronic exceedances for clothianidin were from soil use for citrus and cucurbits, and foliar use on oilseed. For thiamethoxam, the highest chronic exceedances occurred from foliar use on ornamentals, berries and small fruit, and cucurbits.

2.4. Dinotefuran Risk Estimates

Acute Risks: Dinotefuran is highly toxic to adult bees on an acute contact (48-hr LD50 = 0.024 µg a.i./bee) and oral (48-hr LD50 = 0.0076 µg a.i./bee) basis. Dinotefuran is classified as non-toxic with endpoints up to 3.3 µg a.i./larva (111 mg a.i./kg diet) to honey bee larvae on an acute (single dose dietary) exposure basis. RQ exceedances for larvae are orders of magnitude lower than those of adults, with acute contact RQs ranging from 7.4 to 20. Acute RQ exceedances associated with on-field foliar use of dinotefuran range from <0.3 to 760 and soil use exceedances range from <0.1 to 12 (LOC = 0.4). The highest acute foliar RQ exceedances noted are associated with use on brassica head and stem vegetables, fruiting vegetables, cucurbit vegetables, bulb vegetables, stone fruit, and low growing berries (except strawberry); while the highest soil-applied RQ exceedances result from use on potatoes, leafy vegetables, brassica head and stem vegetables, fruiting vegetables, cucurbits, kiwi, tuberous and corm vegetables, and small fruit vine climbing subgroup (except kiwi).

Chronic Risks: One study is available that examines the chronic toxicity of dinotefuran for adult honeybees through dietary exposure. The NOAEC and the LOAEC based on mortality are 0.0015 and 0.0035 µg a.i./bee, respectively. In a larval chronic 21-day study, individual honeybee (Apis mellifera) larvae were exposed in vitro to technical grade dinotefuran. No statistically significant differences were detected between the negative control and treatment groups for pupal mortality, adult emergence, or growth (body weight of emerged bees); however, high mortality in the control group observed at Day 14 limits the extent to which the study can detect treatment effects. The NOAEC is less than the lowest dinotefuran treatment level (i.e., NOAEC: <0.0325 µg a.i./larva/day). As with the acute data, RQ exceedances for honeybee larvae are orders of magnitude lower than those of adults. Chronic RQ exceedances associated with on-field foliar use of dinotefuran range from 28 to 3900 and soil use RQ exceedances range from 0.9 to 60.

2.5. Off-Field Risks

Based on an analysis of Tier I data for foliar applications, potential off-field dietary risks to individual bees exposed to spray drift extend greater than 1000 feet from the edge of the treated field. There is uncertainty in this analysis including: assumptions on available attractive forage off field, use of individual level toxicity data, BeeREX default estimates for residues, and unrefined AgDRIFT™ modeling. Soil applications are assumed to have a low off-field risk because of low potential to drift.

Off-field estimates of risk are based on screening-level exposure estimates, which cannot be refined with available residue data. Moreover, these estimates relied on assumptions regarding crop-attractiveness to bees, exposures, cultural practices (i.e. harvest cycles), environmental conditions (i.e. canopy coverage), wind conditions (i.e. unidirectional and constant), etc. Therefore, potential off-field risks may be overestimated. Additionally, exposure to individual bees from off-site movement of abraded seed dust during planting is noted as a potential exposure route of concern.

2.6. Risk Estimates for Exposure through Poultry Litter Residues

Due to neonicotinoid persistence in the environment, poultry litter usage estimates indicated potential risk to bees when applied at the maximum allowed rate (0.49 lbs. a.i./A; clothianidin only) rate (0.032 – 0.756 lb a.i./A; imidacloprid) when applied on multiple occasions (six whole house treatments) and then utilized as fertilizer on agricultural fields. Based on that maximum rate, RQs calculated using the Bee-REX model showed acute and chronic exceedances for clothianidin to adult bees (RQs 7 and 70, respectively, and chronic risk to larval bees (RQ of 2.3). For Imidacloprid, the exceedances were up to 5.5 (larval chronic) and up to 21 (adult chronic). For the lowest application rate of 0.032 lb ai/A, RQ values are 0.23 (larval chronic) and 0.91 (adult chronic); below the LOC of 1.

2.7. Risk Estimates On a Colony-Level

Potential risks were identified for several scenarios. Since risks to honey bees were identified at the Tier 1 (individual bee) level, the Agency evaluated risks at the colony level (Tier II and Tier III). At the Tier II level, this involved comparing neonicotinoid residues measured in pollen and nectar in various crops to levels that affect honey bee colonies. At the Tier III level, this involved analysis of full field studies with Imidacloprid that were conducted for pumpkin and cotton. Tier III level full field studies were conducted for clothianidin and thiamethoxam seed treatments (various crops). In addition, this involved analysis of full field studies that were conducted on thiamethoxam foliar applications to orchards or melons.

These Tier III studies contained significant uncertainties associated with the study design and availability of data which limited their utility. These uncertainties include the origin of the pollen and nectar brought back to the hives, high variability in the data collected (including in control hives), and inadequate replication or pseudo-replication (e.g. studies conducted using only one field). Ecological incidents were also considered as a line of evidence. For a detailed explanation of these risk estimates, please refer to the *Final Bee Risk Assessment to Support the Registration Reviews* of the individual neonicotinoids. The findings of the higher tier assessment are summarized in section 3.

Relative the risk from dinotefuran on a colony-level, potential risks were identified for several scenarios. Since risks to honey bees were identified at the Tier 1 (individual bee) level, the Agency evaluated risks at the colony level (Tier II and Tier III). At the Tier II level, this involved comparing dinotefuran residues measured in pollen and nectar in various crops to levels that affect honey bee colonies. These analyses may not reasonably represent non-Apis bees (e.g., bumblebees), due to different crop attractiveness.

3. Terrestrial Invertebrates – Refined Risk Characterization

EPA utilized several lines of evidence to better refine the risk calls including: incorporating information on crop bee attractiveness, agronomic practices (e.g., harvest time relative to bloom) to determine if exposure was present, a comparison of residues to adverse effects levels for entire hives (residues above NOAEC and LOAEC), and major categories of incidents. For comparison of residues to adverse effects levels for entire hives, EPA considered duration and frequency of exceedance, the magnitude of exceedance (including the ration of max residue value to NOAEC/LOAEC and percent of diet from the treated field needed to reach the NOAEC/LOAEC), as well as consideration of usage and geographic scale/spatial distribution of exposure.

It is important to note that multiple factors can influence the strength and survival of bees whether they are solitary or social. These factors, including disease, pests (e.g., mites), nutrition, and bee management practices, can confound the interpretation of studies intended to examine the relationship of the test chemical to a receptor (i.e., larval or adult bee). Therefore, most studies attempt to minimize the extent to which these other factors impact the study; however, higher-tier studies afford less control over these other factors, and their role may become increasingly prominent as the duration of the study is extended. Although studies attempt to minimize the confounding effects of other environmental factors, there is uncertainty regarding the extent to which the effects of a chemical may be substantially different had these other factors not been present.

