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OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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MEMORANDUM

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SUBJECT: Final Bee Risk Assessment to Support the Registration Review of Imidacloprid

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This memo transmits the Environmental Fate and Effects Division's Final Bee Risk Assessment to Support the Registration Review of Imidacloprid. This assessment updates the Preliminary Pollinator Assessment (1/4/2016, DP 429937) and incorporates additional information, submitted to the Environmental Protection Agency after completion of the preliminary

document, for assessing the risks of agricultural and non-agricultural uses of imidacloprid to bees. Where appropriate, this assessment incorporates comments received during the public comment period on the preliminary risk assessment document.

Major updates that have been made to this final assessment include the following:

- Tier 3 (full field) studies conducted on pumpkin and cotton have been incorporated.
- A methodology to quantitatively assess colony-level effects of imidacloprid residues in pollen has been added to this document which combines residues from nectar and pollen by taking into account their differential exposure and toxicity at the colony level. This new approach was developed in consideration of comments received on approaches for considering the pollen route of exposure in the preliminary assessments for imidacloprid, clothianidin and thiamethoxam.
- Additional residue study data were considered, which provide residues of imidacloprid in nectar, pollen, and other plant matrices for registered crop uses.
- A residue bridging strategy has been employed to extrapolate, where appropriate, residue data among crops, chemicals and plant matrices to address lack of residue data for certain crops
- This document includes risk conclusions for non-agricultural use sites, which were not included in the Preliminary Bee Risk Assessment.

Risk conclusions for all other non-bee taxa from exposure to imidacloprid were included in separate preliminary risk assessments¹ from the bee assessment. Updates to the non-bee taxa risk assessments and response to public comments received on those documents are addressed separately in the response to comment documents². Four attachments that support the data analysis and scientific basis of the residue bridging strategy and revised pollen-nectar method are included within the imidacloprid docket as separate entries. These attachments provide the detailed methodology and data evaluations that underly the bridging strategy and risk assessment conclusions.

¹ Preliminary Aquatic Risk Assessment to Support the Registration Review of Imidacloprid (12/22/2016, DP 435477); Preliminary Terrestrial Risk Assessment to Support Registration Review of Imidacloprid (11/28/2017, DP 442390)

² Imidacloprid: Response to Public Comments Related to the Preliminary Risk Assessments and Addendum to the Non-Pollinator Risk Assessments in Support of Registration Review (1/8/2020, DB 447632)

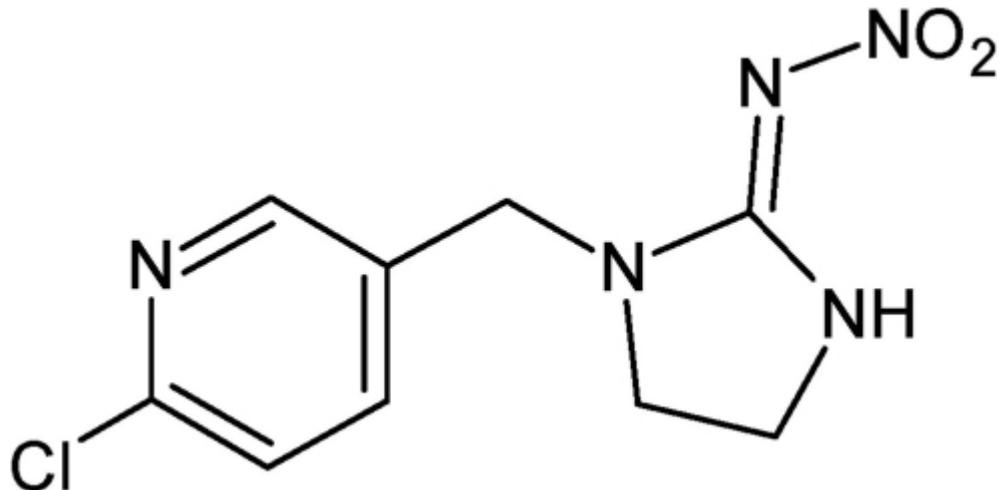
EFED Response to Public Comments Common to the Preliminary Bee and Preliminary Non-Pollinator Registration Review Risk Assessments Across the Four Neonicotinoid Pesticides (Imidacloprid, Thiamethoxam, Clothianidin, and Dinotefuran) (1-6-2020, DB447635)



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Final Bee Risk Assessment to Support the Registration Review of Imidacloprid



January 14, 2020

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Contents

| | | |
|--------|---|----|
| 1. | EXECUTIVE SUMMARY | 15 |
| 1.1. | Background and Scope..... | 15 |
| 1.2. | Use Profile..... | 15 |
| 1.3. | Risk Assessment Approach | 16 |
| 1.4. | Risk Conclusions Summary..... | 16 |
| 1.4.1. | Uses with Low On-Field Risk | 17 |
| 1.4.2. | Uses With On-Field Risk | 17 |
| 1.4.3. | Off Field Risk: | 19 |
| 1.4.4. | Other Lines of Evidence | 25 |
| 1.4.5. | Non-Apis Bees | 25 |
| 1.5. | Environmental Fate and Exposure Summary and Residue Bridging Approach | 26 |
| 1.6. | Ecological Effects Summary | 28 |
| 1.7. | Major Assumptions and Uncertainties | 29 |
| 2. | PROBLEM FORMULATION..... | 31 |
| 2.1. | Registration Review Background | 31 |
| 2.2. | Nature and Scope of Assessment | 31 |
| 2.3. | Pesticide Type, Class, and Mode of Action | 32 |
| 2.4. | Overview of Imidacloprid Uses | 32 |
| 2.5. | Overview of Physicochemical, Fate, and Transport Properties | 33 |
| 2.6. | Stressors of Toxicological Concern..... | 33 |
| 2.7. | Protection Goals and Assessment Endpoints | 34 |
| 2.8. | Conceptual Models and Risk Hypotheses | 35 |
| 2.8.1. | Foliar Spray..... | 35 |
| 2.8.2. | Soil Application | 37 |
| 2.8.3. | Seed Treatment..... | 38 |
| 2.9. | Analysis Plan..... | 39 |
| 2.9.1. | Risk Assessment Methodology | 39 |
| 2.10. | Measures of Exposure..... | 44 |
| 2.11. | Measures of Effects..... | 45 |

| | |
|---|-----|
| 3. USE CHARACTERIZATION | 48 |
| 3.1. Agricultural Uses | 48 |
| 3.1.1. Foliar Applications..... | 49 |
| 3.1.2. Soil Applications..... | 51 |
| 3.1.3. Seed Treatments | 53 |
| 3.1.4. Multiple Application Types (e.g. combinations of seed, soil, and/or foliar)..... | 54 |
| 3.1.5. Usage Information | 55 |
| 3.2. Non-agricultural Uses..... | 57 |
| 4. EXPOSURE ASSESSMENT | 59 |
| 4.1. Physical/chemical and fate and transport properties | 60 |
| 4.1.1. Physical/Chemical properties | 60 |
| 4.1.2. Environmental Fate and Transport Properties | 61 |
| 4.2. Imidacloprid Plant Up-take | 69 |
| 4.2.1. Imidacloprid applied to soil including seed treatment..... | 69 |
| 4.2.2. Imidacloprid applied to foliage and fruits..... | 70 |
| 4.2.3. Imidacloprid: soil versus foliage applied..... | 71 |
| 4.3. Plant Metabolism of Imidacloprid | 72 |
| 4.3.1. Imidacloprid metabolism in various plants..... | 73 |
| 4.3.2. Imidacloprid metabolism profile in plants..... | 74 |
| 4.3.3. Seed Treatment Application Residue Studies – Open Literature | 75 |
| 4.3.4. Imidacloprid metabolism profile in plants | 79 |
| 4.4. Potential for Exposure to Bees..... | 80 |
| 4.4.1. Exposure Potential of Agricultural Uses..... | 81 |
| 4.4.2. Exposure Potential of Non-Agricultural Uses..... | 84 |
| 4.5. Screening-level Exposure Estimation | 85 |
| 4.6. Experimental Residue Studies..... | 89 |
| 4.6.1. Rationale for Residue-based EEC Selection for Refined Tier I | 89 |
| 4.6.2. Rationale for Comparing Residue Data with Tier II Endpoints..... | 91 |
| 4.6.3. Foliar Application Residue Studies – Registrant Submitted..... | 91 |
| 4.6.4. Soil Application Residue Studies – Registrant Submitted | 95 |
| 4.6.5. Soil Application Residue Studies – Open Literature..... | 102 |
| 4.6.6. Seed Treatment Application Residue Studies – Registrant Submitted | 105 |
| 4.6.7. Combined Application Method Residue Studies | 111 |

| | | |
|--------|--|-----|
| 4.6.8. | Non-Agricultural Residue Studies | 116 |
| 4.6.9. | Carry-over of Imidacloprid Residues in Soil | 120 |
| 4.7. | Observational Residue Monitoring Studies | 122 |
| 4.7.1. | Agricultural crop studies | 122 |
| 4.7.2. | Hive monitoring studies | 123 |
| 4.7.3. | Non-Agricultural Monitoring Studies | 129 |
| 5. | EFFECTS ASSESSMENT..... | 130 |
| 5.1. | Tier I Studies..... | 130 |
| 5.1.1. | Review of Registrant-Submitted Studies | 130 |
| 5.1.2. | Review of Open Literature Studies | 131 |
| 5.1.3. | Adult Acute Contact Toxicity..... | 132 |
| 5.1.4. | Adult Acute Oral Exposure | 139 |
| 5.1.5. | Adult Chronic Oral Toxicity (Apis and non-Apis) | 144 |
| 5.1.6. | Larval Acute Oral Toxicity..... | 146 |
| 5.1.7. | Larval Chronic Oral Toxicity..... | 147 |
| 5.1.8. | Acute and Chronic Toxicity of the Degradation Products of Imidacloprid | 149 |
| 5.2. | Tier II Studies..... | 152 |
| 5.2.1. | Registrant-Submitted..... | 153 |
| 5.2.2. | Open Literature Studies | 157 |
| 5.3. | Tier III Studies..... | 185 |
| 5.3.1. | Registrant Submitted | 185 |
| 5.3.2. | Open Literature | 191 |
| 5.4. | Reported Bee Incident Information | 197 |
| 5.4.1. | U.S. Reported Incidents | 197 |
| 5.4.2. | Incidents Outside the U.S..... | 205 |
| 6. | RISK CHARACTERIZATION..... | 207 |
| 6.1. | Tier I Risk Assessment | 207 |
| 6.1.1. | Acute Contact Risk (On-Field, Screening)..... | 207 |
| 6.1.2. | Acute Oral Risk (On-Field, Screening) | 208 |
| 6.1.3. | Acute Oral Risk (Off-Field, Screening)..... | 211 |
| 6.1.4. | Refined Acute Oral Risk (On-field) | 219 |
| 6.1.5. | Uncertainties In Tier 1 Risk Assessment | 224 |
| 6.2. | Higher Tier Risk Assessment for <i>Apis</i> Bees | 225 |

| | | |
|---------|---|-----|
| 6.2.1. | Method to Assess Combined Pollen and Nectar Exposure..... | 226 |
| 6.2.2. | Residue Bridging Strategy | 226 |
| 6.2.3. | Drawing Higher Tier Risk Conclusions..... | 230 |
| 6.2.4. | Higher Tier Uncertainties | 231 |
| 6.2.5. | Crop group 20 – Oilseed..... | 232 |
| 6.2.6. | Crop group 9 – Cucurbit vegetables..... | 247 |
| 6.2.7. | Crop group 10, 11, 12, 14, and others - Orchard crops | 254 |
| 6.2.8. | Crop group 13 – Berry and small fruit..... | 268 |
| 6.2.9. | Crop group 6 – Legumes | 277 |
| 6.2.10. | Other herbaceous crops..... | 279 |
| 6.2.11. | Crops not in a designated crop group..... | 285 |
| 6.2.12. | Non-Agricultural Crops..... | 286 |
| 6.3. | Risk Characterization of Non- <i>Apis</i> Bees | 297 |
| 6.3.1. | Exposure Considerations..... | 298 |
| 6.3.2. | Toxicity Considerations | 300 |
| 6.4. | Additional Lines of Evidence | 303 |
| 7. | CONCLUSIONS..... | 304 |
| 7.1. | Foliar applications | 305 |
| 7.2. | Soil Applications | 306 |
| 7.3. | Seed Treatment Applications..... | 306 |
| 8. | REFERENCES | 312 |

Table of Appendices

- Appendix A. Evaluated Registrant-Submitted and Open Literature Studies Invalid for Risk Assessment Use
- Appendix B. Soil and Seed Treatment Residue Monitoring Study Summaries
- Appendix C. Non-Agricultural Registrant and Open Literature Study Summaries
- Appendix D. Agricultural Residue Monitoring Study Summaries
- Appendix E. Effects Study Summaries
- Appendix F. Registrant Submitted Residue Study Summaries
- Appendix G. Reported Pollinator Incident Summaries (I023737-005 and I024127)
- Appendix H. Supplemental Information for the Tier II Colony Feeding Study (MRID 49510001)
- Appendix I. Additional Environmental Fate Information
- Appendix J. Refined Tier 1 Risk Assessment Description
- Appendix K. Shamblen And Judkins 2012 Poultry House Use

Table of Attachments

- Attachment 1. Tier II Method for Assessing Combined Nectar and Pollen Exposure to Honey Bee Colonies
- Attachment 2. Residue Bridging Analysis for Foliar and Soil Agricultural Uses of Neonicotinoids
- Attachment 3. Residue Bridging Analysis for Foliar and Soil Non-Agricultural Uses of Neonicotinoids
- Attachment 4. Residue Bridging Analysis for Seed Treatment Uses of Neonicotinoids

Table of Tables

| | |
|---|----|
| Table 1-1. Summary of on-field risk findings for honey bees (<i>Apis mellifera</i>) for the registered use patterns of imidacloprid | 20 |
| Table 2-1. Protection goals and examples of associated assessment and measurement (population and individual) endpoints for bees. | 35 |
| Table 3-1. Summary of labeled use information for foliar applications of imidacloprid..... | 49 |
| Table 3-2. Summary of labeled use information for soil applications of imidacloprid..... | 51 |
| Table 3-3. Summary of labeled use information for seed treatment applications of imidacloprid | 53 |
| Table 3-4. Summary of imidacloprid usage data as reported by the SLUA (2004-2013)..... | 55 |
| Table 3-5. Maximum application rates for bee-relevant non-agricultural uses of imidacloprid..... | 58 |
| Table 4-1. Chemical profile of imidacloprid..... | 60 |
| Table 4-2. Fate and transport properties for imidacloprid..... | 61 |
| Table 4-3. Imidacloprid root up-take/distribution and resultant concentrations in cotton, potatoes, corn and eggplant (%= up-take in % of the applied radioactivity and numbers in brackets are resultant concentrations in mg/kg) | 69 |
| Table 4-4. Imidacloprid up-take/distribution and resultant concentrations in various parts of the potato plants and only in the fruits of apples and tomatoes (%= up-take in % of the applied radioactivity and numbers in brackets are resultant concentrations in mg/kg). | 71 |
| Table 4-5. Summary of residue data from imidacloprid-treated seed studies evaluated from the open literature | 78 |

| | |
|---|-----|
| Table 4-6. Observed estimated concentrations of the stressor in parts per million= ppm) (parent imidacloprid + IMI-olefin and IMI-5-OH compounds) in varied crops, plant parts and application procedures based on radioactivity data | 79 |
| Table 4-7. Attractiveness of crops to bees for the registered foliar uses of imidacloprid..... | 82 |
| Table 4-8. Attractiveness of crops to bees for the registered soil uses of imidacloprid. | 83 |
| Table 4-9. Attractiveness of crops to bees for the registered seed treatment uses of imidacloprid. | 84 |
| Table 4-10. Pollinator Attractiveness for Various Tree Species ¹ | 85 |
| Table 4-11. Summary of contact and dietary exposure estimates for foliar applications, soil treatment, seed treatments, and tree trunk injections of pesticides for Tier I risk assessments | 86 |
| Table 4-12. Summary of estimated food consumption rates of bees. | 88 |
| Table 4-13. Summary of available registrant submitted foliar application residue studies | 93 |
| Table 4-14. Summary of available registrant submitted soil application residue studies | 97 |
| Table 4-15. Summary of the soil application residue studies evaluated from the open literature..... | 103 |
| Table 4-16. Summary of the registrant submitted seed treatment application residue studies | 106 |
| Table 4-17. Summary of the registrant-submitted combined application method residue studies (soil application + foliar spray) | 113 |
| Table 4-18. Summary of the registrant submitted combined application method residue studies (seed treatment + foliar spray)..... | 115 |
| Table 4-19. Summary of registrant-submitted residue data for application of imidacloprid to ornamental species..... | 117 |
| Table 4-20. Summary of open literature residue data for the application of imidacloprid to ornamental species..... | 120 |
| Table 4-21. Distribution of samples from corn fields according to their concentration of imidacloprid (Bonmatin, 2005) | 123 |
| Table 4-22. Distribution of residues from corn and sunflower pollen according to their concentration of imidacloprid (Bonmatin, 2007) | 123 |
| Table 4-23. Summary of observational monitoring studies which quantified imidacloprid residues in whole bee tissue | 124 |
| Table 4-24. Summary of observational monitoring studies which quantified imidacloprid residues in various hive and agricultural matrices..... | 126 |
| Table 5-1. Summary of endpoints to be used in screening-level and refined Tier I risk estimation | 132 |
| Table 5-2. Summary of registrant submitted adult acute contact toxicity studies (all studies tested <i>Apis mellifera</i>) | 133 |
| Table 5-3. Summary of adult acute contact toxicity studies to <i>Apis</i> bees evaluated from the open literature | 134 |
| Table 5-4. Summary of registrant submitted adult acute contact toxicity studies for non- <i>Apis</i> bees (Note: both studies concern <i>Bombus terrestris</i>)..... | 135 |
| Table 5-5. Summary of adult acute contact toxicity studies to non- <i>Apis</i> bees evaluated from the open literature | 136 |
| Table 5-6. Summary of registrant submitted adult acute oral toxicity studies (Note: All studies tested <i>Apis mellifera</i>). | 139 |
| Table 5-7. Summary of adult acute oral toxicity studies for <i>Apis</i> bees evaluated from the open literature | 140 |

| | |
|--|-----|
| Table 5-8. Summary of registrant-submitted and evaluated open literature studies assessing the chronic oral toxicity of imidacloprid to <i>Apis</i> and non- <i>Apis</i> adults..... | 144 |
| Table 5-9. Summary of results from Abbott <i>et al.</i> , 2008 examining the effects of imidacloprid TGAI on larval development of blue orchard bees (<i>Osmia lignaria</i>) . ¹ (Note: Study classified as qualitative)..... | 148 |
| Table 5-10. Summary of acute oral toxicity studies testing the degradates of imidacloprid in the open literature | 149 |
| Table 5-11. Summary of chronic adult oral toxicity studies with urea metabolite and 6-CNA (all studies conducted with <i>Apis mellifera</i>) | 151 |
| Table 5-12. Summary of semi-field (feeding) studies available from the open literature (<i>Apis</i>) ¹ | 160 |
| Table 5-13. Summary of semi-field (Tunnel) studies available from the open literature (<i>Bombus</i>) | 173 |
| Table 5-14. Summary of semi-field (feeding) studies available from the open literature (<i>Bombus</i>) | 174 |
| Table 5-15. Measured residues and associated RQs for chemicals found in the cotton field study hives (MRID 50206701)..... | 187 |
| Table 5-16. Summary of Tier III (full field) studies available from the open literature for <i>Apis</i> bees | 193 |
| Table 5-17. Summary of Tier III (full field) studies available from the open literature for <i>Bombus</i> bees. | 196 |
| Table 5-18. Summary of reported pollinator incident reports that are either associated with confirmatory residue analysis or registrant submitted | 199 |
| Table 6-1. Summary of Tier I screening-level RQs for contact exposure resulting from foliar uses of imidacloprid (screening-level contact on-field) | 208 |
| Table 6-2. Summary of Tier I screening-level RQs for oral exposure resulting from foliar uses of imidacloprid (based on model-generated exposure values on-field). ⁴ | 209 |
| Table 6-3. Summary of Tier I screening-level RQs for oral exposure ⁵ resulting from soil uses of imidacloprid (based on model-generated exposure values on-field). ⁴ | 210 |
| Table 6-4. Summary of labeled use information for seed treatment applications of imidacloprid (screening-level oral on-field) ⁴ | 211 |
| Table 6-5. Imidacloprid Use Patterns for Crops with or without Specific Application Restrictions | 211 |
| Table 6-6. Distance from the edge of the field associated with LOC exceedance, for citrus and pome fruits, calculated using AgDRIFT v.1.1.1, the Tier I Orchard/Airblast module, and app rate of 0.25 lbs. a.i./A..... | 213 |
| Table 6-7. Citrus and Pome Fruits: Tier II aerial applications, boom height 10 ft, wind speed 15 mph (label required), non-volatile rate 0.25 lbs./A, spray volume 5 gal/A | 213 |
| Table 6-8. Citrus and Pome Fruits: Tier II aerial applications, boom height 10 ft, wind speed 10 mph (label required), non-volatile rate 0.25 lbs./A, spray volume 5 gal/A | 214 |
| Table 6-9. Globe artichoke (only ground apps allowed): Tier I ground applications, high boom height (50 inches), application rate 0.126 lbs. a.i./A, 90th percentile results | 214 |
| Table 6-10. Globe artichoke (only ground apps allowed): Tier I ground applications, low boom height (20 inches), application rate 0.126 lbs. a.i./A, 90th percentile results | 215 |
| Table 6-11. Stone fruit, Tree nuts: Tier II aerial applications, boom height 10 ft, wind speed 15 mph (label required), non-volatile rate 0.10 lbs./A, spray volume 25 gal/A (label required for these crops) . | 215 |
| Table 6-12. Stone fruit, Tree nuts: Tier II aerial applications, boom height 10 ft, wind speed 10 mph, non-volatile rate 0.10 lbs./A, spray volume 25 gal/A (label required for these crops). | 215 |
| Table 6-13. Tuberous & Corm Vegetables and Certain Other Crops: Tier II aerial applications, boom height 10 ft, wind speed 15 mph (label required), non-volatile rate 0.04 lbs./A, spray volume 5 gal/A . | 216 |

| | |
|---|-----|
| Table 6-14. Tuberous & Corm Vegetables and Certain Other Crops: Tier II aerial applications, boom height 10 ft, wind speed 10 mph, non-volatile rate 0.04 lbs./A, spray volume 5 gal/A | 216 |
| Table 6-15. Summary of Tier I screening-level RQs for oral exposure resulting from soil incorporated poultry litter applications of imidacloprid (based on model-generated exposure values on-field). ⁴ | 218 |
| Table 6-16. Summary of Refined Tier I Risk Conclusions | 221 |
| Table 6-17. Seed treatment uses that are not attractive to honey bees..... | 222 |
| Table 6-18. Seed treatment uses that are harvested prior to bloom..... | 222 |
| Table 6-19. Tier I recommendations for imidacloprid residues in pollen and nectar | 223 |
| Table 6-20. Refined RQs (for adult honey bees) for crops with potential exposure from imidacloprid seed treatments | 223 |
| Table 6-21. Recommended Extrapolation Factors for Converting Neonicotinoid Residues from Surrogate to Target Plant Matrices | 228 |
| Table 6-22. Crop-group specific recommendations for bridging neonicotinoid residue data resulting from foliar and soil applications. | 229 |
| Table 6-23. Lines of evidence considered in characterizing colony-level risk to honey bees from foliar and soil applications of imidacloprid to oilseed crops..... | 234 |
| Table 6-24. Tier II assessment for imidacloprid and oilseed crops | 244 |
| Table 6-25. Summary of imidacloprid residues in tier III cotton study (MRID 50206701) | 246 |
| Table 6-26. Lines of evidence considered in characterizing colony-level risk to honey bees from soil application of imidacloprid to cucurbits. | 248 |
| Table 6-27. Summary of total imidacloprid residues ($\mu\text{g a.i./kg}$) measured in the pumpkin tier III field study..... | 253 |
| Table 6-28. Use and Application information for imidacloprid use on orchard crops and tropical fruits | 254 |
| Table 6-29. Lines of evidence considered in characterizing colony-level risk to honey bees from foliar applications of imidacloprid to orchard crops | 256 |
| Table 6-30. Lines of evidence considered in characterizing colony-level honey bee risk from soil applications of imidacloprid to orchard crops | 258 |
| Table 6-31. Lines of evidence considered in characterizing colony-level risk to honey bees for applications of imidacloprid to berry and small fruit. | 270 |
| Table 6-32. Lines of evidence considered in characterizing colony-level risk to honey bees from imidacloprid application to legume crops | 278 |
| Table 6-33. Seed treatment Tier II assessment for imidacloprid and legume crops | 279 |
| Table 6-34. Maximum application rates for registered uses of imidacloprid on attractive root and tubers, fruiting vegetables and herbs/spices..... | 280 |
| Table 6-35. Lines of evidence considered in characterizing colony-level risk to honey bees from imidacloprid applications to attractive root and tubers (sweet potato ¹) and herbs/spices | 280 |
| Table 6-36. Lines of evidence considered in characterizing colony-level risk to honey bees from imidacloprid foliar and soil applications to attractive fruiting vegetables (chilis, peppers, okra, roselle) | 281 |
| Table 6-37. SLUA data imidacloprid and use patterns registered for additional foliar and soil use patterns (2004-2013) with no available residue data..... | 285 |
| Table 6-38. Tier II assessment for imidacloprid seed treatment of peanuts | 286 |
| Table 6-39. Lines of evidence in characterizing colony-level risk to honey bees from foliar and soil applications of imidacloprid to ornamentals | 289 |

| | |
|---|-----|
| Table 6-40. Summary of imidacloprid and clothianidin residues in white clover nectar following foliar applications to turfgrass | 297 |
| Table 6-41. Comparison of oral exposure to pollen and nectar for adult <i>Apis</i> and Non- <i>Apis</i> bees ¹ | 299 |
| Table 6-42. Comparison of oral exposure to pollen and nectar for larval <i>Apis</i> and Non- <i>Apis</i> bees ¹ | 299 |
| Table 6-43. Comparison of imidacloprid acute contact toxicity to <i>Apis</i> and non- <i>Apis</i> bees..... | 300 |
| Table 6-44. Comparison of imidacloprid acute oral toxicity to <i>Apis</i> and non- <i>Apis</i> bees | 301 |
| Table 7-1. Summary of on-field risk findings for honey bees (<i>Apis mellifera</i>) for the registered use patterns of imidacloprid | 307 |

Table of Figures

| | |
|---|-----|
| Figure 2-1. Conceptual model for risk assessment of foliar spray applications of imidacloprid to honey bees. Red depicts systemic pathways. Dashed lines represent routes of exposure that are not considered major..... | 37 |
| Figure 2-2. Conceptual model for risk assessment of soil applications of imidacloprid to honey bees. Red depicts systemic pathways. Dashed lines represent routes of exposure that are not considered major. | 38 |
| Figure 2-3. Conceptual model for risk assessment of planting of imidacloprid-treated seeds to honey bees. Red depicts systemic pathways. Dashed lines represent routes of exposure that are not considered major..... | 39 |
| Figure 2-4. Tiered approach for assessing risk to honey bees from foliar spray applications..... | 42 |
| Figure 2-5. Tiered approach for assessing risk to honey bees from soil/seed applications | 43 |
| Figure 4-1. Conceptual diagram of imidacloprid application and processes related to bee exposure | 59 |
| Figure 4-2. Expected degradation profile for imidacloprid in compartments of the terrestrial ecosystems. Imidacloprid parent, and the IMI-olefin and IMI-5-OH degradates are considered residues of toxicological concern. | 67 |
| Figure 4-3. Comparison of up-take data obtained for imidacloprid applied to soil and that applied to foliage in potatoes | 72 |
| Figure 4-4. Suggested Imidacloprid degradation profile in plants..... | 75 |
| Figure 4-5. Summarization of the potential scenarios warranting a Tier I on and/or off-field risk assessment..... | 81 |
| Figure 5-1. Scatterplot of adult acute contact LD ₅₀ (48-96 hr) of <i>Apis</i> and non- <i>Apis</i> bees from registrant-submitted and open literature sources conducted with technical grade active ingredient (TGAI) and formulated typical end product (TEP) imidacloprid. Each point is a separate study and the red circle denotes the endpoint used for Tier I risk estimation purposes..... | 138 |
| Figure 5-2. Scatterplot of adult acute oral toxicity of <i>Apis</i> and non- <i>Apis</i> bees from registrant-submitted and open literature sources conducted with technical grade active ingredient (TGAI) and formulated typical end product (TEP) imidacloprid. Red circle denotes endpoint used for Tier I risk estimation purposes..... | 143 |
| Figure 5-3. Queen Production Data from Whitehorn et al (2012) in Controls (A), Low (B) and High Exposure Treatments (C). Legend numbers indicate the concentration in pollen and nectar, respectively. | 183 |
| Figure 6-1. Daily mean concentration (+/- 95% CL) of total imidacloprid in cotton floral nectar (adjusted to the maximum seasonal foliar rate of 0.31 lb a.i./A) following seed + 5 foliar applications in 3 MO trials | |

| | |
|---|-----|
| (MRID 49511702) and 1 foliar application in 5 CA trials (MRID 49103301, supplemental). Dashed and solid horizontal lines represent the colony level NOAEC and LOAEC, respectively..... | 237 |
| Figure 6-2. Mean concentration (+/- 95% CL) of total imidacloprid in cotton extrafloral nectar (adjusted to the maximum seasonal foliar rate of 0.31 lb a.i./A) following seed + foliar application in 3 MO trials (MRID 49511702). Dashed and solid horizontal lines represent the colony level NOAEC and LOAEC, respectively..... | 239 |
| Figure 6-3. Mean daily concentrations of total imidacloprid in cotton floral nectar following soil application of 0.33 lb a.i./A at 9 sites in California over 2 years (MRID 49665202) | 240 |
| Figure 6-4. Mean daily concentrations of total imidacloprid in cotton extrafloral nectar following soil application of 0.33 lb a.i./A at 9 sites in California over 2 years (MRID 49665202) | 240 |
| Figure 6-5. Mean daily concentrations of total imidacloprid in cotton floral nectar following soil application of 0.33 lb a.i./A at 9 sites in California vs. % sand and % organic matter (MRID 49665202). 241 | |
| Figure 6-6. Concentrations of total imidacloprid in cotton floral nectar (A) and extrafloral nectar following one soil application of 0.33 lb a.i./A and three foliar applications of 0.06 lb a.i./A (MRID 49665202). Data represent 9 sites among 1-3 years..... | 243 |
| Figure 6-7. Concentrations of total imidacloprid in cotton floral nectar following one soil application of 0.33 lb a.i./A and three foliar applications of 0.06 lb a.i./A vs. % sand (MRID 49665202). Data represent 9 sites among 1-3 years..... | 244 |
| Figure 6-8. Measured imidacloprid residue data in nectar equivalents (normalized to 0.38 lb a.i./A total annual application) versus imidacloprid endpoints for the cucurbit crop group..... | 250 |
| Figure 6-9. Measured imidacloprid, clothianidin, thiamethoxam, and dinotefuran residue data in nectar equivalents (normalized to 0.38 lb a.i./A total application) versus imidacloprid colony level endpoints..... | 251 |
| Figure 6-10. Mean-measured neonicotinoid residues (expressed as nectar equivalents) in orchard crops (normalized to 0.5 lb a.i./A) from pre-bloom, foliar applications relative to the imidacloprid colony level NOAEC and LOAEC..... | 260 |
| Figure 6-11. Mean measured neonicotinoid residues (expressed as nectar equivalents) in orchard crops (normalized to 0.5 lb a.i./A for orchard uses except tree nuts) from post-bloom, foliar applications relative to the imidacloprid colony level NOAEC and LOAEC..... | 261 |
| Figure 6-12. Mean measured neonicotinoid residues (expressed as nectar equivalents) in orchard crops (normalized to 0.3 lb a.i./A for tree nuts) from post-bloom, foliar applications relative to the imidacloprid colony level NOAEC and LOAEC | 262 |
| Figure 6-13. Mean measured neonicotinoid residues (expressed as nectar equivalents) in citrus (normalized to 0.5 lb a.i./A for citrus, tree nuts & tropical fruits) from soil applications relative to the imidacloprid colony-level NOAEC and LOAEC..... | 264 |
| Figure 6-14. Mean measured neonicotinoid residues (expressed as nectar equivalents) in citrus (normalized to 0.38 lb a.i./A) for pome and stone fruits from soil applications relative to the imidacloprid colony-level NOAEC and LOAEC..... | 265 |
| Figure 6-15. Mean concentration of total imidacloprid (expressed as nectar equivalents) in pome fruit (apples) following soil (0.38 lb ai/A) +foliar (2 x 0.06 lb ai/A) application pre- and post-harvest..... | 266 |
| Figure 6-16. Mean concentration of imidacloprid (total nectar equivalents) in stone fruit (cherry, plum, apricot, peach) following soil (0.38 lb ai/A) +foliar (2 x 0.06 lb ai/A) application pre- and post-harvest. 267 | |
| Figure 6-17. Mean-measured neonicotinoid residues (expressed as nectar equivalents) and modeled 50th and 90th percentiles for pre-bloom foliar applications (normalized to 0.1 lb a.i./A) of neonicotinoids | |

| | |
|---|-----|
| to berry and small fruits.). Dashed and solid horizontal lines represent the imidacloprid colony level NOAEC and LOAEC, respectively..... | 272 |
| Figure 6-18. Measured neonicotinoid residues (expressed as nectar equivalents) normalized to 0.1 lb a.i./A) for post-bloom foliar applications to the berry crop group in relation to and imidacloprid colony-level endpoints..... | 273 |
| Figure 6-19. Mean residue concentrations of imidacloprid (expressed as nectar equivalents) in strawberries following pre-bloom soil application of 0.5 lb ai/A (MRID 49090502)..... | 274 |
| Figure 6-20. Measured neonicotinoid residue data (normalized to 0.5 lb a.i./A) versus imidacloprid endpoints for the low growing berry crop group subgroup (13-07H); Pre-bloom applications..... | 275 |
| Figure 6-21. Mean measured imidacloprid residues (expressed as nectar equivalents) normalized to 0.5 lb a.i./A) for post-bloom soil applications to blueberries in relation to imidacloprid colony-level endpoints | 276 |
| Figure 6-22. Nectar equivalent residues for pollen-only producing fruiting vegetables normalized to the maximum single foliar application rate of imidacloprid (0.08 lb a.i./A) | 283 |
| Figure 6-23. Nectar equivalent residues for pollen-only producing fruiting vegetables normalized to the maximum single soil application rate of imidacloprid (0.5 lb a.i./A) | 284 |
| Figure 6-24. Mean residue concentrations in nectar, expressed as Clothi equivalents, following foliar application of thiamethoxam to ornamental plants (MRID 47303407). Data are normalized to the maximum imidacloprid application rate of 0.4 lb ai/A. | 290 |
| Figure 6-25. Mean residue of total imidacloprid in nectar following soil application to two ornamental shrubs (Mach et al. 2017). Data are normalized to the maximum application rate of 4.6 g a.i./m. | 291 |
| Figure 6-26. Mean residue concentrations (95% C.L.) in nectar of three ornamental plants following soil drench application of imidacloprid. Data are from multiple supplemental studies and are normalized to a maximum rate of 4.6 g/m plant height..... | 292 |
| Figure 6-27. Mean residue concentrations in nectar, expressed as Clothi equivalents, following soil drench application of thiamethoxam to ornamental plants (MRID 47303407). Data are normalized to the maximum imidacloprid application rate of 0.4 lb ai/A..... | 293 |
| Figure 6-28. Mean residue concentrations, expressed in terms of nectar equivalents following trunk injection of total imidacloprid to horse chestnut trees normalized to max app rate of 0.09 g/cm trunk diameter..... | 294 |
| Figure 6-29. Mean residue concentrations expressed in terms of nectar equivalents following trunk injection dinotefuran to the cherry tree normalized to the max app rate of 0.09 g/cm trunk diameter | 295 |
| Figure 6-30. Comparison of effect levels from qualitative Tier II feeding studies on <i>B. terrestris</i> obtained from the open literature (numbers in parentheses refer to the magnitude of effects and/or additional exposure to pollen) | 303 |

1. EXECUTIVE SUMMARY

1.1. Background and Scope

The purpose of this assessment is to characterize the potential risks of registered uses of imidacloprid to bees, focusing quantitative estimates of risk to honey bees (*Apis mellifera*). Risks to non-*Apis* bees (e.g., bumble bees, solitary bees) are evaluated qualitatively based on available information. Imidacloprid, along with the other nitroguanidine-substituted neonicotinoid insecticides, clothianidin, thiamethoxam, and dinotefuran, are currently undergoing Registration Review by the U.S. Environmental Protection Agency (EPA). With imidacloprid, the EPA published a final registration review Work Plan in 2009 and issued a Generic Data Call-in in 2010 to obtain data required for assessing risks to bees and other taxa. In 2016, EPA issued its *Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid* (D429937)³ which evaluated risks to bees associated with the registered agricultural uses of imidacloprid. Following the receipt of public comments on the 2016 Preliminary Pollinator Risk Assessment and additional data, the Agency has issued this 2019 Final Bee Risk Assessment for Imidacloprid which:

1. Incorporates modifications based on public comments where appropriate;
2. Includes additional exposure and effects data the Agency received since the preliminary assessment;
3. Assesses the potential risks to bees associated with registered uses for both agriculture and non-agricultural uses of imidacloprid;
4. Implements a revised method for assessing colony-level risks from combined exposure to nectar and pollen; and
5. Incorporates results from a quantitative analysis of residue data to bridge (extrapolate) residue data to address data gaps.

1.2. Use Profile

Imidacloprid is registered for a variety of agricultural crops, including (but not limited to): root and tuber vegetables, bulb vegetables, leafy, brassica, cucurbit, and fruiting vegetables, beans and other legumes, citrus fruit, pome fruit, stone fruit, berries, tree nuts, cereal grains, herbs, oilseed crops (e.g. canola, cotton), tropical fruits, and other use patterns not associated with a crop group such as peanuts and tobacco. It has been registered for use in the United States since 1994. The maximum application rates vary by crop and method, but typically do not exceed 0.5 lbs. a.i./A (single application or per year). Imidacloprid may be applied to crops via a variety of methods including aerial and ground foliar sprays, soil drench, chemigation, soil injection, in-furrow sprays, and seed treatment, including multiple application methods within the same growing season, so long as the 0.5 lbs a.i./A rate is not exceeded. Additionally, there are a wide variety of registered non-agricultural uses, some examples of which include trunk injection to ornamental trees, forestry, pet spot-on treatments, turf, and applications to ornamentals.

³ Available at: <https://www.epa.gov/pesticides/epa-releases-neonicotinoid-assessments-public-comment>

1.3. Risk Assessment Approach

Consistent with the Agency's 2014 *Guidance for Assessing Pesticide Risks to Bees* (USEPA et al. 2014), risks are quantified for the honey bee, *Apis mellifera*, and to the extent that data are available, characterized qualitatively for other bee species relative to the honey bee. The primary routes of exposure assessed include contact of bees with spray droplets and oral ingestion via pollen and nectar. Initially, the potential for exposure of bees was determined qualitatively based on the expected use pattern and attractiveness of the treated crop. Acute and chronic risk quotients (RQs) were then estimated at the Tier I (individual bee) level using model-generated exposure estimates that reflect default (screening-level) assumptions and laboratory toxicity endpoints. For oral routes of exposure, further refinement of the Tier I RQs was conducted using measured data on residues in pollen and nectar from representative crops when default Tier I RQs exceed the Agency's level of concern (LOC). Additionally, an off-field spray drift assessment was conducted and indicated a Tier I risk above the LOC for all foliar uses. When the refined Tier I RQ values exceeded the LOC values, this same residue information was used to characterize risks based on colony-level effects determined from Tier II (semi-field) studies. In comparing pollen residues to the sucrose-based Tier II endpoints, a method was developed to adjust pollen residues to nectar equivalent levels based on a quantitative analysis of differential exposure and toxicity of nectar and pollen observed at the colony-level. Lastly, information from Tier III (full field) studies was also considered, when available, for characterizing risk.

With the higher tier risk assessment, multiple lines of evidence were used to characterize the strength of evidence supporting the risk conclusions into the following categories: "strongest", "moderate", and "weakest." These lines of evidence included:

- The quality and quantity of available pollen and nectar residue data;
- The magnitude, duration, and frequency that measured residues in nectar and pollen (expressed as nectar equivalence) exceeded the colony-level NOAEC and LOAEC;
- Where applicable, the magnitude and duration that modeled 50th, 70th, and 90th percentile residues exceeded the colony-level toxicity endpoints;
- The extent that residues would need to be diluted from uncontaminated food sources to reduce exposure to levels below the colony-level endpoints;
- The spatial extent of potential exposure based on pesticide usage data or other factors;
- Agronomic practices that affect exposure;
- Results from Tier III (full field) studies; and
- Ecological incidents involving bees.

1.4. Risk Conclusions Summary

Error! Reference source not found. summarizes the risk conclusions for honey bees associated with each crop or crop group⁴ for which imidacloprid is registered. Conclusions that are expressed with red text

⁴ Crops groups are codified in 40 CFR 180.41 and can be found here: <https://www.ir4project.org/crop-grouping/>

indicate uses of imidacloprid which pose risks to bees, while green text indicates uses where the likelihood of adverse effects on bees is considered low.

1.4.1. 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 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 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.

1.4.2. Uses With On-Field Risk

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. For other non-woody crops with limited or no residue data (*e.g.*, attractive root and tubers, certain attractive fruiting vegetables, herbs and spices), residues for herbaceous crops (*e.g.*, cucurbits, cotton, legumes) are used as surrogates. For woody crops that lack residue data (tree nuts, tropical fruits), residues for stone fruit, pome fruit and citrus are used as surrogate measures of exposure. Furthermore, residue data for woody ornamentals are used to represent forestry uses due to lack of data. Generally, this risk assessment finds a potential for oral risk to honey bee colonies from foliar and/or soil applications of imidacloprid to honey-bee attractive crops which are not harvested prior to bloom.

Strongest Evidence of Risk:

For foliar and soil applications of imidacloprid, the lines of evidence are considered “strongest” for supporting the finding of oral risk to honey bee colonies resulting from applications to:

- **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 & soil), and
- **attractive ornamentals and forest trees** (foliar, soil)

These findings are supported by multiple lines evidence indicating 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 applications of imidacloprid, the strength of evidence is considered “moderate” in indicating a colony-level risk from oral exposure of honey bees for the following registered uses:

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

These findings are supported by lines evidence indicating 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 from oral exposure of honey bees for the following registered uses:

- **attractive 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), and

1.4.3. Off Field Risk:

Based on a Tier I analysis, for foliar applications, off-field dietary risks to individual bees exposed to spray drift extend 1000 feet from the edge of the treated field. There are uncertainties with this conclusion which include: assumption of available attractive forage off field, individual level toxicity data, BeeREX default estimates for residues, and AgDRIFT™ modeling.

Soil applications are assumed to have a low off-field risk because of low potential to drift.

Regarding seed treatments, there is a potential for off-site transport of contaminated dust at the time of planting. This concern is supported by multiple bee kill incidents that are associated with the planting of treated seed, particularly with corn, canola, and soybean.