3.1. Imidacloprid

Strongest Evidence of Risk: For foliar and soil applications of imidacloprid, the lines of evidence are considered "strongest" for supporting the finding of colony-level risk resulting from applications to (with corresponding application method and timing of application with highest level of concern):

- citrus, banana/plantain (foliar and soil, pre-bloom),
- cotton (combined foliar + soil)
- berries (foliar and soil, pre-bloom),
- cucurbits (soil)
- attractive fruiting vegetables (chilies, peppers, foliar and soil), and
- attractive ornamentals and forest trees (foliar, soil)

These findings are supported by multiple lines of evidence indicating that residues exceed the imidacloprid colony-level endpoints by a high magnitude, frequency and/or duration. In some cases, they are also supported by modeled residues or ecological incidents involving bees that are associated with the use.

Moderate Evidence of Risk: For foliar, soil, and trunk injection application of imidacloprid, the strength of evidence is considered "moderate" in indicating a colony-level risk to honeybees for the following registered uses:

- citrus (soil, post-bloom),
- tree nuts (soil, post-bloom),
- cotton (foliar and soil),
- turf (including residential lawns), and
- ornamentals and forestry (trunk injection).

These findings are supported by lines evidence indicating that residues exceed the imidacloprid colony-level endpoints but the magnitude, frequency and/or duration of exceedance is limited. In some cases, residues exceed only for a subset of sites or crops, possibly due to the impact of soil type (e.g., soil applications to cotton).

Weakest Evidence of Risk: For foliar, soil and seed treatment applications of imidacloprid, the strength of evidence is considered "weakest" in indicating a colony-level risk to honeybees for the following registered uses:

- root/tubers (foliar, soil),
- legumes (soil, seed, beans),
- citrus (foliar, post-bloom),
- pome and stone fruit (foliar & soil, post-bloom),

- herbs and spices (foliar, soil),
- tropical fruit (foliar & soil, post-bloom), and
- hops/peanut (foliar, soil, seed)

The Final Bee Risk Assessment also lists the following category:

Uses with Low On-Field Risk:

This assessment concludes that registered uses of imidacloprid on the following crops and crop groups pose low risk to honey bees because agronomic practices restrict exposure of bees. Specifically, these crops are either are harvested prior to bloom (according to USDA 2017) or are tented during bloom to prevent bee pollination (e.g., mandarin oranges):

- bulb, leafy and brassica leafy vegetables,
- artichoke,
- tobacco, and
- mandarin oranges.

This assessment concludes that registered uses of imidacloprid on the following crops and crop groups pose a low risk to honey bees because they are not considered attractive to honey bees (according to USDA 2017) and therefore are expected to have a limited potential for on-field exposure:

- root and tuber vegetables (except sweet potato, Jerusalem artichoke, edible burdock, dasheen and horseradish),
- fruiting vegetables (except roselle, okra, peppers and chilies),
- cereal grains (except corn),
- turf (commercial sod), and
- unattractive ornamentals and trees (forestry)

For registered seed treatment uses of imidacloprid on honey bee-attractive crops which are not harvested prior to bloom, results from this assessment indicate there is a low potential for risk from oral exposures to imidacloprid. Specifically, refined Tier I RQ values derived from residue data bridged across chemicals are below their respective acute and chronic risk LOCs except for beans, canola, cotton, peanuts, peas, safflower, soybeans and sunflower. At the Tier II level, residues for all but two uses are below the honey bee colony-level endpoints, indicating a low potential for colony-level risk. The two uses for which a colony-level risk is indicated are bean and peanut; however, the strength of evidence supporting with this risk finding is considered "weakest."

The following uses pose a low potential for on-field risk to honey bee colonies based on comparison of available residue data with colony-level endpoints for imidacloprid:

- post-bloom foliar and soil applications to berries/small fruit,
- post-bloom foliar applications to soybeans, and
- post-bloom foliar application to tree nuts.

3.2. Clothianidin and Thiamethoxam

<u>Strongest Evidence of On-field Risk</u>: For foliar and soil applications, the lines of evidence are considered "strongest" for supporting the finding of colony-level risk resulting from applications to:

- For Clothianidin:
  - Cotton (foliar);
  - Cucurbits (foliar);
  - Grapes (foliar, pre-bloom); and
  - Ornamentals (foliar and soil).
- For Thiamethoxam:
  - Cotton (foliar);
  - Cucurbits (foliar);
  - Orchard crops (i.e., citrus, pome, stone and tropical fruits, tree nuts; foliar, prebloom);
  - Citrus (soil, pre-bloom);
  - Berries (foliar and soil, pre-bloom;
  - Honeybee attractive fruiting vegetables (i.e., okra, roselle, chilis and peppers; foliar);
  - Ornamentals (foliar and soil).

These findings are supported by multiple lines evidence indicating residues exceed the clothianidin and/or thiamethoxam colony-level endpoints by a high magnitude, frequency and/or duration. In some cases, they are also supported by modeled residues or ecological incidents involving bees that are associated with the use.

<u>Moderate Evidence of On-field Risk:</u> For foliar and soil application, the strength of evidence is considered "moderate" in indicating a colony-level risk to honeybees for the following registered uses:

- Clothianidin and Thiamethoxam:
  - Citrus (soil, post-bloom);
  - Cucurbits (soil);
  - Residential lawns (foliar); and
  - Ornamentals (foliar and soil).
- Thiamethoxam only:
  - Honeybee attractive fruiting vegetables (soil).

These findings are supported by lines of evidence indicating residues exceed the clothianidin and/or thiamethoxam colony-level endpoints but the magnitude, frequency and/or duration of exceedance is limited.

<u>Weakest Evidence of On-field Risk</u>: For foliar, soil and seed treatment applications, the strength of evidence is considered "weakest" in indicating a colony-level risk to honeybees for the following registered uses:

- Clothianidin
  - Honeybee attractive root and tuber crops (i.e., sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish; foliar and soil); and
  - Turmeric (seed treatment).
- Thiamethoxam
  - Honeybee attractive root and tuber crops (foliar and soil);
  - Citrus (soil, post-bloom); and
  - Mint (foliar).

For thiamethoxam applications (foliar) to mint, the evidence is considered weakest because risk findings rely exclusively on residue data that are extrapolated (bridged) from other neonicotinoids or different crop groups where the influence of crop on the magnitude of the residue is highly uncertain. The clothianidin use for treated turmeric seed pieces, the evidence is considered weakest because risk findings rely on nectar and pollen exposures extrapolated from the size of treated seeds, but turmeric is planted as large seed pieces.