Table 1-1. Summary of on-field risk findings for honey bees (*Apis mellifera*) for the registered use patterns of imidacloprid

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|---------|-------------------------|-----------------------------------|------------------------------------|---|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| 1 | Root/Tuber Vegetables | No | Foliar | NA | NA | NA | NA | LOW RISK ⁴ |
| | | | Soil | | | | | RISK ⁸ (Weakest evidence) |
| | | | Seed ¹² | | | | | RISK ⁸ (Weakest evidence) |
| | | Yes ⁵ | Foliar | Cucurbits (C, T, D) Oilseed (C, T, D) | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Soil | | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Seed ¹² | | Yes | Yes | No | LOW RISK |
| 3 | Bulb Vegetables | No | Soil | NA | No | NA | NA | LOW RISK ⁴ |
| | | | Seed ¹² | | No | | | |
| 4 | Leafy Greens Vegetables | No | Foliar | NA | No | NA | NA | LOW RISK ⁴ |
| | | | Soil | | No | | | |
| 5 | Brassica Vegetables | No | Foliar | NA | No | NA | NA | LOW RISK ⁴ |
| | | | Soil | | No | | | |
| | | | Seed ¹² | | No | | | |
| 6 | Legumes | Yes | Foliar | Soybean | Yes | No | No | LOW RISK |
| | | | Soil | No | Yes | NA | Yes | RISK ⁸ (Weakest evidence) |
| | | | Seed (soybean, peas) ¹² | Soybean | Yes | Yes | No | LOW RISK |
| | | | Seed (beans) ¹² | No | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| 8 | Fruiting Vegetables | No | Foliar | NA | NA | NA | NA | LOW RISK ⁴ |
| | | | Soil | | | | | |
| | | Yes ⁶ | Foliar | Tomato (T, D), Chili (T), Pepper (D), Cucurbits (C, T, D) Oilseed (C, T, D), Soybean (I, T) Tomato Tomato (T, D), Chili (T), | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | | Soil | | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|---------|---------------------|-----------------------------------|---------------------|--|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| | | | | <i>Pepper (D), Cucurbits (C, T, D) Oilseed (C, T, D), Soybean (I, T)</i> | | | | |
| 9 | Cucurbit Vegetables | Yes | Soil | Melon, watermelon <i>Pumpkin (C, T, D), cucumber (C, T, D), cantaloupe (C), muskmelon (T), melon (D), squash (C, T, D)</i> | Yes | Yes | Yes | RISK⁸ (Strongest evidence) |
| 10 | Citrus Fruits | No ⁹ | Foliar | NA | NA | NA | NA | LOW RISK⁴ |
| | | | Soil | NA | NA | NA | NA | LOW RISK⁴ |
| | | Yes | Foliar (pre-bloom) | Oranges <i>Apple and Orange (T)</i> | Yes | Yes | Yes | RISK⁸ (Strongest evidence) |
| | | | Foliar (post-bloom) | <i>Almonds (C), Apple (C), Cherry (T, D, I), Peach (C, D, T), and Plum (T)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| | | | Soil (pre-bloom) | <i>Lemon and Orange (C, T)</i> | Yes | Yes | Yes | RISK⁸ (Strongest evidence) |
| | | | Soil (post-bloom) | <i>Lemon and Orange (C)</i> | Yes | Yes | Yes | RISK⁸ (Moderate evidence) |
| 11 | Pome Fruits | Yes | Foliar (post-bloom) | <i>Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| | | | Soil (post-bloom) | Apple⁷ <i>Orange and Lemon (C)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| 12 | Stone Fruits | Yes | Foliar (post bloom) | Cherry <i>Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| | | | Soil (post-bloom) | Cherry, peach, apricot, plum⁷ <i>Orange and Lemon (C)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|---------|--------------------------------------|-----------------------------------|---------------------|--|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| 13 | Berries / small fruits | Yes | Foliar (pre-bloom) | Blueberry (D, T), Cranberry (T, D), Grape and Strawberry (T) | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | | Foliar (post-bloom) | Grape (C) | Yes | Yes | No | LOW RISK ⁸ |
| | | | Soil (pre-bloom) | Strawberry (T), Grape (C) | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | | Soil (post-bloom) | Blueberry | Yes | Yes | No | LOW RISK ¹³ |
| 14 | Tree nuts | Yes | Foliar (post-bloom) | Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T) | Yes | Yes | No | LOW RISK ⁸ |
| | | | Soil (post-bloom) | Orange and Lemon (C) | Yes | Yes | Yes | RISK ⁸ (Moderate evidence) |
| 15 | Cereal Grains | Yes | Seed ¹² | Corn | Yes | No | No | LOW RISK |
| | | No | Seed ¹² | NA | NA | NA | NA | LOW RISK ⁴ |
| 19 | Herbs / Spices | Yes | Foliar | Cucurbits (C, T, D) Oilseed (C, T, D) | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Soil | | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| 20 | Oilseed ¹⁰ | Yes | Foliar | Cotton | Yes | Yes | Yes | RISK (Moderate evidence) |
| | | | Soil | Cotton | Yes | Yes | Yes | RISK (Moderate evidence) |
| | | | Soil + Foliar | Cotton ⁷ | Yes | Yes | Yes | RISK (Strongest evidence) |
| | | | Seed ¹² | No | Yes | Yes | No | LOW RISK ⁸ |
| None | Tropical Fruits, coffee, pomegranate | Yes | Foliar (post-bloom) | Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T) | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Soil (post-bloom) | Orange and Lemon (C) | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|--------------|--------------------------|-----------------------------------|--|--|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| | Banana, plantain | Yes | Foliar, Soil (pre-bloom) | Oranges <i>Apple and Orange (T)</i> | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | Tobacco, globe artichoke | No | Foliar, Soil | NA | NA | NA | NA | LOW RISK ⁴ |
| Hops, peanut | Yes | Foliar | Tomato <i>Tomato (T, D), Chili (T), Pepper (D)</i> | Yes | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | Soil | | Yes | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | Peanuts | Yes | Seed ¹² | No | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | Turf (residential lawn) | Yes | Foliar, Soil | No | Yes | Yes | Yes | RISK ¹¹ (Moderate evidence) |
| | Turf (commercial sod) | No | Foliar, Soil | NA | NA | NA | NA | LOW RISK ¹¹ |
| Ornamentals | No | Foliar, Soil, Injection | No | NA | NA | NA | NA | LOW RISK ⁴ |
| | Yes | Foliar | <i>Lilly, mock orange, lilac (T)</i> | NA | NA | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | Soil | Holly, Pepperbush <i>Lilly, mock orange, lilac (T)</i> | Yes | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | injection | | <i>Cherry (D)</i> | NA | NA | Yes | Yes | RISK ⁸ (Moderate evidence) |
| Forestry | No | Foliar, Soil, Injection | NA | NA | NA | NA | NA | LOW RISK ⁴ |
| | Yes | Foliar | <i>Mock orange, lilac (T)</i> | NA | NA | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | Soil | Holly, Pepperbush <i>Mock orange, lilac (T)</i> | Yes | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | Injection | <i>Cherry (D)</i> | NA | NA | Yes | Yes | RISK ⁸ (Moderate evidence) |

NA = not assessed. Residue data for imidacloprid indicated by crops in **bold**; residue data bridged from other neonicotinoids are shown in *italics as follows: C = Clothianidin; D = Dinotefuran; T = Thiamethoxam*.

¹ Based on USDA 2017. *Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen*.

² Green indicates a low potential for risk; red indicates a potential for risk. Strength of evidence refers to the confidence in the risk conclusion based on the available lines of evidence.

³ If crop is not attractive to bees or is harvested prior to bloom (USDA 2017), Tier I RQs are not calculated on the treated field and risk conclusion is “LOW RISK.”

⁴ Agronomic practices indicate root/tubers, globe artichoke, tobacco, bulb, leafy brassica and most fruiting vegetables are harvested prior to bloom, unless grown for seed (USDA 2017). Other members of a crop group are not attractive to bees. These factors limit exposure of bees on the treated field. Exposure may occur on the treated field if crop is grown for seed (*i.e.*, when the crop is allowed to flower). Although imidacloprid may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied/yr and specific geographic areas where crops are grown for seed.

⁵ Exposure is presumed for honey bee-attractive root and tubers (sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish) since available information does not indicate they are harvested prior to bloom (USDA 2017).

⁶ Applies to chilies, peppers, roselle and okra which are considered honey bee attractive (USDA 2017).

⁷ Residue data reflect combined soil + foliar application.

⁸ Due to limited or lack of data for imidacloprid, this risk finding is supported by residue data from other neonicotinoids applied to crops within this crop group using the same application method (but scaled to the imidacloprid application rate). Risk findings for the following crop groups were also supported by residue data from other crop groups. For attractive root/tubers and herbs/spices, risk finding was supported by residue data from other herbaceous crops (cucurbits, cotton, fruiting vegetables, legumes). For tree nuts and tropical fruits, risk finding was supported by residue data from orchard crops. For hops and peanut (soil & foliar, risk conclusions were bridged from pollen only-producing fruiting vegetables. For beans and peanut (seed treatment), risk finding was supported by all available neonicotinoid residue data for seed treatments. For foliar and soil applications to ornamentals, risk finding was also supported by ornamental data for thiamethoxam. Risks from forestry uses were assessed from woody ornamentals.

⁹ During bloom, mandarin orange trees are tented with nets to prevent pollination from bees.

¹⁰ Cotton is registered for all application methods. All other members of the oilseed group including canola and sunflower are registered only for seed treatment use.

¹¹ For uses on residential turf (lawns), a potential for exposure of bees exists for attractive blooming weeds (*e.g.*, clover). Qualitative data suggests that residues of imidacloprid in nectar of clover following turf applications at the maximum label rate can exceed Tier I levels of concern and the Tier II honey bee colony NOAEC for up to two weeks. Uses on commercial sod production are not expected to result in exposure of bees due to management practices which limits the occurrence of weeds.

¹² Risk conclusions for seed treatments are based on the oral route of exposure and drift of abraded seed coat dust is not considered.

¹³ Assumes post bloom applications occur ≥ 200 days prior to bloom during following season.

1.4.4. Other Lines of Evidence

Multiple Tier III (full-field colony-level studies) were available from the registrant and open literature that examined the effects of various seed treatment, soil and foliar uses of imidacloprid on honey bee colonies. The Tier III studies involving seed treatment uses of imidacloprid generally did not indicate a treatment related effect, which is consistent with this application method being associated with relatively low residues in pollen and nectar reported from field residue studies. However, these Tier III studies had 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). A registrant-submitted full field study involving seed, soil and foliar uses of imidacloprid on cotton was determined to be unreliable for multiple reasons, including the application of multiple pesticides (and their documented exposure in honey bee colonies) to both reference and treated sites throughout the exposure phase of the study. A second full field study involving a soil application of imidacloprid to pumpkins was considered of limited use in risk assessment due to relatively low concentrations of imidacloprid (< 5.1 µg/L) found in pollen and nectar, presumably due to the heavy (clay) soils associated with the study sites (heavy soils may reduce systemic uptake of imidacloprid and other neonicotinoids relative to lighter (sandier) soils).

Based on the reported ecological incidents for bees, a clear association between individual bee or colony losses to imidacloprid was often not indicated, generally due to a lack of a confirmatory residue analysis. In the cases where a link between imidacloprid exposure and individual or colony losses was made, these reports generally concerned residential uses or applications made by pesticide control operators (PCOs). Additionally, open literature data on the prevalence of imidacloprid in bee-relevant crop and hive matrices generally indicated relatively infrequent and low levels of detection (typically < 3 µg/L). These hive monitoring studies included surveys across the United States and Europe where imidacloprid residues were investigated in pollen, nectar, bee, and wax samples. These studies indicated that while imidacloprid was detected in various matrices, the frequency of detection was generally below 10% and where the frequency exceeded 10%, the mean values were generally marginally above the limits of quantitation. Although one study reported a mean of detected imidacloprid residues in pollen samples of 39 µg/L, this mean originated from 10 detections out of 350 analyzed samples (2.9%). In the aggregate, the hive monitoring studies suggest that despite widespread use of imidacloprid on crops through multiple application methods, the magnitude and frequency of detection in hive matrices is relatively low. One possible explanation for the low detection frequency in hive matrices is dilution from non-contaminated sources of pollen and nectar.

1.4.5. Non-*Apis* Bees

Comparisons of available Tier I acute toxicity data for non-*Apis* species, including bumble bees, indicates that honey bees are similarly sensitive to imidacloprid compared to other non-*Apis* bees which have been tested. Notably, however, few of the estimated 4,000 species of North American bees have been tested to date. An analysis of food consumption rates (of pollen and nectar) for several non-*Apis* bee species suggests that oral exposure of honey bees is similar to (or protective of) oral exposure of other bee species. In addition, reported incidents involving non-*Apis* bees, including bumble bees, indicate a

complete exposure pathway exists for non-*Apis* bees and suggest that individuals are sensitive when exposed via registered uses. Thus, the available data suggest that honey bees represent a reasonable surrogate for assessing individual-level risks of imidacloprid to at least some species of non-*Apis* bees. The Tier I risk conclusions for honey bees are therefore used to represent risks to solitary bees and individual-level risks to bumble bees. One notable exception relates to differences in attractiveness of crops to different bee species. For example, many fruiting vegetables are attractive to non-*Apis* bees (*e.g.*, bumble bees) but not to honey bees. Therefore, a potential for on-field exposure and risk to non-*Apis* bees may occur with applications to these fruiting vegetables, but this is not expected for honey bees.

Based on higher tier testing reported in the open literature, colony-level effects of imidacloprid on bumble bees were reported at concentrations lower than those reported from the registrant-submitted colony feeding study with honey bees. This suggests that imidacloprid uses with risk identified based on Tier II assessments with honey bees may also be a risk concern for crops which are similarly attractive to bumble bees. However, these higher tier bumble bee studies are considered only for qualitative use in the risk assessment, primarily because they lack analytical verification of the test substance and raw data. Furthermore, a formal process for quantifying risks to non-*Apis* bees has not been developed by the USEPA. As such, while there may be a potential for effects to non-*Apis* species, the ability to reliably determine a no-effect concentration is limited at this time. As the pollinator risk assessment framework used by the EPA indicates the honey bees are intended to be reasonable surrogates for other bee species, conclusions from the weight of evidence for the honey bee can be used to help inform about potential risks to other non-*Apis* species.

1.5. Environmental Fate and Exposure Summary and Residue Bridging Approach

Imidacloprid is a systemic insecticide that is highly soluble in water and exhibits low volatility. These properties, combined with low propensity to partition to organic carbon, suggest that imidacloprid will be highly mobile in the terrestrial environment (*i.e.*, subject to leaching in soils and runoff). The dominant transformation processes for imidacloprid are photolysis (very fast in the presence of water) and aerobic soil degradation. However, aerobic soil metabolism for imidacloprid is very slow (half-lives range from 200 days to more than one year) and therefore, imidacloprid is expected to persist in the soil system. Based on their occurrence as the primary degradates identified in plant metabolism studies and comparable toxicological properties with respect to bees relative to parent imidacloprid, the primary stressors of concern include parent imidacloprid and its metabolites imidacloprid-olefin (IMI-olefin) and imidacloprid-5-OH (5-OH-IMI). As a systemic chemical, imidacloprid is absorbed by plants via the roots, stems and foliage and is considered xylem mobile. Therefore, its dominant uptake and translocation routes in plants is expected to follow the transpiration stream (*i.e.*, no downward transport from leaves to roots). Additionally, numerous field studies have demonstrated that imidacloprid applied via foliar, soil or seed treatment methods can result in residues in pollen and nectar of blooming plants.

Exposure of bees through direct contact by foliar spray of imidacloprid (*i.e.*, interception of spray droplets either on or off the treated field) and oral ingestion (*e.g.*, consumption of contaminated pollen and nectar) represent the primary routes of exposure considered in this assessment. Bees may also be

exposed to imidacloprid through other routes, such as contaminated surface water, plant guttation fluids, honey dew, soil (for ground-nesting bees), and leaves. However, there is high uncertainty regarding the importance of these exposure routes, and the Agency lacks information to quantify risks from these other routes. With respect to potential exposure via drift of abraded seed coat dust, the Agency does not have a method to reliably quantify exposures of bees via abraded seed coat dust and consistent with the Agency's 2014 risk assessment guidance, this risk assessment focuses on quantitative estimates of exposure via contact and ingestion of pollen and/or nectar. However, the Agency is working with different stakeholders to identify best management practices and to promote technology-based solutions that reduce this potential route of exposure. Finally, the "carryover" of imidacloprid residues in soil (*i.e.* the potential for year-to-year accumulation in soil leading to higher residues in pollen and nectar) was considered as a potential route of exposure in this assessment. This potential for carryover was evaluated using multiple lines of evidence. While model results and some empirical data from multi-year applications in soil suggest possible year-to-year accumulation in soils, available residue data in pollen and nectar are not indicative of imidacloprid carryover in treated crops. Furthermore, imidacloprid residues in succeeding crops (*e.g.* white clover following seed treatment applications to corn) are low when detected, such that risk to honey bees is not expected.

In accordance with the 2014 *Guidance for Assessing Pesticide Risks to Bees* (USEPA *et. al.* 2014), the exposure assessment considered Tier I (model-generated/screening-level) exposures of bees via contact and oral routes. Prior to this step, a determination was made on the potential for exposure based on indications of crop attractiveness to bees and cultural practices (*e.g.* whether the crop is harvested before bloom) referenced in the United States Department of Agriculture document, *Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen* (2017). For foliar sprays, off-field exposures via spray drift were also considered. These modeled/screening-level, exposure estimates were then refined using available information on measured imidacloprid residues in pollen and nectar of representative crops to assess risks to individual bees. This same residue information was also used to characterize risks at the colony level.

Tier I exposure estimates are generated with EFED's BeeREX model. A comparison of BeeREX estimated environmental concentrations (EECs) to measured residues in pollen and nectar collected from crops treated with imidacloprid indicates varying levels of confidence in the model's predictive accuracy. For example, modeled values for foliar applications are generally the same order of magnitude to several orders of magnitude higher than measured residues. To account for this potential uncertainty, refined exposure estimates are generated using measured concentrations of imidacloprid in pollen and nectar obtained in available field-residue studies. At the individual bee level, maximum empirical residue values are compared to laboratory toxicity assay endpoints, while at the colony level, residues are compared to a semi-field (colony-based) no effect concentration. These residue studies were mostly conducted at the maximum labeled application rates and generally resulting in pollen concentrations an order of magnitude higher than nectar concentrations. Measured concentrations of imidacloprid in pollen and nectar from field-residue studies are available across a variety of crop groups, including: legumes (soybean), fruiting vegetables (tomato), cucurbit vegetables (melon, watermelon), citrus fruit (orange, grapefruit), pome fruit (apple), stone fruit (cherry, peach, plum, apricot), berry and small fruits (blueberry, strawberry), cereal grains (corn), and oilseed (cotton).

While refined exposure estimates via empirical residue data are available for many crops (e.g., those listed above), there is lack of residue data in bee relevant matrices for several crops and application methods which introduces uncertainty into exposure potential. There is also uncertainty how well empirical residue data from a single crop represent those from botanically similar crops. To address these limitations, this assessment uses a residue bridging approach for quantifying dietary neonicotinoid exposure to honeybee colonies (Tier II) from use of imidacloprid. In this approach, measured residue data from four neonicotinoids⁵ in the nitroguanidine-substituted class are pooled by crop group and application type and analyzed for use as surrogate values in bee-relevant matrices where empirical data are not available for a chemical or crop. When available data allowed (for foliar applications to selected crops), the Agency employed a Monte Carlo approach to estimate median and upper bound exposure values over time.

1.6. Ecological Effects Summary

As with other neonicotinoid insecticides, imidacloprid acts on the insect nicotinic acetylcholine receptors (nAChRs) of the central nervous system via competitive modulation. At the individual organism level, a number of molecular, cellular, physiological, histopathological and behavioral effects of imidacloprid to bees have been reported from laboratory tests at varying levels of exposure for adult and larval bees.

A robust registrant-submitted dataset was available to characterize the acute and chronic toxicity of imidacloprid to adult and larval honey bees at the Tier I (individual) level. Additionally, the EPA, through a joint review effort with Health Canada's Pest Management Regulatory Agency (PMRA) and the State of California's Department of Pesticide Regulation (CDPR) evaluated over 75 studies from the open literature that investigated the toxic effects on *Apis* and non-*Apis* bees at the individual and colony level. Consistent with the Agency's 2014 Risk Assessment Guidance, the focus for this assessment was on apical endpoints which directly related to growth, development, survival, and reproduction known to impact bees at the colony and population/community level.

Based on the evaluated data, imidacloprid is classified as very highly toxic to adult honey bees (*Apis mellifera*) 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, and a 21-day chronic toxicity test did not show significant effects (p>0.05) up to and including the highest concentration tested, 40 µg a.i./L (equivalent to 0.00183 µg a.i./bee). For chronic oral toxicity to adults, a 10-day registrant-submitted study achieved a No Observed Adverse Effect Concentration (NOAEC), based on significant effects (p<0.05) on food consumption at 0.0011 µg a.i./bee/day. The Lowest Observed Adverse Effect Concentration (LOAEC) for this study was 0.0018 µg a.i./bee/day. **Table 1-2** below shows the Tier I endpoints to be used for risk estimation for adult and larval honey bees at the individual level (Tier I).

Currently available data suggest that colony level effects of imidacloprid on honey bees may result through multiple mechanisms including (but not limited to) reduction in number of worker bees available for foraging or maintaining hive temperature (during over-wintering), reduction in foraging efficiency via sublethal effects on workers, decreased number or delayed development of brood either

⁵ Clothianidin, Thiamethoxam, Dinotefuran, and Imidacloprid

from direct exposure or indirectly from reduced brood feeding and maintenance by hive bees, and reduced fecundity and survival of queens. The Tier II colony level effects assessment is based on a registrant-submitted colony feeding study that assessed a 6-week exposure through nectar (spiked sucrose). This study was subjected to a tri-agency review by EPA, PMRA, and CDPR that included a comprehensive statistical re-analysis of the raw data. Although other Tier II studies conducted with *Apis mellifera* were reviewed only this colony feeding study was considered acceptable for quantitative use in this risk assessment. Based on a tri-agency analysis of the statistical and biological considerations of the data, a NOAEC and LOAEC of 23 and 47 µg a.i./L in nectar were determined based on reductions of the number of adult workers, numbers of pupae, pollen stores and honey stores which persisted across much of the study duration.

Table 1-2. Summary of the toxicity endpoints to be used in risk estimation for Tier 1

| Study Type | Endpoint ¹ | Reference | Classification |
|--|--|---------------|----------------|
| Adult Acute Contact Toxicity | 96-hr LD ₅₀ : 0.043 µg a.i./bee | MRID 49602717 | Acceptable |
| Adult Acute Oral Toxicity | 48-hr LD ₅₀ : 0.0039 µg a.i./bee | MRID 42273003 | Acceptable |
| Adult Chronic Oral Toxicity | 10-day NOAEL/LOAEL (food consumption): 0.0011/0.0018 µg a.i./bee/day | MRID 50399101 | Acceptable |
| Larval Acute (single dose) | No data available | | |
| Larval Chronic (repeat dose) | 21-day NOAEL/LOAEL: 0.0018/>0.0018 µg a.i./larva | MRID 49090506 | Supplemental |
| Colony Feeding Study (Tier II, spiked sucrose) | Colony NOAEC/LOAEC: 23/47 µg a.i./L | MRID 49510001 | Acceptable |

¹Represents most sensitive (*i.e.* lowest) of all endpoints within a particular study type for studies for which raw data (to allow for independent statistical verification of the endpoint) are available.

1.7. Major Assumptions and Uncertainties

There are several assumptions and uncertainties associated with both the effects and exposure assessments for imidacloprid. While these assumptions and uncertainties are described in further detail throughout this assessment, a list of the major assumptions and uncertainties is provided below:

- Direct contact and consumption of pollen and nectar are assumed to be the dominant routes of exposure for bees. Potential exposure via abraded seed coat dust is being addressed through separate ongoing development of best management practices.
- The use of honey bees as a surrogate for other bee pollinators has limitations, it is assumed that data on individual organisms as well as colony-level data can provide relevant information on the potential effects of a pesticide on both solitary bees as well as social bees
- Model-predicted, screening-level EECs serve as a conservative estimate for predicting exposure to individual adult and larval honey bees resulting from foliar, soil, and seed treatment applications and therefore may over-estimate exposure.
- It is assumed that pollen and nectar are equally potent routes of exposure when assessing the risk to individual bees.
- Extrapolation of individual bee risk findings to risks at the colony-level is uncertain due to the complexities of exposure and effects at the colony level.

- Off-field estimates of risk are based on screening-level exposure estimates which cannot be refined with available residue data and are assumed to be representative of bee attractive plants with foraging bees present during bloom. Therefore, potential off-field risks may be overestimated when these assumptions are not realized.
- Available data from crop residue studies may not fully capture variation in temporal and spatial factors (*e.g.*, weather patterns, soil type) that affect imidacloprid residues in pollen and nectar for the tested crop.
- Based on multiple lines of evidence, colony-level exposure via pollen is assumed to be 20X less than that for nectar.
- Interpretation of Tier II risks based on the 6-week, sucrose colony feeding study assumes that bees forage on the treated crop nearly 100% of the time to represent the nectar needs of the colony. In the field, bees may forage for significantly shorter periods of time particularly for crops with a shorter blooming duration. Bees may also forage on alternative (untreated) plants. Conversely, bees associated with migratory colonies used for pollination services may feed on treated crops for similar or possibly longer periods of time over the course of a growing season.

2. PROBLEM FORMULATION

Problem formulation serves as the first step of a risk assessment and it provides the foundation for the entire ecological risk assessment. In addition to identifying the risk assessment scope and objectives, the problem formulation includes three major components: (1) assessment and measurement endpoints that reflect management goals and the ecosystem they represent, (2) conceptual models that describe key relationships between a stressor (*i.e.*, pesticide) and assessment endpoint or between several stressors and assessment endpoints, and (3) an analysis plan that summarizes the key sources of data and methods to be used in the risk assessment (USEPA 1998).

2.1. Registration Review Background

As articulated by the Agency's Registration Review Schedule, the nitroguanidine-substituted neonicotinoid insecticides (imidacloprid, clothianidin, thiamethoxam, dinotefuran) are currently undergoing Registration Review. With imidacloprid, the first installment of the Registration Review process was the publication of the Problem Formulation and Preliminary Work Plan documents in 2008, (USEPA 2008a; 2008b). With respect to assessing ecological risk, these documents summarized the available data on ecological effects and environmental fate of imidacloprid, identified key data gaps, and set forth a schedule for obtaining these data and completing the ecological risk assessment. Following its receipt and response to public comments, the Agency published a Final Work Plan in 2009 (USEPA 2009), which was subsequently amended in 2010 to request additional data related to assessing risks to bees (USEPA 2010a). Also in 2010, a Generic Data Call-In (GDCI) was issued (USEPA 2010b) that required registrants to submit certain types of environmental fate and effects data to support the preliminary ecological risk assessment⁶.

2.2. Nature and Scope of Assessment

Unlike most of the Agency's Preliminary Ecological Risk Assessment for pesticides which focus on multiple taxa of aquatic and terrestrial non-target organisms, this preliminary assessment focuses solely on the risk of registered imidacloprid uses to bees. The decision to focus on imidacloprid's potential risk to bees (honey bees [*Apis mellifera*] and non-*Apis* bees) reflects that Agency's desire to evaluate potential risks and appropriate mitigation measures earlier in the Registration Review process relative to other taxa. It also reflects the large volume of information related to environmental exposure and effects of imidacloprid to bees which has been generated over the past decade.

Several other aspects related to the scope of this assessment are important to note. First, this assessment includes a quantitative estimate of risk (*i.e.*, derivation of risk quotients) for the honey bees. Other types, *i.e.* non-*Apis* bees, are also considered in this assessment, *e.g.*, bumble bees (*Bombus* spp.) and solitary bees, but risks are evaluated qualitatively (*i.e.*, without derivation of risk quotients) due to limitations in available data and suitably vetted risk assessment methods for these species. This

⁶ Preliminary Aquatic Risk Assessment to Support the Registration Review of Imidacloprid (12/22/2016, DP 435477); Preliminary Terrestrial Risk Assessment to Support Registration Review of Imidacloprid (11/28/2017, DP 442390)

approach is consistent with the Agency's *Guidance for Assessing Pesticide Risks to Bees* (USEPA/PMRA/CDPR, 2014) which recognizes that methods and data for assessing pesticide effects (and exposure) to bumble bees and solitary bees are still evolving and lack standardized regulatory guidelines.

Second, this assessment considers the agricultural and non-agricultural uses (e.g., ornamental, turf,, forestry uses) whereas the previous preliminary bee assessment considered only agricultural uses.

Finally, the effects data considered in this assessment are centered on the Agency's protection goals and their associated assessment endpoints previously identified for bees (USEPA et. al. 2014). As described further in **Section 2.5**, the assessment and measurement endpoints used to support these protection goals are those that closely relate to survival, growth and reproduction of individual (solitary) bees and overall colony strength and survival (for eusocial bees). A large body of literature has been generated on effects of imidacloprid on bees at lower levels of biological organization (e.g., molecular, organ-level effects) in addition to endpoints relating to behavioral aspects of individual bees. While such data serve as additional lines of evidence in risk assessment and understanding the mechanisms of toxicological effects, they were formally evaluated in this assessment only when they were quantitatively linked to Agency assessment endpoints described in **Section 2.5**.

2.3. Pesticide Type, Class, and Mode of Action

Imidacloprid (IUPAC name: N-[1-[(6-chloropyridin-3-yl)methyl]-4,5-dihydroimidazol-2-yl]nitramide) is a systemic, neonicotinoid insecticide which acts on the insect nicotinic acetylcholine receptors (nAChRs) of the central nervous system via competitive modulation (IRAC 2015). Imidacloprid is in the N-nitroguanidine group of neonicotinoids (IRAC subclass 4A) along with clothianidin, thiamethoxam and dinotefuran.⁷ Its mode of action on target insects involves out-competing the neurotransmitter, acetylcholine, for available binding sites on the nAChRs (Zhang et al. 2008). At low concentrations, neonicotinoids cause excessive nervous stimulation and at high concentrations, insect paralysis and death will occur (Tomizawa and Casida 2005). Imidacloprid is a xylem-mobile systemic compound that is readily taken up by the roots of the plant and translocated throughout the plant via the transpiration stream⁸.

2.4. Overview of Imidacloprid Uses

Imidacloprid is registered on a wide variety of agricultural crops, including (but not limited to): root and tuber vegetables, bulb vegetables, leafy green vegetables, brassica, cucurbit, and fruiting vegetables, cereal grains, citrus fruit, pome fruit, stone fruit, berries, tree nuts, beans and other legumes, herbs, oilseed crops (e.g. canola, cotton) and other use patterns not associated with a crop group such as peanuts and tobacco. It has been registered for use in the United States since 1994. Maximum application rates vary by crop and method, but typically do not exceed 0.5 pounds of active ingredient

⁷ <http://www.irac-online.org/>

⁸ Sur, R. and Stork, A. (2003). Uptake, translocation, and metabolism of imidacloprid in plants. Bulletin of Insectology. 56 (1), 35 – 40.

per acre (lbs a.i/A; single application or per year). Imidacloprid may be applied to crops via a variety of methods including aerial and ground foliar sprays, soil drench, chemigation, soil injection, in-furrow sprays, and seed treatment. There are a wide variety of non-agricultural uses, some examples of which include tree trunk injection, forestry, pet spot-on treatments, turf, and applications to ornamentals. Additionally, there are a number of use patterns that specifically prohibit applications during the pre-bloom or blooming period or whenever bees are foraging. A detailed summary of registered agricultural uses of imidacloprid is provided in **Section 3**.

2.5. Overview of Physicochemical, Fate, and Transport Properties

As described in **Section 4.1**, imidacloprid is a highly water soluble chemical with low vapor pressure and Henry's Law Constants. These properties suggest that the chemical will be readily soluble for movement with water and that it is unlikely to volatilize to a meaningful degree. Furthermore, the organic carbon: water partitioning coefficient (K_{OC}) for imidacloprid is low, indicating that it is mobile.

The dominant transformation processes for imidacloprid are photolysis (very fast in the presence of water) and aerobic soil degradation. However, aerobic soil transformation for imidacloprid is very slow (half-life values range from 200 days to more than a year) and therefore, it is expected to persist in the soil system. Photodegradation may occur on soil surfaces via soil application and on wet foliage in case of foliar application, although photolysis on dry soil appears to be slow. Several metabolites of imidacloprid may be formed in the terrestrial soil/plant system and are of toxicological concern with respect to bees. These include IMI-olefin and IMI-5-OH (5-OH-IMI). In plants, imidacloprid may be taken up via the roots or across plant stems and leaves. Imidacloprid is considered xylem mobile, with dominant uptake routes following the transpiration stream⁹. Details of imidacloprid fate and transformation pathways are provided in **Section 4.1**.

2.6. Stressors of Toxicological Concern

As discussed in **Section 4.1**, imidacloprid is considered persistent in the terrestrial environment with the exception of conditions that favor aqueous photolysis. Metabolites identified from aerobic soil metabolism studies include IMI-olefin, nitrosamine, guanidine, and 5-keto urea isomers. Based on plant metabolism studies submitted to the Agency, metabolites of imidacloprid detected in various plants include guanidine, IMI-5-OH, IMI-olefin, IMI-4,5-OH, 6-chloronicotinic acid (6-CNA), 6-chloropicolylalcohol (6-CPA), nitrosamine and urea. Data on the relative toxicity of these metabolites are discussed in **Section 5** while information of the residues of these toxic metabolites is described in **Section 4.6**. These data indicate that two metabolites (IMI-olefin and IMI-5-OH) are of similar toxicity as parent imidacloprid to the honey bee, while other metabolites are much less toxic (e.g. 6-CNA and urea). These two toxic metabolites were included for analysis in the submitted residue studies of pollen and nectar. Therefore, based on relative toxicity of various imidacloprid metabolites to bees and their occurrence in pollen and nectar, the primary stressors of toxicological concern for this assessment are:

⁹ *Ibid*

- Imidacloprid (parent)
- IMI-olefin, and
- IMI-5-OH.

2.7. Protection Goals and Assessment Endpoints

The Agency has recently defined protection goals for assessing pesticide risks to bees which include: 1) maintenance of pollination services, 2) hive product production (*e.g.*, honey, wax, propolis), and 3) bee biodiversity (**Table 2-1**; USEPA/PMRA/CDPR 2014). These goals do not apply uniformly across *Apis* and non-*Apis* bees; however, they are considered relevant for both social and solitary bees, and honey bees are generally used a surrogate for non-*Apis* bees. Protection goals dictate assessment endpoints for which specific measurement endpoints are identified. As EPA regulates pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act, which directs EPA to weigh ecological risks associated with a pesticide product against the benefits of that product, protection goals serve to clarify the potential risks against which benefits can be balanced.

The management goals, assessment endpoints and measurement endpoints depicted in **Table 2-1** reflect the Agency's use of honey bees as a surrogate for other bee pollinators. Although this approach has limitations, it is assumed that data on individual organisms as well as colony-level data can provide relevant information on the potential effects of a pesticide on both solitary bees as well as social bees. In addition, protection of honey bees would contribute to pollinator diversity indirectly by preserving the pollination and propagation of the many plant species pollinated by honey bees, which also serve as food sources for other pollinating insects. In evaluating potential risks specific to honey bees, the protection goals of preserving pollination services and production of hive products (*e.g.*, honey, wax) are readily assessed through the assessment of population size and the stability (*e.g.*, presence of a queen, uniform brood pattern) of the colony and through direct and indirect measures of the quantity and quality of hive products¹⁰. As such, the sensitivity of individual larval or adult honey bees based on laboratory-based acute and chronic toxicity studies are used as measurement endpoints for screening-level assessments of potential adverse effects on colony strength, survival and capacity of the colony to produce any products. While these measurement and assessment endpoints are tested using individual bees from managed honey bee colonies, they apply to feral honey bee colonies and, in the absence of data specific to other bees, these measurement endpoints provide useful information for assessing the survival and development of solitary bees and potential effects on bee species richness and biodiversity. To the extent that data are available for other species such as the bumble bee (*e.g.*, *Bombus terrestris*), blue orchard bee (*Osmia lignaria*), and the alfalfa leafcutting bee (*Megachile rotundata*), the effects of imidacloprid on these species are also considered in this risk assessment.

¹⁰ USEPA. 2012. White Paper in Support of the Proposed Risk Assessment Process for Bees. Submitted to the FIFRA Scientific Advisory Panel for Review and Comment September 11 – 14, 2012. Office of Chemical Safety and Pollution Prevention Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Protection Agency, Washington DC; Environmental Assessment Directorate, Pest Management Regulatory Agency, Health Canada, Ottawa, CN; California Department of Pesticide Regulation
<http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0004>

Table 2-1. Protection goals and examples of associated assessment and measurement (population and individual) endpoints for bees.

| Protection Goal | Assessment Endpoints | Example Measurement Endpoints | |
|-----------------------------------|---|---|--|
| | | Population level and higher | Individual Level |
| Contribution to Bee Biodiversity | Species richness ¹ and abundance | Individual bee survival (solitary bees) and colony strength and survival (social bees) Species richness and abundance ¹ | Individual worker and larval survival assays; larval emergence; queen fecundity/reproduction |
| Provision of Pollination Services | Population size ² and stability of native bees and commercially managed bees | Colony strength and survival; colony development | Individual worker and larval survival assays; queen fecundity; brood success; worker bee longevity |
| Production of Hive Products | Quantity and quality of hive products | Quantity and quality of hive products; including pesticide residue levels on honey/wax | Individual worker and larval survival assays; queen fecundity/reproduction; larval emergence |

¹ Use of honey bees as a surrogate for other insect pollinators has limitations; however, it is assumed that as with all surrogates, data on individual organisms as well as colony-level data would provide some relevant information on the potential effects of a pesticide on both solitary bees as well as “eusocial” taxa. In addition, protection of honey bees would contribute to pollinator diversity indirectly by preserving the pollination and propagation of the many plant species pollinated by honey bees, which also serve as food sources for other pollinating insects.

² For managed honey bees, population size can include numbers of colonies.

2.8. Conceptual Models and Risk Hypotheses

The risk hypothesis and conceptual model are used to depict the hypothesis in terms of the source of the stress, route of exposure, receptor, and changes in the receptor attribute(s) of concern (USEPA, 1998). With imidacloprid, the conceptual models are depicted separately for each method of application to agricultural crops (*i.e.* foliar spray, soil application and seed treatment).

2.8.1. Foliar Spray

There are many factors that determine the exposure of bees to a pesticide, including methods and timing of application, application rate, attractiveness of the crop to bees, and agronomic practices such as harvesting crops prior to bloom. In general, however, foliar application of systemic pesticides such as imidacloprid are expected to result in exposure of bees via two dominant routes: 1) direct contact with the bee via interception of pesticide spray droplets and newly-sprayed vegetation, and 2) oral ingestion through contaminated pollen and nectar (Figure 2-1). With foliar sprays, these routes of exposure may occur on the treated field or adjacent to the treated field in the case of spray drift. With honey bees, nectar and pollen foragers are expected to receive high exposure via their frequent interaction with blooming crops. Dominant exposure routes of in-hive bees (*e.g.*, nurse, queen, drone bees) include ingestion and processing of pollen and nectar and exposure through production. Stored honey is expected to be an important exposure route for over wintering bees. Processed bee bread, brood food,

and royal jelly are major routes of exposure for developing larvae and the queen, although limited evidence suggests pesticide levels in royal jelly are orders of magnitude below those found in pollen and nectar (USEPA 2012).

Exposure through the vapor phase is not expected to be a significant route of exposure for imidacloprid, regardless of application method. Exposure of honey bees through contact with contaminated soil is also not expected to be a major route of exposure, although this may be important for ground-nesting bees on or near the treated site. Other routes of exposure are also possible, including consumption of plant guttation fluids, water from dew droplet formation on leaves, puddles, and other surface water. Although relatively high concentrations of neonicotinoid insecticides have been reported in plant guttation fluid (*e.g.* Girolami *et al.* 2009), recent reviews of honey bee exposure routes indicate high uncertainty in the importance of guttation fluid ingestion relative to other oral ingestion sources of pesticides (*e.g.*, nectar and pollen). This uncertainty is partly due to the availability of guttation fluid at times of the year when crops are generally unattractive to pollinators and there are other sources of water (Godfray *et al.* 2014; USEPA 2012). Furthermore, there is presently a lack of robust information on water intake rates by bees from surface water and multiple factors that affect these rates. Therefore, this pathway is not currently considered for quantitative estimation of risk to bees.

Changes in the assessment endpoints (*e.g.*, size and stability of bee colonies, production of hive products, pollinator species richness and abundance) as a result of the aforementioned pesticide exposure routes may occur through various means, including reduction in number of worker bees available for foraging or maintaining hive temperature (over wintering), reduction in foraging efficiency via sublethal effects on workers, decreased number or delayed development of brood either from direct exposure to pesticide or indirectly from reduced brood feeding and maintenance by hive bees, and reduced fecundity and survival of queens. Changes in these assessment endpoints are directly related to impacts on protection goals of maintaining pollination services, production of hive products and contribution to pollinator biodiversity.

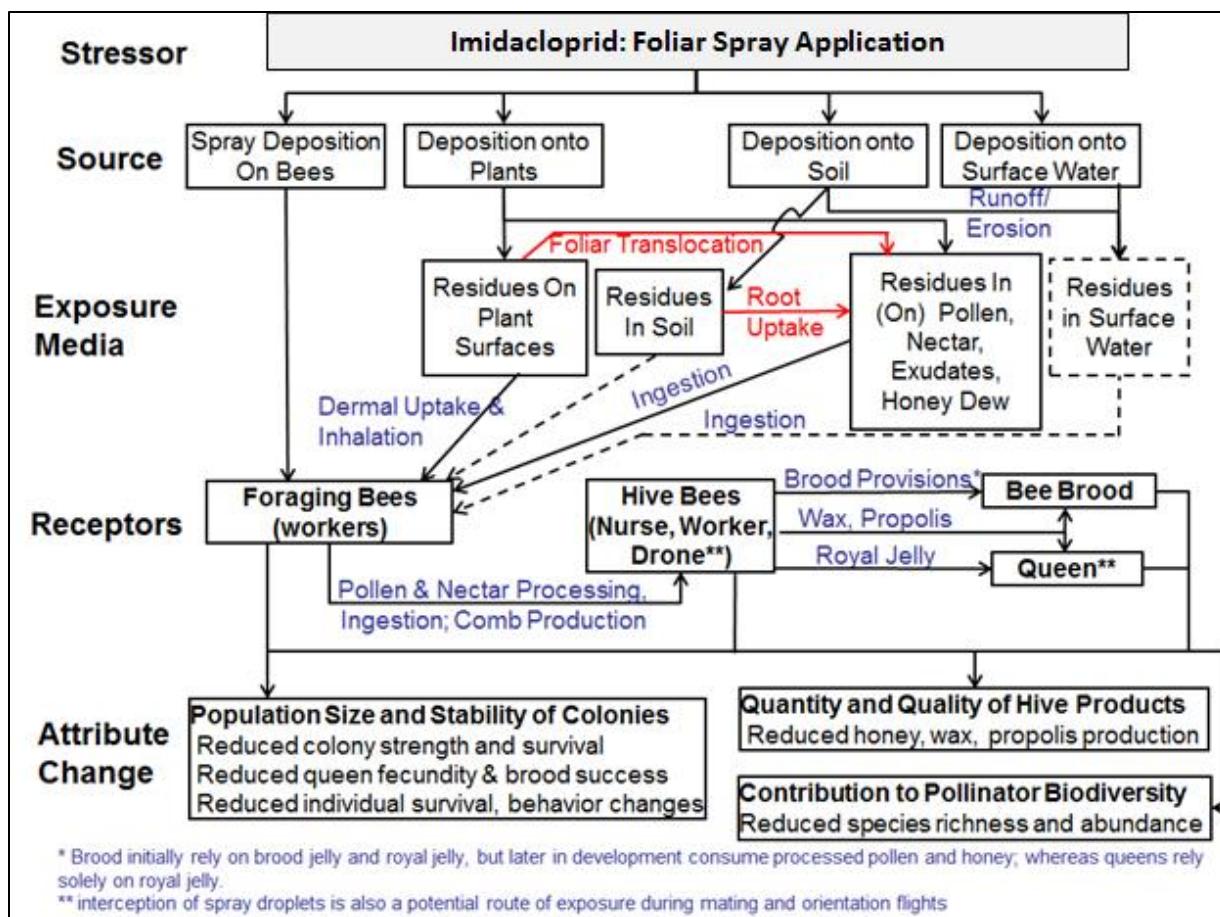


Figure 2-1. Conceptual model for risk assessment of foliar spray applications of imidacloprid to honey bees. Red depicts systemic pathways. Dashed lines represent routes of exposure that are not considered major.

2.8.2. Soil Application

Exposure of honey bees to imidacloprid via soil applications (e.g., drench, injection, in-furrow sprays and chemigation) are expected to follow the same routes of exposure as shown previously with foliar sprays, except that contact exposure (on-field and off-field) is not expected to be significant since applications are typically made close to soil surfaces where the likelihood of drift is reduced (**Figure 2-2**).

Furthermore, the nature of these applications is not expected to result in substantial spray drift to adjacent sites relative to foliar sprays. Depending on the timing of rainfall events, there is some potential for exposure via imidacloprid runoff and subsequent translocation into plants adjacent to the treated field. Also, given its persistence in soil, there is potential for soil applications of imidacloprid to be taken up by rotational plants (e.g., cover crops) that are planted after crop harvest. Some of these rotational crops may be attractive to bees as sources of pollen and/or nectar (e.g., clover).

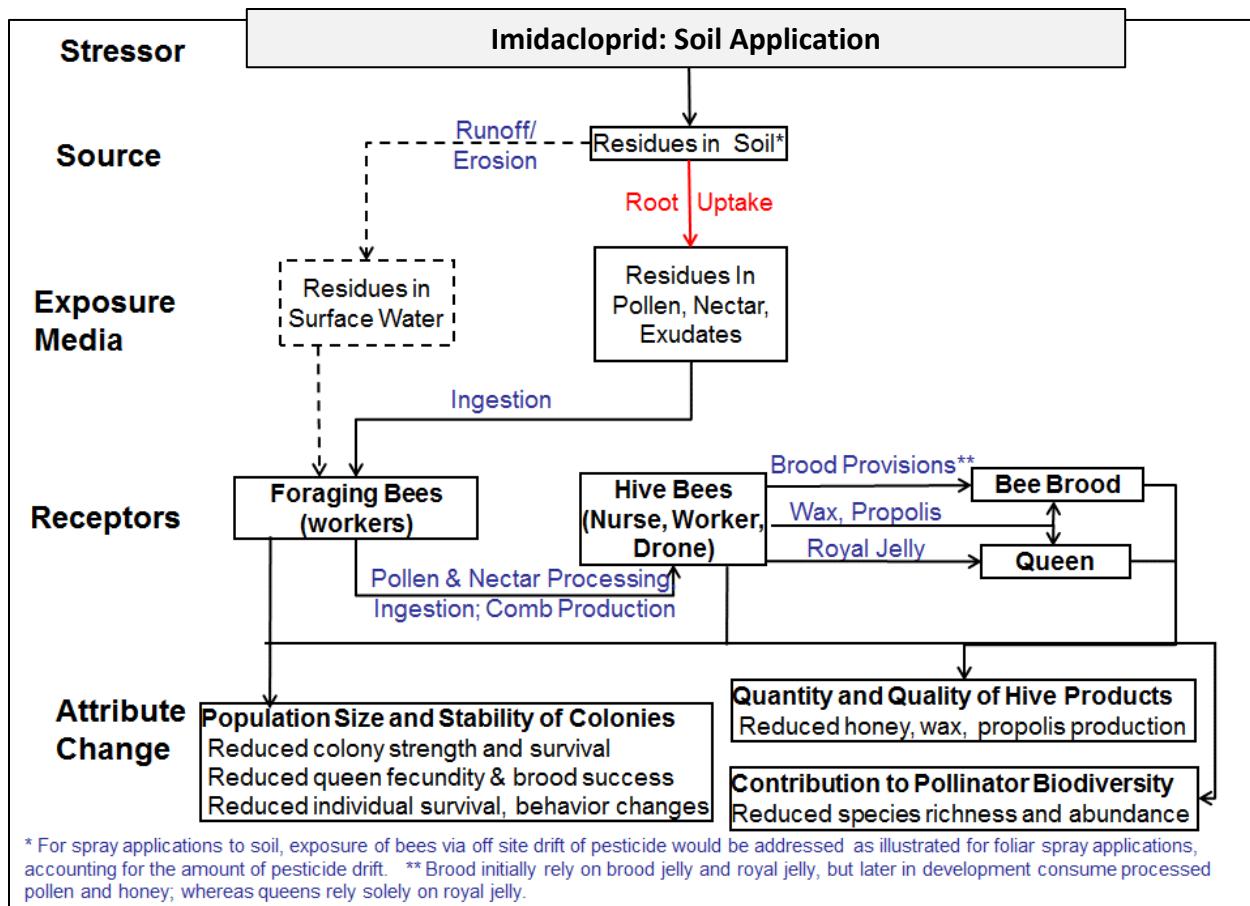


Figure 2-2. Conceptual model for risk assessment of soil applications of imidacloprid to honey bees. Red depicts systemic pathways. Dashed lines represent routes of exposure that are not considered major.

2.8.3. Seed Treatment

Potential exposure routes of honey bees to imidacloprid used as seed treatments include pollen, nectar, exudates (e.g., guttation fluid), and honey dew resulting from translocation from the seed to growing plant tissues (**Figure 2-3**). Another route of exposure includes contact with abraded seed coat dust during planting. The latter pathway has been associated with incidents of honey bee mortality (Pistorius *et al.* 2009, Forster *et al.* 2009) and is the focus of considerable research (e.g., Tapparo *et al.* 2012, Krupke *et al.* 2012). The extent to which honey bees are exposed via contact with abraded seed coat dust is determined by many factors including the physico-chemical properties of the seed coating, seed planting equipment, use of fluency agents (e.g., talc), environmental conditions (wind speed, humidity), and hive location in relation to sowing. Off-site drift of contaminated seed coat dust also may contribute to residues on plants, soil, and surface water to which bees may be exposed through direct contact and ingestion of surface water, pollen, and nectar. This is further described in **Section 2.10** (Measures of Exposure). One important attribute of the seed treatment exposure pathway is that exposure to pesticides may occur over a wide time scale (e.g., at seed sowing, during plant growth and flowering, and potentially at plant harvest from exposure to contaminated plant dust).

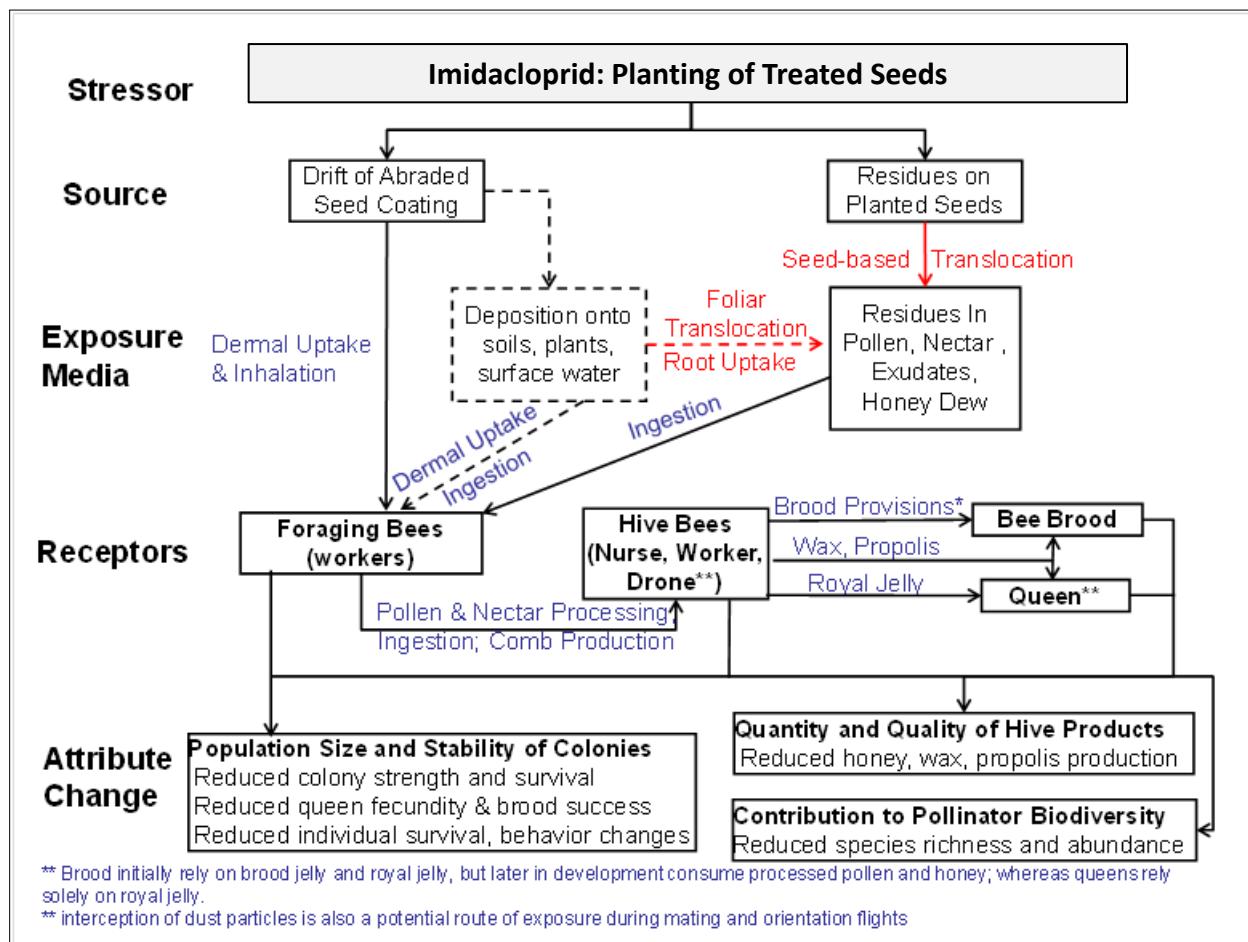


Figure 2-3. Conceptual model for risk assessment of planting of imidacloprid-treated seeds to honey bees. Red depicts systemic pathways. Dashed lines represent routes of exposure that are not considered major.

2.9. Analysis Plan

The analysis plan provides a rationale for selecting and omitting risk hypotheses in the actual analysis. As with any risk assessment process, the analysis plan also articulates data gaps, the methods used to evaluate existing and anticipated data, and the assumptions that will be made where data may be missing. The analysis plan also identifies the specific measures of exposure (e.g., estimated environmental concentrations; EECs) and effect (e.g., median lethal dose for 50% of the organisms tested; LD₅₀) which will be used to develop risk estimates.

2.9.1. Risk Assessment Methodology

For assessing the risks of registered agricultural uses of imidacloprid to bees, this assessment follows the Agency's guidance entitled: "Guidance for Assessing Pesticide Risks to Bees" (USEPA *et al.* 2014). The risk assessment consists of an iterative, tiered process that considers multiple lines of evidence related

to exposure and effects of pesticides to bees. The overall risk assessment framework for foliar spray applications and soil/seed applications are shown in **Figure 2-4** and **Figure 2-5**, respectively.

Assessing the Potential for Exposure. The first step of this process is to determine whether exposure to adult and larval bees is of concern. This determination is made based on information about the application methods, application timing, attractiveness of crops to bees, and agronomic practices for the treated crops. This process also considers the potential for bees to be exposed both by foraging on the treated field (*i.e.*, on-field exposure) and from foraging at sites adjacent to the treated field (*i.e.*, off-field exposure). With foliar spray applications of pesticides such as imidacloprid, it is presumed that off-field exposure would occur due to spray drift to adjacent areas regardless of the attractiveness or agronomic practices pertaining to the treated crop.

Tier I Assessment (Screening-level). The next step in this process is to conduct a Tier I risk assessment based on estimated exposure via contact and oral routes and effects on individual bees tested in the laboratory. The (EECs) are first calculated at a screening-level using conservative (high end) assumptions of potential exposure. For foliar sprays, these screening-level EECs are calculated for both “on-field” and “off-field” exposures. The screening-level EECs are then compared to acute and chronic toxicity endpoints for adult and larval bees (oral exposure) and acute toxicity endpoints for adult bees (for contact exposure) for the purposes of calculating risk quotients (*i.e.* the ratio of the EEC to toxicity endpoints).

Tier I Assessment (Refined). If the screening-level tier I Risk Quotient (RQ) values exceed the acute or chronic risk level of concern (LOC), then refinements to the Tier I screening-level RQs are considered. These refinements include additional information on the potential exposure of bees to the pesticide, such as field studies that quantify the pesticide residue in pollen and nectar of treated crops, *i.e.* using measured rather than estimated exposure levels. The Tier I RQ values are then recalculated using the refined EECs and again compared to the acute (0.4) and chronic (1.0) LOCs. If the acute or chronic risk LOCs are again exceeded using the refined Tier I, then mitigation options may be considered and/or a higher tier assessment may be conducted.

Tier II Assessment. The Tier II assessment is based on effect studies that characterize pesticide effects at the whole-colony level and therefore, reduce uncertainty associated with extrapolating effects on individual bees under laboratory conditions (Tier I toxicity studies) to effects on the colony. It is important to recognize that Tier II effect studies are conducted under semi-field conditions where the high-end exposure at the colony level is generally expected. Often, Tier II semi-field studies are conducted in which whole colonies are exposed to the pesticide of concern, either in enclosed mesh tunnels or via the diet, such as through feeding spiked sucrose. In Tier II studies other stressors may be present and potential compensatory mechanisms of the colony may occur. Unlike Tier I, characterization of risk in Tier II does not involve the calculation of RQ values *per se*. Rather, risks at the colony level are usually characterized in relation to pesticide application rate and/or measured residue levels in their diet. Interpretation of such whole-colony effects studies is often much more complex than Tier I studies and relies on comprehensive considerations of the extent to which adverse effects are likely to occur at the colony level. Based on the risks identified at lower-tier assessments, their

associated uncertainties, and other lines of evidence, the risk assessor considers the impact of any risk mitigation options identified for the pesticide of concern.

Tier III Assessment. The need for more refined information conducted at the Tier III level is determined depending on the nature of the estimated risks, the associated uncertainties, and available risk mitigation options. Tier III studies are full-field studies that are designed to mimic actual pesticide applications and exposure of bees encountered in the environment. Tier III full field studies are usually highly complex and require a high level of effort to design and conduct so as to address specific sources of uncertainties and potential risks identified in lower risk assessment tiers. Similar to risk characterization at Tier II, risk characterization at Tier III considers multiple lines of evidence available from lower Tiers and other information sources (*e.g.*, open literature) that meet the respective Agency's standard for inclusion in risk assessments. Risk assessment conclusions are made based on the weight of evidence, available risk mitigation options, and uncertainties in the available data and methods.

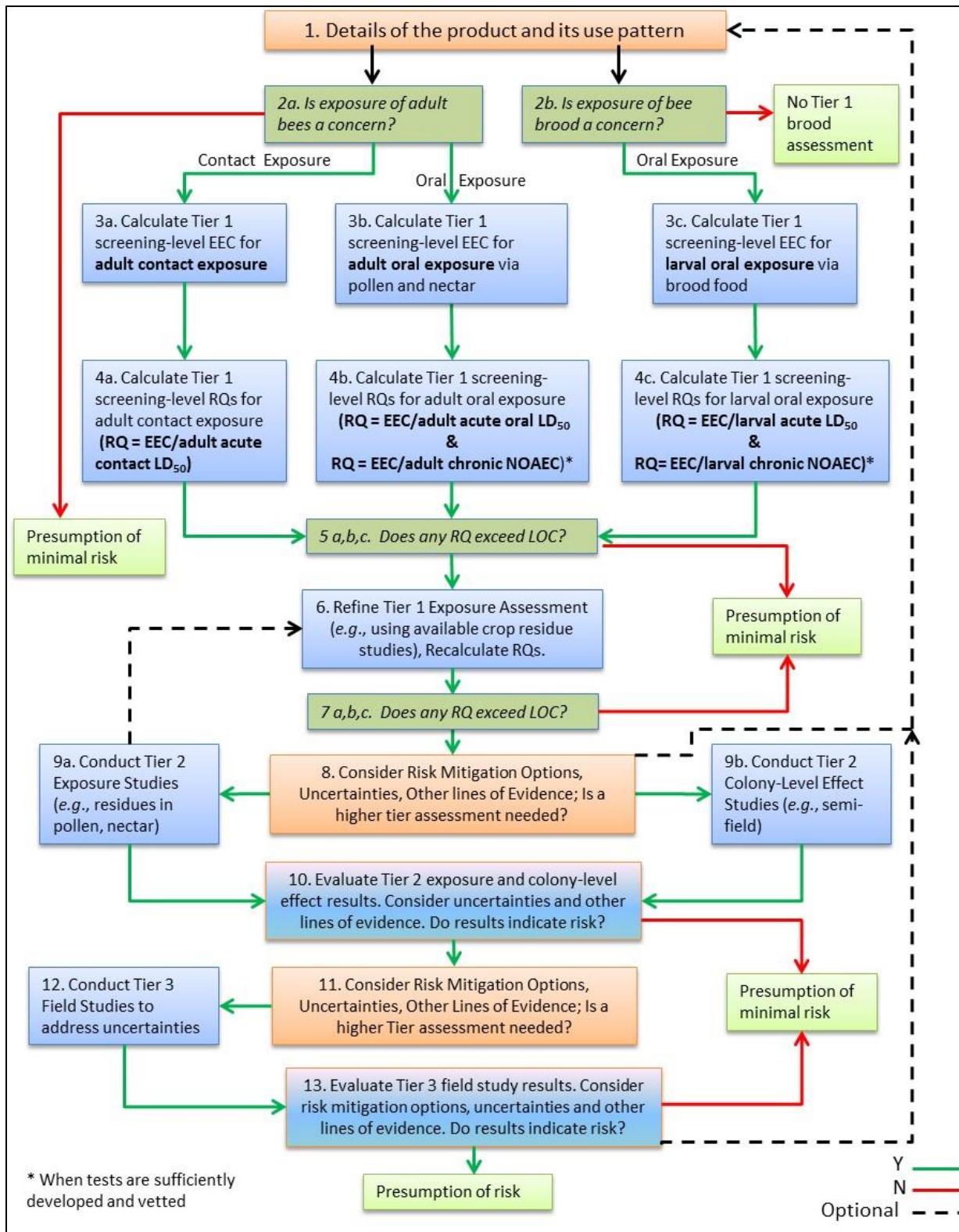


Figure 2-4. Tiered approach for assessing risk to honey bees from foliar spray applications

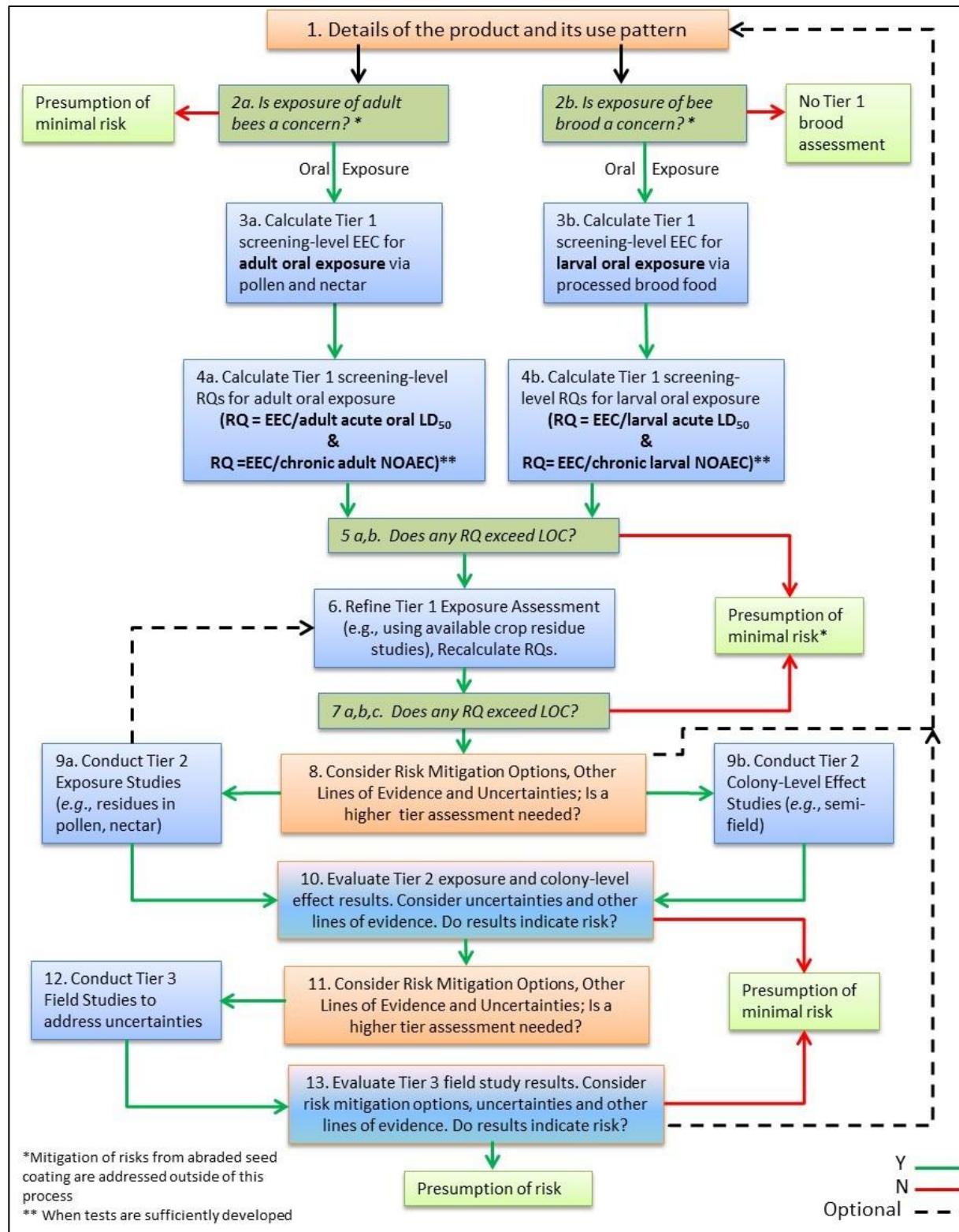


Figure 2-5. Tiered approach for assessing risk to honey bees from soil/seed applications

2.10. Measures of Exposure

The primary routes of exposure being assessed quantitatively in this assessment are the contact and oral routes. These are considered the dominant exposure routes for imidacloprid. Measures of contact exposure include the estimated contact dose on a per bee basis (*e.g.*, µg a.i./bee). Contact exposure is also incorporated into Tier II semi-field (tunnel) studies; however, it is not quantified on a per bee basis. Oral exposure is also determined on a mass a.i. per bee basis and considers ingestion of contaminated pollen and nectar. Detailed methods for estimating contact and oral exposure to honey bees are described later in **Section 4**.

Bees may also be exposed to pesticides via other routes of exposure such as through plant guttation fluid, surface water, soil (for ground nesting bees) and drift of abraded seed coat dust. As noted previously, the extent to which bees are exposed via plant guttation fluids and surface water is considered uncertain. Furthermore, the Agency currently lacks reliable methods for evaluating these exposure routes in a quantitative manner (*i.e.*, derivation of Tier I EECs). Therefore, consistent with the Agency's 2014 risk assessment guidance, this risk assessment will focus on quantitative estimates of exposure via contact and ingestion of pollen and nectar only. Although exposure and effects to bees via abraded seed coat dust has been documented, obtaining quantitative estimates of this route of exposure is also considered highly uncertain. Rather than assess the risks of abraded seed coat dust, the Agency is focusing its resources on mitigating risks from this exposure pathway through best management practices and working with the regulated community in the development of alternative technologies to reduce dust-off during planting (*e.g.*, alternative fluency agents, equipment modifications, etc.)¹¹

An additional potential route of exposure is carryover of imidacloprid residues in soil from one planting season to another. As will be discussed, environmental fate data suggest a high persistence in the soil. Additionally, a subset of residue studies which contained multi-season applications are considered for evaluating the potential carryover of imidacloprid in soil and bee-relevant plant matrices.

In the Tier II assessment, the maximum mean measured residues in nectar are compared to endpoints from colony-level studies where endpoints are expressed in terms of the concentration in spiked sucrose solution diet. This exposure route considers exposure from consuming contaminated sucrose (*i.e.* nectar) but does not consider exposure via consumption of contaminated pollen. This assessment differs from the preliminary assessment (USEPA 2017) in the way exposure is estimated via consumption of contaminated pollen. The previous assessment considered exposure via contaminated nectar separately from consumption of contaminated pollen based on a pollen-only feeding study from the open literature. This assessment replaced that method of evaluating exposure using a combined total dietary approach which takes the measured values of pollen and nectar in single crop and adjusts the concentration based on relative consumption rates for a single estimated dietary dose. Details on this method are further summarized in **Section Error! Reference source not found.** (Tier II risk characterization) and the full analysis is presented in **Attachment 1**.

¹¹ <http://www2.epa.gov/pollinator-protection/2013-summit-reducing-exposure-dust-treated-seed>

As mentioned above, for tier II exposures are estimated using the maximum mean measured residues in pollen and nectar, summing them (to get a total nectar exposure value) and then comparing these values to endpoints from colony-level studies expressed in terms of the concentration in spiked sucrose solution diet. This necessitates a data set of empirical residue values from specific crops available to compare to colony effect levels. As part of the Registration Review of the nitroguanidine-substituted neonicotinoid insecticides (*i.e.*, imidacloprid, clothianidin, thiamethoxam, dinotefuran), EPA required technical registrants submit data on the concentrations of these compounds and their residues of concern in bee-relevant matrices¹². While these individual chemical data sets are expansive, it is not feasible to perform trials to capture residues for all registered crops. Thus, this assessment uses a Residue bridging approach to supplement, and in the cases where no chemical specific data available act as a surrogate for, empirical residue data in pollen and nectar. Details on this method are further summarized in **Section 6.2.2** (Tier II risk characterization) and the full analysis is presented in **Attachments 2, 3 and 4**.

2.11. Measures of Effects

The primary species of focus in this risk assessment is the honey bee and reflects the dominant role this species maintains in providing managed pollination services for agricultural crops throughout the U.S. It also reflects the availability of standardized methods for estimating exposure and effects on *A. mellifera*. As such, this assessment will consider a variety of measures of effects for quantifying risk to honey bees which differ according to the level of biological organization being assessed. At the Tier I (organism) level, measures of effects include:

- The acute contact LD₅₀ to adult worker bees,
- The acute oral LD₅₀ to adult worker bees
- The chronic (10-d) oral NOAEL¹³ for adult worker bees, and
- The chronic (21-d) NOAEL for larval bees.

The acute contact and oral endpoints are derived from standardized laboratory toxicity tests conducted according to EPA Office of Chemical Safety and Pollution Prevention (OCSPP) and the Organization for Economic Cooperation and Development (OECD) guidelines and consider lethality as its primary test endpoint, although sublethal effects are commonly noted. Guidance for the chronic oral adult study has been recently finalized by the OECD¹⁴. This test measures lethality and food consumption of adult bees during a 10-d oral exposure. For larval honey bees, measures of effect at the Tier I level include the acute oral LD₅₀, conducted by OECD Test Guideline 237 and the chronic oral NOAEL following OECD guidance¹⁵. Acute effects on honey bee larvae are based on lethality while chronic effects include larval bee mortality and the percent emergence of adult bees following pupation. While, the acute LD₅₀ for

¹² The registrants also submitted residue data for other matrices that could potentially be used as surrogates for pollen and nectar (*e.g.*, anthers, flowers, leaves).

¹³ No Observed Adverse Effect Level

¹⁴ <http://www.oecd.org/env/test-no-245-honey-bee-apis-mellifera-l-chronic-oral-toxicity-test-10-day-feeding-9789264284081-en.htm>.

¹⁵ [https://one.oecd.org/document/ENV/JM/MONO\(2016\)34/en/pdf](https://one.oecd.org/document/ENV/JM/MONO(2016)34/en/pdf)

larval bees is also commonly included as a measure of effect, the acute data for honey bee larvae were not available for imidacloprid.

At the Tier II and Tier III levels, measures of effect at the colony level typically include:

- forager bee mortality,
- fecundity (e.g., eggs production),
- brood development and survival,
- hive weight, strength and survival,
- foraging activity, and
- the quantity and quality of food provisions.

These effects may be expressed in terms of a particular pesticide application rate (e.g., lbs. a.i./A) or the concentration of the active ingredient in the diet (e.g., µg a.i./L in sucrose). As discussed in USEPA et al. (2014), other sublethal endpoints such as proboscis extension reflex (PER), histopathological effects, and behavior anomalies are not considered as regulatory endpoints by themselves. However, to the extent that these effects contribute to impairment of the aforementioned colony level effects, they are indirectly incorporated into Tier II and Tier III measure of effect and the ensuing risk assessment.

Although the focus of this risk assessment is on the honey bee, 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, 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*), and 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, besides their overall ecological importance via maintaining biological diversity. Although standard methods are currently not available to quantitatively assess exposure and effects to non-*Apis* bees, this assessment will include data on the effects of imidacloprid to non-*Apis* bees and qualitatively assess risks to non-*Apis* bees.

As noted in the White Paper (USEPA et al. 2012) and as discussed in the FIFRA SAP's response (SAP 2012), there is uncertainty regarding the extent to which any risk assessment process that relies on data on a specific species (e.g., *A. mellifera*) can be considered representative of an entire taxon or multiple taxa. This is especially true for honey bees, which are a highly social (eusocial) species, where the colony/hive is dependent on the collective tasks of multiple castes and function as a “superorganism”; whereas, the majority of other bee species, particularly those species native to North America, are solitary.

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, 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 been in place.

3. USE CHARACTERIZATION

As noted in the problem formulation, imidacloprid is registered for the control of insects on a large variety of agricultural and non-agricultural sites, including vegetable crops, tree nuts, tree fruits, stone fruits, cotton, tobacco, grapes, citrus, turf, and ornamentals. Target pests include aphids, thrips, whiteflies, termites, turf insects, soil insects and some beetles. Imidacloprid formulations are available as wettable powder, granular, seed dressing (flowable slurry concentrate), and soluble concentrate.

Overall agricultural use of imidacloprid includes a large component as a seed treatment where approximately 520,000 pounds are used, and main seed-treatment uses include soybean, followed by cotton, then corn and potato. Use of imidacloprid appears to have increased, where approximately 5 million acres received an imidacloprid treatment in 1998, and approximately 30 million acres received an imidacloprid treatment in 2012. Part of this usage increase (as a foliar or soil treatment) has occurred on a number of specialty crops such as on apples, carrots, cauliflower, cherries; other usage increase, as a seed treatment, has occurred on crops such as soybean and wheat.

3.1. Agricultural Uses

Table 3-1 shows the maximum application rates and maximum number of applications for the different crops for imidacloprid with *foliar* applications, as well as other labeled use information. **Table 3-2** shows use information for the different crops for imidacloprid with *soil* applications, and **Table 3-3** shows use information for different crops for *seed-treatment* applications. Each of the tables provides additional comments where there are caveats to the federal labels.

It is noted that several crops have restrictions on applications made during the pre-bloom and bloom period. These include use patterns that have either a pre-bloom interval associated with them or prohibit applications made pre-bloom, during bloom or when bees are foraging (*i.e.* only post-bloom applications are permitted).

Those use patterns and associated application methods that require a 10-day pre-bloom interval include:

- Foliar applications to strawberries
- Foliar applications to citrus fruits

Those use patterns and associated application methods that prohibit applications made during the pre-bloom or during bloom period, or when bees are foraging include:

- Soil applications to strawberries (annual and perennial varieties)
- Soil and foliar applications to bushberries (*e.g.* blueberry)
- Soil and foliar applications to caneberry (*e.g.* blackberry and raspberry)
- Soil (containerized) applications to citrus fruits
- Soil and foliar applications to coffee

- Soil applications to cranberry
- Soil and foliar applications to pome fruits
- Soil and foliar applications to stone fruits
- Soil and foliar applications to tropical fruits
- Soil and foliar applications to tree nuts

3.1.1. Foliar Applications

Table 3-1. Summary of labeled use information for foliar applications of imidacloprid

| Crop Group (Use Pattern) | Max. Single Appl. Rate (lbs a.i/A) | Max # of Appl. | Appl. Interval | Annual total (lbs a.i/A) | Appl. Method | Appl. Timing | Comment |
|--|--|-------------------------------|-------------------|--------------------------------|---------------|---|--|
| 1 (Potato) | 0.05 | 4 | 7 | 0.2 | Ground/Aerial | From emergence to 7 days prior to harvest | |
| 1C (Tuberous and corm vegetables) | 0.04 | 3 (1 only on radish) | 5 | 0.13 (per season) | Ground/Aerial | After planting up to 7 days prior to harvest. | |
| 4A (Leafy greens vegetables) | 0.05 | 5 | 5 | 0.23 (per season) | Ground/Aerial | After planting up to 7 days prior to harvest. | |
| 5 (Brassica (Cole) Leafy vegetables) | 0.05 | 5 | 5 | 0.23 (per season) | Ground/Aerial | After planting up to 7 days prior to harvest. | |
| 6 (Legume vegetables (except soybean) | 0.04 | 3 | 7 | 0.13 (per season) | Ground/Aerial | After planting up to 7 days prior to harvest. | |
| 6 (Soybeans) | 0.05 | 3 | 7 | 0.14 | Ground/Aerial | At bloom to 21 days prior to harvest | |
| 8 (Fruiting vegetables) | 0.08 | 3 | 5 | 0.24 (per season) | Ground/Aerial | After planting up to 0 days prior to harvest. | |
| 10 (Citrus Fruits) | 0.25 | 2 | 10 | 0.5 | Ground/Aerial | Anytime up to 0 days prior to harvest. | * |
| 11 (Pome fruits) | 0.25 (for pears only) ¹ | 2 | 10 | 0.5 | Ground/Aerial | Anytime up to 7 days prior to harvest. | 0.25 lbs./A is only for pear, other crops have max. of 0.1 lbs./A Do not apply pre-bloom or during bloom or when bees are foraging. |
| | 0.1 (for other crops in group) | 5 | | | | | |
| 12 (Stone fruits) | 0.10 | 5 | 7 or 10 | 0.5 | Ground/Aerial | Anytime up to 0- 7 days prior to harvest. | * Yearly maximum 0.3 lbs./A for Apricot, |

| Crop Group (Use Pattern) | Max. Single Appl. Rate (lbs a.i./A) | Max # of Appl. | Appl. Interval | Annual total (lbs a.i./A) | Appl. Method | Appl. Timing | Comment |
|-------------------------------------|---|-------------------|-------------------|---------------------------------|---------------|---|---|
| | | | | | | | Nectarine, Peach; 0.5 lbs./A for Cherry, Plum, Plumcot, Prune. |
| 13A (Caneberry) | 0.1 | 3 | 7 | 0.3 | Ground/Aerial | After bloom up to 3 days prior to harvest. | * |
| 13B (Bushberry) | 0.1 | 5 | 7 | 0.5 | Ground/Aerial | After bloom up to 3 days prior to harvest. | * |
| 13 (Grape only) | 0.05 | 2 | 14 | 0.1 | Ground | Anytime up to 0 days prior to harvest. | |
| 13 (Strawberry only) | 0.05 | 3 | 5 | 0.14 (per season) | Ground/Aerial | After planting up to 7 days prior to harvest. | * |
| 14 (Tree nuts) | 0.10 | 3 | 6 | 0.36 | Ground/Aerial | Anytime up to 7 days prior to harvest. | * |
| 19A (Herbs) | 0.04 | 3 | 5 | 0.13 (per season) | Ground/Aerial | After planting up to 7 days prior to harvest. | |
| 20 (Cotton) | 0.06 | 5 | 7 | 0.31 | Ground/Aerial | Anytime up to 14 days prior to harvest | |
| Pomegranate ² | 0.10 | 3 | 7 | 0.3 | Ground/Aerial | Anytime up to 7 days prior to harvest. | * |
| Banana and plantain ² | 0.1 | 5 | 14 | 0.5 | Ground/Aerial | Anytime up to 0 days prior to harvest. | |
| Tropical fruit ² | 0.10 | 5 | 10 | 0.5 | Ground/Aerial | Anytime up to 7 days prior to harvest. | * |
| No group (Hops) | 0.10 | 3 | 21 | 0.3 | Ground/Aerial | Anytime up to 28 days prior to harvest. | |
| No group (Peanut) | 0.04 | 3 | 5 | 0.13 | Ground/Aerial | From emergence to 14 days prior to harvest | |
| No group (Globe artichoke) | 0.13 | 4 | 14 | 0.5 | Ground/Aerial | After planting up to 7 days prior to harvest. | |
| No group (Tobacco) | 0.05 | 5 | 7 | 0.28 | Ground/Aerial | From emergence to 14 days prior to harvest | * |

NA = not applicable; lbs a.i./A = pounds of active ingredient/acre

¹ the pear rate is 0.1 lb ai/A for most pests; there is only one insect that requires the higher 0.25 lb ai/A foliar rate

² Although part of the tropical fruit group (Crops Groups 23 and 24), registered labels include only specific commodities of the group instead of the entire group

*Some labels state "Do not apply during bloom or within a set number of days prior to bloom or when bees are foraging"

3.1.2. Soil Applications

Table 3-2. Summary of labeled use information for soil applications of imidacloprid

| Crop Group (Use Pattern) | Max. Single Appl. Rate (lbs a.i./A) | Max # of Appl. | Appl. Interval | Annual total (lbs a.i./A) | Appl. Method | Appl. Timing | Comment |
|---------------------------------------|--|----------------------|-------------------|------------------------------------|--|--|---|
| 1 (Sugar beet) | 0.18 | 1 | NA | 0.18 | In-furrow | Prior to or at planting | For use only in California |
| 1B (Root vegetables) | 0.38 | 1 | NA | 0.38 (per season) | In-furrow / band / chemigation | At or after planting up to 21 days prior to harvest. | |
| 1 (Potato) | 0.31 | 1 | NA | 0.31 | in-furrow / band / subsurface side-dress | At Planting | |
| 1C (Tuberous and corm vegetables) | 0.38 | 1 | NA | 0.38 (per season) | In-furrow / shank / side-dress | At or after planting up to 3 days (leaves) or 125 days (corms) prior to harvest. | |
| 3 (Bulb Vegetables) | 0.5 | 1 | NA | 0.5 (per season) | In-furrow / band / chemigation / drench | Prior to, at, or after planting up to 21 days prior to harvest. | Generally applied at planting for greatest benefit |
| 4A (Leafy greens vegetables) | 0.38 | 1 | NA | 0.38 (per season) | In-furrow / band / chemigation / drench | At or after planting up to 21 days prior to harvest. | |
| 4B (Leafy petiole vegetables) | 0.38 | 1 | NA | 0.38 (per season) | In-furrow / band/ chemigation / drench | At or after planting up to 45 days prior to harvest. | |
| 5 (Brassica (Cole) leafy vegetables) | 0.38 | 1 | NA | 0.38 (per season) | In-furrow / band / chemigation /drench | At or after planting up to 21 days prior to harvest. | |
| 6 (Legume vegetables (except soybean) | 0.38 | 1 | NA | 0.38 (per season) | In-furrow / band/ chemigation / drench | At or after planting up to 21 days prior to harvest. | |
| 8 (Fruiting vegetables) | 0.5 | 1 | NA | 0.5 (per season) | In-furrow/band/ chemigation / drench | At or immediately following planting up to 21 days prior to harvest | - 0.5 lbs./a for pepper and okra, 0.38 lbs./a for other crops (per crop season) |
| 9 (Cucurbit vegetables) | 0.38 | 1 | NA | 0.38 | In-furrow /band /chemigation /drench | At Planting up to 21 days prior to harvest | |
| 10 (Citrus fruits) | 0.5 | 1 | NA | 0.5 | Chemigation / band/drench | Anytime up to 0 days prior to harvest. | |
| 11 (Pome fruits) | 0.38 | 1 | NA | 0.38 | Chemigation | Anytime up to 21 days prior to harvest. | * |
| 12 (Stone fruits) | 0.38 | 1 | NA | 0.38 | Chemigation | Anytime up to 21 days prior to harvest. | * |
| 13A (Caneberry) | 0.5 | 1 | NA | 0.5 | Chemigation /drench | After bloom up to 7 days prior to harvest. | * |
| 13B (Bushberry) | 0.5 | 1 | NA | 0.5 | Chemigation / band | After bloom up to 7 days prior to harvest. | * |

| Crop Group (Use Pattern) | Max. Single Appl. Rate (lbs a.i/A) | Max # of Appl. | Appl. Interval | Annual total (lbs a.i/A) | Appl. Method | Appl. Timing | Comment |
|--|---|----------------------|-------------------|-----------------------------------|--|---|---|
| 13 (Grape only) | 0.5 | 1 | NA | 0.5 | Chemigation / side-dress/drench | Anytime up to 30 days prior to harvest. | |
| 13 (Cranberry) | 0.5 | 1 | NA | 0.5 | Chemigation / direct app. | Anytime up to 30 days prior to harvest. | * |
| 13 (Strawberry only annual and perennial) | 0.5 | 1 | NA | 0.5 (per season) | Chemigation / band | Prior to, at, or after planting up to 14 days prior to harvest. | * |
| 13-07G (Strawberry only perennial and post- harvest) | 0.38 | 1 | NA | 0.38 | Chemigation / band | During renovation up to 14 days prior to harvest. | |
| 14 (Tree nuts) | 0.50 | 1 | NA | 0.5 | Chemigation / side-dress/drench | Anytime up to 7 days prior to harvest. | * |
| 19A (Herbs) | 0.38 | 1 | NA | 0.38 (per season) | in-furrow / shank / drench /chemigation | At or after planting up to 14 days prior to harvest. | |
| 20 (Cotton) | 0.33 | 1 | NA | 0.33 | In-furrow / band /chemigation | At Planting | Labels allow both at planting AND foliar applications |
| Banana and plantain ¹ | 0.5 | 1 | NA | 0.5 | Chemigation | Anytime up to 0 days prior to harvest. | |
| Pomegranate ¹ | 0.50 | 1 | NA | 0.5 | Chemigation | Anytime up to 0 days prior to harvest. | * |
| Tropical fruit ¹ | 0.50 | 1 | NA | 0.5 | Chemigation | Anytime during the year up to 6 days prior to harvest. | * |
| No group (Coffee) | 0.5 | 1 | NA | 0.5 | Chemigation / side-dress/drench | Anytime up to 7 days prior to harvest. | * Basal treatment available on 264-827, 264-758 |
| No group (Globe artichoke) | 0.5 | 1 | NA | 0.5 | In-furrow /chemigation | Prior to, at, or after planting up to 7 days prior to harvest. | |
| No group (Hops) | 0.3 | 1 | NA | 0.3 | Chemigation / side-dress/drench | Anytime up to 60 days prior to harvest. | |
| No group (Peanut) | 0.38 | 1 | NA | 0.38 | In-furrow / chemigation | At Planting | |
| No group (Tobacco) | 0.04 | | NA | 0.5 | In-furrow / tray drench /chemigation | Prior to or At Planting up to 14 days prior to harvest | Single app rate is based on lbs. a.i./1000 plants. Optimum plant population = 6200 to 7200 plants per acre. |
| No Group (Poplar/Cotton wood) | 0.5 | 1 | NA | 0.5 | Chemigation by drip; or shank into root zone | | * |
| Poultry House Treatment ² | 0.132 & 0.771 | 1 | NA | 0.771 | Liquid spray to poultry litter | NA | Off field application of treated poultry litter to crops attractive to bees |

NA = not applicable; lbs a.i./A = pounds of active ingredient/acre

¹ Although part of the tropical fruit group (Crops Groups 23 and 24), registered labels include only specific commodities of the group instead of the entire group

*some labels state "Do not apply during bloom or within a set number of days prior to bloom or when bees are foraging"

² Calculations supporting a range of application rates are provided in Appendix K. Lower rate reflects a potential label mitigation option, higher rate is the overall maximum rate.

3.1.3. Seed Treatments

The maximum single application rate in (lbs a.i./A) was estimated based on the amount of product applied to seeds coupled with the number of seeds planted per acre. The number of seeds per acre were either provided or calculated from parameters listed in *Acres Planted per Day and Seeding Rates of Crops Grown in the United States*. (US EPA, March 24, 2011).