For clothianidin and thiamethoxam applications to honeybee attractive root and tuber crops, the evidence is considered weakest because of the following. Clothianidin residue data are available for potato pollen; however, this crop does not produce nectar like other crops in this group (e.g., sweet potatoes). Residues in potato (*Solanum tuberosum*) pollen are below the colony level endpoints, however, the agency cannot conclude that nectar-producing honeybee attractive root and tuber crops pose a low risk because there are no residue data for nectars in this crop group. When considering residue data for other field crops (e.g., cotton, cucurbits), foliar and soil applications result in residues in nectar that are above the colony level endpoints. This suggests a potential concern for nectar-producing root and tuber crops. Available information suggests that several of these honeybee attractive root and tuber crops are cultivated primarily through their roots and not through setting seed, however without further information on the timing of cultivation relative to bloom periods, honeybee exposure cannot be precluded.

The final bee risk assessment also includes the following category:

<u>Uses with Low On-Field Risk</u>:

This assessment concludes that clothianidin and thiamethoxam application to the following crops and crop groups pose a low risk to honey bees because they are harvested prior to bloom (according to USDA 2017) and have limited on-field exposure to bees:

- bulb, leafy and brassica leafy vegetables;
- artichoke and tobacco.

Therefore, any type of applications (i.e., foliar, soil or seed) to these crops would pose a low on-field risk to bees. For these crops, one exception would be cases where the crop is grown for seed, thus, the crop would not be harvested prior to bloom. Although clothianidin and/or thiamethoxam may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied and specific geographic areas where crops are grown for seed.

This assessment concludes that the following crops and crop groups pose a low risk to honey bees because they are not attractive to honey bees (according to USDA 2017) and have limited on-field exposure to honey bees: root and tuber vegetables (except sweet potato, Jerusalem artichoke, edible burdock, dasheen and horseradish), fruiting vegetables (except roselle, okra, chilies and peppers). Therefore, any type of applications (i.e., foliar, soil or seed) to these crops would pose a low on-field risk to honey bees.

For crops where clothianidin or thiamethoxam are applied as seed treatment, there is a low risk from exposures of clothianidin and thiamethoxam to honey bees. These conclusions are based on available empirical residue data for seed treated crops (i.e., corn, cotton, canola and soybeans) and bridging toother crops receiving seed treatments. Although the default BeeREX RQs are above LOCs, the majority of refined RQs (with empirical residues) are below LOCs. For clothianidin, the following uses had refinedTier I RQs above the LOCs for adult bees: canola, cereal grains, legumes, sorghum and soybeans. When residues were compared to the Tier II honey bee colony endpoints, residues were all below the NOAEC, indicating low risk of colony level effects. For thiamethoxam, the following uses had refined Tier 1 RQs above the LOC for adult bees: beans, cucurbits, legumes, lentils, peanuts, peas, sorghum, soybeans and sunflower. All uses had residues below the clothianidin and thiamethoxam colony level NOAEC (both are considered because both chemicals are part of thiamethoxam's residues of concern), except for cucurbits. The weight of evidence indicates a low risk from thiamethoxam seed treatments to cucurbits.

In summary, a low risk conclusion is made for on field exposures associated with all clothianidin and thiamethoxam seed treatment uses, except clothianidin applications to turmeric seed. Low risk conclusions are also made for several foliar or soil uses because residues were below colony level endpoints. This applies to the following crops (or groups):

- Foliar applications of clothianidin and thiamethoxam to soybeans;
- Foliar, post-bloom applications of clothianidin and thiamethoxam to orchard crops;
- Foliar and soil, post-bloom applications of clothianidin and thiamethoxam to berries;
- Soil, pre-bloom applications of clothianidin to grapes.

3.3. Dinotefuran

Strongest Evidence of Risk: For foliar, soil, and trunk injection applications of dinotefuran, the lines of evidence are considered "strongest" for supporting the finding of colony-level risk resulting from applications to (with corresponding application method and timing of application with highest level of concern):

- cotton (foliar)

- stone fruit (foliar, pre-bloom)
- berries (foliar, pre-bloom),
- pollinator-attractive fruiting vegetables (foliar), and
- pollinator-attractive ornamentals and forest trees (foliar, soil, trunk injection)

These findings are supported by multiple lines of evidence indicating that residues exceed the dinotefuran colony-level NOAEC by a high magnitude, frequency and/or duration. In some cases, they are also supported by modeled residues or ecological incidents involving bees that are associated with the use.

<u>Moderate Evidence of Risk:</u> For foliar and soil application of dinotefuran, the strength of evidence is considered "moderate" in indicating a colony-level risk to honey bees for the following registered uses:

- cucurbits (foliar),
- berries (soil, pre-bloom), and
- turf (residential lawns with bee-attractive blooming weeds).

These findings are supported by lines of evidence indicating that residues exceed the dinotefuran colony-level NOAEC but the magnitude, frequency and/or duration of exceedance is limited.

<u>Weakest Evidence of Risk</u>: For foliar and soil applications of dinotefuran, the strength of evidence is considered "weakest" in indicating a colony-level risk to honey bees for the following registered uses:

- pollinator-attractive root/tubers (foliar, soil),
- pollinator-attractive fruiting vegetables (soil), and
- stone fruit (soil, pre-bloom)

Honeybees in particular play an important role in commercial pollination services for certain crops. Although the focus of the pollinator risk assessments is on honeybees, the agency recognizes that numerous other species of bees occur in North America and that these non-*Apis* bees have ecological importance in addition to commercial importance in some cases. For example, it is important to note that several species of non-Apis bees are commercially managed for their pollination services, including bumble bees (*Bombus* spp.), leaf cutting bees (*Megachile rotundata*), alkali bees (*Nomia melanderi*), blue orchard bees (*Osmia lignaria*), and the Japanese horn-faced bee (*Osmia cornifrons*). Importantly, a growing body of information indicates native bees play an important role in crop and native plant pollination, in addition to their overall ecological importance via maintaining biological diversity.

Off-field drift of dinotefuran (from foliar spray applications) is another potential route of exposure which can present risks to bees. Off-field drift was calculated via the AgDRIFT model which considers a variety of factors including wind speed, spray nozzle type, release height, etc. Spray drift from foliar treatments resulted in risks at greater than 1,000 feet from the field for honey bees. Off-field estimates of risk are based on exposure estimates which cannot be refined with available residue data. Moreover, these estimates relied on conservative assumptions regarding crop-attractiveness to bees, exposures, cultural practices (i.e. harvest cycles), environmental conditions (i.e. canopy coverage), wind conditions (i.e. unidirectional and constant), etc. Therefore, potential off-field risks may be overestimated. Additionally, adult chronic endpoints were considered very sensitive, even with the additional modeling (section….).

The final bee risk assessment also includes the following category:

<u>Uses with Low On-Field Risk</u>:

This assessment concludes that registered uses of dinotefuran on the following crops and crop groups pose a low risk to honey bees because agronomic practices restrict exposure of bees. Specifically, these crops are harvested prior to bloom (according to USDA 2017):

- Bulb vegetables,
- leafy vegetables, and
- brassica leafy vegetables.

This assessment concludes that registered uses of dinotefuran on the following crops and crop groups pose a low risk to honey bees because they are not considered attractive to honey bees (according to USDA 2017 and other sources) and therefore are expected to have a limited potential for on-field exposure:

- root and tuber vegetables (except sweet potato, Jerusalem artichoke, edible burdock, dasheen
- and horseradish),
- fruiting vegetables (except roselle, okra, peppers and chilies),
- rice,
- turf (commercial sod), and
- unattractive ornamentals and trees (Christmas trees, forestry).

The following uses pose a low potential for on-field risk to honey bee colonies based on comparison of available residue data with colony-level NOAEC for dinotefuran:

- soil applications to cucurbits,
- post-bloom foliar and soil applications to berries/small fruit, and
- post-bloom foliar and soil applications stone fruit.

4. Risks to Other Non-Target Organisms

4.1. Aquatic Risks

Neonicotinoid are applied through aerial and ground application methods, which includes sprayers, chemigation and soil drenching, and seed treatment. For aquatic wildlife, the agency modeled potential exposure based on the likelihood of imidacloprid residues reaching aquatic waterbodies. Neonicotinoids' chemical properties indicate it is readily soluble in water and that volatilization and bioaccumulation in aquatic organisms are negligible. Neonicotinoids are generally considered persistent in aquatic environments with the exception of conditions that favor aqueous photolysis. The major routes transporting neonicotinoid from treatment sites to aquatic habitats include runoff and spray drift.

Freshwater Invertebrates: Based on the preliminary aquatic risk assessment to support the registration review of the neonicotinoids, acute and chronic risks of concern to freshwater invertebrates for of neonicotinoids were identified for both agricultural and non-agricultural soil, foliar, and combined application method uses. All uses associated with foliar spray and combination application methods showed the potential for acute and chronic risks to freshwater invertebrates. For Imidacloprid, acute RQs ranged from <0.01 to 44 and exceeding the LOC of 0.5, while chronic RQs ranged from <0.01 to 2130 exceeding the chronic LOC of 1.0. Chronic freshwater RQ exceedances were generally highest for combined applications (39 to 2130), then foliar (82 to 1020), followed by soil (<0.01 to 699), and then seed (<0.01 to 84). A similar trend was seen with acute risks of concern.

Comparative Analysis of Aquatic Invertebrate Risk Quotients: While imidacloprid had a fairly comprehensive dataset for the agency to estimate potential aquatic risk, the other neonicotinoids in this group had much more limited dataset for the draft aquatic risk assessment. The agency generated a *Comparative analysis of Aquatic Invertebrate Risk Quotients* generated for neonicotinoids using Raby et al. (2018) toxicity data, which became available following publication of the *Preliminary Aquatic Risk Assessment to Support the Registration Review of Imidacloprid* (2016). The studies, located in the docket, were used to determine RQs using acute and chronic toxicity data provided in the two open literature papers published by researchers from the University of Guelph, Raby data (Raby et al. 2018 and Raby et al. 2018). With use of the available raw data, EPA determined the results could be used quantitatively for risk assessment purposes (i.e., to derive RQs). Upon the review of the Raby data, risks of concern were identified for all four neonicotinoid insecticides (dinotefuran, clothianidin, thiamethoxam, and imidacloprid) to freshwater invertebrates on both an acute and chronic basis.

On an acute basis across all tested species, LC50 values for dinotefuran were similar, but slightly higher than imidacloprid. LC50 values for clothianidin on average were 2.4 times higher than those of imidacloprid and dinotefuran, suggesting that clothianidin may be somewhat less toxic on an acute basis than imidacloprid and dinotefuran. Thiamethoxam LC50 values were 5.6 times higher than those of imidacloprid across all tested species, suggesting that thiamethoxam is potentially the least toxic on an acute basis.

All four neonicotinoids present risks of concern to freshwater invertebrates on a chronic basis as well, with clothianidin and imidacloprid having similar toxicity, dinotefuran being ~2.3 times less sensitive, and thiamethoxam being ~5.3 times less sensitive than imidacloprid and clothianidin based on midge data (which was generally more sensitive than mayfly, the other tested species in the chronic test). There is a ~4 times difference in sensitivity across the four neonicotinoids with dinotefuran being the least sensitive; despite an almost 20 times difference between mayfly toxic endpoints. There is a similar trend with the mayfly data with dinotefuran (and thiamethoxam) being the least sensitive.

4.2. Risk to Mammals and Birds

Overall, acute risks to avian and mammalian species from foliar and soil treatments of the neonicotinoids appear to be low. Soil incorporation following soil treatments, including incorporation of treated poultry litter (Imidacloprid, Clothianidin, Thiamethoxam), decreases potential risks from this use pattern considerably. Exposures from treated seed (Imidacloprid, Clothianidin, Thiamethoxam) result in the highest acute and chronic risks to terrestrial organisms. However, the risks vary considerably.

A low number of small treated seeds (e.g. lettuce and sugar beets) are required to reach levels of concern for smaller birds and mammals because the surface of these seeds have higher concentrations of a.i. applied. Also, these smaller seeds are easier for small birds and mammals to consume because of their small size. However, larger seeds (e.g. corn and soybean) pose far lower risks to birds and mammals because lower concentrations of a.i. are applied to the seed surface. Also, the larger size of these seeds prevents smaller birds and mammals from consuming them.

Although EPA's risk estimates indicate the potential for acute risks of concern, specifically for smaller sized mammals, there is uncertainty associated with the percentage of an individual mammal is likely ot be treated seed. Overall, risk of concern is more likely from chronic (long-term) consumption of treated seed.

4.3. Birds, Reptiles, and Terrestrial-Phase Amphibians

In field conditions, the exposure of birds to neonicotinoid-treated seed is dependent upon many variables beyond the amount of active ingredient on a given treated seed. These factors include whether or not the treated seed is buried or on the surface of a field (as in the case of an accidental seed spill), the depth at which buried seed is buried, the number and density of treated areas across the landscape, and the seed size relative to the size and foraging patterns of birds. For birds of any size, the attractiveness of the treated seed as a source of food is relative to the color or size of other available food sources. The size of a bird is also important in predicting effects expected from exposure, because larger birds generally need to consume more treated seeds before toxicological effects are observed.

5. PROPOSED INTERIM REGISTRATION REVIEW DECISIONS

5.1. Proposed Risk Mitigation and Regulatory Rationale

EPA recognizes that the neonicotinoids are a key tools for growers and land managers that provide unique and effective pest control. However, the agency has identified ecological risks of concern, *particularly to pollinators and aquatic invertebrates*, as a result of many of the same attributes that make the neonicotinoids effective pest management tools. Risk mitigation measures are being proposed to ecological risks of concern identified for pollinators, birds, mammals, and to aquatic invertebrates.