Table 3-3. Summary of labeled use information for seed treatment applications of imidacloprid

| Crop Group (Use pattern) | Max. Single Appl. Rate (mg a.i./seed) | Comment ¹ |
|---|---------------------------------------|--|
| 1A (Sugar beet) | 1.3 | Calculated from labeled application rate of 0.2 lbs a.i./2.2 lbs seed. Application rate = ((1/2.2) * 0.2 * 3.24)). 3.24 is the number of pound of seed per acre |
| 1A, 1B (Carrot) | 0.01 | Calculated from labeled application rate of 0.0025 lbs a.i./lbs seed and lbs of seed/acre (11.95). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 1C (Potato) | 6.5 | Calculated from labeled application rate of 0.000125 lbs a.i./lbs seed. As the rate that was calculated from number of seeds per acre and number of seeds per pound exceeded the maximum single application rate the label specifies a maximum seed treatment rate of 0.25 lb ai/A and therefore the rate was capped at 0.25 lbs a.i./A. |
| 03-07A, 03-07B (onions/leeks/scallions) | 0.06 | Calculated from labeled application rate of 0.002 oz./1000 seed and lbs seed per acre. Rate = ((0.002 / 16) * 1,229,929 seeds / 1000)) |
| 5A (Broccoli) | 0.39 | Calculated from labeled application rate of 0.014 oz./1000 seed and lbs seed per acre. Rate = ((0.014 / 16) * 210,845 seeds / 1000)) |
| 6A (Soybean) | 0.38 | Calculated from labeled application rate of 0.00125 lbs a.i./lbs seed and lbs of seed/acre (167). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 6 (Beans and peas) | 0.43-0.54 | Planting of treated seed not permitted in California. Calculated from labeled application rate of 0.000125 lbs a.i./lbs seed. As the rate that was calculated from number of seeds per acre and number of seeds per pound exceeded the maximum single application rate (in lbs a.i./A) of all imidacloprid uses, the rate was capped at 0.5 lbs a.i./A |
| 15 (Barley) | 0.05 | Calculated from labeled application rate of 0.00094 lbs a.i./lbs seed and lbs of seed/acre (138). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 15 (Buckwheat) | 0.01 | Calculated from labeled application rate of 0.000023 lbs a.i./lbs seed and lbs of seed/acre (72). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 15 (Corn, field) | 1.41 | Calculated from labeled application rate of 0.004 lbs a.i./lbs seed and lbs of seed/acre (29.57). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |

| Crop Group (Use pattern) | Max. Single Appl. Rate (mg a.i./seed) | Comment ¹ |
|--------------------------|---------------------------------------|--|
| 15 (Corn, pop) | 0.83 | Calculated from labeled application rate of 0.0025 lbs a.i./lbs seed and lbs of seed/acre (22.04). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 15 (Corn, sweet) | 0.63 | Calculated from labeled application rate of 0.0025 lbs a.i./lbs seed and lbs of seed/acre (31.52). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 15 (Millet) | 0.01 | Calculated from labeled application rate of 0.0025 lbs a.i./lbs seed and lbs of seed/acre (30). |
| 15 (Oats) | 0.03 | Calculated from labeled application rate of 0.0009 lbs a.i./lbs seed and lbs of seed/acre (90). |
| 15 (Rye) | 0.02 | Calculated from labeled application rate of 0.0009 lbs a.i./lbs seed and lbs of seed/acre (109). |
| 15 (Sorghum) | 0.06 | Calculated from labeled application rate of 0.0025 lbs a.i./lbs seed and lbs of seed/acre (12). |
| 15 (Wheat) | 0.05 | Calculated from labeled application rate of 0.0009 lbs a.i./lbs seed and lbs of seed/acre (188). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 15 (Triticale) | 0.03 | Calculated from labeled application rate of 0.0009 lbs a.i./lbs seed and lbs of seed/acre (109). |
| 19B (Mustard) | 0.05 | Calculated from labeled application rate of 0.01 lbs a.i./lbs seed and lbs of seed/acre (7). |
| 20 (Canola/Rape) | 0.05 | Calculated from labeled application rate of 0.01 lbs a.i./lbs seed and lbs of seed/acre (8.23). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 20 (Cotton) | 0.51 | Calculated from labeled application rate of 0.005 lbs a.i./lbs seed and lbs of seed/acre (18.89). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 20 (Sunflower) | 0.32 | Calculated from labeled application rate of 0.005 lbs a.i./lbs seed and lbs of seed/acre (4). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| 20 (Safflower) | 0.30 | Calculated from labeled application rate of 0.005 lbs a.i./lbs seed and lbs of seed/acre (35). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |
| No group (Peanuts) | 0.61 | Calculated from labeled application rate of 0.00062 lbs a.i./lbs seed and lbs of seed/acre (228). Pounds of seed/acre calculated from number of seeds per acre and number of seeds per pound. |

¹Number of seeds per acre either provided or calculated from parameters listed in BEAD Memo entitled "Acres Planted per Day and Seeding Rates of Crops Grown in the United States." (US EPA, March 24, 2011). Note: rates were calculated by considering several labels and taking the rate from the label with the highest rate.

3.1.4. Multiple Application Types (e.g. combinations of seed, soil, and/or foliar)

As indicated above, the maximum annual application rate for several use patterns of imidacloprid is 0.5 lbs a.i./A. Several use patterns stipulate that a variety of application methods (*i.e.* foliar, soil, and seed treatment) can be used so as long as the applied rate does not exceed 0.5 lbs a.i./year. As will be discussed, there are residue studies available for combined application methods of soil + foliar treatments and seed + foliar treatments.

3.1.5. Usage Information

As mentioned previously, imidacloprid is registered on a wide variety of agricultural and non-agricultural use patterns. For agricultural uses, usage data from the Screening Level Usage Analysis (SLUA) compiled by the Biological and Economic Analysis Division (BEAD) is summarized below in **Table 3-4**. The reporting time for this data is from 2004 – 2013 and indicates the lbs applied per year, and the average and maximum percent crop treated for each use pattern where data are available. Additionally, **Table 3-4** indicates the attractiveness of the use pattern and whether it is harvested before the bloom period per USDA 2017. It is worth noting that although the SLUA indicates the poundage applied to certain use patterns as seed treatments, the report does not distinguish between foliar and soil applications for a given use pattern.

Table 3-4. Summary of imidacloprid usage data as reported by the SLUA (2004-2013).

| Crop Group | Use pattern | Lbs. Applied/yr. | % Acreage Treated (average) | % Acreage Treated (max) | Honey Bee Attractive? (Pollen or nectar) (Y/N) | Harvested Before Bloom? (Y/N) |
|---------------------|--------------------------|------------------|-----------------------------|-------------------------|--|-------------------------------|
| Root & Tubers | Potatoes | 70,000 | 35 | 50 | N | -- |
| | Carrots | 4,000 | 15 | 45 | Y | Y |
| | Sugar Beets ² | 2,000 | <2.5 | 5 | Y (nectar) | Y |
| Leafy Vegetables | Chicory* | <500 | 10 | 20 | Y | Y |
| | Lettuce | 40,000 | 65 | 85 | Y | Y |
| | Spinach | 2,000 | 25 | 40 | N | Y |
| | Celery | 1,000 | 10 | 20 | Y | Y |
| Brassica (Cole) | Brussels Sprouts* | <500 | 50 | 85 | Y | Y |
| | Broccoli | 10,000 | 65 | 90 | Y | Y |
| | Cauliflower | 5,000 | 60 | 90 | Y | Y |
| | Cabbage | 4,000 | 30 | 45 | Y | Y |
| Legumes | Dry Beans/Peas | <500 | <1 | <2.5 | Y | -- |
| | Peas, green | <500 | <2.5 | <2.5 | Y | -- |
| | Soybeans | 30,000 | <2.5 | <2.5 | Y | -- |
| | Beans, Green | 3,000 | 5 | 10 | Y | -- |
| Fruiting vegetables | Tomatoes | 30,000 | 30 | 60 | N | -- |
| | Peppers | 9,000 | 35 | 50 | Y (pollen) | -- |
| Cucurbit Vegetables | Cantaloupes | 9,000 | 40 | 60 | Y | -- |
| | Cucumbers | 3,000 | 10 | 20 | Y | -- |
| | Honeydews | 2,000 | 30 | 50 | Y | -- |
| | Pumpkins | 2,000 | 10 | 20 | Y | -- |
| | Squash | 2,000 | 15 | 30 | Y | -- |
| | Watermelons | 9,000 | 25 | 45 | Y | -- |
| Citrus | Grapefruit | 8,000 | 30 | 60 | Y | -- |
| | Lemons | 3,000 | 10 | 25 | Y | -- |

| Crop Group | Use pattern | Lbs. Applied/yr. | % Acreage Treated (average) | % Acreage Treated (max) | Honey Bee Attractive? (Pollen or nectar) (Y/N) | Harvested Before Bloom? (Y/N) |
|--------------------|--|------------------|-----------------------------|-------------------------|--|-------------------------------|
| | Oranges | 60,000 | 25 | 40 | Y | -- |
| | Tangelos | <500 | 15 | 20 | Y | -- |
| | Tangerines | 6,000 | 25 | 40 | Y | -- |
| Pome Fruit | Apples | 10,000 | 30 | 45 | Y | N |
| | Pears | 1,000 | 5 | 15 | Y | -- |
| Stone fruit | Cherries | 4,000 | 25 | 50 | Y | N |
| | Nectarines | <500 | <2.5 | <2.5 | Y | -- |
| | Peaches | 1,000 | 5 | 15 | Y | -- |
| | Plums/Prunes | <500 | <2.5 | 10 | Y | -- |
| | Pluots | <500 | 20 | 65 | Y | -- |
| Berry& Small Fruit | Caneberries (blackberry and raspberry) | <500 | 15 | 25 | Y | -- |
| | Grapes | 60,000 | 30 | 50 | Y (pollen) | N |
| | Strawberries | 2,000 | 5 | 15 | Y | -- |
| | Blueberries | 1,000 | 10 | 20 | Y | N |
| Tree Nuts | Hazelnuts | <500 | 5 | 20 | Y (pollen) | -- |
| | Pecans | 20,000 | 15 | 20 | N | -- |
| | Pistachios | 3,000 | 5 | 15 | N | -- |
| | Walnuts | 3,000 | 10 | 20 | Y (pollen) | -- |
| | Almonds | 1,000 | <2.5 | <2.5 | Y | N |
| Cereal grain | Corn (Seed Treatment) ¹ | 30,000 | <2.5 | <2.5 | Y (pollen) | -- |
| | Sorghum (seed treatment) ¹ | 10,000 | 15 | 20 | Y (pollen) | -- |
| | Wheat (seed treatment) ¹ | 100,000 | 15 | 20 | N | -- |
| Oilseed | Cotton | 50,000 | 5 | 10 | Y (nectar) | -- |
| | Cotton (Seed Treatment) ¹ | 50,000 | 10 | 20 | Y (nectar) | -- |
| No Group | Artichokes | <500 | 15 | 60 | Y | Y |
| | Pluots* | <500 | 20 | 65 | -- | -- |
| | Sugarcane | <500 | <2.5 | <2.5 | N | -- |
| | Tobacco | 10,000 | 25 | 40 | Y (pollen) | Y |
| | Avocados | 59,950 | <1 | 2.5 | Y | N |
| | Pomegranates * | 4,000 | 45 | 65 | -- | -- |

NA = not available

¹ The surveying period for seed treatment uses does not always cover the entire period of the SLUA

² For use in California only according to Admire® Pro label (EPA Reg. No. 264-827) soil only

*Based on CDPR PUR data only (80% or more of total acreage is in California)

3.2. Non-agricultural Uses

Imidacloprid is registered for a wide variety of non-agricultural uses, some examples of which include applications to:

- Turf (commercial and residential);
- Ornamentals (Nurseries, residential and commercial areas);
- Forestry (including Poplar/Cottonwood and Christmas Tree Plantations);
- Building/perimeter treatments in farms/residential/commercial areas;
- Indoor uses in commercial and domestic dwellings
- Pet spot-on treatments; and
- Wood treatment

A detailed review of the non-agricultural uses of imidacloprid is found in the Appendix A of the 2017 Preliminary Aquatic Risk Assessment (USEPA 2017).

Uses of imidacloprid pertaining to applications indoors, pet spot on treatments, wood preservation and building/perimeter treatment are expected to result in little or no exposure of bees and therefore, these uses are not considered further in this risk assessment. Uses on turf, ornamentals and forestry are considered further due to the potential for significant exposure of bees.

For the purposes of this assessment, the distinction between ornamental and forestry uses pertains to the environmental setting of use rather than the type of plant being treated. Forestry uses are considered those that involve application to trees in plantation or natural forest settings. Ornamental uses may involve the same tree species as a forestry use, but the settings include residential or nursery use sites.

Turf uses include foliar and soil applications (spray and granule) while ornamental and forestry uses include foliar, soil, and tree injection application methods. Turf is registered for applications via a broadcast soluble granule followed by rainfall or irrigation. Imidacloprid can be applied on both commercial and residential turf. Commercial turf uses include application on golf courses and sod farms; these areas of turf are expected to be a monoculture with little to no flowering weeds that would be attractive to pollinators. Therefore, uses on commercial turf are not expected to present an exposure pathway for oral exposure to pollinators. However, residential turf uses include applications at cemeteries, playgrounds, recreational areas and parks where it cannot be reliably assumed that bee-attractive flowering weeds would be absent. Therefore, it is presumed that imidacloprid uses on residential turf have the potential to result in exposure of bees via contaminated pollen and nectar.

Maximum registered application rates for ornamental, forestry and turf uses of imidacloprid are shown in **Table 3-5**.

Table 3-5. Maximum application rates for bee-relevant non-agricultural uses of imidacloprid

| Use Pattern | Maximum Single Application Rate | | | |
|--|--|--|---------------------------|-------------------------------|
| | Soil ⁽¹⁾ | Foliar | Trunk Injection | Total Seasonal ⁽²⁾ |
| Ornamentals: (trees, shrubs, and other ornamentals in residential & field nursery settings) | 0.4 lb a.i./A 4.6 g ai/m plant height | 0.4 lb a.i./A 4.6 g ai/m plant height | 0.9 g/10 cm stem diameter | 0.4 lb a.i./A |
| Forestry: (poplar, Xmas trees, cottonwood & other trees in forest\plantation settings) | 0.5 lb a.i./A | 0.1 lb a.i./A x 5 apps | 0.9 g/10 cm stem diameter | 0.5 lb a.i./A |
| Turf: (residential settings) | 0.5 lb a.i./A | 0.5 lb a.i./A | N/A | 0.5 lb a.i./A |

⁽¹⁾ includes soil spray, drench, granule or tablet applications

⁽²⁾ applies to soil and foliar applications

⁽³⁾ for foliar and soil applications to poplar/cottonwood, applications restricted to post-bloom and when bees are not foraging

4. EXPOSURE ASSESSMENT

Imidacloprid is a systemic insecticide that is associated with multiple use patterns. Exposure of bees to imidacloprid is determined by many factors that are expected to affect the concentration of the chemical in plant parts visited by bees. Two main procedures are used for applying this pesticide: soil and foliar applications.

- (1) Direct Soil application including in-furrow, drench, chemigation (through drip irrigation), band, shank injection and planting treated seeds: These types of applications deliver most of the pesticide mass into the soil system with the potential for relatively low amount of drift such as seed drilling dust; and
- (2) Foliar application by ground and air equipment. These types of applications deliver the pesticide onto the plant foliage (target) with a percentage being deposited or drifting to the soil upon application (also, later from plant wash-off).

Figure 4-1 depicts important processes governing exposure of bees to imidacloprid through the plant. In this figure, it is assumed that imidacloprid alone is systemic as it is uncertain if any of imidacloprid metabolites are systemic.

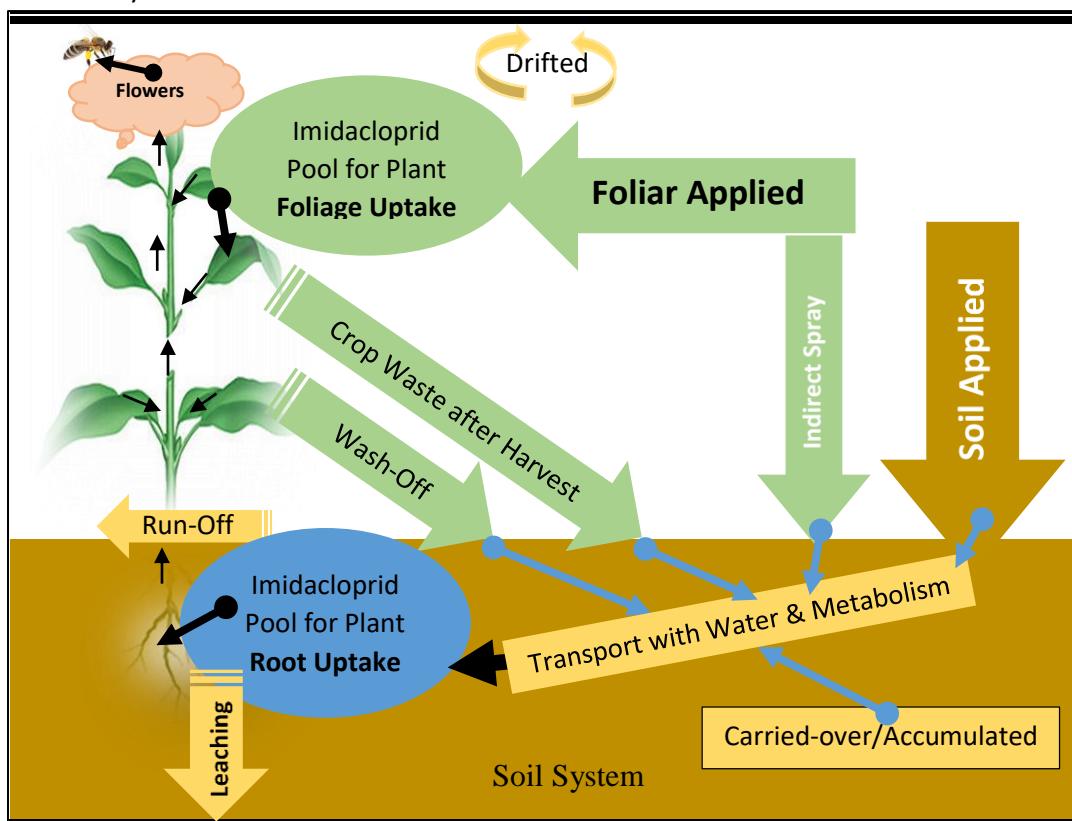


Figure 4-1. Conceptual diagram of imidacloprid application and processes related to bee exposure

As shown in **Figure 4-1**, the extent of bee exposure to imidacloprid through the plant is a function of the source and movement of the compound from the point of application into the point of plant entry (roots and/or foliage). Conceptually, two virtual imidacloprid pools can be assumed: a pool that is available for plant root uptake and a pool that is available for plant foliage uptake. Sources of the “root up-take pool” include imidacloprid from direct soil application including seed treatment, indirect spray following foliar application, and that reaching the soil later by plant wash-off. Other potential sources include imidacloprid carried-over from applications to previous rotational crop(s) (accumulated in the soil and/or added from treated plant material left in the field after harvest). Sources of the “foliage up-take pool” include imidacloprid from direct foliar application noting that part of the foliage-applied chemical is expected to reach the soil during application and later through wash-off. The dynamic nature of these two virtual pools is expected because chemical species present in these pools and their concentrations will vary with time following application. Other factors likely to influence the characteristics of these virtual pools include: mode (e.g., soil, foliar), procedure (e.g., ground, aerial), rate, and timing of application; crop growth stage; physiochemical, fate and transport properties (solubility, mobility and persistence), and soil properties affecting mobility and bioavailability.

Currently, plant/pesticide uptake models do not enable quantification of how most of these factors affect pesticide uptake and expression in bee-relevant tissues of plants. As a result, refined estimates of imidacloprid exposure via residues in pollen and nectar rely on empirical measurements derived from field residue studies (USEPA/PMRA/CDPR 2014). Nonetheless, a conceptual understanding of the how these factors may affect imidacloprid pollen and nectar residues is important when interpreting and applying field residue data for bee risk assessment.

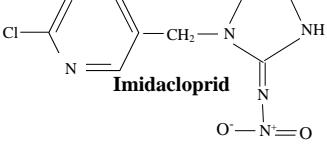
4.1. Physical/chemical and fate and transport properties

Data in **Table 4-1** indicate that imidacloprid is highly soluble with low vapor pressure and Henry's Law Constants. These properties suggest that the chemical will be readily soluble for movement with water and that it is unlikely to volatilize to a meaningful degree. Furthermore, the octanol: water coefficient (K_{ow}) for imidacloprid is low, and this property along with the high solubility are known attributes of systemic pesticides although the systemic nature of the pesticide should be based on residue and fate analyses to reduce uncertainties (Bonmatin *et al.*, 2015).

4.1.1. Physical/Chemical properties

Table 4-1 contains a summary of the chemical profile of imidacloprid.

Table 4-1. Chemical profile of imidacloprid

| Property | Value |
|--------------------------|---|
| Chemical Structure: Name |  <p style="text-align: center;">Imidacloprid</p> <p style="text-align: center;">1-(6-chloro-3-pyridin-3-ylmethyl)-N-nitroimidazolidin-2-ylidenamine</p> |
| Molecular Formula | C ₉ H ₁₀ ClN ₅ O ₂ |

| Property | Value |
|---------------------------------------|--|
| Molecular Weight (CAS No.) | 255.7 g/mole (13826-41-3) |
| Water Solubility @ 20 °C | 580 mg/L |
| Octanol: Water Coefficient K_{ow} | 3.7 @ 21 °C |
| Vapor pressure (Henry's Law Constant) | 1.5×10^{-9} torr (9.9×10^{-13} atm m ³ mol ⁻¹) @ 20 °C |

Available data indicate that imidacloprid is highly soluble with low vapor pressure and Henry's Law Constants. These properties suggest that the chemical will be readily soluble and thus available for movement with water, and that it is unlikely to volatilize to a meaningful degree. Furthermore, the K_{ow} for imidacloprid is low, and this property along with the high solubility are known attributes of systemic pesticides that can move upward in the plant within the xylem and phloem. Furthermore, the relatively high persistence of imidacloprid in the soil system and its predicted mobility are characteristics of pesticides that are expected to leach and may contaminate vulnerable ground water resources.

4.1.2. Environmental Fate and Transport Properties

The environmental fate and transport characteristics of imidacloprid are summarized in **Table 4-2**. These data suggest that the compound is relatively stable to multiple routes of degradation other than photolysis in water and is therefore likely to be persistent in soils. Given the persistence in soil and the mobility of imidacloprid, the compound has the potential to leach into ground water and to run-off into surface waters for extended periods of time depending on soil and climatic conditions.

Table 4-2. Fate and transport properties for imidacloprid

| Property | Values¹ | MRID Reference |
|--|--|-----------------------|
| Hydrolysis t $\frac{1}{2}$ | Stable @ pH 5, 7 and hydrolyzed slowly (Extrapolated t $\frac{1}{2} = 355$ d) in sterile alkaline solutions @ pH 9 | 420553-37 |
| Environmentally Relevant Direct Aqueous Photolysis t $\frac{1}{2}$ (Two hours study) | <p>0.2 days</p> <p>Major Metabolites: Guanidine or desnitro compound (NTN-38014): Max 17% and urea compound (NTN-33519): Max 10% @ End of study (EOS)</p> <p>Additionally, three major un-knowns reached Maximums of 8-13% @ EOS</p> <p>Minor Metabolites: Several un-knowns with a total Max of 13% @ EOS</p> <p>Important Notes:</p> <ul style="list-style-type: none"> (1) UV spectra of the chemical has a maximum absorption at 269 nm, therefore degradation by sunlight is expected (2) Under natural sunlight, in a dilute aqueous solution in the greenhouse: 60% of the chemical degraded within 4 hours supporting the results of the study | 422563-76 |
| Environmentally Relevant Soil Photolysis t $\frac{1}{2}$ (15-d study) | <p>171 days in a sandy loam soil from Kansas (pH= 5.2; O.C= 1.4% and CEC= 22 meq/100 g)</p> <p>Major Metabolites: None</p> <p>Minor Metabolites: 5-hydroxy compound (WAK-4103): Max 6%; Nitosimine compound (WAK-3839): Max 1% and a mixture of urea compound (NTN-33519) and Olefin compound (NTN-35884): Max 3%; and 6-Choronictonic acid: Max 2%; All Maximums @ EOS. Additionally, two unidentified reached Maximums of >>5% @ EOS</p> <p>Un-extracted Residues (UER): Max 11% @ EOS</p> | 422563-77 |
| Aerobic soil t $\frac{1}{2}$ @ 20 ± 2 °C | 608 days (SFO*; Extrapolated value because parent reached only 62% @ EOS) in a sandy loam soil from Kansas (pH= 4.8; O.C= 1.4% and CEC= 16 meq/100 g). | 420735-01 |

| | | |
|---|---|--------------------------------|
| (End of study “EOS”= 366 day; Pyridinyl- ¹⁴ C- methylene imidacloprid) | <p>Note: Levels of metabolites were insufficient to permit their identification (Needed 20x to 100x the rate)</p> <p>Major Metabolites: None</p> <p>Minor Metabolites: Olefin compound (NTN-35884), WAK-4230-1, Nitrosimine compound (WAK-3839), Guanidine or desnitro compounds (NTN-33014) and the two isomers of 5-keto-urea compounds. Additionally, one unidentified reached Maximums of nearly 1% @ EOS</p> <p>Un-extracted Residues (UER): Max 30% @ EOS reduced to 13% after additional reflux extraction yielding parent which was considered as bound parent because of harsh extraction</p> <p>Mineralization to CO₂: Max 7.4% @ EOS</p> | |
| Aerobic soil t ½ @ 20 ± 2 °C (End of study “EOS”= 100 day; Pyridinyl- ¹⁴ C- methylene imidacloprid) | <p>172 days (Slow DFOP; Extrapolated value because parent reached only 63% @ EOS) in BBA 2.2, a loamy sand soil from Germany (pH= 5.5; O.C= 2.2% and CEC= 10 meq/100 g).</p> <p>Note: Levels of metabolites were insufficient to permit their identification (Needed 20x to 100x the rate)</p> <p>Major Metabolites: None</p> <p>Minor Metabolites: Same as in the soil, above</p> <p>Mineralization to CO₂: Max 10% @ EOS</p> <p>Un-extracted Residues (UER): Max 22% @ 30 d- EOS reduced to 14% after additional reflux extraction yielding parent which was considered as bound parent because of harsh extraction</p> | 452393-01 |
| Aerobic soil t ½ @ 22 ± 2 °C (End of study “EOS”= 100 day; Pyridinyl- ¹⁴ C- methylene imidacloprid) | <p>193 days (SFO; Extrapolated value because parent reached only 67% @ EOS) in Hoefchen, a loamy soil from Germany (pH= 5.3; O.C= 1.2% and CEC= 11 meq/100 g).</p> <p>Major Metabolites: None</p> <p>Minor Metabolites: Several metabolites occurred at very low levels: total= 7% (not identified nor quantified)</p> <p>Mineralization to CO₂: Max 6.4% @ EOS</p> <p>Un-extracted Residues (UER): Max 11-13% @ 35 d- EOS after additional reflux extraction yielding parent</p> | 452393-02 |
| Aerobic soil t ½ @ 22 ± 2 °C (End of study “EOS”= 366 day; Pyridinyl- ¹⁴ C- methylene imidacloprid) | <p>336 days (SFO; Parent reached 52% @ EOS) in Monheim 1, a sandy loam soil from Germany.</p> <p>Major Metabolites: None</p> <p>Minor Metabolites: None were tracked, if any</p> <p>Mineralization to CO₂: Max 5% @ EOS</p> <p>Un-extracted Residues (UER): Max 12-22% @ 100- EOS after additional reflux extraction yielding parent which was considered as bound parent because of harsh extraction</p> | 452393-03 |
| Aerobic soil t ½ @ 20 ± 0.2 °C (End of study “EOS” = 120 days; Pyridinyl- ¹⁴ C- methylene imidacloprid) | <p>139 days (slow DFOP*; Parent reached 40% @ EOS) in Sarotti (silt loam, pH 7.0, O.C= 1.46% and CEC= 13 meq/100 g) soil from Germany</p> <p>242 days (slow DFOP*; Parent reached 50% @ EOS) in Laacherhof (sandy loam, pH 6.2, O.C= 1.88% and CEC= 9 meq/100 g) soil from Germany</p> <p>332 days (slow DFOP*; Parent reached 57% @ EOS) in Wurmwiese (sandy loam, pH 5.4, O.C= 1.69% and CEC= 10 meq/100 g) soil from Germany</p> <p>177 days (slow DFOP*; Parent reached 38% @ EOS) in Hoefchen am Hohenseh 4a (silt loam, pH 6.5, O.C= 2.59% and CEC= 14 meq/100 g) soil from Germany</p> <p>Major Metabolites: None</p> | 498358-02 with 498358-03 |

| | | |
|---|--|---|
| | <p><u>Minor Metabolites:</u> Multiple unknowns with Max ranging from 9.8 to 11.3% consisting of minor multi degradate residues. Attempts to identify residues was not successful (MRID 498358-03)</p> <p><u>Mineralization to CO₂:</u> Max 12-28% @ EOS</p> <p><u>Un-extracted Residues (UER):</u> Max 15-21% @ EOS</p> | |
| Anaerobic Aquatic t½ @ 22 ± 1°C (End of study "EOS" = 358 days; Pyridinyl-14C-methylene imidacloprid) | <p>33 days (SFO) in pond water sediment system from Stanly, Kansas (Water: Total organic carbon (TOC) 5 mg/L; Sediment: silt loam, pH 6.9, O.C= 3.15% and CEC= 14 meq/100 g) soil from Germany</p> <p>Major Metabolites: Guanidine= Max 21% @ 60 d declined to 16% @ EOS</p> <p>Minor Metabolites: None</p> <p>Mineralization to CO₂: Max 0.2-0.5% @ 249 d to EOS</p> <p>Un-extracted Residues (UER): Max 73% @ EOS Noting that harsh reflux boiling with acetone: 1 N HCl yielded high levels of Guanidine. Therefore, the authors suggested that the major part of the UER is Guanidine noting (without data) that parent could withstand the harsh extraction and that Guanidine is not an artificial product resulting from the effect of harsh extraction on parent. The possibility of parent artificially converting to Guanidine may not be ruled out without submittal of data supporting the claim that parent could withstand the harsh extraction. The 73% of radioactivity, above, contains radioactivity attributed to the UER (left after the harsh extraction) plus the radioactivity attributed, by the authors, to be Guanidine.</p> | 422563-78 |
| Aerobic Aquatic t½ @ 22 °C (End of study "EOS" = 92 days; Pyridinyl-14C-methylene imidacloprid) | <p>32 days (SFO) in an orchard ditch water: loamy silt sediment system (Water: pH 8.4 and TOC= 5 mg/L; Sediment: OC%= 4.1%) from IJzendoorn, Netherlands</p> <p>Major Metabolites: Guanidine= 12% @ EOS</p> <p>Minor Metabolites: 6-chloronictonic Acid= Max 1% @ 29 d declined to <1% @ EOS; and DIJ 9646-2= Max <1% throughout and un-characterized residues= Max 6% @ 29 d declining to 4% @ EOS</p> <p>Mineralization to CO₂: Max 1.4% @ EOS</p> <p>Un-extracted Residues (UER): Max 66% @ EOS</p> <p>159 days (SFO) in a re-cultivated quarry water: loamy sand sediment system (water: pH 8.1 and TOC= 4 mg/L; sediment: OC%= 0.9%) from Lienden, Netherlands</p> <p>Major Metabolites: None</p> <p>Minor Metabolites: Guanidine= Max 9% and 6-chloronictonic Acid= 4% @ EOS; and DIJ 9646-2= Max 2% @ EOS and un-characterized residues= Max 4% @ 60-EOS</p> <p>Mineralization to CO₂: Max 2% @ EOS</p> <p>Un-extracted Residues (UER): Max 15% @ EOS</p> | 484169-01 |
| Aerobic Aquatic t½ @ 22 °C (End of study "EOS" = 30 days; Pyridinyl-14C-methylene imidacloprid) | <p>>30 days (parent was 84% @ EOS) in a pond water: silty clay sediment system (water: pH 8.5 and TOC= 4 mg/L; sediment: pH 7.6 and OC%= 2.1%) from Kansas, USA</p> <p>Major Metabolites: None</p> <p>Minor Metabolites: WAK 4103= Max 3% @ 7 d declined to 2% @ EOS; Nitrosimine, Cyclic Urea & GBH 4315= 1% 14 d- EOS</p> <p>Mineralization to CO₂: Max 0.7% @ EOS</p> <p>Un-extracted Residues (UER): Max 8-10% 21 d-EOS</p> | 484169-02 |
| Terrestrial Field Dissipation | All studies were unacceptable | GA: 422563-79 MN: 422563-80 CA: 422563-81 |
| K _{oc} (L Kg _{oc} ⁻¹) | Parent | 425208-01 |

| | | |
|--|--|--|
| | <p>266 (n=15) ranging from 98-487 in soils with varied texture, Clay= 1 to 43%, Organic carbon (O.C) = 0.23 to 3.95%, pH= 4.5 to 7.8, and Cation exchange capacity (C.E.C) = 4 to 41 meq/100 g</p> <p>Guanidine Compound (a metabolite)</p> <p>Average= 742 (n=4) ranging from 327 to 942 in soils with varied texture (Sand, Loamy sand, Sandy loam and Loam, O.C= 0.23 to 1.51%, pH= 5.1 to 6.5, and C.E.C= 4 to 16 meq/100 g</p> | <p>and 425208-02</p> |
|--|--|--|

¹ Values for half-lives were estimated as per NAFTA degradation kinetic: SFO model= Single Order; DFOP model= Double First Order; and IORE model= Indeterminate Order Rate Equation

Persistence

Fate data suggest that imidacloprid is persistent in terrestrial and aquatic environments with the exception of conditions that favor aqueous photolysis. It is noted however, that imidacloprid persistence in aerobic soil system is more than that expected in anaerobic/aerobic aquatic systems. Photo-degradation may occur on soil surfaces in the case of direct/indirect soil application and on foliage in case of foliar application. Photolysis on soil data suggest that dissipation of imidacloprid through this process is expected to be slow ($t_{1/2} = 171$ days). In contrast, aqueous photolysis is expected to be a significant process for imidacloprid transformation on wet foliage during daylight when the chemical is applied directly to foliage. The significance of this process is dependent on the presence of light and moisture (rain and/or irrigation) and on factors that determine **how much** of the chemical is present on foliage: application rate, formulation, tank mixes, timing, procedure and plant foliage density/characteristics) and for **how long** (affected by plant wash-off by rain and/or irrigation). Although many factors are required for dissipation of the chemical by aqueous photolysis, laboratory data suggest that abiotic photolysis may play an important role in imidacloprid dissipation ($t_{1/2} = 0.2$ days).

As will be shown later in this assessment, available field data do not show that the aqueous photolysis process is important from a dissipation standpoint. Aerobic and anaerobic aquatic transformation are expected to contribute to dissipation of imidacloprid reaching aquatic systems by run-off and drift.

Metabolism appears to be more pronounced in anaerobic conditions ($t_{1/2} = 33$ days; n=1) compared to aerobic conditions (upper 90th confidence limit on the mean $t_{1/2}$ 236 days; n=2). Aerobic soil transformation of imidacloprid is expected to be relatively slow with degradation half-lives ranging from 172 to 608 days and upper 90th confidence limit on the mean $t_{1/2}$ of 254 days (n=8). Based on this route of degradation alone, imidacloprid is expected to be highly persistent in the soil system. This persistence in soils may lead to accumulation over the years with repeated applications. However, the magnitude of soil accumulation is expected to be highly affected by other important routes of dissipation including: leaching, run-off and plant up-take which are expected to reduce this accumulation.

For persistence of imidacloprid in the field, available terrestrial field dissipation studies are all classified as invalid for several reasons including application rates not confirmed, and metabolites were not tracked. However, it could be stated that the chemical showed relative stability in the field.

Additionally, available rotational crop studies confirmed occurrence of soil carry-over from application to one crop to the following crop based on data obtained for magnitude of residues in rotational crops (MRIDs: 432459-01 and 440637-01). In these studies, detectable residues of imidacloprid were found in variable quantities in rotational crops planted after 1, 4, 8, and 11 months rotational intervals following a single granular application of 0.29-0.32 lb. a.i/A. Measured average residues of imidacloprid plus its metabolites (parent plus metabolites containing the 6-chloropyridinyl moiety) were observed in

California: wheat forage/straw (0.12-0.19 (mg/L), turnip tops (0.58 mg/L), and spinach leaves (0.32 mg/L) all planted-back after 8 months. It is noted however, that residues were much lower in other parts of the plant such as roots and grain (e.g., grains: <0.05 mg/L) and that the magnitude of residues varies within a given crop depending on the planting location (*i.e.*, CA vs. KS or MS). It is noted that the list of degradates containing the 6-chloropyridinyl moiety includes the two degradates of concern (IMI-olefin and IMI-5-OH) plus guanidine, 4-5-hydroxy, nitrosimine and urea compounds.

In the soil-applied blueberry residue study (MRID 495356-02), field soil residues of total imidacloprid (imidacloprid, IMI-olefin, and IMI-5-OH) were measured in three locations (Site 1: Loam soil in NY, Site 2: Silt loam soil in IL and Site 3: Sand soil in MI). In each site, nine samples, from the top 6" of the soil, were analyzed (after the first application of 0.50 lbs a.i/A) at two separate sampling intervals (245 and 361 days after the 1st application at site 1 and 275 and 357 days after the 1st application at site 2). At 366, 360 and 366 days after the 1st application a 2nd application of 0.50 lbs. a.i/A was applied to sites 1, 2 and 3, respectively. After this 2nd application, the same scheme of sampling/ analyses were performed after 588, 611 and 608 days following the 1st application at sites 1, 2 and 3, respectively (**Appendix I**). Parent was the major constituent of the tracked residues (on the average 72% of the applied after nearly a year following the 1st application at sites 1 and 2). The IMI-olefin metabolite constitutes 2 to 5% of the applied after same period at site 1 and 2. Within the year after the first application, each of the three sites received a second application of 0.5 lbs a.i./A. Residue analyses was not performed just before and just after this 2nd application but rather within a year after the application (nearly two years after the 1st application). Again, residue data indicate that parent was the major constituent of the tracked residues (on the average 50, 69 and 48% of total applied "% of the 1st plus the 2nd applications" after nearly two years following the 1st application at sites 1, 2, and 3, respectively). The IMI-olefin metabolite constitutes 2, 5 and 2% of the applied after same period at sites 1, 2 and 3, respectively. The IMI-5-OH metabolite was not detected at sites 1 and 2 within the first year from the first application but was sporadically detected, after two years in the three sites, at very low level (<0.4% of the total two applications). A wide range of concentrations was observed and some were even higher than what is expected from the amount applied (further details in **Appendix I**). This may reflect the small width of the band application (18" on each side) in relation to the larger area of sampling (100 x 200 ft and 200 x 400 ft). However, the large number of samples may reflect the real concentration present resulting from application followed by dissipation (degradation and movement).

Mobility

Based on laboratory batch equilibrium studies, parent imidacloprid is expected to be moderately mobile ($K_{oc} = 266 \text{ L Kg}_{oc}^{-1}$, n=125; FAO Classification). Persistence/mobility data suggest that imidacloprid has the potential to leach into groundwater and to move into surface waters through run-off for long periods of time. The mobility of imidacloprid was confirmed in the field by two prospective ground water (PGW) studies. One of the studies was conducted in Montcalm County, Michigan (0.34 lbs. a.i/A to potatoes; MRID 458582-01) and the other in Monterey County, California (0.45 lb. a.i/A to broccoli; 458787-01). In both studies, the registrant monitored for imidacloprid parent, imidacloprid guanidine, imidacloprid olefin, and imidacloprid urea in the vadose zone (area between ground surface and where groundwater is at atmospheric pressure) and in shallow ground water. In both studies, the predominant compound detected in soil, soil-pore water throughout the vadose zone, and in ground-water (when

detectable) was parent imidacloprid. Of the three degradates analyzed for (guanidine, olefin, and urea compounds) only the urea compound leached at concentrations that were frequently detectable in the shallow ground water. It was noted that detections in ground water (*i.e.*, breakthrough) started after 500 days from application and continued five years after application. Residues of imidacloprid in ground water were most frequently observed under use conditions which promoted greater ground-water recharge and/or when imidacloprid was used in multiple growing seasons at the same site.

Degradation Profile

Based on various laboratory fate studies (**Table 4-2**), abiotic direct photolysis appears to be the major degradation pathway for imidacloprid. In contrast, the chemical is expected to resist biotic metabolism in the aerobic soil. Based on this data, **Figure 4-2** is suggested to represent the degradation pathways for imidacloprid in terrestrial ecosystems.

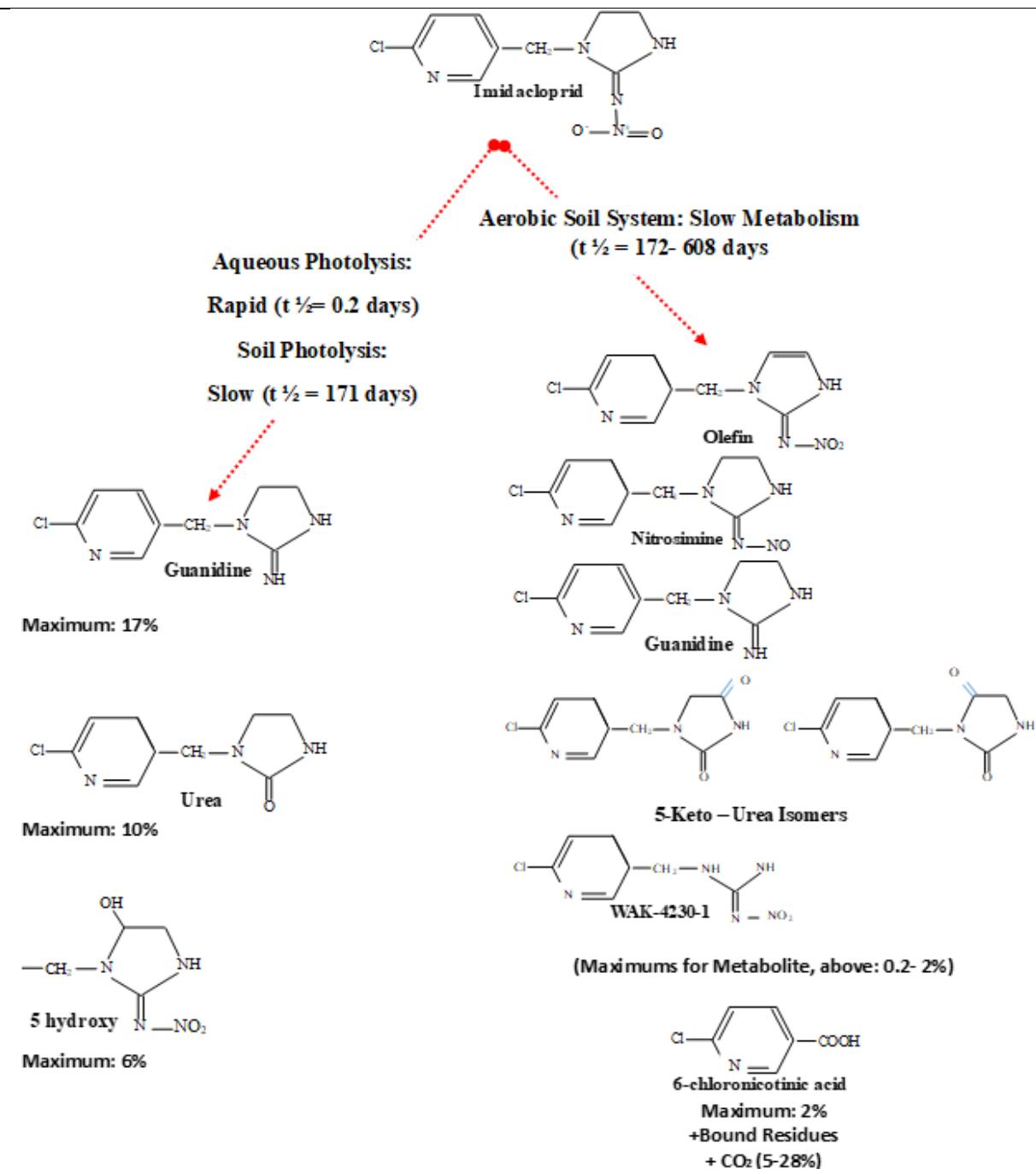


Figure 4-2. Expected degradation profile for imidacloprid in compartments of the terrestrial ecosystems. Imidacloprid parent, and the IMI-olefin and IMI-5-OH degradates are considered residues of toxicological concern.

Data in **Figure 4-2** show the following:

- Direct aqueous photolysis: photolysis is expected to be rapid ($t_{1/2} = 0.2$ days) producing the following metabolites: guanidine/desnitro compound (NTN-38014) at a maximum of 17% and imidacloprid

urea (NTN-33519) at a maximum of 10%. Both maxima occurring at the end of the study suggesting their stability to further photo-degradation. Many other metabolites were not identified with only three of them at levels ranging from 8-13% of the applied residues. Availability of water and sunlight is necessary for this process to occur and therefore is expected to be important in clear shallow surface water exposed to sunlight and could be important on wet foliage exposed to sunlight; and

- Biotic aerobic soil metabolism: this process is expected to be very slow producing metabolites at very low concentrations. Although it is very slow, aerobic soil degradation is the only degradation pathway that is expected to affect applied parent reaching the soil directly upon soil or seed application or indirectly from foliar applications and later from wash-off. Limited, biotic degradation in aerobic soil systems is expected to produce the following minor metabolites: olefin (NTN-35884), WAK-4230-1, nitrosimine (WAK-3839), guanidine/desnitro (NTN-38014) and the two isomers of 5-keto-urea compounds.

The degradation profile of imidacloprid suggests the following:

- Imidacloprid parent is expected to be the major species present in the soil system of the terrestrial eco-systems because it resists aerobic soil bio-degradation and abiotic photolysis on soil. Therefore, parent is expected to be the dominant species in both imidacloprid pools (root and foliage), noting that metabolites are also expected to be present but at low concentrations. In addition to parent, the only other two metabolites that are reported to be of toxicological concern for bees are the olefin and 5-hydroxy imidacloprid (these are included as analytes in the submitted residue data); and
- Although aqueous photolysis is expected to be a significant process for imidacloprid transformation on wet foliage during daylight ($t_{1/2} = 0.2$ days) the importance of this parameter was not demonstrated in the examined field trials herein.

In terrestrial ecosystems, there are two dissipation processes that appear to be of varying importance in imidacloprid exposure: degradation and movement. Degradation in the soil system is expected to have minimal effects on parent imidacloprid and available field data do not show that photolysis is important in degradation of imidacloprid reaching foliage. In contrast to degradation, imidacloprid exposure is expected to be highly affected by its movement including leaching down the soil profile, movement into the plant (plant up-take) and with surface water run-off. Imidacloprid mobility is necessary for its movements towards the root system from the point of application for root up-take but it may also reduce its availability for the same root up-take, by leaching downwards, as it reduces the available pool of imidacloprid from which the roots could up-take the pesticide. In this respect, it should be noted that dense深深 plant root systems may overcome effects of imidacloprid leaching. This factor depends on the plant type and the stage of growth in relation to application timing of the pesticide. Although the compound is expected to leach and no longer be available for root uptake for crops with shallow/thin root systems, it would still be available for those plants with deep/dense root systems. Similarly, reduction of the available pool of imidacloprid for root-uptake is expected as a result of its movement away from the application site in run-off waters. This dissipation pathway is highly dependent on many factors such as soil type/slope and rainfall intensity/timing in relation to pesticide application timing.

4.2. Imidacloprid Plant Up-take

Several studies were evaluated in order to understand root and foliage up-take. These studies were not specifically designed for this purpose but rather for determining the nature of imidacloprid residues in varied raw agricultural commodities (apples, corn, tomatoes, potatoes and eggplants). In this section, plant up-take will be examined for imidacloprid applied to soil (including seed treatment) as well as applied to foliage.

4.2.1. *Imidacloprid applied to soil including seed treatment*

In four studies, radio-labeled compound (¹⁴C-imidacloprid) was soil applied to cotton, potatoes, corn and eggplant (MRIDs: 425561-05/06/10 and 11, respectively). Only a summary of the results obtained from these studies is included herein and more details are included in **Appendix I**.

Results from these four studies are summarized in **Table 4-3**. In this **Table 4-3**, observed up-take in percent of applied and resultant concentrations are included. It is noted, that data for foliage were combined from stems and leaves but most of the radioactivity assigned for foliage in **Table 4-3** is present in leaves rather than stems.

Table 4-3. Imidacloprid root up-take/distribution and resultant concentrations in cotton, potatoes, corn and eggplant (% = up-take in % of the applied radioactivity and numbers in brackets are resultant concentrations in mg/kg)

| | | | | | | | |
|----------|-------------------|---|--------------|--------------|--------------|--------------|--------------|
| Cotton | Timing 1 | 211 days | | | | | |
| | Type ² | Foliage | | Seeds | | | |
| | Data | 4.7% | 0.2% | (0.11) | (0.007) | | |
| Potatoes | Timing 1 | 129 days | | | | | |
| | Type ² | Foliage | | Tubers | | | |
| | Plant | 2.2% (5.76) | | 0.3% (0.091) | | | |
| | Soil | 98.4% (0-20 cm: 0.98-0.47; 20-50 cm: 0.007-0.002) | | | | | |
| Corn | Timing 1 | 33 days | 61 days | 134 days | | | |
| | Type ² | Foliage | Foliage | Foliage | Husks | Cobs | Grain |
| | Plant | 4.2% (5.84) | 10.2% (1.52) | 19.7% (3.08) | 0.12% (0.21) | 0.15% (0.12) | 0.14% (0.04) |
| Eggplant | Timing 1 | 14 days | 35 days | | 69 days | | |
| | Type ² | Foliage | Foliage | F/FC/IMMF | Foliage | F/FC/IMMF | Calyx |
| | Plant | 2.7% (5.89) | 2.7% (3.63) | 0.03% (0.73) | 1.6% (1.47) | 0.04% (0.74) | 0.01% (0.17) |

| | | | | |
|--|-------------|-------------------|-------------------|-------------------|
| | Soil | 79% (1.67) | 74% (1.43) | 78% (1.60) |
|--|-------------|-------------------|-------------------|-------------------|

¹ **Timing:** Timing in days from imidacloprid application which coincides with planting time noting that it was transplanting time for eggplant plantlets which were transplanted at the eight leaves stage

² **Type:** Type of sample noting that **Foliage**= Stems and leaves/vines; **F/FC/IMMF**= Flowers, flower clusters and immature fruits

Data in **Table 4-3** suggest that the total root uptake for soil-applied imidacloprid, appeared to take place upon application reaching equilibrium in the early growth stage of the plant. Uptake was generally very low (ranged from 2-5% of the applied in cotton, potatoes and eggplant). In corn, much higher uptake was observed with quantities increasing towards maturity (from 4 to 20% of the applied). In all cases, radioactivity that was taken up through the roots concentrated in foliage (leaves and stems) with minor amounts reaching the productive parts of the plant at maturity (ranged from 0.1 to 0.5% of the applied). As a result of the differing distribution of radioactivity within the plant, concentrations in the foliage ranged from 0.1 to 5.89 mg/L compared to 0.007 to 0.2 mg/L in the reproductive parts of the plant.

Radioactivity left in the soil was measured in only two studies in eggplant at 14, 35 and 69 days showing that radioactivity left in the soil was almost constant (74 to 79% of the applied). The same was observed in the soil planted with potatoes in which 98.4% of the applied radioactivity remained in the soil. Loss of radioactivity may be related to leaching, in addition to expected analytical errors. Transformation of imidacloprid was observed in the soil planted in eggplant as observed parent concentrations were between **62** and **82%** with not more than 2% of the metabolites 5-hydroxy and nitrosimine compounds and 6-CNA.

Data, not shown in **Table 4-3**, suggest that the presence of high concentrations of imidacloprid in the soil lead to high root up-take. This was demonstrated in the cotton study by applying an additional soil drench of imidacloprid to some of the cotton plants (60 X the seed treatment amount applied in the main experiment).

4.2.2. Imidacloprid applied to foliage and fruits

In three studies, ¹⁴C-imidacloprid was applied as formulated liquid spray to the foliage of potato plants and to the fruits of apple and tomato plants planted in the greenhouse (MRIDs: 425561-07/08 and 09, respectively). These studies represent application of the chemical directly to foliage and depending on the growth stage of the plant, it may also be directly applied to flowers and fruits. In this case, plant up-take is determined by the amount of chemical inside the fruits in the case of application to fruits (tomato and apple experiments). However, uptake can be only confirmed in the case of foliage (the potato experiment) by the occurrence of plant metabolism inside leaves and stems (when metabolism on the surface can be discounted) and by translocation to other plant parts that are not directly sprayed by the chemical (such as tubers when no chemical is present in the soil). Only a summary of the results obtained from these studies is included herein and more details are included in **Appendix I**. Data obtained from the three studies for radioactivity distribution and resultant concentrations are summarized in **Table 4-4**.

Table 4-4. Imidacloprid up-take/distribution and resultant concentrations in various parts of the potato plants and only in the fruits of apples and tomatoes (%= up-take in % of the applied radioactivity and numbers in brackets are resultant concentrations in mg/kg).

| Potatoes | Timing ¹ | 7/90 days | | 28/111 days | | 64/147 days | |
|----------|---------------------|--|--------------|----------------|---|--------------------|-------------------|
| | Type ² | Vines | Tubers | Vines | Tubers | Vines | Tubers |
| | Plant | 40.1% (2.51) | 0.02% (0.01) | 48.5% (1.97) | 0.02% (0.01) | 49.0% (1.35) | 0.20% (0.01) |
| | Soil | 50.75% (0-15 cm: 0.006-0.004; 15-55 cm: 0.001-<0.001); Samples for 64/147 days only and the depth of sampling, in cm, is indicated | | | | | |
| Tomatoes | Timing ¹ | 4 days | | 7 days | | 14-21 days | |
| | Type ² | Fruit Surfaces | Fruit Pulp | Fruit surfaces | Fruit Pulp | Fruit surfaces | Fruit Pulp |
| | Fruits | 88% (0.89) | 12% (0.12) | 77% (0.64) | 23% (0.19) | 76-60% (0.65-0.39) | 24-40% (0.2-0.25) |
| Apples | Timing ¹ | Zero Day (Just After) the Last of 3 Applications | | | 14 Days After the Last of 3 Application | | |
| | Type ² | Fruit Surfaces | Fruit Peel | Fruit Pulp | Fruit Surfaces | Fruit Peel | Fruit Pulp |
| | Fruits | 74.2% (1.31) | 15.9% (0.28) | 9.9% (0.17) | 64.9% (0.94) | 21.1% (0.31) | 14.0% (0.2) |

¹ Timing: Timing in days from imidacloprid application; For potato 7/90 days mean that (vines)/tubers were sampled 7 days after application on plants at age of 90 days)

² Type: Column: Type of sample noting that **Potato Vines**= Stems and leaves

Data in **Table 4-4** indicate that only half of the chemical reached/stayed on/in the foliage of the potato plants (40-49% of the applied radioactivity), the other half reached the soil and only 0.2% reached tubers presumably by direct up-take from the contaminated soil or by translocation from the foliage. In the case of tomato and apples, most of the applied radioactivity stayed on the surface of the fruits (60 to 88%) with relatively substantial amounts entering the fruits (12 to 40% in tomatoes and 26-35% in apples). Additionally, increasing residence time on the fruit surfaces appears to increase radioactivity that enters the fruits (an increase from 26 to 35% in apple peel+ pulp after a resident time of 21 days and from 12 to 40% in tomato pulp after a resident time of 14 days. The results suggest the likelihood of an increase in residues in fruits sprayed at younger age compared to those sprayed at older age. Data suggest that important translocation may have occurred from the fruit surface to the interior. In contrast, no apparent transport of radioactivity occurs from plant leaves into fruits for both apples and tomatoes in a separate imidacloprid translocation experiment (refer to **Appendix I**).

4.2.3. *Imidacloprid: soil versus foliage applied*

As expected, the chemical residues present on/in foliage from foliar applied imidacloprid was much higher than that resulting from soil application (a total of 49.2% on mature plants, 64 days after application compared to a total of 2.5% on mature plants, 129 days after application). In the first case, imidacloprid reaches foliage directly and the soil indirectly while in the second case, a comparatively small fraction of the chemical reaches foliage by root up-take. It is noted that the level of chemical ending up in the foliage, from foliar application, depends on many factors that were not investigated here such as photolysis on wet foliage, use of stickers and levels of wash-off (weather dependent).

Soil (at planting) and foliar applications were investigated in parallel in potatoes. Data obtained from previously stated experiments are summarized in **Figure 4-3**. It is important to note that in the soil applied part of the graph: radioactivity in the soil is from application and that radioactivity in foliage is from root up-take and radioactivity in the tubers is from soil/root up-take; however, in the foliar applied part of the graph radioactivity in *BOTH* soil and foliage are from direct/indirect application and *ONLY* the amount in tubers is from soil/foliage up-take. These data indicate that a large percentage (49%) of imidacloprid was present on foliage due to direct application while a relatively low percentage (2.2%) reached the foliage from the soil by root up-take. However, the amount of radioactivity moving from the foliage into the tubers was almost the same (0.3% in the case of soil application and 0.2% in case of foliar application). Although radioactivity reaching tubers was the same, it is noted that measured concentrations in tubers from soil-applied imidacloprid is relatively higher than that present in the tubers from foliar applied imidacloprid (0.09 mg/kg compared to 0.01 mg/kg). A possible explanation to the observed may be related to higher yield of tubers in the foliar applied experiment compared to that in the soil applied experiment.

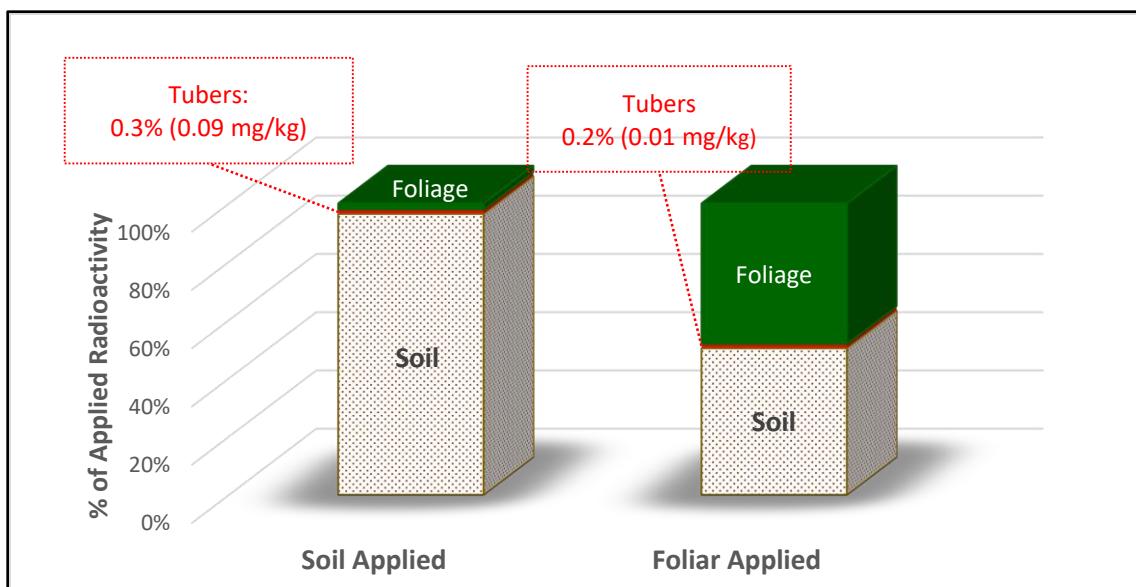


Figure 4-3. Comparison of up-take data obtained for imidacloprid applied to soil and that applied to foliage in potatoes

4.3. Plant Metabolism of Imidacloprid

In the experiments discussed in the preceding section, radioactivity that was applied and/entered into the plant, as parent, was examined to obtain data on imidacloprid plant metabolism during the period from initial exposure (application time) to fruit maturity. Only a summary of the results obtained from these studies is included herein and more details are included in **Appendix I**.

4.3.1. Imidacloprid metabolism in various plants

In contrast to the persistence of imidacloprid in the soil system, plant metabolism appears to play an important role in its degradation within various plant parts. Biotransformation occurs as a result of changes in moieties associated with the imidazole ring with the backbone structure of the chemical staying intact in addition to cleavage of the chemical structure between the imidazole and chloropyridinyl rings. The following is a summary of the data obtained for metabolism of imidacloprid in various plants:

- (a) In cotton (seed treated), almost all parent (99 to 97%) was transformed into mainly guanidine and glucoside in the leaves and 6-CNA in seeds with relatively high percentages of un-identified compounds (extracted and un-extracted);
- (b) In potatoes (soil applied), high percentage of parent persisted in both leaves and tubers (25 and 48%). Transformation in potatoes produced the major metabolites 5-hydroxy, guanidine and 6-CNA and the minor metabolites nitrosimine, IMI-olefin and 6-CPA with relatively high percentages of un-identified compounds (extracted and un-extracted) in the leaves compared to the tubers;
- (c) In corn (seed treated), relatively high percentages (65 to 47%) of imidacloprid parent appear to persist in the whole plant throughout the plant growth stages up to maturity as it then decreases to 22%. High concentrations were observed in corn husks and cobs (43 to 47%) with lower concentrations in grains (24%). Imidacloprid appears to be transformed primarily into IMI-5-OH and guanidine with minor amounts of IMI-olefin, 4, 5-hydroxy, nitrosimine, 6-CNA, 6-CPA and open ring guanidine. Higher percentage of un-identified compounds (extracted and un-extracted) appear to form as the corn plant matures;
- (d) In transplanted eggplant (soil applied), Imidacloprid parent appears to decrease (i.e., degrade) in foliage as the plant matures (decrease from 33 to 9% of the total residues) with relatively higher percentage of parent persisting in the fruits (22% of the residues). In all cases, parent degradation resulted in formation of imidacloprid transformation products and substantial amounts of un-identified compounds (extracted and un-extracted). Transformation products found in foliage included the major metabolite guanidine with minor amounts of IMI-olefin, IMI-5-OH, nitrosimine, glucoside and 6-CNA but glucoside and 6-CNA were the major metabolites in fruits;
- (e) In potatoes (foliar applied), parent imidacloprid dominated the percentage of radioactive residues in the vines at Day 90 but declined (i.e., degraded) as the plant matured. Metabolite residues in young and immature vines consisted primarily of the metabolites guanidine, 4,5-hydroxy and IMI-5-OH and minor amounts nitrosamine, IMI-olefin and glucoside. Residues in the tubers were primarily 6-CNA with a large percentage of un-identified compounds (extracted and un-extracted).
- (f) In potatoes, comparison between two cases: **Case 1** in which the chemical entered potato plant through the leaves from foliar application (root up-take from soil may not be discounted as imidacloprid was present in the soil during foliar application), and **Case 2** in which the chemical

entered the leaves from soil through root up-take following a soil application suggested the following:

- Plant transformation of imidacloprid in the leaves, following foliar application in **Case 1** (38% of the applied persisted and 62% metabolized), is less pronounced than in **Case 2** in which imidacloprid was applied as a soil treatment (25% of the applied persisted and 75% metabolized). This might be resulting from the longer resident time of imidacloprid in the plant in **Case 2** compared to **Case 1** (129 days compared to 64 days) giving more time for metabolism to occur; and
- Chemical residues reaching the tubers in **Case 1** (0.2% of the applied) contain 11% as parent and those reaching the tubers in **Case 2** (0.3% of the applied) contain 48% as parent. Residues in both cases are at least partly translocated from other parts of the plant, therefore, no conclusions can be drawn on possible imidacloprid transformation in the tubers. The high amounts of parent in tubers in **Case 2** compared to **Case 1** (48% compared to 11%) appear to suggest the tubers are affected by direct up-take of parent from the soil. It is noted however, that imidacloprid parent was available, in the soil, for tuber up-take in both cases.

(g) In apple and tomato fruits, parent imidacloprid was applied to the surfaces of immature fruits. Data indicated the following:

- Parent dominates residues in both outside and inside apple and tomato fruits with no major transformation products present in either outside or inside the fruits;
- Minor metabolites were observed on the surface of the apple fruits including: guanidine, 4-5-hydroxy, urea and nitrosimine. The same minor metabolites were present on the surface of tomatoes with 5-hydroxy replacing 4-5-hydroxy. Authors suggested minimal abiotic transformation (assume minimum photolysis possibly due to lack of moisture (plant in greenhouse irrigated through the soil));
- Minor metabolites were observed inside the apple fruits including guanidine, 4-5 & 5-hydroxy, olefin and glucoside. minor metabolites identified inside tomatoes included: guanidine, 5-hydroxy, nitrosimine, olefin and glucoside.

Finally, it is generally noted that the importance of plant metabolism in the fate of imidacloprid appears to differ from one species of plant to another. Additionally, un-identified compounds (extracted and un-extracted) appear to form as the plant matures due to association of residues with natural plant compounds resulting in compounds that are difficult to identify.

4.3.2. Imidacloprid metabolism profile in plants

Based on data presented earlier, parent imidacloprid appears to be metabolized in the plant through two main processes:

- (1) Changes occurring in moieties associated with the imidazole ring with the backbone structure of the chemical staying intact. This includes reduction and loss of the nitro group as well as hydration of the imidazole ring and subsequent loss of H₂O; and
- (2) Breakage of the backbone of the chemical structure between the imidazole and chloropyridinyl rings resulting in the formation of the metabolite 6-CPA followed by either association with glucose forming glucoside or oxidation into 6-CNA.

Figure 4-4 contains a summary of the plant metabolism profile of imidacloprid based on submitted data. It is noted that not all of the plant metabolism radioactive residues were extracted/identified (due to possible incorporation into the natural plant constituents) or were extracted but not identified. The first fraction of the residues is termed herein as un-extracted residue (UER) while the second is termed as unidentified residue (UN-ID).

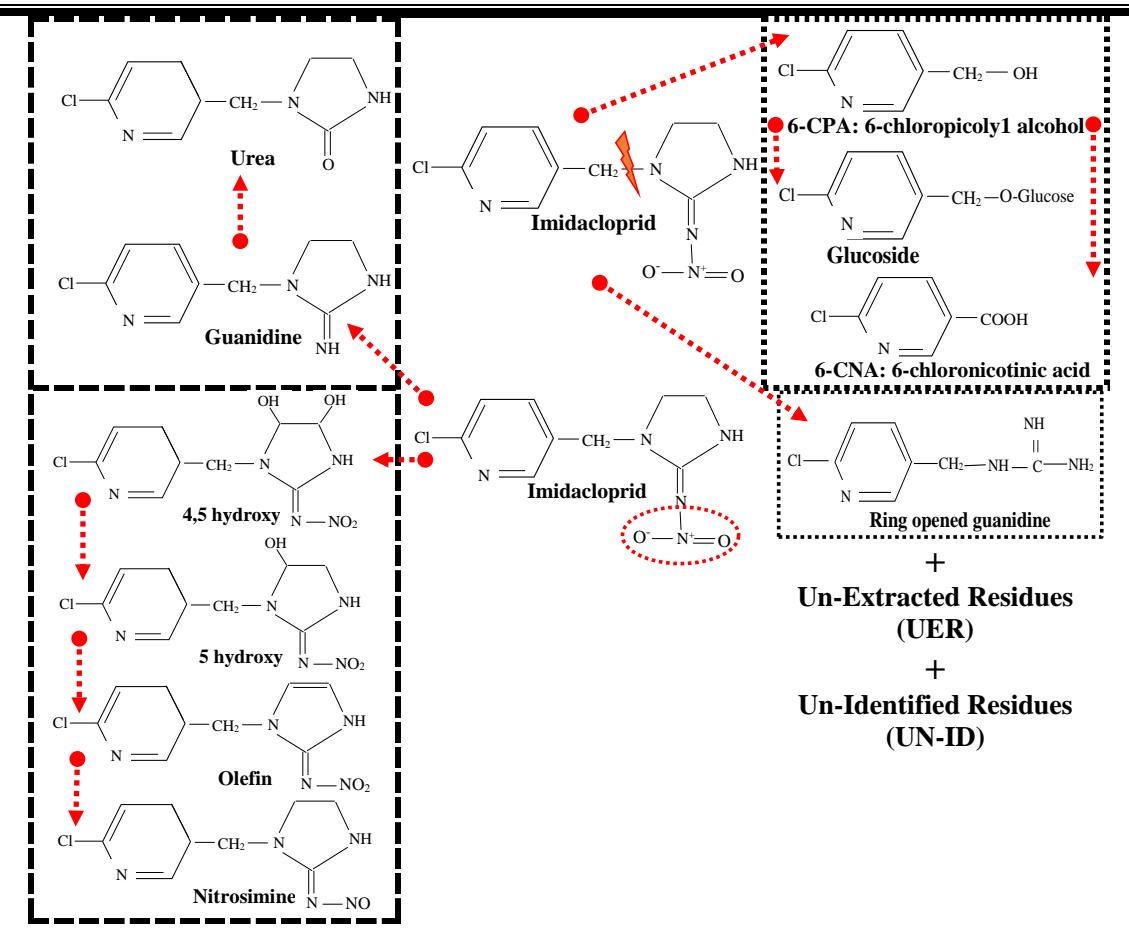


Figure 4-4. Suggested Imidacloprid degradation profile in plants

4.3.3. Seed Treatment Application Residue Studies – Open Literature

Additionally, there were 5 studies available from the open literature that investigated the residues of imidacloprid in pollen and nectar following seed treatment applications either as a targeted residue study or as part of a semi-field or full-field study design. As these studies originated from the open

literature, only the maximum and average residue values were available and not the entire dataset to verify the findings. **Table 4-5** below summarizes the key elements from each of the studies. Summaries of each study including methods and results are provided in **Appendix B**.

In a study by Donnarumma *et al.* (2011, MRID 49719614), seed-treated corn (Gaucho® 350 FS at 1.0 mg/seed, insufficient information to provide rate in terms of lbs a.i./A) were planted and samples were collected at 30, 45, 60, 80, and 130 days after initial sowing. Analysis of pollen residues 130 days after sowing indicated residues below the LOQ of 1 µg/L. The study also indicated that residues in the soil declined steadily as the trial progressed, *i.e.*, 652 µg/L at 30 days after sowing to 11 µg/L 130 days after sowing.

In a study by Laurent and Rathahao (2003; MRID 48077902), the uptake and distribution of seed treated-imidacloprid in sunflowers was examined under controlled conditions in the laboratory and uncontrolled conditions using an outdoor lysimeter. Sunflower seeds were dressed with Gaucho® 70 WS (1 mg a.i./seed). The dressed seeds were also radiolabeled with ¹⁴C (radiochemical purity of >97%). Pollen residues were collected when approximately ½ of the florets on the treatment plots were blossoming and indicated a mean residue level of 13 µg/L and a maximum of 36 µg/L. It was also determined from the radiolabeling analysis that between 3 – 10% of the total applied radioactivity was taken up by the plant depending on whether the plant was grown under controlled laboratory conditions or within an outdoor lysimeter.

Schmuck *et al.* (2001), conducted an uptake and metabolism study of imidacloprid-treated sunflower seeds in a greenhouse as well a residue component of imidacloprid-treated sunflower seeds in a honey bee field study. For the greenhouse component, sunflower seeds were dressed with labeled [methylene-¹⁴C] imidacloprid formulated as the commercial 700g/ kg WS (Gaucho® WS 70) at a rate of 0.7 mg a.i./seed. The field residue component was conducted with a rate of 1 mg a.i./seed. Parent imidacloprid, IMI-olefin and IMI-5-OH were assessed. The LOD and LOQ were reported to be 1.5 and 5 µg/L, respectively. Pollen and nectar residues in both study components were reported to be below the LOD with sampling interval of 62 – 66 days after application.

In Stadler 2003 (MRID 47796301), while the primary focus was to evaluate the effects of imidacloprid on honey bee colonies exposed to imidacloprid-treated sunflower seed, the residues in bee-collected nectar and pollen as well as hive wax were quantified with an LOD of 1.5 µg/L in all matrices. The honey bee colonies were exposed to seed-treated sunflower for 10 days, monitored through an overwintering period, and after which nectar and pollen samples were taken. Parent imidacloprid, IMI-olefin and IMI-5-OH were below the LOD in all matrices assessed. The interval between samples being collected and analyzed was approximately 216 days.

Stewart *et al.* (2014) evaluated concentrations of multiple neonicotinoids in bee-relevant matrices of corn, cotton and soybean grown in the mid-south, USA. With imidacloprid, only flowers of soybean seed treatments were evaluated (Gaucho® 600, 0.78 g a.i./kg seed) from four test sites. Flowers were sampled in early bloom and residues of imidacloprid and its metabolites quantified with a limit of detection of 1 ng a.i./g. Stewart *et al* report that imidacloprid (and metabolites) were not detected in soybean flower samples from the four seed treatment test sites. Although other matrices were

analyzed for the presence of imidacloprid in this study (*e.g.*, wildflowers adjacent to fields, forager bees and hive pollen from adjacent apiaries), the relationship of these residues to the seed-treated soybean is uncertain due to potential exposure from other imidacloprid applications at nearby locations.

Table 4-5. Summary of residue data from imidacloprid-treated seed studies evaluated from the open literature

| Crop Group (Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix | Max Value ($\mu\text{g/L}$) ² | Average Value ($\mu\text{g/L}$) ³ | DAA (days) | Study Notes | Classification (Reference) |
|--|---|--|--|--|--|-------------------------------|---|---|
| Cereal Grain - 15 (Corn/Maize) | 1 site Italy (Study Year NR) | Gaucho® 350 FS 1 mg/seed Sowing time NR | Pollen | <LOQ | NR | 130 | <ul style="list-style-type: none"> • Soil composition was 54.3% clay, 43.4% silt, and 2.3% sand • LOD: NR, LOQ: 1 $\mu\text{g/L}$ | <i>Qualitative</i> (Donnarumma, 2011 MRID 49719614) |
| Oilseed – 20 (Sunflower) | 1 site, Argentina (2000 – 2001) | Gaucho® 60 FS 0.26 mg a.i./seed , Seeds sown 12/7/1999 | Honey (b) Pollen (b) Wax | <LOD <LOD <LOD | NR NR NR | 13 days 13 days 13 days | <ul style="list-style-type: none"> • Full field study • No soil characterization Pollen analysis showed 20-30% of pollen collected was from sunflower • LOD: 1.5 $\mu\text{g/L}$, LOQ: 5 $\mu\text{g/L}$ | <i>Qualitative</i> (Stadler, 2000 also part of open lit effort as Stadler 2003, MRID 47796301) |
| Oilseed – 20 (Sunflower) | 1 site, France (Year of study not reported) | Gaucho® 70 WS 1 mg a.i./seed Grown in controlled conditions for 4-5 days until emergence then moved outdoors | Pollen | 36 | 13 | NR | <ul style="list-style-type: none"> • Reported that uptake of radiolabeled imidacloprid into plant from treated seeds ranged from 3-10% • LOD: NR, LOQ: 0.5 $\mu\text{g/L}$ | <i>Qualitative</i> (Laurent and Rathahao, 2003 MRID 48077902) |
| Oilseed – 20 (Sunflower) | 1 site, Germany | Gaucho® WS 70 0.7 mg a.i./seed (greenhouse component) Gaucho® WS 70 1 mg a.i./seed | Pollen Nectar Pollen Nectar | <LOD <LOD <LOD <LOD | NR NR NR NR | 62-66 days | <ul style="list-style-type: none"> • Greenhouse component: LOD: 1 $\mu\text{g/L}$; LOQ: NR • Full field study: LOD: 1.5 $\mu\text{g/L}$; LOQ: 5 $\mu\text{g/L}$ • Full field component seeds also treated with carbendazim, metalaxyl and copper oxyquonolate | <i>Qualitative</i> (Schmuck 2001, MRID 47812303) |
| Legume-6 (Soybean) | 4 sites, Southern UAA | Gaucho® 600 0.78 g a.i./kg seed | Flower | <LOD | <LOD | NR | <ul style="list-style-type: none"> • 4 test sites • flowers sampled in early bloom • LOD = 1 ng/g | <i>Qualitative</i> (Stewart et al. 2014) |

¹Unless delineated as "h" (hive collected), "b" (bee collected), or "t" (trapped pollen), nectar and pollen refer to hand collected pollen and nectar

²If study provided a low to high range of residues, the high-end value is reported here

³Value reflect the reported mean value of all residues within the provided scenario. Studies generally did not provide information on the numbers of sampling intervals from which the average was derived and therefore it is assumed to be one sampling period unless otherwise noted.

4.3.4. Imidacloprid metabolism profile in plants

As a result of plant metabolism, the quantity of parent entering the plant through root or foliage/fruit up-take is expected to decrease with time. However, plant metabolism produces two metabolites that are considered of concern: IMI-5-OH and IMI-olefin and olefin. **Table 4-6** contains a summary of the estimated stressor concentrations in various plants and plant parts.

Table 4-6. Observed estimated concentrations of the stressor in parts per million= ppm) (parent imidacloprid + IMI-olefin and IMI-5-OH compounds) in varied crops, plant parts and application procedures based on radioactivity data

| Soil Applied | | | | | | | | | |
|----------------|---------------------|--|---------|-------------|---|----------------|---------------|--|--|
| Cotton | Timing ¹ | 211 days | | | | | | | |
| | Type ² | Foliage | Seeds | | | | | | |
| | Data | 0.004 | <0.001 | | | | | | |
| Potatoes | Timing ¹ | 129 days | | | | | | | |
| | Type ² | Foliage | | Tubers | | | | | |
| | Plant | 2.016 | | 0.054 | | | | | |
| Corn | Timing ¹ | 33 days | 61 days | 134 days | | | | | |
| | Type ² | Foliage | Foliage | Foliage | Husks | Cobs | Grain | | |
| | Plant | 4.497 | 0.851 | 0.893 | 0.118 | 0.074 | 0.019 | | |
| Eggplant | Timing ¹ | 14 days | 35 days | | 69 days | | | | |
| | Type ² | Foliage | Foliage | F/FC/IMMF | Foliage | F/FC/IMMF | Calyx | | |
| | Plant | 2.533 | 0.436 | 0.088 | 0.206 | 0.163 | 0.037 | | |
| Foliar Applied | | | | | | | | | |
| Potatoes | Timing ¹ | 7/90 days | | 28/111 days | | 64/147 days | | | |
| | Type ² | Vines | Tubers | Vines | Tubers | Vines | Tubers | | |
| | Plant | 2.033 | 0.000 | 1.162 | 0.000 | 0.635 | 0.001 | | |
| Tomatoes | Timing ¹ | 4 days | | 7 days | | 14-21 days | | | |
| | Type ² | Surface | Pulp | Surface | Pulp | Surface | Pulp | | |
| | Fruits | 0.748 | 0.012 | 0.461 | 0.036 | 0.0455- 0.0700 | 0.068- 0.1040 | | |
| Apples | Timing ¹ | Zero Day (Just After) the Last of 3 Applications | | | 14 Days After the Last of 3 Application | | | | |
| | Type ² | Surface | Peel | Pulp | Surface | Peel | Pulp | | |
| | Fruits | 0.865 | 0.031 | 0.019 | 0.526 | 0.040 | 0.026 | | |

¹Timing: Timing in days from imidacloprid application;

²Type: Column: Type of sample noting that **Potato Vines**= Stems and leaves; **Foliage**= Stems and leaves/vines; **F/FC/IMMF**= Flowers, flower clusters and immature fruits

4.4. Potential for Exposure to Bees

As described in the Problem Formulation (**Section 2**), the first step in assessing a pesticide's risk to bees involves a determination of the potential for exposure of adult and larval honey bees from a given use pattern. In this step, the potential for exposure of bees is evaluated qualitatively based on the attractiveness of the treated crop to bees, agronomic practices and timing of application. If a use pattern is considered to have a reasonable potential for exposure to bees, risk is further evaluated quantitatively using the tiered assessment approach. If a use pattern is not considered to exert a reasonable potential for exposure of bees, it is not considered further for risk assessment.

Figure 4-5 below summarizes the process for determining whether an on-field or off-field Tier 1 risk assessment is warranted for imidacloprid. Consistent with the 2014 risk assessment guidance, it is assumed that contact exposure on the treated field would be negligible for soil or seed treatment uses.¹⁶ However, oral exposure to residues in pollen and nectar may occur, provided the crop is attractive and is not harvested prior to bloom. As spray drift would not be present from these use patterns, there would be no off-field exposure expected.

For any use with a foliar spray component, a Tier I off-field assessment would be conducted for contact and oral exposure routes regardless of whether the crop is attractive or is harvested prior to bloom. An off-field Tier 1 assessment would be indicated due to the potential of bees visiting pollinator-attractive plants in fields adjacent to the treated crop which may be subject to spray drift. If the crop is attractive and is harvested after bloom, a Tier I on- and off-field assessment is conducted for contact and oral exposure routes.

When uncertainty exists regarding attractiveness of the crop to bees or its time of harvest, it is assumed that the crop will be attractive to bees and harvested after the bloom period, thereby necessitating on-field and off-field Tier I assessments for contact and oral exposure routes.

¹⁶ Per the 2014 Guidance for Assessing Pesticide Risk To Bees, exposure of bees via drift of abraded seed coatings of treated seeds is being addressed through implementation of best management practices.

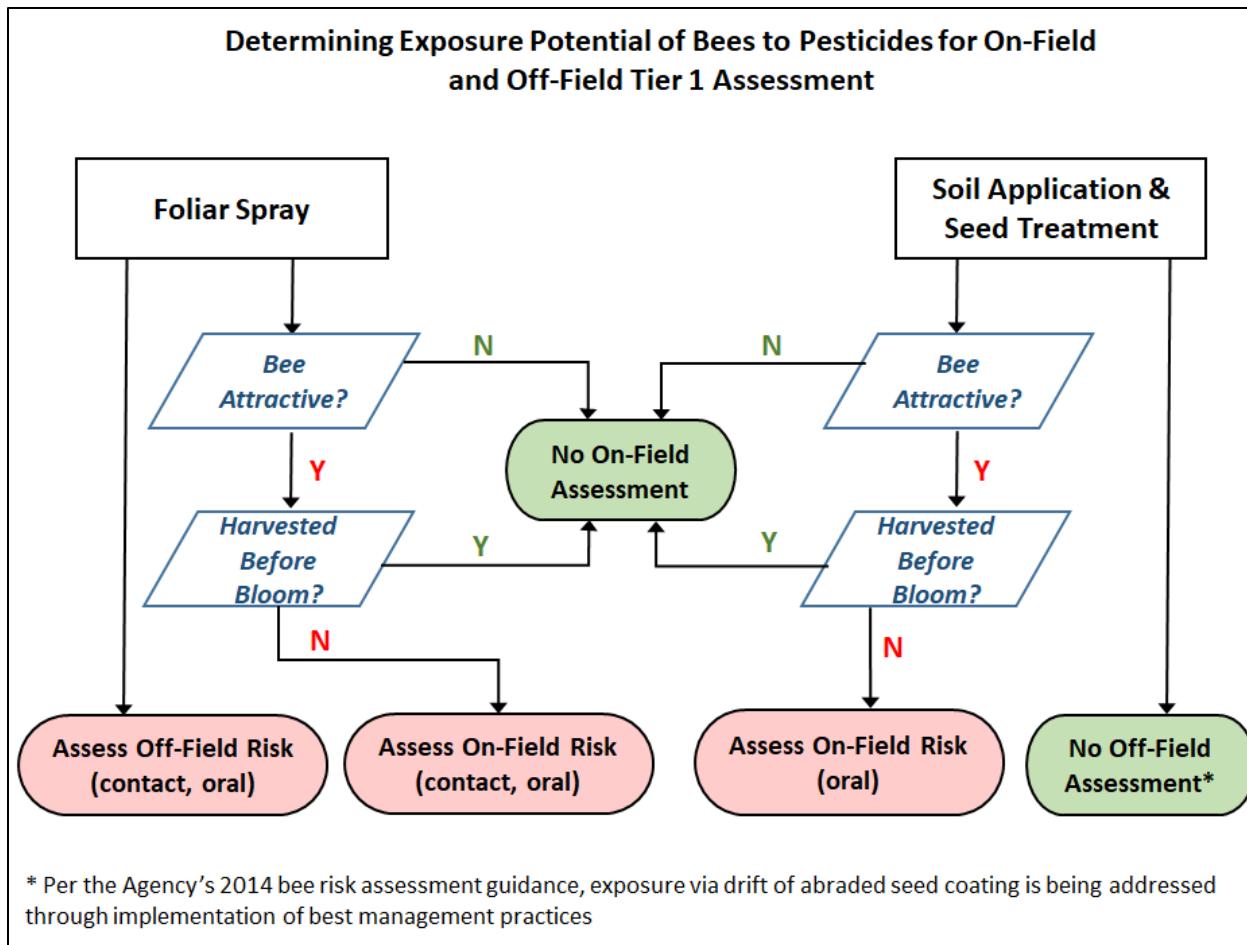


Figure 4-5. Summarization of the potential scenarios warranting a Tier I on and/or off-field risk assessment.

4.4.1. *Exposure Potential of Agricultural Uses*

Tables 4-7 and **4-8** below summarizes the potential for on-field and off-field exposure of bees from each of the registered agricultural use patterns for imidacloprid, organized by application method. This determination is informed by the USDA's review of the attractiveness of U.S. crops to bees (USDA 2017). Due to the persistent and systemic nature of imidacloprid, the potential for on-field exposure of bees is presumed for crops harvested after bloom and which are attractive to visiting honey bees, while off-field exposure is pertinent only for foliar uses, whether the crop is attractive to bees or not, as a result of spray drift.

For the tables below, the attractiveness and harvesting information presented represents the most conservative scenario that would warrant a Tier I on-field and off-field assessment. For example, if a certain member of a crop group indicates no attractiveness to bees, yet another crop within the group is considered attractive, a Tier I on-field and off-field assessment would be conducted.

Table 4-7. Attractiveness of crops to bees for the registered foliar uses of imidacloprid.

| Crop Group Number (Crop Group Name) | Attractiveness | | | Notes | Tier I On-Field Contact/Oral Assessment? | Tier I Off-Field Contact/Oral Assessment? |
|--|-----------------------|------------|--------------|--|---|---|
| | Honey Bee | Bumble Bee | Solitary Bee | | | |
| 1 (Root and Tuber Vegetables) ¹ | Y (N&P) | Y | Y | Bees important for seed production, typically harvested prior to bloom. Potatoes noted to be harvested after bloom | Y | Y |
| 4A (Leafy Green Vegetables) | Y (N&P) | Y | Y | Bees important for seed production, crop harvested prior to bloom when not used for seed production. | N | Y |
| 5 (Brassica Leafy Vegetables) | Y (N&P) | Y | Y | Harvested prior to bloom | N | Y |
| 6 (Legume Vegetables) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | Y |
| 8 (Fruiting Vegetables) | Y (N&P)) ⁴ | Y | Y | May be grown in glasshouses, with bumble bees for pollination | Y | Y |
| 10 (Citrus Fruit)* | Y (N&P) | Y | Y | -- | Y | Y |
| 11 (Pome Fruit) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | Y |
| 12 (Stone Fruit)* | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | Y |
| 13 (Berry and Small Fruit) ² | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | Y |
| 14 (Tree Nuts) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | Y |
| 9 (Herbs) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | Y |
| 20 (Oilseed) ^{3,5*} | Y (N) | Y | Y | -- | Y | Y |
| Non-crop group uses (Globe artichoke, banana and plantain, peanut, pomegranate, tobacco, coffee, hops, tropical fruit) | Y (Pollen and Nectar) | Y | Y | Globe artichoke harvested before bloom, tobacco deflowered as part of the harvest process | N (globe artichoke, tobacco) Y for all others | Y |

Groups where members have residue data available are indicated with *

When information was not available from USDA 2017 document, cell was indicated with a “--”

¹Refer to members of subgroups 1C (potato) and 1D (yams, ginger, others) only

²Includes 13A, 13B, 13-07D, 13-07F, 13-07G

³Cotton represents sole member in oilseed group with registered foliar uses.

⁴Okra nectar and pollen indicated to be attractive to honey bees (USDA, 2017)

⁵Cotton is only attractive for nectar but other members of this group are attractive for nectar and pollen.