Risks of concern were identified to *aquatic invertebrates*, which play a foundational role in aquatic ecosystems. The agency is proposing several risk mitigation measures for reducing exposure to aquatic invertebrates, including targeted annual application rate reductions, along with spray drift and runoff management measures.

Risks of concern were identified to honeybees in EPA's assessments. The protection of honeybee populations is particularly important as honeybees play a critical role in the pollination needs of many U.S. crops. In 2017, pollination services from operations with more than 5 colonies were valued at over 160 million dollars, and annual honey production in the US was valued at over 340 million dollars9. Although the focus of the pollinator risk assessments is on honeybees, the agency recognizes that numerous other species of bees occur in North America and that these non-Apis bees have ecological importance in addition to commercial importance in some cases. For example, it is important to note that several species of non-Apis bees are commercially managed for their pollination services, including bumble bees (Bombus spp.), leaf cutting bees (*Megachile rotundata*), alkali bees (*Nomia melanderi*), blue orchard bees (*Osmia lignaria*), and the Japanese horn-faced bee (*Osmia cornifrons*). Importantly, a growing body of information indicates native bees play an important role in crop and native plant pollination, in addition to their overall ecological importance via maintaining biological diversity. EPA is therefore proposing mitigation that reduces impact to honeybees that are also expected to benefit other pollinating insects. Of these measures, reductions in maximum application rates for certain crops where pollinator/bee exposure may occur, or crop stage restrictions which limit exposure during critical periods in the growing season, are expected to have the highest potential impact in reducing risks to all pollinators. These measures were developed in a manner intended to preserve the majority of pest management utility, while also considering risk reductions for bees.

EPA reached out to a variety of stakeholders while developing the mitigation strategy in order to gain a better grasp of growing practices and potential benefits. As part of its assessments of the impacts of potential mitigation, EPA reviewed available information on the distribution of application rates used by applicators, and this information contributed to identifying when assumptions were made in the risk assessments regarding maximum rates may have overestimated certain risks. These analyses also allowed the EPA to determine where targeted rate reductions would decrease overall potential risks, while minimizing potential impacts to users. Proposed risk mitigation measures were identified by evaluating each neonicotinoid active ingredient and each use scenario for each crop individually, to determine the best path forward.

5.2. Imidacloprid

Overall, EPA is proposing addressing risk posed by current registered uses of imidacloprid uses through the following risk mitigation measures:

- Cancel residential spray applications to turf, on-farm seed treatment (of canola, millet, and wheat), and use on bulb vegetables;
- Require additional PPE;

- Reduce maximum application rates or restricting applications during pre-bloom and/or bloom, targeting certain uses with potentially higher pollinator risks and lower benefits;
- Preserve the current restrictions for application at-bloom;
- Require advisory language for residential ornamental uses;
- Apply targeted application rate reductions for higher risk uses;
- Require additional spray drift and runoff reduction label language; and,
- Promote voluntary stewardship efforts to encourage employment of best management practices, education, and outreach to applicators and beekeepers.

In selecting appropriate mitigation, EPA considered both the risks and benefits of imidacloprid use. Due to the potential impact to growers' ability to address certain critical pest issues, the agency did not propose risk mitigation on several uses, including citrus and grapes. For citrus crops, the neonicotinoids are a key element in programs to control the ACP, an invasive pest that transmits HLB, a devastating and incurable disease. In grapes, the neonicotinoids are used similarly to combat sharpshooters which vector Pierce's Disease, a fatal bacterial disease for grapes that can result in 100% yield loss. For other uses where mitigation was proposed, the mitigation does not completely eliminate all risks of concern from the use of imidacloprid, however does reduce overall risk and/or exposure. The agency finds the remaining risks to be reasonable under FIFRA given the benefits of the use of imidacloprid. The EPA is also proposing label changes to address general labeling improvements for all imidacloprid products.

5.3. Clothianidin and Thiamethoxam

Overall, EPA is proposing to address potential risks posed by current registered uses of clothianidin and/or thiamethoxam through the following risk mitigation measures:

- Cancelling certain clothianidin uses
- Restricting certain thiamethoxam uses
- Requiring additional PPE
- Reducing maximum application rates or restricting applications during pre-bloom and/or bloom, targeting certain uses with potentially higher pollinator risks and lower benefits
- Preserving the current restrictions for application at-bloom
- Requiring additional label language reducing use by homeowners
- Applying targeted rate reductions for higher risk uses
- Requiring additional spray drift and runoff reduction label language
- Promoting voluntary stewardship efforts to encourage the use of best management practices, education, and outreach to applicators and beekeepers

In selecting appropriate mitigation, EPA considered both the risks and benefits of imidacloprid use. Due to the potential impact to growers' ability to address certain critical pest issues, the agency did not propose risk mitigation on several uses, including citrus and grapes.

The proposed mitigation does not eliminate all potential risks of concern from the use of clothianidin or thiamethoxam, however, the proposed mitigation reduces the overall potential of risk and/or exposure.

The agency finds the remaining risks to be reasonable under FIFRA, given the benefits of using clothianidin and thiamethoxam. The EPA is also proposing label changes to address general labeling improvements for all clothianidin and thiamethoxam products and uses.

5.4. Dinotefuran

Overall, EPA is proposing addressing risk posed by current registered uses of dinotefuran uses through the following risk mitigation measures:

- Cancel use on bulb vegetables;
- Reduce maximum application rates or restricting applications during pre-bloom and/or bloom, targeting certain uses with potentially higher pollinator risks and lower benefits;
- Preserve the current restrictions for application at-bloom;
- Require advisory language for residential ornamental uses;
- Apply targeted application rate reductions for higher risk uses;
- Require additional spray drift and runoff reduction label language; and,
- Promote voluntary stewardship efforts to encourage employment of best management practices, education, and outreach to applicators and beekeepers.

In selecting appropriate mitigation, EPA considered both the risks and benefits of dinotefuran use. Due to the potential impact to growers' ability to address certain critical pest issues, the agency did not propose risk mitigation on several uses, including citrus and grapes. For citrus crops, the neonicotinoids are a key element in programs to control the ACP, an invasive pest that transmits HLB, a devastating and incurable disease. In grapes, the neonicotinoids are used similarly to combat sharpshooters which vector Pierce's Disease, a fatal bacterial disease for grapes that can result in 100% yield loss. For other uses where mitigation was proposed, the mitigation does not completely eliminate all risks of concern from the use of dinotefuran, however does reduce overall risk and/or exposure. The agency finds the remaining risks to be reasonable under FIFRA given the benefits of the use of dinotefuran. The EPA is also proposing label changes to address general labeling improvements for all dinotefuran products.

6. Acetamiprid

Since Acetamiprid belongs to the subclass of chloropyridinyl neonicotinoids, information is presented separately from the N-nitroguandine neonicotinoids.