Table 4-8. Attractiveness of crops to bees for the registered soil uses of imidacloprid.

| Crop Group Number (Crop Group Name) | Honey Bee Attractive? | Bumble Bee Attractive? | Solitary Bee Attractive? | Notes | Tier I On- Field Oral Assessment? | Tier I Off Field Contact/Oral Assessment? |
|--|--------------------------|------------------------------|--------------------------------|--|---|--|
| 1 (Root and Tuber Vegetables) | Y (N&P) | Y | Y | Bees important for seed production, typically harvested prior to bloom. Potatoes noted to be harvested after bloom | Y | N |
| 3 (Bulb Vegetables) | Y (N&P) | Y | Y | Typically harvest prior to bloom. | N | N |
| 4 (Leafy Vegetables) | Y (N&P) | Y | Y | Crop harvested prior to bloom when not used for seed production. | N | N |
| 5 (Brassica Leafy Vegetables) | Y (N&P) | Y | Y | Harvested prior to bloom | N | N |
| 6 (Legume Vegetables) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 8 (Fruiting Vegetables)* | N | Y | Y | May be grown in glasshouses, with bumble bees for pollination | Y | N |
| 9 (Cucurbit Vegetables)* | Y (N&P) | Y | Y | -- | Y | N |
| 10 (Citrus Fruit)* | Y (N&P) | Y | Y | -- | Y | N |
| 11 (Pome Fruit) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 12 (Stone Fruit) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 13 (Berry and Small Fruit) ^{1*} | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 14 (Tree Nuts) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 19 (Herbs) | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 20 (Oilseed) ^{2,3*} | Y (N) | Y | Y | -- | Y | N |
| Non-crop group uses (Globe artichoke, banana/plantain, peanut, pomegranate, tobacco, coffee, hops, tropical fruit) | Y (N&P) | Y | Y | -- | Y | N |

Groups where members have residue data available are indicated with *

When information was not available from USDA 2017 document, cell was indicated with a "--"

¹Includes 13A, 13B, 13-07D, 13-07F, 13-07G, 13-07H

²Cotton represents sole member in oilseed group with registered soil uses.

³Cotton is only attractive for nectar but other members of this group are attractive for nectar and pollen.

Table 4-9. Attractiveness of crops to bees for the registered seed treatment uses of imidacloprid.

| Crop Group Number (Crop Group Name) | Honey Bee Attractive? | Bumble Bee Attractive? | Solitary Bee Attractive? | Notes | Tier I On-Field Oral Assessment? | Tier I Off-Field Contact/Oral Assessment? |
|--|-----------------------|------------------------|--------------------------|--|----------------------------------|---|
| 1 (Root and Tuber Vegetables) ¹ | Y (N&P) | Y | Y | Bees important for seed production, typically harvested prior to bloom. Potatoes noted to be harvested after bloom | Y | N |
| 3 (Bulb Vegetables) ² | Y (N&P) | Y | Y | Typically harvest prior to bloom. | N | N |
| 5 (Brassica Leafy Vegetables) ³ | Y (N&P) | Y | Y | Requires pollination only when grown for seed; small % of acreage; harvested prior to bloom | N | N |
| 6 (Legume Vegetables) ⁴ | Y (N&P) | Y | Y | Not harvested prior to bloom | N | N |
| 15 (Cereal grains) ^{5*} | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 19 (Herbs) ⁶ | Y (N&P) | Y | Y | Not harvested prior to bloom | Y | N |
| 20 (Oilseed) ^{7,8} | Y (N&P) | Y | Y | -- | Y | N |
| Non-crop group uses (peanut) | Y (N&P) | Y | Y | -- | Y | N |

Groups where members have residue data available are indicated with *

When information was not available from USDA 2017 document, cell was indicated with a "--"

¹Labels specify sugarbeet (1A), carrot (1B), and potato (1C)

²Labels specify onions/leeks and scallions (03-07A, 03-07B)

³Labels specify broccoli (5A)

⁴Labels specify soybean (6A) and beans/peas (6)

⁵Labels specify buckwheat, triticale, wheat, barley, oats, millet, sorghum, rye, and corn (pop, sweet, field)

⁶Labels specify borage (19A) and mustard (19B)

⁷Labels specify flax, sunflower, safflower, cotton, canola, and crambe

⁸Cotton is only attractive for nectar but other members of this group are attractive for nectar and pollen.

4.4.2. Exposure Potential of Non-Agricultural Uses

Currently the USDA Pollinator Attractiveness Document does not include attractiveness to ornamental or forestry species. The Arbor Day Foundation¹ lists several trees that produce nutrient-rich pollen and nectar for foraging bee (**Table 4-10**). Furthermore, Hill and Webster (1995) discusses the potential economic benefits of combining apiculture and forestry operations as many of the commercially valuable trees produce nectar and pollen that are available during the spring, when other resources are limited. In addition to the trees in **Table 4-10**, Hill and Webster (1995) includes paulownia (*Paulownia tomentosa*), tulip-poplar (*Liriodendron tulipifera*), and persimmon (*Diospyros virginiana*). In addition,

The IR-4 has published a list of over 400 ornamental plants that are considered attractive to pollinators (primarily bees)¹⁷.

Therefore, a reasonable potential is presumed for exposure of bees to imidacloprid applications to forestry and ornamentals.

Table 4-10. Pollinator Attractiveness for Various Tree Species¹

| Species | Bee Attractive |
|--|----------------|
| Maples (<i>Acer sp.</i>) | Yes |
| Serviceberry (<i>Amelanchier sp.</i>) | Yes |
| <i>Koelreuteria sp.</i> | Yes |
| Crapemyrtle (<i>Lagerstroemia sp.</i>) | Yes |
| Black tupelo (<i>Nyssa sylvatica</i>) | Yes |
| Sourwood (<i>Oxydendrum arboreum</i>) | Yes |
| Black locust (<i>Robinia pseudoacacia</i>) | Yes |
| Linden (<i>Tilia sp.</i>) | Yes |

¹<https://www.arborday.org/trees/health/pests/article-trees-for-bees.cfm>

4.5. Screening-level Exposure Estimation

As described above in **Section 2**, the pollinator risk assessment process is a tiered approach that begins with model-generated (based on consumption rates of pollen and nectar and application rate) or default estimates of exposure and laboratory toxicity data at the individual level (Tier I). These estimates are also based on the bee's life stage (*i.e.* adult vs larvae) and the method of application (*i.e.* foliar, soil, or seed treatment applications).

In order to quantify contact exposures due to direct spray, the proposed upper bound value is 2.7 µg a.i./bee per 1 lb a.i./A, or 2.4 µg a.i./bee per 1 kg a.i./ha, based on data published by Koch and Weisser (1997). These values were derived from studies conducted on direct contact with the bee via interception of pesticide spray droplets and newly-sprayed vegetation. As with the dietary exposure, the contact exposure value can be adjusted to account for application rate.

In Tier I, pesticide exposures are estimated based on honey bee castes with known high-end consumption rates. For larvae, food consumption rates are based on 5-day old larvae, which consume the most food compared to other days of this life stage. For adults, the screening method relies upon nectar foraging bees, which consume the greatest amount of nectar of all castes while nurse bees consume the greatest amount of pollen. It is assumed that this value will be comparable to the consumption rates of adult drones (males) and will be protective for adult queens as well. Although the queen consumes more food than adult workers or drones, the queen consumes "processed" food (*i.e.*, royal jelly produced by the hypopharyngeal glands of nurse bees) that is assumed, based on currently available data, to contain orders of magnitude less pesticide than that consumed by adult workers.

¹⁷ <http://campaign.r20.constantcontact.com/render?m=1104982944285&ca=a7e26b54-c915-4491-8bd1-e2aea4ddfb1b>

Nectar is the major food source for foraging honey bees as well as nurse bees (young, in-hive females). Therefore, pesticide residues in nectar likely account for most of the exposures to bees, and may represent most of the potential risk concerns for adult bees. However, if residues in pollen are of concern, exposures to nurse bees, which consume more pollen than any other adult honey bees, should be considered. This is the case especially when pesticide concentrations in pollen are much greater than in nectar, or for crops that mainly provide pollen to bees and would be assessed on a case-by-case basis. In fact, the screening level Tier I risk estimation model for honey bees (Bee-Rex; v.1.0) allows calculation of exposure and resulting risk quotients (RQs) for all types of bee castes. As described in the 2012 White Paper (USEPA et al. 2012) presented to the FIFRA Scientific Advisory Panel and the final Guidance Document for Assessing Risk to Bees (USEPA et al. 2014), for dietary exposure from foliar applications, it is assumed that pesticide residues on tall grass (from the Kenaga nomogram of T-REX which is incorporated into Bee-REX) are a suitable surrogate for residues in pollen and nectar of flowers that are directly sprayed. The Bee-REX model is a screening level tool that is intended for use in a Tier I risk assessment to assess exposures of bees to pesticides and to calculate risk quotients. This model is individual-based and is not intended to assess exposures and effects at the colony-level (*i.e.*, for honey bees).

The Tier I exposure method is intended to account for the major routes of pesticide exposure that are relevant to bees (*i.e.*, through diet and contact). Exposure routes for bees differ based on application type. In the model, bees foraging in a field treated with a pesticide through foliar spray could potentially be exposed to the pesticide through direct spray as well as through consuming contaminated food. For honey bees foraging in fields treated with a pesticide through direct application to soil (*e.g.*, drip irrigation), through seed treatments, or through tree injection, direct spray onto bees is not expected. For these application methods, pesticide exposure through consumption of residues in nectar and pollen are expected to be the dominant routes.

Table 4-11 below (extracted from *Guidance for Assessing Pesticide Risks to Bees*, USEPA et al. 2014) summarizes the exposure estimates for contact and dietary exposures for adult and larvae resulting from foliar, soil, seed treatment and tree injection application of pesticides.

Table 4-11. Summary of contact and dietary exposure estimates for foliar applications, soil treatment, seed treatments, and tree trunk injections of pesticides for Tier I risk assessments

| Measurement Endpoint | Exposure Route | Exposure Estimate* |
|------------------------------|----------------|--|
| Foliar Applications | | |
| Individual Survival (adults) | Contact | $AR_{English}^*(2.7 \mu\text{g a.i./bee})$ $AR_{Metric}^*(2.4 \mu\text{g a.i./bee})$ |
| Individual Survival (adults) | Diet | $AR_{English}^*(110 \mu\text{g a.i./g})*(0.292 \text{ g/day})$ $AR_{Metric}^*(98 \mu\text{g a.i./g})*(0.292 \text{ g/day})$ |
| Brood size and success | Diet | $AR_{English}^*(110 \mu\text{g a.i./g})*(0.124 \text{ g/day})$ $AR_{Metric}^*(98 \mu\text{g a.i./g})*(0.124 \text{ g/day})$ |
| Soil Treatments | | |
| Individual Survival (adults) | Diet | (Briggs EEC)*(0.292 g/day) |
| Brood size and success | Diet | (Briggs EEC)*(0.124 g/day) |
| Seed Treatments | | |

| Measurement Endpoint | Exposure Route | Exposure Estimate* |
|---|----------------|--|
| Individual Survival (adults) | Diet | (1 µg a.i./g)*(0.292 g/day) |
| Brood size and success | Diet | (1 µg a.i./g)*(0.124 g/day) |
| Tree Trunk Applications⁺⁺ | | |
| Individual Survival (adults) | Diet | (µg a.i. applied to tree/g of foliage)*(0.292 g/day) |
| Brood size and success | Diet | (µg a.i. applied to tree/g of foliage)*(0.124 g/day) |

AR_{English} = application rate in lbs a.i./A; AR_{Metric} = application rate in kg a.i./ha

*Based on food consumption rates for larvae (0.124 g/day) and adult (0.292 g/day) worker bees and concentration in pollen and nectar.

⁺⁺Note that concentration estimates for tree applications are specific to the type and age of the crop to which the chemical is applied.

The consumption of nectar and pollen vary depending on the bee's life stage and caste within the hive. The consumption rates tabulated below inform the exposure estimates and resultant RQs in the default Tier I and refined Tier I analyses that are presented in **Section 6. Table 4-12** below is extracted from *Guidance for Assessing Pesticide Risks to Bees*, USEPA et al. 2014, and additional detail of the derivation of these consumption rates can be found in the White Paper (USEPA et al. 2012).

Table 4-12. Summary of estimated food consumption rates of bees.

| Life Stage | Caste (task in hive ^a) | Average age (in days) ^a | Daily consumption rate (mg/day) | | | |
|------------|--|---------------------------------------|---------------------------------|------------------------------|-------------------------|-----------|
| | | | Jelly | Nectar ^b | Pollen | Total |
| Larval | Worker | 1 | 1.9 | 0 | 0 | 1.9 |
| | | 2 | 9.4 | 0 | 0 | 9.4 |
| | | 3 | 19 | 0 | 0 | 19 |
| | | 4 | 0 | 60 ^c | 1.8 ^d | 62 |
| | | 5 | 0 | 120 ^c | 3.6 ^d | 124 |
| | Drone | 6+ | 0 | 130 | 3.6 | 134 |
| | Queen | 1 | 1.9 | 0 | 0 | 1.9 |
| | | 2 | 9.4 | 0 | 0 | 9.4 |
| | | 3 | 23 | 0 | 0 | 23 |
| | | 4+ | 141 | 0 | 0 | 141 |
| Adult | Worker (cell cleaning and capping) | 0-10 | 0 | 60 ^f | 1.3 - 12 ^{g,h} | 61 - 72 |
| | Worker (brood and queen tending, nurse bees) | 6-17 | 0 | 113 - 167 ^f | 1.3 - 12 ^{g,h} | 114 - 179 |
| | Worker (comb building, cleaning and food handling) | 11-18 | 0 | 60 ^f | 1.7 ^g | 62 |
| | Worker (foraging for pollen) | >18 | 0 | 35 - 52 ^f | 0.041 ^g | 35 - 52 |
| | Worker (foraging for nectar) | >18 | 0 | 292 (median) ^c | 0.041 ^g | 292 |
| | Worker (maintenance of hive in winter) | 0-90 | 0 | 29 ^f | 2 ^g | 31 |
| | Drone | >10 | 0 | 133 - 337 ^c | 0.0002 ^c | 133 - 337 |
| | Queen (laying 1500 eggs/day) | Entire life stage | 525 | 0 | 0 | 525 |

^aWinston (1987)

^bConsumption of honey is converted to nectar-equivalents using sugar contents of honey and nectar.

^cCalculated as described in this paper.

^dSimpson (1955) and Babendreier *et al.* (2004)

^ePollen consumption rates for drone larvae are unknown. Pollen consumption rates for worker larvae are used as a surrogate.

^fBased on sugar consumption rates of Rortais *et al.* (2005). Assumes that average sugar content of nectar is 30%.

^gCrailsheim *et al.* (1992, 1993)

^hPain and Maugenet 1966

4.6. Experimental Residue Studies

In cases where the screening-level Tier I RQs exceed the level of concern (LOC, discussed below), estimates of exposure may be refined using measured pesticide concentrations in pollen and nectar of treated crops, and further calculated for other castes of bees using their food consumption rates (see **Table 4-12**).

As discussed above in **Section 4.2**, the most conservative (highest) exposure estimates for contact and/or diet exposure routes are selected for the Tier I screening-level assessment. These exposure estimates are based on adult and larval bees with the highest food consumption rates among bees. The Bee-REX tool also calculates dietary exposure values and associated RQs for larvae of different ages, adult workers with different tasks (and associated energy requirements) and the queen. This is accomplished using the food consumption rates provided in **Table 4-12**. Those food consumption rates are based on work described in the White Paper¹⁸ and updated to reflect comments from the Scientific Advisory Panel (SAP). Exposure values for other groups of bees within a hive along with their RQs can be used to characterize risks of dietary exposures of different bees within the hive. Empirical data can be used to refine conservative exposure estimates and reduce uncertainties associated with the Tier I exposure assessment by providing direct measurements of pesticide concentrations resulting from actual use settings. Studies investigating pesticide concentrations in pollen and nectar should be designed to provide residue data for crops and application methods of concern. The available residue studies for imidacloprid for foliar, soil, and seed treatment applications from both registrant and open literature sources are summarized below. For detailed summaries of the methods and findings of each study, please see **Appendix F**.

4.6.1. *Rationale for Residue-based EEC Selection for Refined Tier I*

The Agency has a long-standing practice of deriving estimated environmental concentrations (EECs) using model-derived exposure data (USEPA, 2000). For example, acute EECs for aquatic organisms are based on the maximum peak (daily) concentration with an estimated return interval of 1-in-10 years while chronic EECs are based on the 21-d average (invertebrates) or 60-d average (fish) concentration with the same return interval. Generally speaking, these EECs are considered “high-end” estimates of exposure within the context of the available model output. Terrestrial EECs produced by the T-REX model similarly reflect high-end estimates of exposure to birds and mammals. The general rationale behind the Agency’s selection of EECs from its exposure models relates to the desire to achieve an EEC that is sufficiently protective given the temporal and spatial variability in exposure concentrations that can be expected to occur across the United States.

Unlike EEC selection from its standard exposure models, the Agency does not yet have a standard process for selecting EECs in pollen and nectar obtained from field residue studies. This partly reflects the wide diversity of residue study designs from which residue data are obtained and the relatively

¹⁸ USEPA, PMRA, CDPR (2012) White paper in support of the proposed risk assessment process for bees. United States Environmental Protection Agency, Office of Pesticide Programs, Washington DC. Pest Management Regulatory Agency, Health Canada, Ottawa. California Department of Pesticide Regulation, Sacramento, CA.

recent adoption of a quantitative risk assessment process for bees. Nonetheless, the conceptual approach used by the Agency for selecting model-based EECs appropriate to other taxa (*e.g.*, fish, birds) is used here to guide the selection of pollen and nectar EECs obtained from field residue studies. Residue studies submitted to the agency used a total toxic residue approach where parent imidacloprid and the two degradates of concern (IMI-olefin and IMI-5-OH) were measured to give a total imidacloprid residue.

In selecting the acute and chronic EECs from field residue data in pollen and nectar, the following factors were considered:

1. Field residue data typically have relatively coarse resolution with respect to capturing the temporal variability in pollen and nectar residues that would be expected to occur for a given crop in the U.S. This reflects the technical and resource constraints associated with the conduct of these studies. Specifically, pollen and nectar residue trials sample residues at discrete times following pesticide application, usually 5 or fewer sampling intervals. Often, these sampling intervals may span one or more weeks such that the pattern of residues in between the sampling events is not known. Furthermore, data are usually available for 1 or 2 growing seasons, which likely underestimates the temporal variation associated with pesticide residues in pollen and nectar over multiple growing seasons.
2. From a spatial variability perspective, field residue data for pollen and nectar generally reflect a limited number of sites in the U.S. (commonly 3 or less). Where a substantially greater number of sites have been included in pollen and nectar residue studies (*e.g.*, 10), these tend to be located in one specific region or State for practical reasons. Therefore, available field residue data sets currently available to the Agency likely underestimate the extent of spatial variation that exists in pollen and nectar residues in the U.S. per crop system.
3. From a toxicological perspective, the averaging period associated with a given EEC should reflect the time period necessary to elicit adverse effects in the toxicity studies to which it is being compared. In the case of honey bee toxicity studies, acute toxicity endpoints obtained from Tier I studies reflect a single oral or contact dose to the bee. Therefore, the EEC averaging period appropriate for comparing to acute toxicity endpoints should be relatively short (*e.g.*, 1 day). Chronic toxicity endpoints derived from Tier I toxicity studies reflect exposure durations of 10 days (adult) and 21-days (larvae). However, the actual dosing in chronic larval tests last only for 3-4 consecutive days, after which larvae undergo pupation and emergence. Based on these considerations, it seems appropriate for the chronic EEC to reflect several days at most, given that toxicological effects may be manifest from exposure periods that are shorter than the duration of a chronic test.
4. Most of the residue studies available to the Agency with imidacloprid contained multiple sample replicates for a given sampling period. Therefore, some variation due to sampling and pesticide application methods was captured in these cases.

Tier I Acute EEC. Given the limitations of residue trial data to account for temporal and spatial variability, the Agency defines the field residue acute EEC as the overall maximum residue value measured for each matrix (pollen, nectar). If replicate data are reported (*i.e.*, multiple samples on a given sampling day), then the acute EEC would be the maximum of the replicates. These field residue

acute EECs are then used to calculate the acute RQ for adult and larval bees (caste and life stage/task specific).

Tier I Chronic EEC. Given the short exposure windows of chronic adult and larval toxicity tests and relatively coarse temporal resolution associated with the field residue data, the Agency defines the field residue chronic EECs as high average residue value determined from a given sampling event (usually a daily average).

Additional characterization of RQ values derived from the aforementioned EECs will be conducted using the entire pollen and nectar data set obtained for each representative crop where the totality of the data will be compared to the Tier I endpoints to yield a set of resultant RQs. This will be expressed as a percentage of the RQs which exceed the respective LOC.

4.6.2. Rationale for Comparing Residue Data with Tier II Endpoints

According to the 2014 *Guidance for Assessing Pesticide Risks to Bees*, RQ values are not determined in evaluating risks at higher tiers. Rather, risks are evaluated qualitatively and consider multiple lines of evidence. In the case of the Tier 2 colony feeding study, consideration is given not only to the magnitude of the residue in nectar relative to the NOAEC and LOAEC, but also the duration and frequency that residues exceed these Tier 2 endpoints. Additionally, information regarding the duration that the crop remains in bloom is also factored into the Tier 2 risk characterization to characterize the potential for long-term exposure of bees to contaminated pollen and nectar. The quality and quantity of available residue data are also carefully considered at the Tier 2 level. For example, available information suggests that soil applications of imidacloprid in coarse soils results in substantially greater residues in pollen and nectar compared to fine/heavy soils. Thus, if no data are available for coarse soils for a particular soil application, this information will be considered when evaluating the uncertainty associated with the Tier 2 risk characterization.

4.6.3. Foliar Application Residue Studies – Registrant Submitted

There are five registrant submitted studies available to characterize the total residues of parent imidacloprid and the metabolites IMI-olefin and IMI-5-OH in pollen and nectar. There were no studies that were available from the open literature that examined residues on crops following foliar applications of imidacloprid. **Table 4-13** summarizes the key elements of the available registrant submitted foliar application residue studies. Further details of each residue study are provided in **Appendix F**.

Available studies on soybeans, oranges, cherries, and cotton were conducted at rates that represent 20% (cotton) – 127% (soybean) of the maximum permitted annual rate for these crops (and respective crop groups, noting that no foliar applications are permitted for other members of the oilseed group, of which cotton is a member). In the case of the foliar cotton study, an additional 4 foliar applications of 0.06 lbs a.i/A are permitted during the indeterminate bloom period, but the available study only assessed one application. Cotton represents one of the few use patterns of imidacloprid where there

are no restrictions for foliar applications associated with the bloom period given the protracted period of time over which cotton blooms.

In the study on oranges conducted in Florida in 2012-2013 (MRID 49521301), imidacloprid as the formulated product Admire® Pro SC (42.9% a.i) was applied twice at 0.25 lbs a.i/A with a reported 8 – 10 day reapplication interval and the last application prior to the 10-day pre-bloom interval, in accordance with labeled parameters and represents the highest single and annual rate on oranges and other citrus fruits. Maximum residues across all individual replicates (*i.e.* acute EEC) and the maximum average concentration among all individual sampling events (*i.e.* chronic EEC) were noted to be an order of magnitude higher in pollen as compared to nectar (acute and chronic EEC of 4,100 and 3,000 µg/L, respectively in pollen compared to 430 and 324 µg/L, respectively in nectar).

There were two studies submitted on soybeans conducted in Brazil; one in 2014 and one in 2015 (MRID 40025901 and 50025902, respectively). Two pre-flowering foliar spray applications were conducted at an interval of 12 days (BBCH 14 and 22) with Connect® 112. 5 SC (Imidacloprid + Beta-Cyfluthrin 100+ 12.5 SC) at a nominal rate of 0.089 lb a.i./A. Two applications at this rate are not in accordance with currently registered labels in the United States, which specify a maximum of 3 applications of 0.05 lb a.i./A with no bloom restrictions. Acute and chronic EECs were <LOD in the 2014 study and were similar in pollen and nectar in the 2015 study. Acute and chronic EECs in pollen were 2.5 and 1.25 µg/L, respectively and 5.2 and 2.7 µg/L, respectively in nectar.

In the cherry study (conducted in New York and Oregon in 2013 - 2014), 5 applications of Admire Pro® (42.9% a.i) at 0.1 lbs a.i/ A and a retreatment interval of 8-11 days were made post-bloom after harvest in the first year of the study and pre-harvest in the second year of the study (MRID 49535601). This scenario is in accordance with labeled parameters and represents the highest single and annual rate of foliar application on cherries and other stone fruits. Acute and chronic EECs in pollen were noted to be two orders of magnitude higher than in nectar (1000 and 545 µg/L, respectively in pollen as compared to 10 and 5.6 µg/L, respectively in nectar). It is noted that the label permits foliar applications to stone fruits only after the bloom period.

As indicated previously, the available foliar-applied cotton study represents approximately 20% of the permitted maximum annual application rate. For this study (conducted in California from 2008 – 2010, MRID 49103301) one application of imidacloprid (as Provado® 1.6 F, 17.4% a.i) of 0.06 lbs a.i/A was made during the bloom period. It was noted that previous applications of Admire® Pro (42.9% a.i) were made as soil application in 2008 and 2009 to other crops with rates ranging from 0.18 – 0.38 lbs a.i/A in the same fields as the cotton. Due to the lower annual application rate the acute and chronic EEC of 66 and 56 µg/L, respectively, are considered underestimates of the potential risk associated with foliar applications on cotton.

Table 4-13. Summary of available registrant submitted foliar application residue studies

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|-----------------------------|-----------------------------------|---|----------------------|---|---|-------------------------|--|--|
| Legumes – 6 (Soybean) | 3 tents in Brazil (2013) | Connect 112.5 SC (Imidacloprid + Beta-Cyfluthrin, 100+12.5 SC) 2 x 0.089lb a.i/A @ 12 d interval (0.18 lb a.i/A total) Foliar applied, before flowering | Nectar Pollen | <LOQ N/A | <LOQ N/A | | <ul style="list-style-type: none"> Commercial fields Sandy Loam soils Single growing season Low number of experimental replicates (3 tents) LOQ reported to be 1 ug/kg in pollen and nectar | Supplemental (MRID 50025901) |
| Legumes – 6 (Soybean) | 3 tents in Brazil (2014) | Connect 112.5 SC (Imidacloprid + Beta-Cyfluthrin, 100+12.5 SC) 2 x 0.89 lb a.i/A @ 10 d interval (0.18 lb a.i/A total) Foliar applied, before flowering | Nectar Pollen | 2.5 5.2 | 1.25 2.7 | 29 29 | <ul style="list-style-type: none"> Commercial Fields Sandy Clay soils Single growing season Low number of experimental replicates LOQ reported to be 1ug/kg in pollen and nectar | Supplemental (MRID 50025902) |
| Citrus Fruits – 10 (Orange) | 3 sites (FL) 2 years (2012, 2013) | Gaucho® 600 FL Admire® Pro SC 2 x 0.25 lbs. a.i/A @ 8-10d interval (0.5 lbs. a.i/A total) Ground applied ~10d pre-bloom | Pollen Nectar | 4,100 430 | 3,300 324 | 7, 4 4 | <ul style="list-style-type: none"> Experimental trials (sandy soils); Data are from trials NT005 and NT006 only; Nectar residues declined with time; pollen usually remained constant or declined (one trial/year); Year-to-year residue carryover uncertain LOQ and LOD for total imidacloprid residues were 1 and 0.7 µg/L in nectar, | Acceptable (NT005 & NT006 only) (Murphy et al. 2014, MRID 49521301) |

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|--|--|--|----------------------|---|---|-------------------------|---|---|
| | | | | | | | respectively, and 1 and 0.5 µg/L in pollen, respectively | |
| Stone Fruit – 12 (Cherry) | 4 sites, (NY, OR) 2 years (2013-2014) | Gaucho 600® FL Admire® Pro SC (airblast) post bloom 5 x 0.1 lbs. a.i/A @ 8-11d interval (0.5 lbs. a.i/A total) Year 1: Post harvest (fall) Year 2: Pre-harvest (summer) | Pollen Nectar | 1000 10 | 545 5.6 | 208 208, 212 | <ul style="list-style-type: none"> • Experimental trials • Sandy loam soils • NY sites 10X higher pollen residues vs. OR, • Post-harvest (fall) appl. > residues vs. Pre-harvest (summer) appl. • Year to year residue carry over is uncertain • LOQ and LOD for total imidacloprid residues were 1 and 0.7 µg/L in nectar, respectively, and 1 and 0.5 µg/L in pollen, respectively | <i>Acceptable</i> (Miller <i>et al.</i> 2014, MRID 49535601) |
| Oilseed – 20 (Cotton)⁵ | 5 sites (CA) 2-3 years (2008-2010) | <u>2010:</u> Provado® 1.6F 1 x 0.06 lbs. a.i/A during bloom (aerial) <u>2008-2009:</u> Admire® Pro: 0.18-0.38 lbs. a.i/A (chemigation to other crops) | Nectar | 66 | 56 | 6 | <ul style="list-style-type: none"> • Commercial fields; • Heavy (clay) soils; • Field portion of study was non-GLP • Only 1 sampling event post application (nectar only) • Less than max seasonal rate tested • LOQ reported to be 1 µg/L in nectar | <i>Supplemental</i> (Beedle and Harbin 2011, MRID 49103301) |

NR: Not reported; LOQ: limit of quantitation; LOD: limit of detection; DAA: Days after application

¹Refers to hand collected pollen and nectar

²Acute EEC chosen as the maximum reported concentration among all individual replicates following application, refers to parent + IMI-olefin and IMI-5-OH

³Chronic EEC chosen as the maximum average concentration among all individual sampling events following application, refers to parent + IMI-olefin and IMI-5-OH

⁴DAA = Days after the last application of the pesticide

⁵Cotton represent sole member of oilseed group with registered foliar uses.

4.6.4. Soil Application Residue Studies – Registrant Submitted

There are nine registrant-submitted studies available to characterize the total residues of parent imidacloprid and the IMI-olefin and IMI-5-OH metabolites in pollen and nectar; 8 studies are nectar and pollen field residue trials and one study was a full field study that provided residue information. **Table 4-14** summarizes the key elements of the available registrant-submitted soil application studies. Detailed methods and findings of each study are provided in **Appendix F**.

Studies on tomatoes, melons, pumpkins, citrus fruits, blueberries, strawberries, and cotton are available that represent 47% (tomatoes) – 100% (tomatoes, citrus, melons, blueberries, strawberries, and cotton) of the maximum permitted annual rate for these crops (and associated groups).

There are two studies available for tomato with one study (California, 2009 – 2010; MRID 49090503) testing 47 – 66% of the maximum annual rate permitted for tomatoes and other fruiting vegetables while a more recent study (California, 2013 – 2014; MRID 49090503) assessed the highest annual rate of 0.38 lbs a.i/A. Both studies tested the formulated product Admire® Pro (42.9% a.i) and applications ranged from being made at transplant to 25 days after transplant, depending on the trial. Both studies employed a drip irrigation method of soil application. It is noted that tomato does not produce nectar, and therefore only pollen data is available. In the case of the more recent study testing the higher application rate, the residues in pollen collected by bumble bees was assessed. The higher acute and chronic EECs resulted, as expected from the more recent study and were 242 and 198 µg a.i/L (parts per billion; µg/L), respectively.

In the available melon study (California, 2008 – 2011; MRID 49090501), cantaloupe and unidentified varieties of melons were treated with Admire® Pro (42.9% a.i), Alias® (40.6% a.i), and an unidentified formulation of imidacloprid at application rates ranging from 0.23 – 0.38 lbs a.i/A, representing 60 – 100% of the maximum annual rate permitted for melons and other cucurbit vegetables. Applications were made via soil drip or seed line drench at transplant depending on the trial. Bee-collected (trapped) pollen and hive (comb) nectar were sampled as opposed to hand-collected nectar and pollen directly from the melon flowers. Acute and chronic EECs in trapped pollen were 32 and 19 µg/L, respectively, and 8 and 4.9 µg/L in hive nectar, respectively.

In the study with watermelon (Brazil 2014; MRID 50357101), plants were treated with one drench treatment of Evidence® 700 WG at a nominal rate of 0.187 lb a.i./A which represents 50% of the maximum labelled annual rate of soil applications to cucurbit vegetables that is permitted in the United States. Bee-collected (trapped) pollen and bee-collected nectar were sampled as opposed to hand-collected nectar and pollen, directly from the watermelon flowers. At some sampling time points there were a limited number of samples leading to limited ability to determine residue averages. Acute and chronic EECs in trapped pollen were both 53 µg/L, and 11 and 8.9 µg/L in hive nectar, respectively.

In a Tier III full field study on pumpkins (South Dakota (2015-2016; MRID 50263061) imidacloprid as Admire® Pro Systemic Protectant was applied as sub-surface side dress at 0.38 lb/acre once pumpkins had attained the six true leaf stage. As part of this study, residue data was collected in nectar and pollen from pumpkin flowers. Acute and chronic EECs in flower nectar was 5.1 and 2.7 µg/L, respectively, and

14.5 and 7.1 µg/L in flower pollen, respectively. It was noted from this study that the soils used were predominately heavy (*i.e.* clay) soils which may limit the uptake of imidacloprid relative to coarser soil types.

In a soil-applied citrus study (California, 2009 – 2011; MRIDs 49090504 and 49090505), orange, tangerine, and grapefruit orchards were treated in multiple trials at application rates ranging from 0.25 – 0.50 lbs a.i/A which represent 50 – 100% of the maximum labelled annual rate of soil application to citrus fruits. The trials were conducted either in tunnels or open fields, all with Admire® Pro (42.9% a.i.). Only one field trial assessed the residues in pollen, which was the sole trial in the study that assessed the lower 0.25 lbs a.i/A. Maximum residues in nectar from individual replicates (*i.e.* acute EECs) were similar (29.1 – 35.5 µg/L) across the three trials that tested the highest maximum annual rate of 0.5 lbs a.i/A. In the trial that tested the half rate of 0.25 lbs a.i/A, maximum residues were approximately 50% reduced, at 18.3 µg/L. The magnitude of residues in pollen from this study are uncertain given the trials with the higher application rate did not sample residues in pollen.

For the blueberry study (New York, Illinois, Michigan, 2012 – 2013; MRID 49535602), one application of Admire® Pro 600 SC (42.9% a.i.) at 0.5 lbs a.i/A (representing the highest permitted soil-applied rate for blueberries and other bushberries) was made 3 days post-harvest. Honey bee hive nectar and bee-collected (*Apis* and *Bombus*) pollen were assessed with acute and chronic EECs of 16 and 8.8 µg/L, respectively in hive nectar and 42 and 16.5 µg/L, respectively in bee-collected pollen (*i.e.* honey bee and bumble bees that were within a flight cage during the course of the nectar and pollen collection period.). The highest concentrations were noted to have been determined in coarser soils.

In the strawberry study (California, 2010 – 2011; MRID 49090502), although the highest application rate of 0.5 lbs a.i/A to strawberries was made (Admire® Pro [42.9% a.i.] or Alias® 4F [40.6% a.i.]), its timing in relation to bloom as well as the interval between application and sampling of residues is unknown. Labels prohibit soil applications to strawberries prior to bud opening, during bloom, or when bees are foraging. Additionally, this study did not investigate the residue levels in nectar, which is considered to be attractive to honey bees (USDA 2014). The acute and chronic EECs in pollen were 320 and 280 µg/L, respectively, and due to the absence of residue data for nectar, the exposure to residues in pollen alone is considered to be an underestimation of the potential exposure to imidacloprid for foraging honey bees.

Finally, in the cotton study (California, 2013 – 2014, MRID 49665202), a single soil application of Admire® Pro SC (42.9% a.i.) application was made at planting at the maximum single and annual application rate for cotton at 0.33 lbs a.i/A. Residues in pollen, nectar, and extra-floral nectar were assessed, with the maximum nectar residue samples being roughly 3 - 3.5 fold higher than those in pollen or the extra-floral nectar (acute EEC of 127, 43.4 and 35.9 µg/L in floral nectar, pollen and extra-floral nectar, respectively).

Table 4-14. Summary of available registrant submitted soil application residue studies

| Crop Group (Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² ($\mu\text{g}/\text{L}$) | Residue-based Chronic EEC ³ ($\mu\text{g}/\text{L}$) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|---|---|--|----------------------------------|--|--|----------------------------|---|---|
| Fruiting Vegetable – 8 (Tomato) | 9 Sites Kings & Kern Co, CA 2 years (2009-2010) | Admire® Pro <u>3 sites: 1 x 0.18 lbs.</u> <u>a.i/A per year, 2-25d</u> post transplant (drip chemigation) <u>6 sites: 2 x 0.13 lbs.</u> <u>a.i/A per year; at/near</u> transplant & during bloom (drip chemigation) | Pollen (including anthers) | 54 | 46 | 100 | <ul style="list-style-type: none"> Commercial fields; heavy and medium soils Residues from 2 composites from a single sampling time in 2010 Tested rates reflect 47-66% of maximum single application rate Field sampling not GLP | <i>Supplemental</i> (Freeseman and Harbin, 2011; MRID 49090503) |
| Fruiting Vegetables – 8 (Tomato) | 9 sites CA 2 years (2013-2014) | Admire® Pro Systemic Protectant SC 0.38 lbs. a.i/A @ 7d post- transplant (soil drip/ drench) | Pollen (b) | 242 | 198 | 36-38 | <ul style="list-style-type: none"> Experimental fields; fine, medium, and coarse soils Year 2 ongoing for 5 sites 1-2 replicates from bumble bee-collected pollen Most residue data reflect coarse soils Limited data indicates no year-to-year carry over (leaves) LOQ and LOD for total imidacloprid residues were 1 and 0.7 $\mu\text{g}/\text{L}$ in nectar, respectively, and 1 and 0.5 $\mu\text{g}/\text{L}$ in pollen, respectively | <i>Acceptable</i> (Gould and Jerkins, 2015, MRID 49665201) |

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² ($\mu\text{g}/\text{L}$) | Residue-based Chronic EEC ³ ($\mu\text{g}/\text{L}$) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|--|--|--|--|---|---|-------------------------|--|--|
| Cucurbit Vegetable - 9 (Cantaloupe & unknown melons) | 10 sites CA 2-4 years (2008-2011) | Admire® Pro, Alias®, and unknown formulation 0.23-0.38 lbs. a.i./A per yr. soil drip or seed line drench at transplant (2011) | Pollen (t) Nectar (h) | 32 8 | 19 4.9 | Approx. 90-120 | <ul style="list-style-type: none"> Commercial fields; heavy & Medium soils LOQ in nectar and pollen were 1 and 10 $\mu\text{g}/\text{L}$, respectively | <i>Supplemental</i> (Beedle 2012 MRID 49090501) |
| Cucurbit Vegetable - 9 (Watermelon) | 3 tunnels, Brazil, 2014 | Evidence® 700 WG 1 x 0.187 lbs a.i./A Soil drench 2 days after transplanting (Dec 14, 2013) | Nectar (b) Pollen (h) Pollen (t) | 10.9 1.4 53.1 | 10.9 0.7 41.3 | 7 1 7 | <ul style="list-style-type: none"> 3 tunnels with 1 hive/tunnel Only one test site Problems obtaining in hive pollen and nectar | <i>Supplemental</i> (Bocksch 2015 MRID 50357101) |
| Cucurbit Vegetable - 9 (Pumpkin) | Tier III study, 6 sites (2015) | Admire® Pro Systemic 1 x 0.38 lb a.i./A Sub-surface side dress one month after planting | Nectar Pollen | 5.1 15.8 | 2.7 7.1 | 23-76 | <ul style="list-style-type: none"> Large test fields Heavy (clay) soil type in each field Low exposure to pumpkin pollen as indicated by pollen grain analysis | <i>Supplemental</i> (MRID 50263061) |

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² ($\mu\text{g}/\text{L}$) | Residue-based Chronic EEC ³ ($\mu\text{g}/\text{L}$) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|---------------------------------|---|--|--|---|---|-------------------------|--|--|
| Citrus – 10 (Orange) | 3 Tunnels Exeter, CA 1 year | Admire® Pro 1 x 0.5 lbs. a.i/A; post bloom via soil drench (Sept 3, 2009) | Nectar Nectar (b) Nectar (h) | 34.6 37.1 95.2 | 21.2 17.5 72.8 | ~230 (4/22/10) | <ul style="list-style-type: none"> 3 trees/tunnel; 1 hive/tunnel Loam soil, weekly irrigation Higher conc. in hive nectar may be partly due to water loss | <i>Supplemental</i> (Byrne et al. 2011, MRID 49090504; Fischer and Bowers, 2012, MRID 49090505) |
| Citrus – 10 (Orange, Tangerine) | Multiple Open fields, CA (1-2 mi radius around hives) 1 year (2009-2010) | Various formulations (unspecified); 1 x 0.25 lbs. a.i/A @ post bloom (Fall 2009) Presumed soil drench | Nectar Nectar (b) Nectar (h) Pollen (t) | 18.3 16.0 15.5 10.2 | 9.4 7.6 11.6 9.4 | ~230 (April 2010) | <ul style="list-style-type: none"> Commercial citrus fields Loamy soil Small # of pollen samples could be collected Half of maximum single application rate | <i>Supplemental</i> (Byrne et al. 2011, MRID 49090504; Fischer and Bowers 2012, MRID 49090505) |
| Citrus – 10 (Orange) | 2 sites Open fields Lindcove Research and Extension Center (LREC) and Bakersfield, CA | Admire® Pro 1 x 0.5 lbs. a.i/A @ post-bloom via soil drench (Sept 3 & 8, 2009) | Nectar | 29.1 | 19.3 | Spring 2010 | <ul style="list-style-type: none"> 3.9 ac commercial field and LREC site (size unspecified) 2X (1 lbs. a.i/A) also tested. Loamy soil Residues scaled with application rate | <i>Supplemental</i> (Byrne et al. 2011, MRID 49090504; Fischer and Bowers 2012, MRID 49090505) |
| Citrus – 10 (Grapefruit) | Multiple fields: Helmet, Temecula, LREC, CA | Admire® Pro 1 x 0.5 lbs. a.i/A per yr. <u>Helmet & LREC = post-bloom appl.</u> (2 years; Fall '08/09) <u>Temecula = summer '08 & spring '09</u> | Nectar | 35.5 | 23.8 | Spring 2010 | <ul style="list-style-type: none"> Study designed to evaluate carry over (1 x 1X rate shown here) <u>Helmet</u> = commercial orchard, sandy loam soil, weekly irrigation | <i>Supplemental</i> (Byrne et al. 2011, MRID 49090504; Fischer and |

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² ($\mu\text{g}/\text{L}$) | Residue-based Chronic EEC ³ ($\mu\text{g}/\text{L}$) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|---------------------------|--|---|--------------------------|---|---|-------------------------|---|---|
| | | Presumed soil drench | | | | | <ul style="list-style-type: none"> <u>Temecula</u> = 6 commercial fields (soil type not specified) <u>LREC</u> = 5 citrus blocks, loamy soil Residues generally reflect most recent appl. | Bowers 2012, MRID 49090505) |
| Berries – 13 (Blueberry) | 3 sites NY, IL, MI 2 years (2012, 2013) | Gaucho® 600 FL Admire® Pro 600 SC 1 x 0.5 lbs. a.i/A 3-d post-harvest (Fall) Banded soil appl. | Pollen (b) Nectar (h) | 42 | 16.5 | 240 233 | <ul style="list-style-type: none"> Experimental fields, irrigated Sandy, silt loam, loam soils; Highest conc. in sandy soils Residues steady/ increase during sampling No obvious year-to-year carryover LOQ and LOD for total imidacloprid residues were 1 and 0.7 $\mu\text{g}/\text{L}$ in nectar, respectively, and 1 and 0.5 $\mu\text{g}/\text{L}$ in pollen, respectively | Acceptable (Gould et al. 2014; MRID 49535602) |
| Berries – 13 (Strawberry) | 7 sites, CA 2 years (2010, 2011) | Alias® 4F, Admire® Pro, or unknown formulation 1 x 0.5 lbs. a.i/A in 2010 & 2011 Presumed soil appl. Bloom timing unknown | Pollen | 320 | 280 | Not known | <ul style="list-style-type: none"> Commercial fields, light (sand) and medium (loam) soils; Field portion non-GLP; application method and timing unknown Residues from sandy soils higher than loam (<LOD) LOD and LOQ in pollen were 2.6 and 10 $\mu\text{g}/\text{L}$, respectively | Supplemental Gould et al 2012 MRID 49090502 |

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|------------------------------------|---|--|---|---|---|-------------------------|---|---|
| Oilseed – 20 (Cotton) ⁵ | 9 sites CA 2 years (2013-2014) | Admire® Pro SC 0.33 lbs. a.i/A per yr. @ plant In furrow spray | Pollen Nectar Exfl. Nectar | 43.4 | 41.1 | 78 | <ul style="list-style-type: none"> • 2 fine, 1 medium and 6 coarse soils • 3 trials = 1 yr. only; 6 trials = 2 yr. • No indication of carryover • LOQ and LOD for total imidacloprid residues were 1 and 0.7 µg/L in nectar, respectively, and 1 and 0.5 µg/L in pollen, respectively | <i>Acceptable</i> (Fischer and Jerkins, 2015; MRID 49665202). |

NR: Not reported; LOQ: limit of quantitation; LOD: limit of detection; DAA: Days after application

¹Refers to hand collected pollen and nectar unless otherwise specified: "h" (hive collected), "b" (bee collected), or "t" (trapped pollen),

² Acute EEC chosen as the maximum reported concentration among all individual replicates following application, refers to parent + IMI-olefin and IMI-5-OH

³ Chronic EEC chosen as the maximum average concentration among all individual sampling events following application, refers to parent + IMI-olefin and IMI-5-OH

⁴ DAA = Days after the last application of the pesticide

⁵Cotton represents sole member of oilseed group with registered soil uses.