6.1. Risk Summary and Characterization

<u>Terrestrial Risks, Mammals</u>:

Acetamiprid is highly toxic to mammals on an acute oral exposure basis, based on a 14-day LD50 (lethal dose to 50% of the test subjects) of 149 mg a.i./kg bw (where bw=bodyweight) in rats. The chronic toxicity endpoint (the no observed adverse effect concentration, or NOAEC=160 mg a.i./kg diet) is based on reduced body weight and reduced body weight gains.

While there are no acute (Level of Concern or LOC=0.5) or chronic (LOC=1.0) risks of concern from foliar applications of acetamiprid, there are both acute and chronic risks of concern from consumption of acetamiprid-treated seeds. The maximum acute seed treatment risk quotient (RQ) is 2.65 and the maximum chronic RQ is 48.31. (RQs greater than the established LOC represent potential risks of concern for a given exposure scenario). For context, a small mammal (weighing approximately 15 g) would receive an acutely lethal dose of acetamiprid after ingesting 214 treated canola seeds, or 30% of its diet over a foraging area of 2.53% of its home range. Similarly, a small mammal would reach the chronic LOC after consuming 107 acetamiprid-treated canola seeds, representing 15% of its diet.

Birds, Reptiles, and Terrestrial-Phase Amphibians

Acetamiprid is very highly toxic to passerine species—e.g., zebra finch (*Taeniopygia guttata*)— and moderately toxic to larger birds—e.g., mallard duck (*Anas platyrhynchos*)—on an acute oral exposure basis. The 14-day LD50 is 5.68 mg a.i./kg bw in zebra finches and 84.4 mg a.i./kg bw in mallard ducks. The chronic toxicity endpoint (NOEAC=99 mg a.i./kg diet) is based on reduced number of eggs laid and hatched.

There are both acute (LOC=0.5) and chronic (LOC=1.0) risks of concerns to birds from both foliar applications and seed treatments with acetamiprid. From foliar applications, the maximum acute RQ is 23.51 and the maximum chronic RQ is 1.26. For seed treatments, the maximum acute RQ is 167.83 and the maximum chronic RQ is 40.49. For context, a passerine bird would receive an acutely lethal dose of acetamiprid after ingesting as few as 5.4 acetamiprid-treated seeds, or 0.5% of its diet over a foraging area of 0.06% of its home range. Similarly, a passerine bird would reach the chronic LOC after consuming 88 acetamiprid-treated canola seeds, representing 7.8% of its diet and approximately 1% of its home range.

Terrestrial Invertebrates (honey bees)

Since the publication of the *Preliminary Environmental Fate and Ecological Risk Assessment* (PRA), the agency has revised the toxicity estimates and resulting RQs for larval bees upwards by approximately an order of magnitude. The information presented below reflects these updated estimates. The toxicity and resulting RQs for adult bees remain unchanged since the PRA.

Honey bees may be exposed to acetamiprid through ingestion of residues in nectar and pollen foraged from treated plants, contact with pesticide residues on plants treated with foliar applications, and direct contact via spray drift. Acetamiprid is classified as moderately toxic to adult bees and highly toxic to larvae on an acute exposure basis. For adult bees, the acute contact LD50 is 10.53 µg a.i./bee and the acute oral LD50 is 8.96 ug a.i./bee. For larvae, the acute oral LD50 was 8.96 µg a.i./larva. The chronic endpoint for bees (the no observed adverse effects level, or NOAEL=0.12 ug a.i./bee/day) is based on a decrease in larval survival.

There are acute (LOC= 0.4) and chronic (LOC=1.0) risks of concern to adults and larvae from registered uses of acetamiprid. For adult bees, the maximum acute RQ is 1.86 and the maximum chronic RQ is 6.59. For larvae, the maximum acute RQ is 6.59 and the maximum chronic RQ is 63.7.

Measured residue data suggest that the actual residues of acetamiprid on treated plants may be up to 99% lower than the estimated environmental concentrations (EECs) used to generate RQs. Moreover, though there are risks of concern to individual honey bees, which serve as a surrogate for non-Apis bees, colony-level studies show that these risks are not likely to translate into long-term adverse effects on the colony. These studies indicate that adverse effects of acetamiprid are likely transitory and so will probably not pose long-term risks to colony health. However, there are 37 reported incidents associated with the use of acetamiprid involving honey bees, with the numbers of colonies affected per incident ranging from 9 to 12,000. The majority (76%) of the bee-related incidents occurred in Canada. Of the eight incidents that occurred inside of the U.S., six were classified as either "unlikely" or were the result of illegal use of acetamiprid.

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 acetamiprid, the problem formulation and registration review Data Call-In (DCI) for acetamiprid were both issued prior to the EPA 's issuance of the June 2014 Guidance for Assessing Pesticide Risks to Bees . This 2014 guidance lists additional pollinator studies that were not included in the acetamiprid registration review DCI. Therefore, the EPA is currently determining whether additional pollinator data are needed for acetamiprid. If the agency determines that additional pollinator exposure and effects data are necessary, then the EPA will issue a DCI to obtain these data.

Aquatic Risk:

Freshwater and Estuarine/Marine Invertebrates: Since the publication of the PRA, the agency has revised the toxicity estimates and resulting RQs for freshwater invertebrates upwards by approximately an order of magnitude. Aquatic invertebrates may become exposed to acetamiprid through residues in runoff, flooding of treatment sites, and spray drift. Acetamiprid is very highly toxic to both freshwater and estuarine/marine invertebrates on an acute exposure basis. The 96-hr LC50 for freshwater invertebrates is 3.31 µg a.i./L. The 96-hr LC50 for estuarine/marine invertebrates is 66 µg a.i./L. The freshwater invertebrate chronic toxicity endpoint (NOAEC=0.36 µg a.i./L) is based on adult emergence and on the average number of days to emergence. The estuarine/marine invertebrate chronic toxicity endpoint (NOAEC=2.5 µg a.i./L) is based on reduced body weight in males.

There are both acute (LOC=0.5) and chronic (LOC=1.0) risks of concern to both freshwater and estuarine/marine invertebrates from registered uses of acetamiprid. For freshwater invertebrates, the maximum acute RQ is 10.2 and the maximum chronic RQ is 91.7. For estuarine/marine invertebrates, the maximum acute RQ is 0.57 and the maximum chronic RQ is 14.56.

6.2. Proposed Risk Mitigation and Regulatory Rationale for Acetamiprid

EPA has identified risks to mammals and birds that consume treated seeds, to birds from foliar applications, to terrestrial invertebrates from foliar applications, to aquatic invertebrates from foliar applications, and to terrestrial plants.

Overall, EPA is proposing addressing risk posed by current registered uses of acetamiprid uses through the following risk mitigation measures:

- Advisory statements for Acetamiprid seed treatment uses;
- Environmental Hazard Statement for Pollinators;
- Additional spray drift and runoff reduction label language;
- Proposed spray drift buffers from water bodies.

7. Summaries of Proposed Actions and Proposed Label Changes for the Neonicotinoids

Summary tables are provided in the following appendices:

- Appendix A1 – A4 list the proposed actions for the neonicotinoids
- Appendix B contains a summary of proposed label changes

8. Schedule for Registration Review of Neonicotinoids and Links to Dockets

The following EPA webpage provides information on the schedule for review of neonicotinoids. Links to the dockets for each neonicotinoid are also listed. The dockets provide access to all publicly available documents related to the registration review of these pesticides.

Schedule for Review of Neonicotinoid Pesticides

Web link: https://www.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides

The dockets for all the neonicotinoid pesticides have been opened. Our goal is to review the pesticides in this class in the same timeframe so we can ensure consistency across the class. As EPA completes risk assessments for the neonicotinoids, the Agency will pursue risk mitigation, as appropriate.

Chemical Name and Docket Number	Planned Completion	Milestones

Imidacloprid EPA-HQ-OPP-2008-0844	2021	• preliminary pollinator-only risk assessment issued for public comment in 2016 • preliminary aquatic-only ecological assessment issued for public comment in 2017 • preliminary human health risk assessment issued for public comment in 2017 • remaining non-pollinator ecological risk assessment issued for public comment in 2017 • updated pollinator risk assessment and released a proposed interim decision released in January 2020
Clothianidin EPA-HQ-OPP-2011-0865	2021	• preliminary pollinator-only risk assessment issued for public comment in 2017 • preliminary human health and non-pollinator ecological assessments issued for public comment in 2017 • updated pollinator risk assessment and released a proposed interim decision released in January 2020
Thiamethoxam EPA-HQ-OPP-2011-0581	2021	• preliminary pollinator-only risk assessment issued for public comment in 2017 • preliminary human health and non-pollinator ecological assessments issued for public comment in 2017 • updated pollinator risk assessment and released a proposed interim decision released in January 2020
Dinotefuran EPA-HQ-OPP-2011-0920	2021	• preliminary pollinator-only risk assessment issued for public comment in 2017 • preliminary human health and non-pollinator ecological assessments issued for public comment in 2017 • updated pollinator risk assessment and released a proposed interim decision released in January 2020
Acetamiprid	2021	• preliminary human health and ecological risk

EPA-HQ-OPP-2012-0329		assessments issued for public comment in 2018 • proposed interim decision released in January 2020
Thiacloprid EPA-HQ-OPP-2012-0218	Voluntarily canceled by registrant Registration review case closure issued in November 2014	

Try Pesticide Chemical Search for additional information on these and other pesticide ingredients.

Appendix A1: Summary of Proposed Actions for Imidacloprid

Registration Review Case#: 7605
PC Code: 129099
Chemical Type: Insecticide
Chemical Family: Neonicotinoids
Mode of Action: Nicotinic acetylcholine receptor (NACHR) competitive modulators

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions
Pollinators	Residues on treated site	Ingestion and contact	Acute and chronic	Acute and chronic toxicity	• Reduce application rates • Crop stage restrictions • General other use restrictions • Spray drift reduction
Occupational Handlers	Aerial and ground application	Dermal and inhalation	Short and intermediate term	Portal of entry effects	• Require additional PPE (e.g., double layer clothing, gloves) • Precautionary statements • Prohibition of on-farm seed treatments for canola, millet, and wheat
Residential post-application (adults and children)	Ground application	Dermal and inhalation	Short and intermediate term	Portal of entry effects	• Use deletion for residential spray applications to turf
Aquatic Invertebrates	Runoff from treated sites	Ingestion and contact	Acute and chronic	Acute and chronic toxicity	• Reduce application rates • Spray drift and runoff reduction • Vegetative filter strips • Use deletion for bulb vegetables • Reduce perimeter treatment applications
Birds and Mammals	Residues on ingested seeds	Dietary and ingestion	Acute and chronic	Acute and chronic toxicity	• Clean up spills of treated seeds

Appendix A2: Summary of Proposed Actions for Clothianidin and Thiamethoxam

Table 1: Summary of Proposed Actions for Clothianidin

Registration Review Case#: 7620
PC Code: 044309
Chemical Type: insecticide Chemical Family: nitroguanidine-substituted neonicotinoid
[Mode or Mechanism (for herbicides)] of Action: Nicotinic acetylcholine receptor (NACHR) competitive modulators

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions
Occupational Handlers	Aerial and ground application, treated seeds	Dermal and inhalation	Short and intermediate term	Systemic effects	• Require additional PPE (*e.g.*, gloves and respirators) • Precautionary statements • Use Restrictions
Pollinators	Residues on treated site	Ingestion and contact	Acute and chronic	Acute and chronic toxicity	• Reduce application rates • Crop stage restrictions • Use deletions • Use restrictions • Buffers • Spray drift reduction
Aquatic Invertebrates	Runoff from treated sites	Contact and ingestion	Acute and chronic	Acute and chronic toxicity	• Spray drift reduction • Prevent runoff • Vegetative filter strips • Reduce perimeter treatment applications
Birds and Mammals	Residues on ingested seeds	Dietary and ingestion	Acute and chronic	Acute and chronic toxicity	• Clean up spills of treated seeds

Table 2: Summary of Proposed Actions for <u>Thiamethoxam</u> Registration Review Case#: 7614 PC Code: 060109 Chemical Type: insecticide Chemical Family: nitroguanidine-substituted neonicotinoid [Mode or Mechanism (for herbicides)] of Action: Nicotinic acetylcholine receptor (NACHR) competitive modulators					
Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions
Occupational Handlers	Aerial and ground application	Dermal and inhalation	Short and intermediate term	Systemic effects	• Require additional PPE (gloves and respirators) • Precautionary statements • Require closed loading for seed treatment • Cancel equipment/application uses
Pollinators	Residues on treated site	Ingestion and contact	Acute and chronic	Acute and chronic toxicity	• Reduce application rates • Bloom restrictions • Use deletions • Use restrictions • Buffers • Spray drift reduction
Aquatic Invertebrates	Runoff from treated sites	Contact and ingestion	Acute and chronic	Acute and chronic toxicity	• Spray drift reduction • Prevent runoff • Vegetative filter strips • Reduce perimeter treatment applications
Birds and Mammals	Residues on ingested seeds	Dietary and ingestion	Acute and chronic	Acute and chronic toxicity	• Clean up spills of treated seeds

Appendix A3: Summary of Proposed Actions for <u>Dinotefuran</u>

Registration Review Case#: 7441
PC Code: 044312
Chemical Type: insecticide
Chemical Family: Neonicotinoids
[Mode or Mechanism (for herbicides)] of Action: Nicotinic acetylcholine receptor (NACHR) competitive modulators