4.6.5. Soil Application Residue Studies – Open Literature

Additionally, there were 3 studies available from the open literature that investigated the residues of imidacloprid in pollen and nectar following soil applications (*i.e.*, 2 studies on cucurbit vegetables and 1 study on the carryover of imidacloprid residues from soil applications to potatoes). These studies generally reported the range of residues determined as well as an average. **Table 4-15** summarizes the key elements from each of the studies. Summaries of each study including methods and results are provided in **Appendix B**.

In a study that assessed the residues of imidacloprid in clover (Rogers and Kemp, 2003 MRID 49719626), soil applications to potatoes were made in one year, followed by underseeded grain in the following year (treated with imidacloprid), and finally clover in the following year (not treated with imidacloprid). Applications to potatoes and underseeded grain were 0.18 lbs a.i/A for each of potatoes and underseeded grain. Residues in clover pollen and nectar were determined to be below the LOQ (2 µg/L) although were noted to be as high as 32 µg/L in soil (underseeded grain fields).

In one study assessing residues in pollen and nectar from squash (Stoner and Eitzer, 2012; MRID 49719616), applications of Admire® Pro (42.9% a.i.) were made at 0.32 lbs a.i/A (slightly lower than the maximum single application rate of 0.38 lbs a.i/A) in two consecutive years, with one year having application at one day pre-plant and the other year at 5-days post-transplant in a green house. The pollen and nectar residues from both trials were pooled which resulted in residues as high as 28 µg/L in pollen and 14 µg/L in nectar. As these data were pooled, the potential differences in year-to-year results as well as the potential effect of differing applications regimens on the magnitude of residues could not be ascertained.

In another residue study with pumpkins (Dively and Kamel, 2012; MRID 49719612), various treatment regimens of imidacloprid were tested with applications rates ranging from 0.027 to 0.38 lbs a.i/A (representing 7 – 100% of the maximum annual application rate for soil application to cucurbit vegetables). The lowest residues (6.7 µg/L in pollen and 0.5 µg/L in nectar) resulted from the bedding drench method at 0.027 lbs a.i/A while the highest (101 µg/L in pollen and 13.7 µg/L in nectar) were associated with a split application of 0.19 lbs a.i/A as a transplant water treatment followed by 0.19 lbs a.i/A as a drip irrigation treatment. In a subsequent trial the following year, the maximum residues in pollen and nectar (associated with the split application method described above) were 44 and 16 µg/L, respectively.

Table 4-15. Summary of the soil application residue studies evaluated from the open literature

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Max Value ($\mu\text{g/L}$) ² | Average Value ($\mu\text{g/L}$) ³ | DAA (days) | Study Notes | Classification (Reference) |
|--|---|--|--|--|--|---|--|--|
| Root & Tuber Vegetables – 1 (Potato), Cereal Grains – 15 (unspecified), Non-grass animal feed – 19 (Clover) | 23 sites (18 in Prince Edward Island; 5 in New Brunswick) 3 years (1999-2001) | Admire® Pro 240F 0.18 lbs a.i/A , 1999 (Year 3 – clover), 2000 (Year 2 – under seeded grain), 2001 (Year 1 – potato) (All applications made in Spring) | Pollen (b) – clover only Nectar (b) – clover only | <LOQ <LOQ | NR NR | NR NR | <ul style="list-style-type: none"> • Study examined carryover of residues primarily in soil over the course of three years and different crops. • Pollen and nectar measurements only in clover. • LOD: NR; LOQ: 2 $\mu\text{g/L}$ | <i>Qualitative</i> (Rogers and Kemp, 2003 MRID 49719626) |
| Cucurbit Vegetable – 9 (Squash) | 2 sites, Connecticut, 2 trial years (2009/2010) | Admire® Pro, 0.32 lbs a.i/A @ 1 d pre-plant (soil spray) Admire® Pro, 0.32 lbs a.i/A @ 5 d post-transplant in greenhouse (drip irrigation) | Pollen Nectar | 28 14 | 14 10 | Variable Variable | <ul style="list-style-type: none"> • Residue values pooled across appl. methods (effect of appl. method unknown) • Pollen and nectar samples obtained at varying times depending on the treatment regimen and trial year, • LOD: 0.5 – 2 $\mu\text{g/L}$ depending on the matrix (no further information provided), LOQ: NR | <i>Qualitative</i> (Stoner and Eitzer, 2012 MRID 49719616) |
| Cucurbit Vegetable – 9 (Pumpkin) | 1 site, NC, 2 trial years (2009, 2010) | Admire® Pro, 0.027 lbs a.i/A bedding drench (2009) Admire® Pro, 0.25 lbs a.i/A , transplant water treatment (2009) Admire® Pro, 0.38 lbs a.i/A , transplant water treatment, (2009) | Pollen Nectar Pollen Nectar Pollen Nectar Pollen | 6.7 0.5 40.1 7.3 86.6 11.9 101 | 4.9 0.4 36.7 5.7 60.9 7.4 80.2 | NR NR 42-45 42-45 42-45 42-45 42-45 | <ul style="list-style-type: none"> • Soil characteristics not provided • The metabolites IMI-olefin, IMI-5-OH, desnitro-imidacloprid, urea metabolite, and 6-CNA were 14-31% of the values of parent (based on means) in pollen and 25 – 57% in nectar (breakdown of metabolite not provided) | <i>Qualitative</i> (Dively and Kamel, 2012 MRID 49719612) |

| Crop Group (Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Max Value (µg/L) ² | Average Value (µg/L) ³ | DAA (days) | Study Notes | Classification (Reference) |
|----------------------|-------------------------------------|--|---------------------|-------------------------------------|---|----------------|--|-------------------------------|
| | | Admire Pro, 0.19 lbs a.i/A x 2 , transplant water / drip irrigation (2009) | Nectar | 13.7 | 11.2 | 42-45 | • LOD and LOQ of 0.2 and 0.66, respectively | |
| | | Admire® Pro, 0.027 lbs a.i/A , bedding drench (2010) | Pollen Nectar | <LOD <LOD | <LOD <LOD | NR NR | • Soil characteristics not provided • Weather/more frequent irrigation in 2010 may contribute to lower residues in 2010 vs. 2009. | |
| | | Admire® Pro, 0.25 lbs a.i/A , transplant water treatment, (2010) | Pollen Nectar | 23.9 6.7 | 18.2 6.1 | 42-45 42-45 | • The metabolites IMI-olefin, IMI-5-OH, desnitro-imidacloprid, urea metabolite, and 6-CNA were not detected in nectar and pollen | |
| | | Admire® Pro, 0.19 lbs a.i/A x 2 , transplant water / drip irrigation (2010) | Pollen Nectar | 44.0 16.0 | 31.8 9.1 | 42-45 42-45 | • LOD and LOQ of 0.2 and 0.66, respectively | |

NR: Not reported; LOQ: limit of quantitation; LOD: limit of detection

¹Unless delineated as "h" (hive collected), "b" (bee collected), or "t" (trapped pollen), nectar and pollen refer to hand collected pollen and nectar

²If study provided a low to high range of residues, the high end value is reported here

³Value reflect the reported mean value of all residues within the provided scenario. Studies generally did not provide information on the numbers of sampling intervals from which the average was derived and therefore it is assumed to be one sampling period unless otherwise noted.

4.6.6. Seed Treatment Application Residue Studies – Registrant Submitted

Three registrant-submitted studies are available to characterize the total residues of parent imidacloprid and the metabolites IMI-olefin and IMI-5-OH in nectar and pollen in seed treated soybean and in pollen in seed-treated corn followed by a subsequent planting of clover as a rotational crop to examine the uptake of imidacloprid from soil. Additionally, there are several other registrant-submitted studies that were either a semi-field tunnel or full-field study design that had a residue component in addition to characterizing the effects of imidacloprid on honey bee colonies. While these studies will not be individually discussed, it is noted here that they generally reported no residues in pollen and nectar (hand collected from plant, bee-collected, and hive sources) above the LOD or LOQ, which depending on the study, ranged from 1.5 to 10 µg/L (inclusive of LOD and LOQ). Due to several deficiencies associated with each study (which are summarized in **Appendix A**), these studies are designated as supplemental from an exposure (*i.e.* residue information) standpoint and invalid with respect to effects. **Table 4-16** summarizes the key elements of the available registrant-submitted seed-treatment residue information.

In the available seed-treatment soybean study (Brazil, 2014 and 2015; MRID 50025901 and 50025902), imidacloprid (as Gaucho® FS) was applied at a rate of 120 g imidacloprid ai/100 kg seeds were planted with a target sowing rate of 90 kg seeds/ha which is the highest labeled equivalent application rate for seed-treated corn. Nectar was collected from both bees and comb matrices while pollen was only collected from the comb. Acute and chronic EECs for pollen were 4.2 and 2.5 µg/L, respectively and for bee-collected nectar 1.5 and <LOQ, respectively. For nectar collected from the comb imidacloprid was not detected above LOD at any sampling time.

In the available seed-treatment corn study (conducted in Kansas and Nebraska, 2012-2013; MRID 49511701), imidacloprid (as Gaucho® 600 ST) was applied at a rate of 1.34 mg a.i./seed (equivalent to 0.12 lbs a.i./A) which is the highest labeled equivalent application rate for seed-treated corn). Residues were only available in pollen as corn does not produce nectar. Acute and chronic EECs for pollen were 39.7 and 22.3 µg/L, respectively. Notably, while the average and maximum residues values were similar in two of the three trials (*i.e.* sites), residues were generally higher in the third trial. The percent sand in soils from the third trial (36%) is about 2X (16%) and 30% greater (28%) from that of the other two trials, respectively suggesting that the higher imidacloprid residues in pollen for this trial may be the result of its greater fraction of sand in soil.

Additionally, this study planted clover as a rotational crop to investigate the residues in pollen and nectar following seed treatment applications to corn the previous year. The majority of samples were below the LOD; however, in samples with detectable levels, the maximum measured residues in pollen and nectar were 3.8 and 1.3 µg/L, respectively. A more detailed description of the methods and results of this study can be found in **Appendix F**.

Table 4-16. Summary of the registrant submitted seed treatment application residue studies

| Crop Group Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA (days) | Study Notes | Classification (Reference) |
|--------------------------------------|---|---|----------------------|---|--|---------------------|---|---|
| Legume – 6 (Soybean) | 3 tents in Brazil (2013) | Gaucho® FS (Imidacloprid 600 FS) 120 g ai/100 kg seeds sowing rate of 90 kg seeds/ha Seeds sown 12/06/2013 | Nectar Pollen | 1.5 4.15 | <LOQ 2.53 | 67 61/62 | <ul style="list-style-type: none"> Commercial fields Sandy Loam soils Single growing season Limited number of experimental replicates LOQ reported to be 1ug/kg in pollen and nectar | Supplemental (MRID 50025901) |
| Legume – 6 (Soybean) | 3 tents in Brazil (2014) | Gaucho® FS (Imidacloprid 600 FS) 120 g ai/100 kg seeds sowing rate of 90 kg seeds/ha Seeds sown 12/06/2014 | Nectar Pollen | <LOQ 3.10 | <LOQ 2.07 | 66 | <ul style="list-style-type: none"> Commercial Fields Sandy Clay soils Single growing season Limited number of experimental replicates LOQ reported to be 1ug/kg in pollen and nectar | Supplemental (MRID 50025902) |
| Cereal Grain – 15 (Corn/Maize) | 3 sites, KS, NE 2 years (2012, 2013) | Gaucho 600 ST 1.34 mg a.i./seed (0.12 lbs. a.i/A) | Pollen | 39.7 | 22.3 | 84 | <ul style="list-style-type: none"> Experimental fields Loam, silty loam, silty clay soils Residues increase during sampling time LOD and LOQ in pollen were 0.5 and 1 µg/L, respectively | Acceptable (Miller et al. 2014, MRID 49511701) |
| Rotational Crop (Clover) | 3 sites KS, NE (2013) | White clover planted on fields with prior year planting of seed-treated corn @ 1.34 mg a.i./seed | Pollen Nectar | 3.8 1.3 | 2.3 1.1 | 461, 456 401 | <ul style="list-style-type: none"> Vast majority of residues were < LOD Residues at 1 µg/L reflect assumptions of | |

| Crop Group Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue- based Acute EEC ² (µg/L) | Residue- based Chronic EEC ³ (µg/L) | DAA (days) | Study Notes | Classification (Reference) |
|--------------------------------------|--|--|---------------------|---|--|---------------------------|--|--|
| | | | | | | | ½ the LOD for non-detects. | |
| Cereal Grain - 15 (Corn/Maize) | 1 site, (tunnel) Germany 1 year | Gaucho 70 WS, 1 mg a.i./seed , seeds sown on 5/10/2000 | Pollen | <LOQ | NR | 70-77 | <ul style="list-style-type: none"> Semi-field tunnel study Pollen from seed treated corn fed to bees for 38 day exposure No soil information LOD: NR, LOQ: 5 µg/L | <i>Supplemental (exposure only)</i> (Maus et al. 2000, MRID 47699416) |
| Cereal Grain - 15 (Corn/Maize) | 1 site, (tunnel) Germany 1 year | Imidacloprid FS 600, 1 mg a.i./seed , seeds sown 11/23/2000 (in Brazil) | Pollen | <LOQ | NR | 63 | <ul style="list-style-type: none"> Semi-field tunnel study Pollen from seed treated corn fed to bees for 45 day exposure Soil characterized as: 3.1% coarse sand, 7.3% fine sand, 37.6% clay, 51.9% silt) LOD: NR, LOQ: 5 µg/L | <i>Supplemental (exposure only)</i> (Maus et al. 2002, MRID 47699414) |
| Oilseed – 20 (Sunflower) | 1 site, Germany 1 year (1998) | Gaucho 70 WS, 0.7 mg a.i./seed (0.05 lbs a.i./A) seeds sown on 5/8/1998 | Nectar (b) | <LOQ | NR | 14 (exposure duration) | <ul style="list-style-type: none"> Full field study, % foraging on treated crop not quantified Control field had sandy, gravelly soil (no data on treatment field soil) LOD: NR, High LOQ: (10 µg/L) | <i>Supplemental (exposure only)</i> (Schmidt et al. 1998 – MRID 49766206) |

| Crop Group Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA (days) | Study Notes | Classification (Reference) |
|--|---|---|--|---|--|--|--|---|
| Oilseed – 20 (Rapeseed/ canola) | 4 sites, (tunnels) Germany 1 year (1999) | Poncho FS 500 (formulated with beta-cyfluthrin) 0.03 lbs a.i./A seeds sown 5/12/1999 | Nectar (h) Nectar Pollen (b) Pollen | <LOD <LOD <LOD <LOD | NR NR NR NR | 10 54 - 59 10 54 - 59 | <ul style="list-style-type: none">• Semi field tunnel study• Silty clay soil type• Sites had various prior regimens of imidacloprid use• LOD: 1.5 µg/L, LOQ: 5 µg/L | <i>Supplemental (exposure only)</i> (Schmuck, Schöning, Schramel 1999, MRID 47699417) |
| Oilseed – 20 (Sunflower) | 4 sites, (tunnels) Germany 1 year (1999) | Gaucho WS 70 0.05 lbs a.i./A seeds sown 5/12/1999 | Pollen Pollen (h) Nectar (h) | <LOD <LOD <LOD | NR NR NR | NR 10 NR | | |
| Cereal Grain - 15 (Corn/Maize) | 4 sites (tunnels) Germany 1 year (1999) | Gaucho WS 70 0.08 lbs a.i./A seeds sown 5/12/1999 | Pollen | <LOD | NR | NR | | |
| Oilseed – 20 (Rapeseed/ canola) | 4 sites (tunnels) Germany 1 year (1999) | Poncho FS 500 (formulated with beta-cyfluthrin) 0.06 lbs a.i./A seeds sown 05/11/1999 | Nectar Pollen (b) Pollen Pollen (h) | <LOD <LOD <LOD <LOD | NR NR NR NR | NR 10 59 – 69 10 | <ul style="list-style-type: none">• Semi field tunnel study loamy silt soil type• Sites had various prior regimens of imidacloprid use• LOD: 1.5 µg/L, LOQ: 5 µg/L | <i>Supplemental (exposure only)</i> (Schmuck, Schöning, Schramel 1999, MRID 47699422, 47699425, 47699423) |
| Oilseed – 20 (Sunflower) | 4 sites (tunnels) Germany 1 year (1999) | Gaucho® WS 70 0.04 lbs a.i./A Seeds sown 5/10/1999 | Pollen (h) Nectar (h) Pollen | <LOD <LOD <LOD | NR NR NR | 4 2-8 NR | | |
| Cereal Grain - 15 (Corn/Maize) | 4 sites (tunnels) Germany 1 year (1999) | Gaucho® WS 70 0.08 lbs a.i./A Seeds sown 05/09/1999 | Pollen | <LOD | NR | NR | | |

| Crop Group Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA (days) | Study Notes | Classification (Reference) |
|---------------------------------------|--|---|--|---|--|------------------------------|---|--|
| Oilseed – 20 (Rapeseed/ canola) | 1 site (tunnel) Sweden (1999) | Poncho® FS 500 (formulated with beta cyfluthrin) 0.05 lbs a.i./A (Planting date not specified, exposure period July 2-6) | Nectar (b) Nectar | <LOQ <LOQ | NR NR | 4 NR | <ul style="list-style-type: none"> Semi-field tunnel study LOD: NR, High LOQ: (10 µg/L) | Supplemental (exposure only) (Schmuck, Schöning, 1999, MRID 47699418) |
| Oilseed – 20 (Rapeseed/ canola) | 2 sites, Ontario, Canada, and Minnesota, USA (2000) | Gaucho® + Vitavax (carboxin and thiram), 6-7 lbs product/A (Ontario), planting time not reported Gaucho + Vitavax (carboxin and thiram), 4.5 lbs product/A (Ontario), planting time not reported | Nectar (b) Pollen (b) Nectar (b) Pollen (b) | <LOQ <LOQ 0.81 7.6 | NR NR NR NR | 8 8 8 8 | <ul style="list-style-type: none"> Full field study, Ontario Loam soil (Ontario), no soil information for MN component Vitavax (carboxin and thiram) + Lindane was used as negative control % foraging on crop not quantified LOD: 0.3 µg/L, LOQ: 1 µg/L | Supplemental (exposure only) (Scott-Dupree et al, 2001 – MRID 45422435) |
| Oilseed – 20 (Rapeseed/ canola) | 1 site, Germany (1999) | Imidacloprid + beta cyfluthrin FS 0.03 lbs a.i./A Seeds sown 08/23/1999 | Nectar | <LOD | NR | NR | <ul style="list-style-type: none"> Full field study Soil type not reported % foraging on crop not quantified LOD: 1.5 µg/L, LOQ: 5 µg/L | Supplemental (exposure only) (Schuld, 2002 MRID 49073605) |
| Oilseed – 20 (Rapeseed/ canola) | 1 site France (1998) | Poncho® (formulation with beta-cyfluthrin) 0.05 lbs a.i./A Seeds sown 03/19/1998 | Nectar (b) Nectar | <LOQ <LOQ | NR NR | NR NR | <ul style="list-style-type: none"> Semi field tunnel study LOD: NR; LOQ: (10 µg/L) | Supplemental (exposure only) (Schmuck, Schöning, 1999) |

| Crop Group Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue- based Acute EEC ² (µg/L) | Residue- based Chronic EEC ³ (µg/L) | DAA (days) | Study Notes | Classification (Reference) |
|---------------------|-------------------------------------|--|---------------------|---|--|---------------|-------------|-------------------------------|
| | | | | | | | | MRID 47699419) |

NR: Not reported; LOQ: limit of quantitation; LOD: limit of detection

¹Unless delineated as "h" (hive collected), "b" (bee collected), or "t" (trapped pollen), nectar and pollen refer to hand collected pollen and nectar

²Acute EEC chosen as the maximum reported concentration among all individual replicates following application, refers to parent + IMI-olefin and IMI-5-OH (applies only to Miller *et al.* 2014, MRID 49511701).

³Chronic EEC chosen as the maximum average concentration among all individual sampling events following application refers to parent + IMI-olefin and IMI-5-OH (Miller *et al.* 2014, MRID 49511701)

4.6.7. Combined Application Method Residue Studies

There are five registrant-submitted studies available to characterize the total residues of parent imidacloprid, IMI-olefin, and IMI-5-OH in pollen and nectar following applications made via two different methods (*i.e.* a combination of two applications via seed treatment, soil, or foliar methods).

Additionally, there is residue information provided from a full field study which simulated a soil + foliar application regimen. It is noted that labels stipulate maximum annual rate of 0.5 lbs a.i/A for several use patterns and allow for a combination of methods to get to that maximum rate. Two studies in tomato and cotton examine a soil application followed by multiple foliar applications while one study in cotton involves a seed treatment application followed by foliar spray applications. None of the residue studies evaluated from the open literature combined application method design. **Table 4-17** and **Table 4-18** below summarize the key elements of the soil + foliar and seed treatment + foliar residue studies. A more detailed description of each study is provided in **Appendix F**.

In a study assessing residues from the combined soil + foliar applications to tomatoes (conducted in California, 2013 – 2014; MRID 49665201; same study as that discussed in the soil-applied section), 2 foliar applications of 0.06 lbs a.i/A each were made at bloom following a soil application of 0.38 lbs a.i/A for a total rate that approximates the highest annual application rate for imidacloprid on fruiting vegetables. Tomatoes do not produce nectar and therefore only pollen data (bumble bee-collected) are available¹⁹. The acute and chronic EECs were 1521 and 1268 µg/L, respectively, and are approximately 6-fold higher than acute and chronic EECs for the soil-applied component alone.

For the combined soil + foliar study on apples (California, 2013 -2015; MRID 49662101), two foliar applications of 0.059 to 0.064 lbs a.i/A were applied during post-bloom after a 0.38 lbs. a.i/A soil application for a total rate that approximates the highest annual application rate for imidacloprid on pome fruit (0.5 lbs a.i/A). In 2013, applications were made after harvest whereas in 2014, applications were prior to harvest. Based on this study, the application pre or post-harvest appears to not have an effect on magnitude of imidacloprid residues. At some sampling time points there were a limited number of samples leading to limited ability to determine residue averages. Acute and chronic EECs were both 36.3 µg/L in nectar as compared to 103 and 81 µg/L, respectively in pollen. The nectar EEC is driven by a single nectar sample (36 µg/L) which is 4X greater than the sample from the same location/day for leaf and pollen residues. Since nectar residues of neonicotinoids are typically a fraction of those in pollen and leaf, this sample is considered uncertain. Additionally, all nectar values but this sample for pome fruit was below 10 µg/L.

For the combined soil + foliar study on stone fruit crops including cherry, plum, apricot, and peach (California, 2013 -2015; MRID 49819401), two foliar applications of 0.058 to 0.064 lbs a.i/A were applied during post-bloom after a 0.38 lbs. a.i/A soil application for a total rate that approximates the highest annual application rate for imidacloprid on stone fruit (0.5 lbs a.i/A). In 2013, all applications were made after harvest whereas in 2014, applications were prior to harvest. Based on this study the application pre or post-harvest appears to affect the relative magnitude of imidacloprid residues. Specifically, applications of imidacloprid prior to harvest resulted in lower average concentrations in residues the

¹⁹ Greenleaf, S. and Kreman, C. (2006). Wild bee species increase tomato production and respond differently to surrounding land use in Northern California. *Biological Conservation*, 133. 81-87.

following year. Acute and chronic EECs were 33.6 and 32.8 µg/L, respectively, in nectar as compared to 341 and 237 µg/L, respectively, in pollen.

For the combined soil + foliar study on cotton (conducted in California, 2013 -2014; MRID 49665202; same study as that discussed in the soil-applied section), 3 foliar applications of 0.06 lbs a.i./A each were applied during bloom after a 0.33 lbs. a.i./A soil application for a total rate that approximates the highest annual application rate for imidacloprid on cotton. Based on this study the method of application appears to affect the relative magnitude of imidacloprid in floral vs extrafloral nectars. Specifically, the soil-alone component found floral nectar residues above those of extra-floral. When the foliar applications were added, the extra-floral nectar residues were an order of magnitude higher than floral nectar. Acute and chronic EECs were 2775 and 1952 µg/L, respectively in extra-floral nectar as compared to 171 and 152 µg/L, respectively in floral nectar. Acute and chronic EECs in pollen were similar at 328 and 324 µg/L, respectively.

A tier III full field study with cotton also provided residue information for the combined soil + foliar applications of imidacloprid (conducted in California, 2015; MRID 50206701). Combined application rates ranged from 0.382 – 0.481 lbs a.i./A with a variety of application combinations, including two sites with two soil-only applications. One site (N008) had accidental applications for a total application rate of 0.931, which is approximately double the permitted maximum annual rate. Acute and chronic EECs were 28.1 and 13.6 µg/L, respectively in extra-floral nectar as compared to 36.4 and 18.7 µg/L, respectively, in floral nectar. Acute and chronic EECs in pollen were lower at 8.7 and 6.7 µg/L, respectively.

Finally, in the seed treatment + foliar study on cotton (conducted in Missouri, 2012 – 2013; MRID 49511702), 5 applications of 0.06 lbs a.i./A (Admire® Pro – 42.9% a.i.) followed a seed treatment with Gaucho® 600 Flowable equivalent to an application rate of 0.05 lbs a.i./A. This scenario represents the highest annual application rate of foliar applications made to cotton (0.31 lbs a.i./A). Residues in pollen, floral nectar, and extra-floral nectar were assessed. Similar to the soil-applied alone component of the study, residues in floral nectar were higher than that of extra-floral nectar (acute and chronic EEC of 40 and 29 µg/L, respectively for floral nectar as compared to 30 and 16.2 µg/L, respectively for extra-floral nectar). These residues were also approximately 3.5-fold lower than those determined in the soil-applied alone study component of the soil + foliar study discussed above, despite 5 foliar applications at bloom. Acute and chronic residues in pollen were 57 and 25 µg/L, respectively. Additionally, this study investigated residues in white clover as a rotational crop planted following foliar applications the previous year. Total residues were near or below the level of detection (0.7 µg/L) in the majority of samples analyzed (detection frequency = 38% for clover nectar and 53% for clover pollen). The maximum concentrations of total imidacloprid measured in clover nectar in trials NT014 and NT015 are 1.6 and 2.7 µg/L, respectively. The maximum concentrations of total imidacloprid measured in clover pollen in trials NT014 and NT015 are 8 and 8.6 µg/L, respectively.

Table 4-17. Summary of the registrant-submitted combined application method residue studies (soil application + foliar spray)

| Crop Group (Crop) | No. Sites/ Location/ Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|---|---|---|----------------------|---|--|----------------------------|---|---|
| Fruiting Vegetables - 8 (Tomato) | 9 sites CA 3 years (2013-2015) | 1 x 0.38 lbs. a.i/A Admire® Pro SC (soil @ transplant + 2 x 0.06 lbs. a.i/A Admire® Pro SC (foliar, at bloom) | Pollen (b) | 1762 | 1268 | 2-8 | <ul style="list-style-type: none"> Experimental fields; fine, medium, and coarse soils 1 trial = 1 yr. only; 8 trials = 2 yr. 1-2 replicates from bumble bee-collected pollen Most residue data reflect coarse soils Limited data indicates no year-to-year carry over (leaves) LOQ and LOD for total imidacloprid residues were 1 and 0.7 µg/L in nectar, respectively, and 1 and 0.5 µg/L in pollen, respectively | <i>Acceptable</i> (Gould and Jerkins, 2015, MRID 49665201) |
| Pome fruit - 11 (Apple) | 9 sites, CA, (2013, 2014) | Admire Pro® Systemic Protectant 1 x 0.38 lb a.i./A soil 3-5d int. 2 x 0.059 to 0.064 lb a.i./A foliar 8-10d int. post bloom near apple harvest | Nectar Pollen | 36.3⁶ 103 | 36.3⁶ 81 | 193 131 | <ul style="list-style-type: none"> Three soil type categories utilized (fine, medium, and coarse) Only one sample per year of each matrix, resulting in limited information on the behavior of residues over time LOQ and LOD for total imidacloprid residues were 1 and 0.3 µg/L in nectar, respectively, and 1 and 0.4 µg/L in pollen, respectively | <i>Acceptable</i> (Miller and Jerkins 2016, MRID 49662101) |

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix ¹ | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA ⁴ (days) | Study Notes | Classification (Reference) |
|---|--------------------------------|--|---|--|--|---------------------------|--|---|
| Stone fruit – 12 (Cherry, Plum, Apricot, Peach) | 9 sites, CA, (2013, 2014) | Admire Pro® Systemic Protectant 1 x 0.38 lb a.i./A soil 3-7d int. 2 x 0.058 to 0.064 lb a.i./A foliar 7-10d int. post bloom near stone fruit harvest | Nectar Pollen | 33.6 341 | 32.8 237 | 152 133 | <ul style="list-style-type: none"> Only one sample per year of each matrix, resulting in limited information on the behavior of residues over time LOQ and LOD for total imidacloprid residues were 1 and 0.7 µg/L in nectar, respectively, and 1 and 0.5 µg/L in pollen, respectively | <i>Acceptable</i> (Gould and Jerkins 2016, MRID 49819401) |
| Oilseed – 20 (Cotton) ⁵ | 9 sites CA 3 years (2013-2015) | 1 x 0.33 lbs. a.i/A Admire® Pro SC @ plant (in furrow spray) + 3 x 0.06 lbs. a.i/A Admire® Pro SC (@ bloom) | Pollen Nectar Exfl. Nectar | 2906 171 2775 | 2316 153 1952 | 4 4 5 | <ul style="list-style-type: none"> 2 fine, 1 medium and 6 coarse soils 1 trial = 1 yr. only; 8 trials = 2 yr. No indication of carryover LOQ was 1 µg/L in pollen, nectar and extra-floral nectar | <i>Acceptable</i> (Fischer and Jerkins, 2015; MRID 49665202) |
| Oilseed – 20 (Cotton) ⁵ | Tier III CA (2015) | Ref – foliar+soil Treat 1 foliar only Treat 2x soil only Treat 2x foliar+soil | Pollen Nectar Exfl. Nectar | 8.7 36.4 28.1 | 6.9 18.7 13.6 | ~17 ~60 ~17 | <ul style="list-style-type: none"> Mixture of foliar and soil treatments with various rates of application Fields with a history of pesticide application | <i>Supplemental</i> (MRID 50206701) |

¹Refers to hand collected pollen and nectar; “b” refers to bee-collected sample

²Acute EEC chosen as the maximum reported concentration among all individual replicates following application, refers to parent + IMI-olefin and IMI-5-OH

³Chronic EEC chosen as the maximum average concentration among all individual sampling events following application, refers to parent + IMI-olefin and IMI-5-OH

⁴DAA = Days after the last application of the pesticide

⁵Cotton represents sole member of oilseed group with registered soil and foliar uses.

⁶All but one sample for pome fruit was below 20 µg/L. This value, however, is driven by a single nectar sample (36 µg/L) which is 4X greater than the sample from the same location/day for leaf and pollen residues. Since nectar residues of neonicotinoids are typically a fraction of those in pollen and leaf, this sample is considered uncertain.

Table 4-18. Summary of the registrant submitted combined application method residue studies (seed treatment + foliar spray)

| Crop Group (Crop) | No. Sites/Location/Duration | Formulation, Appl. Rate, Interval, Timing | Matrix | Residue-based Acute EEC ² (µg/L) | Residue-based Chronic EEC ³ (µg/L) | DAA ⁴ (days) | Study Notes | Reference |
|------------------------------------|--|---|------------------------------|---|---|----------------------------|---|---|
| Oilseed – 20 (Cotton) ⁵ | 3 sites MO 2 years (2012, 2013) | Gaucho® 600 FL Admire® Pro SC 5 x 0.06 lbs. a.i./A x 5 (foliar) , 5-8 d int. @ bloom + Gaucho® 600 Flowable 0.05 lbs. a.i./A (seed trt) @ planting | Pollen Nectar ExNectar | 56.7 39.5 30 | 25.2 29 16.2 | 26, 14 21, 14 14, 29 | <ul style="list-style-type: none"> • Experimental fields, sand, sandy loam, silty loam soils • General decline in nectar and extra floral nectar residues during 10-20 DAA • Unclear whether higher residue in nectar (year 2) is due to carryover. • LOQ and LOD for total imidacloprid residues were 1 and 0.7 µg/L in nectar, respectively, and 1 and 0.5 µg/L in pollen, respectively | Acceptable (Gould <i>et al.</i> 2014, MRID 49511702) |
| Rotational Crop (Clover) | 3 sites MO (2013) | Untreated white clover planted on fields with prior year planting of seed-treated cotton @ 0.05 lbs. a.i./A and foliar spray of 5 x 0.06 lbs. a.i./A | Pollen Nectar | 8.6 2.7 | 4.8 1.3 | 439 405, 411 | <ul style="list-style-type: none"> • Vast majority of residues were < LOD • Residues at 1 µg/L reflect assumptions of ½ the LOD for non-detects. • LOQ and LOD for total imidacloprid residues were 1 and 0.7 µg/L in nectar, respectively, and 1 and 0.5 µg/L in pollen, respectively | |

¹ Refers to hand collected pollen and nectar

² Acute EEC chosen as the maximum reported concentration among all individual replicates following application, refers to parent + IMI-olefin and IMI-5-OH

³ Chronic EEC chosen as the maximum average concentration among all individual sampling events following application, refers to parent + IMI-olefin and IMI-5-OH

⁴ DAA = Days after the last application of the pesticide

⁵ Cotton represent sole member of oilseed group with registered foliar uses

4.6.8. Non-Agricultural Residue Studies

4.6.8.1. Registrant-Submitted

Non-agricultural uses of imidacloprid encompass a wide variety of application methods, species of plants and types of use sites, only which a portion are considered relevant to bee risk assessment. In this assessment, non-agricultural uses of imidacloprid considered most relevant to bee risk assessment include applications to ornamentals, turf and forestry.

For imidacloprid, registrant-submitted residue data are available only for soil and trunk injection application of imidacloprid to ornamental trees and bushes, including azalea, hibiscus, hedge cotoneaster, shadbush, cherry, horse chestnut, lime and apple tree. Furthermore, all data pertain to concentrations in flowers, which are less relevant for bee exposure compared to nectar and pollen. Therefore, concentrations of imidacloprid in nectar were estimated by multiplying concentrations in flowers by a factor of 0.3. This flower-to-nectar conversion factor is based on an analysis of paired flower and nectar data for all neonicotinoids for both agricultural crops and ornamental plants (**Attachment 2**).

A summary of the flower and estimated nectar residue data for ornamental plants is provided in **Table 4-19**. Importantly, the primary goal of most of these studies was to document imidacloprid effects on foraging behavior rather than quantification of residues. Therefore, the residue portion of these studies are classified as supplemental and considered only for qualitative use in risk assessment. The following limitations are noted in these studies:

- Measurement made in flowers (not nectar or pollen)
- Insufficient documentation of analytical QA/QC procedures and results (e.g., spike recoveries, replicates, blanks);
- Lack of information on storage stability of the samples;
- Prior year applications to various plants which were not accompanied by residue measurements;
- Variable and relatively small sample size for residue measurements;
- Insufficient documentation of sampling methods;
- Limited temporal coverage of sampling events (*i.e.*, wide gaps in sampling times)

Table 4-19. Summary of registrant-submitted residue data for application of imidacloprid to ornamental species

| Species | App Method | Timing of Application | Application Rate ¹ | DALA | Mean Imidacloprid Total Residues in Matrix ($\mu\text{g ai/kg}$) | | Reference |
|-----------------------------------|-------------|--|---|---------|--|-------------------------------|--|
| | | | | | Blossom | Nectar Estimated ² | |
| Azalea <i>Rhododendron sp.</i> | Soil drench | Pre-bloom applications made on May 9 2013; Post bloom applications made on June 5 2013 | 5 g/m plant height | Day 11 | 11.4 | 3.4 | 47303401 (Supplemental) 47303404 (Supplemental) |
| | | | | Day 17 | 13.8 | 4.1 | |
| | | | | Day 356 | 623 | 186 | |
| | | | 2.5 g/m plant height | Day 11 | 8.4 | 2.5 | |
| | | | | Day 17 | 9.8 | 2.9 | |
| | | | | Day 356 | 235 | 71 | |
| | | | 0.2 g/m plant height | Day 11 | 3.5 | 1.0 | |
| | | | | Day 356 | 120 | 36 | |
| Azalea <i>Rhododendron sp.</i> | Soil drench | January 13, 3005; Blooming stage not reported | 4.3 g/m plant height | Day 126 | 1252 | 376 | 47303405 (Supplemental) |
| | | | 2.15 g/m plant height | Day 126 | 467 | 140 | |
| Azalea <i>Rhododendron sp.</i> | Soil drench | 4.3 g/m plant height | April 12, 2006; Blooming stage not reported | Day 35 | 291 | 87 | 47303406 (Supplemental) |
| Azalea <i>Rhododendron sp.</i> | Soil drench | October 28, 2004; Blooming stage not reported | 4.3 g/m plant height (0.5 m plant) | 216 | 356 | 107 | 47303407 (Supplemental) |
| | | | 2.15 g/m plant height (0.5 m plant) | 216 | 191 | 57 | |
| | | | 1.075 g/m plant height (0.5 m plant) | 216 | 138 | 41 | |
| | | | 4.3 g/m plant height (1 m plant) | 216 | 87 | 26 | |
| | | | 2.15 g/m plant height (1 m plant) | 216 | 89 | 27 | |
| | | | 1.075 g/m plant height (1 m plant) | 216 | 53 | 16 | |
| | | | 4.3 g/m plant height | 175 | 357 | 107 | |
| Azalea <i>Rhododendron sp.</i> | Soil drench | November 26 Blooming stage not reported | 2.15 g/m plant height | 175 | 196 | 58 | 47303412 (Supplemental) |
| | | | 4.3 g/m plant height | 106 | 3764 | 1129 | |
| Hibiscus | Soil drench | April 12 Blooming stage not reported | 4.3 g/m shrub width | 117 | 1887 | 566 | 47303406 (Supplemental) |
| Shadblush | Soil drench | | 4.3 g/m plant height | 166 | 3.0 | 0.9 | 47303402 |

| Species | App Method | Timing of Application | Application Rate ¹ | DALA | Mean Imidacloprid Total Residues in Matrix ($\mu\text{g ai/kg}$) | | Reference |
|---------------------------------------|----------------|---|---|------|--|-------------------------------|----------------------------|
| | | | | | Blossom | Nectar Estimated ² | |
| <i>Amelanchier sp.</i> | | | 2.15 g/m plant height | 540 | 3548 | 1064 | (Supplemental) |
| | | | | 166 | 3.0 | 0.9 | |
| | | | | 540 | 2046 | 614 | |
| Cornelian Cherry <i>Cornus mas</i> | Soil drench | Autumn Blooming stage not reported | 4.3 g/m plant height | 505 | 2108 | 632 | 47303403 (Supplemental) |
| | | | 2.15 g/m plant height | 505 | 2328 | 698 | |
| Horse Chestnut | Soil drench | March 13 Blooming stage not reported | 0.28 g/cm stem diameter | 58 | 3.9 | 1.2 | 47303408 (Supplemental) |
| | | | | 408 | 3.9 | 1.2 | |
| | Tree Injection | May 9 Blooming stage not reported | 0.06 g/cm stem diameter | 2 | 5.0 | 1.5 | 47303413 (Supplemental) |
| | | | | 7 | 181 | 54 | |
| | | | | 351 | 3.9 | 1.2 | 47303409 (Supplemental) |
| | | | | 227 | 9.2 | 2.8 | |
| Lime Tree | Soil drench | November 4 Blooming stage not reported | 0.28 g/cm stem diameter | 230 | 14.5 | 4.4 | 47303410 (Supplemental) |
| | | | | 237 | 6.6 | 2.0 | |
| | | | | 227 | 3.6 | 1.1 | 47303410 (Supplemental) |
| | | | 0.14 g/cm stem diameter | 230 | 3.0 | 0.9 | |
| | | | | 237 | 3.0 | 0.9 | |
| | | | | 181 | 3.0 | 0.9 | 47303411 (Supplemental) |
| Apple Tree | Soil drench | 0.28 g/cm stem diameter | October 31 Blooming stage not reported | 181 | 3.0 | 0.9 | |
| | | 0.14 g/cm stem diameter | | 181 | 3.0 | 0.9 | |

¹ Maximum labeled rates for imidacloprid soil applications for ornamentals/forestry uses are 4.6 g/m plant height; 0.55 g/cm trunk width (< 15 cm dbh); that for tree injection is 0.09 g/cm trunk width.

² Based on the relationship between flower and nectar of ornamental plants treated with thiamethoxam, equivalent concentrations of imidacloprid in nectar were estimated by multiplying blossom concentrations by 0.3 (Attachment 2)

Variation in residues measured in flower (and estimated in nectar) vary widely among and within the ornamental residue studies. Part of this variation relates to the variable application rates used in these studies (and different units of application). Most labeled rates for ornamentals are expressed in lb ai/A, thus it is hard to compare the rates that were used within the studies to the maximum labeled application rates for imidacloprid. For shrubs, the application rates used in the studies ranged from 1.075 g/m plant height to 4.3 g/m plant height. In the case of horse chestnut, apple, and lime trees the rates ranged from 0.06 to 0.28 g/ cm stem diameter up to only half of the maximum labeled rates (when compared to trees with a diameter at breast height [dbh] < 15 inches) based on per centimeter stem diameters.

For soil drench applications to ornamentals, it is evident that measurements shortly after application do not always capture the highest concentrations within a study. In many cases, maximum concentrations occur a year or longer after soil application, however, whether these concentrations represent “peak” levels is unknown due to the limited sampling over time. Estimated residues in nectar greater than 500 ppb are recorded for hibiscus, shadbush and Cornelius cherry (**Table 4-19**). On the other hand, estimating nectar concentrations are relatively low for soil drench applications to horse chestnut, lime and apple tree. Residue data associated with trunk injection are very limited (only 1 trial for horse chestnut with measurements made at 3 sampling events).

4.6.8.2. Open Literature

Several open literature studies are available which report residues in ornamentals, turf, and trees; however, the matrices that are measured within the studies (*e.g.* twig, xylem, leaf, nut) are not relevant matrices currently used to assess risk to bees (*e.g.* pollen, nectar, blossom). A complete summary of open literature that was considered for analysis can be found in **Appendix C**. However, there are two open literature studies available measuring the magnitude of residues in nectar, pollen and blossoms that were used quantitatively in analysis. These studies have been summarized in Error! Reference source not found..

In an open literature study by Mach *et al.* (2017; MRID 51037901), residues of imidacloprid were measured in nectar and leaves of a broadleaf evergreen tree (foster holly) and a deciduous shrub (sweet pepperbush). In the study, plants were treated with Merit 2F at a rate of 1.06 g/ 0.305 m of plant height (3.48 g/m), representing 73.6% of the maximum labeled rate, via simulated soil injection. Applications were made late post-bloom (autumn), pre-bloom (spring), or early post-bloom (summer) to evaluate the impact of application timing on residues. Residue measurements were taken over the course of a 2-year sampling window to evaluate the persistence of imidacloprid in plant tissues. Nectar was extracted from flowers. Due to variable bloom times, each nectar harvest required several days to collect sufficient material for analysis. Detailed information was provided on analytical methods and QA/QC. In addition, raw data were obtained from the study author. This study is classified as supplemental but acceptable for quantitative use in risk assessment.