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions
Pollinators	Residues on treated site	Ingestion and contact	Acute and chronic	Acute and chronic toxicity	• Reduce application rates • Crop stage restrictions • General/other use restrictions • Spray drift reduction
Aquatic Invertebrates	Runoff from treated sites	Ingestion and contact	Acute and chronic	Acute and chronic toxicity	• Reduce application rates • Spray drift and runoff reduction • Vegetative filter strips • Use deletion for bulb vegetables • Reduce perimeter treatment applications

Appendix A4: Summary of Proposed Actions for Acetamiprid

Registration Review Case #: 7468
PC Code: 099050
Chemical Type: Insecticide
Chemical Family: Neonicotinoid
Mode of Action: Group 4: Nicotinic Acetylcholine Receptor Competitive Modulators

Affected Population(s)	Source of Exposure	Route of Exposure	Duration of Exposure	Potential Risk(s) of Concern	Proposed Actions
Occupational Handlers	Backpacks for basal bark treatments	Dermal exposure	Short- and intermediate-term	Reproductive and neurotoxic effects	Addition of double layer clothing and gloves to PPE
Mammals and Birds, Reptiles, and Terrestrial-Phase Amphibians	Seed treatments	Dietary exposure	Acute and chronic	Acute toxicity and weight loss, behavioral changes, labored breathing, and reproductive effects	Require specific handling and management of treated seeds
Birds, Reptiles, and Terrestrial-Phase Amphibians	Foliar applications	Dietary and dermal exposures	Acute and chronic	Acute toxicity and reproductive effects	Spray drift and runoff mitigation language
Terrestrial Invertebrates (Pollinators)	Foliar treatments	Dietary exposure	Acute and chronic	Acute toxicity and increased mortality in adult and larval workers and drones	Environmental hazard statement on labels Spray drift and runoff mitigation language
Terrestrial Plants	Drift; runoff	Contact	Not applicable	Seedling emergence and vegetative vigor	Spray drift and runoff mitigation language
Aquatic Invertebrates	Foliar treatments; runoff	Dermal exposure	Acute and chronic	Acute toxicity and decreased size and reproductive effects	Spray drift and runoff mitigation language

Appendix B

Summary of Proposed Label Changes for the Neonicotinoids

	CLOTHIANIDIN	THIAMETHOXAM	IMIDACLOPRID	DINOTEFURAN	ACETAMPRID
Update/Added Protective Equipment	X	X	X	X	X
Pollinator Specific Labeling	X	X	X	X	X
Delete residential spray use on turf			X		
Delete foliar spray and soil drench use on bulb vegetables			X	X	
Wind speed limits	X	X	X	X	X
Droplet size (medium to coarse)	X	X	X	X	X
Intended for professional use (Ornamentals ground cover & trees)	X	X	X	X	
Setbacks to water		X	X	X	X
Changes in label rates	X	X	X	X	
Vegetative buffer required for Ag. Foliar sprays	X	X	X	X	
Limit how outdoor non-ag use can be performed	X	X	X	X	
Turn off nozzle at end of row (Ag/Airblast)	X	X	X		
Drift Advisory Language	X	X	X	X	X

Appendix C

Responses from EPA to Comments Submitted by the Massachusetts Office of the Attorney General

In Proposed Interim Decision for Imidaclorid PID, p.9; and in Proposed Interim Decision for Clothianidin/Thiamethoxam PID: p. 12:

Comment Submitted by the Massachusetts Office of the Attorney General (EPA-HQ-OPP-2011-0920-0725):

Comment: The Massachusetts Office of the Attorney General (MA-OAG) expressed concerns regarding risks to pollinators from residential homeowner applications of neonicotinoids on gardens, lawns and ornamentals. MA-OAG also highlighted that many retailers have voluntarily committed to phasing out the sale of plants and other products containing neonicotinoid insecticides. MA-OAG suggests that the agency severely curtail the use of neonicotinoids.

EPA Response: EPA thanks the Massachusetts Office of the Attorney General for its comment. The agency recognizes the potential risks to pollinators from homeowner applications of neonicotinoids on gardens, lawns, and ornamentals. In response, the agency is proposing certain rate reductions and require advisory label language for residential ornamental labels stating, "Intended for use by professional applicators". Please refer to Section IV.A of this PID for additional details regarding the proposed label changes.

***In:* MEMORANDUM SUBJECT: Response from the Pesticide Re-evaluation Division to Comments on the Draft Risk Assessments and Benefits Assessments Supporting the Registration Review of the Nitroguanidine-substituted Neonicotinoid Insecticides DATE: January 16, 2020**

Request to Ban or Severely Restrict the Use of Neonicotinoids

i. Multiple comments.

1. Description of Comments: Multiple commenters**, including the Massachusetts Office of the Attorney General,** stated that the EPA should ban or severely restrict the use of neonicotinoids due to unreasonable adverse effects on the environment with reference to FIFRA.

2. Agency Response: Under section 3(c)(5), FIFRA requires that a pesticide not cause "unreasonable adverse effects on the environment" in order to be registered. FIFRA 7 U.S.C. § 136a(c)(5). Section 2(bb) defines "unreasonable adverse effects on the environment" as, among other things, "any unreasonable

risk to man or the environment, taking into account the economic, social and environmental costs and benefits of the use of any pesticide…”. This language creates a “risk-benefit” standard that requires the agency to compare the potential risks from the use of a pesticide with the benefits to users of the pesticide. To determine whether neonicotinoids meet this standard, the agency carefully considered the risks and benefits of each neonicotinoid. The agency determined that there are potential chemical-specific risks of concern that can be managed via mitigation (e.g., PPE, application rate reductions, spray drift language) that also considers the benefits of each neonicotinoid., These potential risks, benefits and proposed mitigation measures can be found in the chemical-specific PIDs, which are available in the dockets for each case.

Appendix D

EPA use of Open Literature Studies:

In: Proposed Interim Decision for Clothianidin and Thiamethoxam: p. 13:

Summary of Comments (BK, BP, CBD, CCM, CFS, DBG, GC, NCC, NRDC, NWF, SFEI, UCR, UCSD):

Several commenters asked the agency to refer to open literature studies for data and/or methodologies to be incorporated into the EPA's pollinator assessment. These studies covered a range of considerations including, but not limited to, assessing risk to additional pollinator species (e.g. non-Apis), sub-lethal effects, and toxicity endpoints.

EPA Response: EPA relies on the best available science at the time of conducting its assessments. In the risk assessment process, numerous studies are considered and evaluated for inclusion in the assessments based on the agency's open literature guidance. Open literature studies that meet the guidance criteria are then selected for inclusion in the risk assessments. The selected studies are then weighted based on the scientific evaluation. EPA acknowledges the growing body of studies/data/methodologies and has considered additional studies in the final pollinator assessments that were brought to the agency's attention as comments received on the preliminary pollinator assessments.