A second open literature study examined imidacloprid (and clothianidin) residues in bee attractive weeds following foliar application to turfgrass (Larson *et al.*, 2015; MRID 51026401). In this study,

Larson et al. quantified residues of imidacloprid (and clothianidin) in white clover following a single application of 0.4 lb ai/A (MERIT® 75 WSP) liquid formulation to turfgrass. Separate trials were conducted in June and August 2013 (4 replicates per trial) in which applications were made during bloom of clover in the turfgrass. This study is classified for qualitative use in risk assessment due to lack of raw data for independent analysis.

Results from Larson et al (2015; MRID 51026401) indicate relatively high levels of imidacloprid residues occur in clover nectar 1 day after receiving direct foliar spray application; mean residues in 2 trials ranged from approximately 5,500 to 6,600 ppb. However, 21 days later after mowing, mean residues of imidacloprid in nectar of newly bloomed clover were much lower (8-26 ppb).

Table 4-20. Summary of open literature residue data for the application of imidacloprid to ornamental

| Species | App Method | Timing of Application | App. Rate ¹ | DALA | Mean Total Imidacloprid in Nectar ($\mu\text{g ai/kg}$) | Reference (Classification) | |
|--|-------------|---------------------------|------------------------|-------------------|---|---|--|
| Foster Holly <i>Ilex attenuata</i> | Soil drench | Autumn Nov. 10, 2014 | 3.48 g/m plant height | 204 | 466 | Mach et al. 2017; MRID 51037901 (Quantitative) | |
| | | Pre-Bloom Mar. 27, 2015 | | 546 | 51 | | |
| | | Post-Bloom June 15, 2015 | | 67 | 273 | | |
| | | | | 409 | 58 | | |
| | | | | 329 | 12 | | |
| Sweet Pepperbush <i>Clethra alnifolia</i> | Soil drench | Autumn Nov. 10, 2014 | 3.48 g/m plant height | 253 | 845 | Mach et al. 2017; MRID 51037901 (Quantitative) | |
| | | Pre- Bloom Mar. 27, 2015 | | 617 | 201 | | |
| | | Post- Bloom June 15, 2015 | | 117 | 617 | | |
| | | | | 481 | 146 | | |
| | | | | 352 | 78 | | |
| Kentucky Blue Grass & Tall Fescue with 30% White Clover <i>(Trifolium repens)</i> | Foliar | June 3 | 0.4 lb ai/A | 1 | 5493 | Larson et al. 2015, MRID 51026401 (Qualitative) | |
| | | | | 21 (after mowing) | 8.4 | | |
| | | Aug. 15 | | 1 | 6,588 | | |
| | | | | 21 (after mowing) | 26 | | |

species

4.6.9. Carry-over of Imidacloprid Residues in Soil

The carryover of imidacloprid residues in soil (i.e. year-to-year accumulation in pollen and nectar) was considered as a potential exposure route. As discussed in **Section 4.1**, imidacloprid is persistent in the soil, with half-lives ranging from 305 days to several years in studies that were terminated after one year and up to 71% of the applied imidacloprid was still present in the soil. Several lines of evidence were considered in evaluating the potential impact of this exposure route including modeling results, rotational crop studies, and field trials in pollen and nectar, with a subset of these latter studies exploring the residues of pollen ad nectar in a rotational crop (white cover) in fields that were previously treated with imidacloprid.

The modeling of potential residues present after carryover accumulation in soil indicated an accumulation of about 5 times the annual rate is potential within 10 years of repeated annual applications. This simulation does not take into account important routes of dissipation including leaching, run-off, and plant up-take of imidacloprid residues which are expected to reduce to the potential magnitude of this accumulation.

Available rotational crop studies confirmed occurrence of soil carry-over from application to one crop to the following crop based on data obtained for magnitude of residues in rotational crops. In these studies, detectable residues of imidacloprid were found in variable quantities in rotational crops planted after 1, 4, 8 and 11-month rotational intervals following a single granular application of 0.29-0.32 lb. a.i/A. While residues reached as high as 0.58 mg/L in the edible portions of various crops, residues in pollen and nectar were not available from these studies. Furthermore, these studies considered the total residues of imidacloprid as parent plus 7 other degradation products including those that are not identified as being of toxicological concern.

Additionally, the available field trials in pollen and nectar were evaluated. In several studies that were conducted in one growing season, where only one sampling interval was included (as was the case with the foliar-applied cotton study, soil-applied melon study, and soil-applied strawberry study) the potential for carryover could not be assessed due to limited data from one year only. Additionally, the foliar applied studies with citrus fruits (oranges) had uncertainties associated with it that confound the ability to ascertain a carryover effect. These include inadvertent applications of imidacloprid to the trial field and differing nectar and pollen sampling measurements across trials. In other cases (soil + foliar applied tomato and soil + foliar applied cotton) there was insufficient information present to determine whether a carryover effect was present. Finally, 3 studies (soil-applied blueberry, seed treatment corn, and seed + foliar-applied cotton) included sufficient information to assess whether a carryover effect was present across the multiple trial years within a study. For 2 of these studies (seed treatment corn seed + foliar-applied cotton) a rotational crop (white clover) was planted in the season directly following the trial years to investigate the residues in pollen and nectar resulting from plant uptake of imidacloprid residues from the soil in the previous season. These studies are further discussed below.

In the soil applied blueberry study conducted across two trial years, there was no indication of carryover as nectar residues decreased from year 1 to year 2 (7.25 µg/L vs 1.8 µg/L) while residues in pollen remained essentially the same (13.7 vs 14.0 µg/L) from year 1 to year 2. In the seed treatment corn study, there did not appear to be a consistent increase or decrease in pollen residues in year 2 values relative to year 1. This finding is despite the fact that residues in soil measured prior to planting in year 2 (9-80 µg/L) are elevated compared to those measured prior to planting in year 1 (2-4 µg/L) which suggests a year-to-year carryover in soil. Finally, the seed + foliar treatment cotton study indicated that year 2 mean residues in floral and extra floral nectar increase by 1.2X to 2.7X over year 1 mean residues. With cotton pollen, yearly averages of mean residues increase by 1.5X to 2.9X from year 1 to year 2. Interestingly, the two trials with the highest coarseness in soils show the greatest relative increase in yearly average residues from year 1 to year 2 in nectar and pollen (1.7X to 2.9X) compared to the trial where the soil type was described as mostly silt (1.2-1.5X). It is not certain whether this differential

increase is related to differences in soil composition, but all three trials had similar amounts of imidacloprid in soil prior to the 2nd year planting (24-42 µg/L).

In the rotational crop (clover) component of the seed treatment corn study, the mean residues in pollen and nectar following planting and harvesting corn the previous year were near or below the combined limits of detection (1.24 µg/L for pollen; 1.33 µg/L for nectar) in the majority of samples analyzed (detection frequency = 28% for clover pollen and 0% for clover nectar). The maximum concentrations of imidacloprid residues in clover pollen in three trials is 3.8 µg/L. Similarly, in the rotational component of the seed + foliar treatment cotton study, mean residues of imidacloprid were near or below the level of detection (0.7 µg/L) in the majority of samples analyzed (detection frequency = 38% for clover nectar and 53% for clover pollen). The maximum average and single concentrations of imidacloprid in nectar were 1.6 and 2.7 µg/L, respectively. The maximum average and single concentrations of imidacloprid residues in pollen were 8 and 8.6 µg/L, respectively.

Based on the available data for which sufficient information is present to indicate an effect, there is limited indication of a carryover effect from year-to-year accumulation of imidacloprid residues in soil that translates to increased residues in pollen and nectar, even in the case where a year-to-year build up in soil residues was present (as with the seed treatment corn study). Additionally, two studies that investigated the residues in pollen and nectar in a rotational crop (white clover) found detectable levels of imidacloprid, however overall these residues were low and very close to the limits of quantitation.

4.7. Observational Residue Monitoring Studies

In addition to the registrant submitted and open literature field residue trials discussed previously which characterized the residues in pollen and nectar following a specific application regimen and sampling schedule, there are several monitoring studies available from the open literature to characterize the residues of imidacloprid. Rather than a targeted study as those described above, these studies surveyed residues of pollen and nectar in crops on agricultural fields with known imidacloprid use as well as samples from various matrices (nectar, pollen, wax) from honey bee hives.

4.7.1. Agricultural crop studies

The studies by Bonmatin 2005 (MRID 47523411) and 2007, investigated the residues in various plant parts from fields known to have been planted with imidacloprid-treated seed. As a result, it is not possible to tie a particular application rate or sampling interval relative to the application timing to the residues of imidacloprid that were determined. The work in 2005 investigated the residues in corn pollen and trapped pollen originating from corn fields while the study in 2007 assessed corn and sunflower pollen. The findings of the 2005 and 2007 studies are summarized below. Full study summaries with a discussion of the methods are provided in **Appendix D**.

Despite the aforementioned uncertainty of an unknown application rate or sampling interval, **Table 4-21** and **Table 4-22** below indicate low mean residues of imidacloprid in sampled corn and sunflower pollen with values either below the LOQ or a maximum of 3-fold above it.

Table 4-21. Distribution of samples from corn fields according to their concentration of imidacloprid (Bonmatin, 2005)

| Sampled Matrix | Number of samples | Number of samples below LOD ¹ | Number of samples between LOD and LOQ ^{1,2} | Number (Percent) of samples above LOQ ^{2,3} | Mean concentration ($\mu\text{g}/\text{L} \pm \text{SD}$) ³ |
|----------------|-------------------|--|--|--|--|
| Corn pollen | 47 | 6 | 18 | 23 (49%) | 2.1 ± 2.7 |
| Trapped pollen | 11 | 5 | 2 | 4 (36%) | 0.6 ± 1.0 |

¹LOD = 0.3 $\mu\text{g}/\text{L}$

² LOQ = 1 $\mu\text{g}/\text{L}$

³Refers to samples above the LOQ

Table 4-22. Distribution of residues from corn and sunflower pollen according to their concentration of imidacloprid (Bonmatin, 2007)

| Sampled Matrix | Number of samples | Percentage of samples exceeding LOQ ¹ | Mean concentration ($\mu\text{g}/\text{L}$) ² |
|------------------|-------------------|--|--|
| Corn pollen | 47 | 2 | 2.0 |
| Sunflower pollen | 24 | 58 | 3.0 |

¹LOQ: 1 $\mu\text{g}/\text{L}$

²Refers to samples above the LOQ

4.7.2. Hive monitoring studies

In addition to the crop monitoring studies discussed above, several studies are available from the open literature that survey residues of in-hive pollen, wax, honey, nectar, and dead bee samples, for various chemicals, including imidacloprid (**Table 4-23** and **Table 4-24**). These studies were not part of the suite of studies that received a review for their utility in terms of quantitative or qualitative use for this assessment for the exposure and effects assessments. Rather, these studies serve to characterize the potential extent to which bees are exposed to imidacloprid in the field. What follows is a summary of these studies while more detailed summaries are provided in **Appendix D**.

The available studies that survey various matrices for pesticide contamination, including hive pollen (bee bread), trapped pollen (pollen collected from bees as they enter the colony), honey, beeswax, and honey bee samples provide a broad picture of the overall in-hive residues that result from use of imidacloprid and other chemicals. While the studies differed in the location of sampled hives, as well as the condition of the colony from which the samples originated (with Mullin 2010, Kasiotis 2014, and Cepero 2016 indicating that healthy and known diseased colonies were sampled), all studies had similar sampling procedures for a given matrix and appropriately low LOQ values reported for the analytical methods used (LOQs varied from study to study, see **Appendix D** for further information).

In several of the available studies, regardless of whether they were conducted in the United States or Europe, imidacloprid was generally detected in 10% or less of pollen, honey, wax, or honey bee samples. For those studies, the highest imidacloprid concentration was detected in trapped pollen at 206 $\mu\text{g}/\text{L}$ from Mullin et al 2010. For the remaining studies, imidacloprid was detected in at least one matrix with

a frequency of 10% or more. While there were high frequencies (nearing or above 50%) of detections of imidacloprid in pollen and honey samples in the Chauzat studies, as well as Lu 2015 and Bonmatin 2007, the mean concentrations were generally at or slightly above the reported LOQ. The Chauzat studies (2006, 2009) in particular claim that although certain pesticide residues were frequently detected across various hive matrices, that there did not appear to be relationships between the abundance of brood and adults and the presence of a particular residue. Only two studies that looked for imidacloprid in honey found residues and the majority of those detects were generally at or slightly above the reported LOQ.

An additional point to be made from these studies is that, for all studies except Lu 2015 (which screened only for neonicotinoid pesticides), multiple pesticides were found in the same samples, with some samples containing up to 12 pesticides (Johnston, 2014). In the majority of these cases, the *Varroa* mite (*Varroa destructor*) treatment miticides fluvalinate, coumaphos, and amitraz (DMA and DMPP degradates) were detected, in some cases in up to 98% of the assessed samples, depending on the matrix (Mullin, 2010). Additionally, fungicides, particularly those of the sterol biosynthesis inhibitor class that include the triazole fungicides were detected with high frequency. There are reports in the literature that these chemicals may exhibit a greater than additive (e.g., synergistic) effect on toxicity when bees are exposed simultaneously with neonicotinoid chemicals like imidacloprid Alaux 2010; Gradish 2009; Biddinger 2013; Thompson 2014a; Johnson 2010; Pettis 2013; Blacquiere 2012). While the extent of this relationship is beyond the scope of this assessment, it highlights the complex nature of interactions of different stressors that exist in the hive.

Table 4-23. Summary of observational monitoring studies which quantified imidacloprid residues in whole bee tissue

| Citation | Study location | Purported Pesticide application | Bee/Wax (µg/L) | | | | |
|---------------------------|---|--|---------------------|--------------------|-----|-----|------------------|
| | | | Source ¹ | % Detects (N Size) | Min | Max | Avg ² |
| Chauzat 2009 ⁴ | France | Hives in honey production areas | Bee | 26.2 (187) | NR | NR | 1.2 |
| Mullin 2010 ⁵ | Various states across the United States | Several studies with various pesticide pressures | Bee | 0 (140) | NA | NA | NA |
| | | | Wax | 1.0 (208) | 2.4 | 14 | 8.0 |
| Wiest 2011 | France | Various landscapes | Bee | 0 (140) | NA | NA | NA |
| Kasiotis 2014 | Greece | Hives reporting incidences vs organic | Bee | 6 (34) | 0.3 | 5.2 | 2.8 |
| Hladik 2016 | Colorado | Grass lands near farms | Bee (GL – 2013) | 14 (21) | 21 | 82 | 57 |
| | | | Bee (GL - 2014) | 7.1 (14) | NR | 1.1 | NR |
| | | Grower maintained wheat field | Bee (Wheat Field) | 20 (20) | 1.3 | 14 | 6.4 |
| Vernich 2016 | Spain | Agricultural areas with extensive pesticide use | Bee | 32 (34) | 12 | 223 | 53 |

| Citation | Study location | Purported Pesticide application | Bee/Wax ($\mu\text{g/L}$) | | | | |
|----------------|----------------|--|-----------------------------|--------------------|-----|-----|------------------|
| | | | Source ¹ | % Detects (N Size) | Min | Max | Avg ² |
| Botias 2016 | England | Ornamental public gardens and parks surrounded by houses | Bee (U) | 24 (25) | NR | 10 | <0.72 |
| | | Agricultural land within mixed farms | Bee (A) | 4 (25) | NR | 2.2 | NR |
| Cepero 2015 | Spain | Hives reporting incidences (Nosema, CCD, other) | Bee | 0 (20) | NA | NA | NA |

LOD = limit of detection; LOQ = limit of quantitation; NR = not reported; NA = Not applicable;

¹U urban landscape; A agricultural landscape; GL grasslands

²Average of residues above the limit of quantification (varies depending on the study)

⁴Inclusive of both imidacloprid and 6-CNA

⁵One detection each in pollen of the degradates olefin-imidacloprid

Table 4-24. Summary of observational monitoring studies which quantified imidacloprid residues in various hive and agricultural matrices

| Citation | Study location | Purported Pesticide application | Pollen ($\mu\text{g/L}$) | | | | | Nectar ($\mu\text{g/L}$) | | | | |
|---|---|---|----------------------------|--------------------|------|-----|------------------|----------------------------|--------------------|-----|-----|------------------|
| | | | Source ¹ | % Detects (N Size) | Min | Max | Avg ² | Source ¹ | % Detects (N Size) | Min | Max | Avg ² |
| Bonmatin 2005 | France | Fields treated with IMI vs not in past 3 years or organic | P (Corn) | 49 (47) | NR | NR | 2.1 | N/A | | | | |
| | | | T | 36 (11) | NR | NR | 0.6 | | | | | |
| Chauzat 2006 ³ | France | Hives in single location | T | 49 (81) | >LOD | 5.7 | 1.2 | N/A | | | | |
| Bee Research Institutes (Germany – 2004 – 2007) | Germany | Various locations and pesticide pressures | H (2004) (Beebread) | 4.2 (48) | NR | NR | 1.0 | H | 0 (48) | NA | NA | NA |
| | | | H (2005 – 2006) | 0 (105) | NA | NA | NA | N/A | | | | |
| | | | T (2007) | 0.9 (11) | NA | 3.0 | NA | N/A | | | | |
| Bonmatin 2007 | France | Intensive agricultural areas | P (Corn) | 2 (47) | NR | NR | 2.0 | N/A | | | | |
| | | | P (Sunfl.) | 58 (24) | 1.0 | 11 | 3.0 | | | | | |
| Chauzat 2009 ⁴ | France | Hives in honey production areas | T | 40 (185) | 5.7 | 9.3 | 0.9 | H (Honey) | 30 (239) | NR | NR | 0.7 |
| Mullin 2010 ⁵ | Various states across the United States | Several studies with various pesticide pressures | T & H (beebread) | 2.9 (350) | 6.2 | 206 | 39 | N/A | | | | |
| Wiest 2011 | France | Various landscapes | T | 0 (145) | NA | NA | NA | H (Honey) | 0 (142) | NA | NA | NA |
| Jones 2016 | England | Honey production hives | N/A | | | | | H (honey) | 0 (22) | NA | NA | NA |
| Stoner and Eitzer 2013 ⁶ | Connecticut | Various pressures; urban to managed pollinators | T | 12 (313) | 1.0 | 70 | 5.2 | N/A | | | | |
| Pettis 2013 | CA, PA, ME, NJ, DE | Pollination service hives in seven crops | T | 16 (19) | NR | 36 | 2.8 | N/A | | | | |
| Kasiotis 2014 | Greece | Hives reporting incidences vs organic | H (bee pollen) | 7.1 (14) | NA | 74 | NA | H (honey) | 0 (22) | NA | NA | NA |
| Johnston 2014 | Europe (12 countries) | NR | H (Beebread) | 0 (25) | NA | NA | NA | N/A | | | | |

| Citation | Study location | Purported Pesticide application | Pollen (µg/L) | | | | | Nectar (µg/L) | | | | | |
|------------------------|----------------|--|---------------------|--------------------|------|------|------------------|---------------------|--------------------|-----|-----|------------------|--|
| | | | Source ¹ | % Detects (N Size) | Min | Max | Avg ² | Source ¹ | % Detects (N Size) | Min | Max | Avg ² | |
| | | T | 5.6 (107) | 1.7 | 149 | NR | | | | | | | |
| Botias 2015 | England | Winter sown oilseed rape fields | P (OSR) | 0 (21) | NA | NA | NA | P (OSR) | 0 (13) | NA | NA | NA | |
| | | Wild flowers that were present in the field margins | P (OSR WF) | 11.6 (43) | NR | 12 | 0.56 | P (OSR WF) | 0 (24) | NA | NA | NA | |
| | | Winter-sown wheat fields | P (WWF) | 3.6 (55) | NR | 0.58 | NR | P (WWF) | (8) | NA | NA | NA | |
| | | Vicinity of OSR fields at the beginning of the OSR flowering | T (OSR-June) | 21 (34) | NR | 26 | 2.5 | N/A | | | | | |
| | | | T (OSR-Aug.) | 15 (46) | NR | 2.5 | NR | | | | | | |
| Frazier 2015 | PA, CA, ME | Hives around various crops | T (Apple) | NR | NR | NR | 16 | N/A | | | | | |
| Lu 2015 | MA | Various areas | T | 57 (124) | NR | 43 | 0.1 | H (Honey) | 53 (53) | NR | 15 | 0.58 | |
| Sanchez-Hernandez 2016 | Spain | Hives next to crops with seed treatment | H (beebread) | 0 (34) | NA | NA | NA | H (Honey) | 0 (9) ⁸ | NA | NA | NA | |
| Cepero 2016 | Spain | Hives reporting incidences (Nosema, CCD, other) | H (beebread) | 0 (20) | NA | NA | NA | N/A | | | | | |
| Alburaki 2017 | TN | Various % agriculture and urban areas | T | 25 (4) | NR | NR | 3 | N/A | | | | | |
| Long & Krupke 2016 | IN | Next to seed treated corn fields | T | 7 (30) | 0.94 | 1.05 | NR | N/A | | | | | |

LOD = limit of detection; LOQ = limit of quantitation; NR = not reported; NA = Not applicable; sunfl. = sunflower; OSR = oil seed rape; OSR WF = wildflowers next to OSR fields; WWF = wildflowers next to wheat fields; GL grasslands

¹H = Hive (bee) collected, P = plant collected, T = trapped (at hive entrance)

²Average of residues above the limit of quantification (varies depending on the study)

³The degradate 6-chloronicotinic acid (6-CNA) was also detected in 36 of 81 samples (44%)

⁴Inclusive of both imidacloprid and 6-CNA

⁵One detection each in pollen of the degradates olefin-imidacloprid

⁶One detection of 5-OH imidacloprid in pollen at LOD (5.6 µg/L)

⁷Two detections each of N-desnitro-imidacloprid and N-desnitro-imidacloprid olefin and 6 detections each of IMI-10 and IMI-11 (names not identified in study, measured values not reported)

⁸Three detections each of N-desnitro-imidacloprid and N-desnitro-olefin-imidacloprid (measured values not reported)

4.7.3. Non-Agricultural Monitoring Studies

One non-agricultural crop monitoring study was examined in support of this assessment (Lentola, 2017). The goal of the study was to sample ornamental plants marketed at garden centers as “pollinator friendly” for pesticide residues in leaves, pollen and nectar. The study examined leaf samples from 29 different plants for 8 insecticides and 16 fungicides commonly used in ornamental production; additionally, it examined 18 different plant species for pollen and 11 different ornamental species for nectar. Neonicotinoid insecticides were found in more than 70% of the analyzed plants. For imidacloprid, the mean concentrations sampled in leaves was 3.8 ng/g and the mean concentrations sampled in pollen was 6.9 ng/g. Nectar sampling was not successful due to the limited quantities of nectar available in the test species. The study findings state that the correlation demonstrated in systemic pesticide residues found in leaf and pollen samples show that residues are still available to pollinator insects when the ornamental plants are planted in residential gardens by consumers.

5. EFFECTS ASSESSMENT

5.1. Tier I Studies

At the Tier I (screening) level, effects to individual bee are considered. This is achieved through a suite of laboratory studies that assess different life stages (*i.e.* adults and larvae) and different durations of exposure, *i.e.*, acute (single dose) and chronic (repeat dose). The adult acute contact, adult acute oral, and larval acute oral toxicity studies have formal protocols published from at least one regulatory entity and these protocols are generally adhered to with registrant-submitted data. While test methods originating from the open literature can be more varied, the adult acute contact and adult acute oral tests evaluated from the open literature for imidacloprid were also generally conducted in accordance with one or more published guidelines. The most sensitive endpoints from the Tier I studies (from which findings can be statistically verified) inform the Tier I default and Tier I refined RQs, using screening level estimates and residue data in pollen and nectar (where available), respectively.

5.1.1. Review of Registrant-Submitted Studies

For registrant-submitted studies, the distinction between acute/chronic adult and acute/chronic larval is made as these guidelines are either already released or in development and are in line with the 2014 *Guidance for Assessing the Risk of Pesticides to Bees* (USEPA *et al.* 2014). For the acute contact toxicity, registrant-submitted studies adhered to either the Office of Chemical Safety and Pollution Prevention (OCSPP) Guideline 850.3020²⁰, the Organization for Economic Cooperation and Development (OECD) Test Guideline 214²¹, or the European and Mediterranean Plant Protection Organization (EPPO) guideline 170²² for adult honey bees. For acute oral toxicity to adult honey bees, studies generally adhered to OECD TG 213²³ and EPPO 170. Acute oral toxicity studies with honey bee larvae were conducted in accordance with OECD TG 237²⁴. Finally, the chronic oral larval toxicity tests and chronic adult (10-day) oral toxicity test protocols are currently in development, but the available studies were conducted in accordance with methodology determined to be sufficient for quantitative risk assessment purposes.

As guidelines are well established for most Tier I data requirements (particularly the acute contact and acute oral toxicity tests for adult honey bees), the methodology for each submitted study is not

²⁰ USEPA. 2012a. "Honey Bee Acute Contact Toxicity" Ecological Effects Test Guidelines OCSPP 850.3020. EPA 712-C-019 Web: <http://www.regulations.gov/#/documentDetail;D=EPA-HQ-OPPT-2009-0154-0016>

²¹ OECD. 1998b. OECD Guidelines for the Testing of Chemicals. Test Number 214, Acute Contact Toxicity Test. http://www.oecd-ilibrary.org/environment/test-no-214-honey-bees-acute-contact-toxicity-test_9789264070189-en;jsessionid=43gvto47wnue9.delta

²² EPPO. 2010. Efficacy Evaluation of Plant Protection Products: Side-effects on Honey bees. PP 1/170 (4). OEPP/EPPO Bulletin 40: 313–319

²³ OECD. 1998a. OECD Guidelines for the Testing of Chemicals. Honey bees, Acute Oral Toxicity Test. 213. <http://lysander.sourceoecd.org/vl=5988235/cl=12/nw=1/rpsv=cgi-bin/fulltextew.pl?rpsv=/ij/oecdjournals/1607310x/v1n2/s14/p1.idx>

²⁴ OECD. 2013. OECD Guidelines for Testing Chemicals. Honey bee (*Apis mellifera*) larval toxicity test, single exposure. http://www.oecd-ilibrary.org/environment/test-no-237-honey-bee-apis-mellifera-larval-toxicity-test-single-exposure_9789264203723-en

discussed extensively but rather only when major guideline deviations are noted. As distinguished from the open literature studies, registrant-submitted studies that are designed to satisfy a guideline requirement are classified as acceptable (suitable for quantitative use in risk estimation), supplemental (some deviations noted that render the study useful for either quantitative or qualitative use), or invalid (not suitable for use in risk assessment due to guideline deviations that affect the scientific soundness of a study). Typically, open literature studies are designated as for quantitative, qualitative, or invalid for risk assessment purposes.

5.1.2. Review of Open Literature Studies

Through a joint collaborative effort by the EPA, Canada's Pest Management Regulatory Agency (PMRA), and the state of California Department of Pesticide Regulation (CDPR), over 30 studies in the open literature were evaluated to further characterize the toxic effects of imidacloprid at the Tier I (individual) level. These effects include effects on mortality, food consumption, brood production, and behavioral responses on several subspecies of *Apis*, as well as non-*Apis* bees including bumble bees (*Bombus* spp.) and several solitary bee species including blue orchard bees (*Osmia lignaria*) and alfalfa leafcutting bees (*Megachile rotundata*).

While the *Guidance for Assessing Pesticide Risks to Bees* (USEPA, 2014) stipulates that data from non-*Apis* species can be considered in the risk assessment, it does not provide a process to estimate risk as it does for honey bees (*Apis*). This is due in part to the fact that there are different exposure estimates that would be needed for non-*Apis* species that at the present time have not been sufficiently explored by the Agency. For example, bumble bee workers and drones are larger than their honey bee counterparts, in addition to having higher food consumption rates that would necessitate different contact and oral exposure estimates, respectively. For the sake of discussion of the Tier I data, due to the exposure and test durations varying so greatly as compared to the more standardized registrant-submitted studies (which generally follow established regulatory guidance), those studies with a single exposure or duration <5d are considered acute while those with repeated exposures or durations >6 days are considered chronic.

To obviate the need to state it for every open literature study discussed, it is noted here that generally all open literature studies (with the exceptions noted in the individual discussions) did not provide raw data in order to conduct an independent verification of the statistical results. This limitation was one of the primary reasons that open literature studies were considered to be *qualitative* in their utility; those that were evaluated and considered invalid for utility in this risk assessment are tabulated in **Appendix A**. The studies from the open literature not only serve to broaden the database of species for which effects of imidacloprid can be characterized, but also expand on the suite of effects that are investigated in the registrant-submitted studies, which is generally limited to observations of mortality and clinical signs of toxicity (sublethal effects). Additionally, studies from the open literature serve to examine any differential toxicity that may be present in *Apis* vs. non-*Apis* bees, particularly as it relates to effects on individual bees at the Tier I level.

What follows is a summary of the available registrant-submitted and open literature studies to characterize the acute and chronic effects to *Apis* and non-*Apis* adult bees and larvae. The studies are

organized by species (*e.g.* *Apis* vs. non-*Apis*), duration (acute or chronic), route of exposure (contact or oral) and source (registrant-submitted and open literature). Unless otherwise stated, in the section dealing with *Apis* studies, all studies concern *A. mellifera*. It is also noted here that a limitation to all Tier I data is the uncertainty as to the extent to which the lethal and sublethal effects described in these studies translate to an adverse effect(s) at the colony level.

Table 5-1 below summarizes the most sensitive endpoints from each of the Tier I study types with further discussion of all studies providing Tier I endpoints provided below. Endpoints in this table originate from registrant-submitted studies conducted with *A. mellifera*.

Table 5-1. Summary of endpoints to be used in screening-level and refined Tier I risk estimation

| Study Type | Endpoint ¹ | Reference | Classification |
|---|---|---------------|----------------|
| Adult Acute Contact Toxicity | 96-hr LD ₅₀ : 0.043 µg a.i./bee | MRID 49602717 | Acceptable |
| Adult Acute Oral Toxicity | 48-hr LD ₅₀ : 0.0039 µg a.i./bee | MRID 42273003 | Acceptable |
| Adult Chronic Oral Toxicity | 10-day NOAEC/LOAEC (food consumption): 0.0011/0.0018 µg a.i./bee/day | MRID 50399101 | Acceptable |
| Larval Acute (single dose) | No data available | | |
| Larval Chronic (repeat dose) | 21-day NOAEC/LOAEC: 0.0018/>0.0018 µg a.i./larva | MRID 49090506 | Supplemental |
| Toxicity of Residues on Foliage ² (OCSPP 850.3030 ³) | 2-hr residues of 0.025 lbs a.i./A: 20% mortality 2-hr residues of 0.05 lbs a.i./A: 19% mortality 2-hr residues of 0.1 lbs a.i./A: 28% mortality | MRID 42480503 | Supplemental |

Bolded value to be used in risk estimation if more than one endpoint present for a study type.

¹Represents most sensitive (*i.e.* lowest) of all endpoints within a particular study type for studies for which raw data (to allow for independent statistical verification of the endpoint) are available.

²Although cited in 40 CFR Part 158 as an EPA testing requirement, the results of this study are not used for risk estimation.

³ USEPA. 2012b. "Honey Bee Toxicity of Residues on Foliage." Ecological Effects Test Guidelines OCSPP 850.3030. EPA 712-C-018. Web. <http://www.regulations.gov/#/documentDetail;D=EPA-HQ-OPPT-2009-0154-0017>

5.1.3. Adult Acute Contact Toxicity

5.1.3.1. Apis – Registrant-Submitted Studies

There are five available contact studies to characterize the acute toxicity of imidacloprid to adult honey bees with technical grade active ingredient (TGAI, purities range from 98.6 - 99.8%) and one study conducted with a formulated typical end use product (TEP, 200.9 g/L, 20% a.i., density of 1.1 g/cm³). As indicated above, these studies were conducted in accordance with one or more recognized protocols for testing the acute contact toxicity to honey bees. The observation period (*i.e.* study duration) ranged from 48 – 96 hours and the resultant LD₅₀ values ranged from 0.043 – 0.104 µg a.i./bee. Clinical signs of toxicity were noted in the majority of studies. **Table 5-2** below summarizes the available registrant submitted acute contact toxicity studies to adult honey bees. Summaries for each study are provided in **Appendix E**. It is noted here, as above in **Table 5-1**, that the most sensitive adult acute contact toxicity endpoint is 0.043 µg a.i./bee (MRID 49602717).

Table 5-2. Summary of registrant submitted adult acute contact toxicity studies (all studies tested *Apis mellifera*)

| Test Substance (% a.i) | Study Duration | Endpoint (95% CI) (expressed in terms of µg a.i/bee) | Comments | Classification (Reference, MRID) |
|--|----------------|---|--|----------------------------------|
| TGAI (99.8) | 48-hr | LD ₅₀ : 0.078 (0.068 – 0.090) | No observations (if any) of clinical signs of toxicity were noted to be present in the study report | Acceptable (42273003) |
| TGAI (98.6) | 72-hr | LD ₅₀ : 0.104 (0.080 – 0.131) | - Clinical signs of toxicity include paralysis, spasms, or frozen behavior, and were observed at all treatment groups. | Acceptable (49766209) |
| TGAI (98.6) | 72-hr | LD ₅₀ : 0.048 (0.041 – 0.057) | - Clinical signs of toxicity included bees observed to have been incapacitated and uncoordinated (stumbling) at all treatment groups | Acceptable (49602715) |
| TGAI (98.6) | 96-hr | LD₅₀: 0.043 (0.026 – 0.055) | - Lying on back/difficulty standing and coordination issues reported at all treatment groups | Acceptable (49602717) |
| TGAI (98.6) | 96-hr | LD ₅₀ : 0.069 (0.056 – 0.085) | - Clinical signs of toxicity include lethargy, lack of coordination, and immobility (not specified which treatment groups) | Acceptable (49602714) |
| TEP (Imidacloprid 200 SL) (200 g/L, 20% purity assuming density is 1 g/L) | 96-hr | LD ₅₀ : 0.045 (0.034 – 0.060) 0.0246 µg product/bee | - Clinical signs of toxicity noted were uncoordinated movement in the 4 highest treatment groups | Acceptable (49602707) |

NA: not available; TGAI: technical grade active ingredient; TEP: typical end use product

Bolded value represents endpoint to be used risk estimation

5.1.3.2. *Apis* – Open Literature Studies

There were six studies evaluated from the open literature that investigated the acute contact toxicity to honey bee adults (**Table 5-3**). These studies generally followed at least one of the protocols available for the acute contact toxicity testing to honey bees. The observation period (*i.e.* study duration) ranged from 24 – 72 hours and tests assessed multiple subspecies of *A. mellifera*. The acute contact LD₅₀ values ranged from 0.018 – 0.24 µg a.i/bee. As noted previously, these studies were classified as qualitative primarily due to their absence of raw data provided to statistically verify the results. In contrast to the suite of registrant-studies, clinical signs of toxicity were generally not reported in the open literature studies. Summaries of each study including methods and other limitations and uncertainties are provided in **Appendix E**.

Table 5-3. Summary of adult acute contact toxicity studies to *Apis* bees evaluated from the open literature

| Test Species | Test Substance (% a.i.) | Study Duration | Endpoint (95% CI) (expressed in terms of µg a.i/bee) | Comments | Classification (Reference, MRID) |
|---------------------------------|---|----------------|---|--|---|
| <i>Apis mellifera</i> | TGAI (>99) | 24-hr | LD ₅₀ : 0.018 (0.009 – 0.032) | - Also tested piperonyl butoxide, triflumizole, and propiconazole with imidacloprid to assess potential synergistic effects (no significant differences in all combined LD ₅₀ values relative to imidacloprid alone). | <i>Qualitative</i> (Iwasa 2004, 47523404) |
| <i>Apis mellifera carnica</i> | TGAI (>98) | 48-hr | LD ₅₀ : 0.081 (0.055 – 0.119) | - No mention of whether dose response was present | <i>Qualitative</i> (Schmuck 2001, 47812303) |
| | TEP (70) | | LD ₅₀ : 0.23 (NA) | | |
| | TEP (200 g/L, 20% purity assuming density of 1 g/L) | | LD ₅₀ : 0.24 (0.17 – 0.35) | | |
| | | | LD ₅₀ : 0.060 (0.039 – 0.093) | | |
| <i>Apis mellifera carnica</i> | TGAI (>98) | 48-hr | LD ₅₀ : 0.061 (0.026 – 0.090) | - No mention of whether dose response was present | <i>Qualitative</i> (Schmuck 2003, 47796304) |
| | | | LD ₅₀ : 0.050 (0.009 – 0.071) | | |
| | | | LD ₅₀ : 0.075 (0.062 – 0.091) | | |
| <i>Apis mellifera mellifera</i> | TGAI (98) | 48-hr | LD ₅₀ : 0.024 (0.022 – 0.027) | - Mortality rates increase at low doses, decrease at intermediate doses, and increase again at higher doses. | <i>Qualitative</i> (Suchail 2000, 47800513) |
| <i>Apis mellifera caucasia</i> | | | LD ₅₀ : 0.013 (0.010 – 0.016) | | |
| <i>Apis mellifera</i> | TGAI (99.9) | 48-hr | LD ₅₀ : 0.067 (0.044 – 0.102) | - Also tested myclobutanil, propiconazole, flusilazole, and tebuconazole. | <i>Qualitative</i> (Thompson 2014a, 49750606) |
| <i>Apis mellifera</i> | TEP (Provado® 1.6F) (17.4) | 48-hr | LD ₅₀ : 0.03 µg a.i/bee (0.017 – 0.05) 0.15 µg product/bee; (0.05 – 0.32) | - Range of actual doses tested was not provided. - There was no mention of whether dose response was present. | <i>Qualitative</i> (Biddinger 2013, 49719605) |

NA: not available; TGAI: technical grade active ingredient; TEP: typical end use product

5.1.3.3. Non-*Apis* – Registrant-Submitted studies

There are two available registrant-submitted contact studies to characterize the acute toxicity of imidacloprid to adult bumble bees; one study with TGAI (98.6% purity) and one study with formulated product (30.4%; **Table 5-4**). These studies are limited in their utility as the study with TGAI could not determine a LD₅₀ due to excessive mortality in the majority of concentrations tested by 24 hours after treatment and the formulated product study not indicating a clear dose response in the results. Summaries of each study are provided in **Appendix E**.

**Table 5-4. Summary of registrant submitted adult acute contact toxicity studies for non-*Apis* bees
(Note: both studies concern *Bombus terrestris*)**

| Test Substance (% a.i) | Study Duration (Type) | Endpoint (95% CI) (expressed in terms of µg a.i/bee) | Comments | Classification (Reference, MRID) |
|----------------------------------|-----------------------|--|---|----------------------------------|
| TGAI (98.6) | 72-hr | Could not be determined | - Test concentrations were evidently too high as all but lowest treatment group had at least 90% mortality after 24 hours. - Definitive LD ₅₀ could not be determined. There was 90 – 100% mortality in the 4, 8, 31, 65, and 101 µg a.i/bee and 47% mortality at the lowest dose (0.1 µg a.i/bee). | Supplemental (49766208) |
| TEP (Imidacloprid FS 350) (30.4) | 96-hr | LD ₅₀ : 85.3 (N/A) | - There was no clear indication of a dose response provided (percent mortality was 0, 20, 33, 27, 53, and 47% in the control, 1.23, 3.70, 11.1, 33.3, and 100 µg a.i/bee) - There was 46.7% mortality in the highest treatment group (100 µg a.i/bee) | Supplemental (MRID 49532101) |

NA: not available; TGAI: technical grade active ingredient; TEP: typical end use product

5.1.3.4. Non-*Apis* – Open Literature Studies

There were 5 studies evaluated from the open literature that characterize the acute contact toxicity to non-*Apis* bees including bumble bees (*B. impatiens*), Japanese orchard bees (*Osmia cornifrons*), blue orchard bees, alfalfa leaf cutting bees, and a species of stingless bee (*i.e.*, *Melipona quadrifasciata*; **Table 5-5**). The key elements of these studies are summarized below with full summaries provided in **Appendix E**. Some studies did not estimate endpoints in terms of dose (*i.e.*, µg a.i/bee) and did not provide sufficient information for estimating dose per bee.

Table 5-5. Summary of adult acute contact toxicity studies to non-*Apis* bees evaluated from the open literature

| Test Species | Test Substance (% a.i.) | Study Duration | Endpoint (95% CI) (expressed in terms of µg a.i./bee unless otherwise noted) | Comments | Classification (Reference, MRID) |
|--|----------------------------|----------------|--|---|--|
| Bumble bee (<i>Bombus impatiens</i>) | TGAI (>95) | 72-hr | No endpoint calculated; there was 72, 96, and 100% mortality for the 0.05, 0.5, and 5 lbs a.i./A treatment groups, respectively. | - Contact administration to bees was via a Potter Spray Tower - Notably high test concentrations, particularly the highest dose | <i>Qualitative</i> (Gradish 2009, 48194902) |
| Bumble bee (<i>Bombus terrestris</i>) | TGAI (purity not reported) | 72-hr | LD ₅₀ : 0.02 (NA) | - Doses that bees were exposed to not provided - The purity of imidacloprid was not reported - There was no information on the performance of the control although it was stated that trials in which over one control individual had died were not considered. - There was no indication on whether a dose-response was present | <i>Qualitative</i> (Marletto 2003, 47796306) |
| Japanese orchard bee (<i>Osmia cornifrons</i>) | TEP (17.4) | 48-hr | LD ₅₀ 0.66 (0.30 – 2.19) | - The study also exposed Japanese orchard bees to imidacloprid with fenbuconazole (mixture was 2-fold less toxic relative to imidacloprid alone). - The doses that the bees were exposed to were not provided | <i>Qualitative</i> (Biddinger 2013, 49719605) |
| Bumble bee (<i>Bombus impatiens</i> - (females only)) | TGAI (>95) | 48-hr | LD ₅₀ : 32.2 µg/kg test solution (NA) | - The test groups were presented in terms of percent active ingredient in solution as opposed to actual treatment concentrations. These concentrations were converted to µg/kg by assuming the density of the test solution was 1 g/mL | <i>Qualitative</i> (Scott-Dupree 2009, 48191904) |
| Alfalfa leafcutting bee (<i>Megachile rotundata</i>) | | | LD ₅₀ : 1.7 µg/kg test solution (NA) | | |
| Blue orchard bee (<i>Osmia lignaria</i>) | | | LD ₅₀ : 0.7 µg/kg solution (NA) | | |

| Test Species | Test Substance (% a.i.) | Study Duration | Endpoint (95% CI) (expressed in terms of µg a.i./bee unless otherwise noted) | Comments | Classification (Reference, MRID) |
|--|---|----------------|--|--|--|
| <i>Melipona quadrifasciata</i> (stingless bee) | 700 g a.i./L (70% purity assuming a density of 1 g/L) | 24-hr | LD ₅₀ : 0.023 (NA) | - No mention of control mortality but data in treatment groups were corrected for control mortality - Relatively short (24-hour) observation period -this species of stingless bee does not have a range that extends into North America and its appropriateness as a surrogate for other species of stingless bees is unknown | <i>Qualitative</i> (Tomé, 2015 49719633) |

NA: not available; TGAI: technical grade active ingredient; TEP: typical end use product

There were additional studies evaluated from the open literature that assessed the effects of acute contact exposure to adult honey bees that were determined to be unsuitable for discussion in this assessment due to various uncertainties and limitations. These studies, along with their respective associated uncertainties and limitations, are provided in **Appendix A**.

5.1.3.5. Summary of Adult Acute Contact Exposure Route to *Apis* and non-*Apis* Bees

From the suite of Tier I registrant-submitted studies, the most sensitive *Apis* adult acute contact toxicity endpoint (which could be verified by provided raw data) was a 72-hour LD₅₀ value of 0.048 µg a.i./bee (MRID 49602715). In total, there were ten studies (from both registrant-submitted and open literature sources) that tested the acute contact toxicity of imidacloprid to adult honey bees, inclusive studies listing *A. mellifera* as the test species as well as studies testing two subspecies (*A. mellifera caucasia* and *A. mellifera carnica*).

Data concerning different subspecies of *A. mellifera* and varying study durations are grouped together in **Figure 5-1** below, separated by whether the data were registrant-submitted or were evaluated from the open literature. Additionally, registrant-submitted and open literature studies that tested formulated imidacloprid do not indicate (albeit with a notably limited dataset) an increased or decreased sensitivity as compared to technical grade imidacloprid. Three open literature studies testing formulated imidacloprid on non-*Apis* species (*B. terrestris*, *O. cornifrons*, and *M. quadrifasciata*), show a range of values spanning over an order of magnitude. It is noted that for two non-*Apis* studies (Gradish, 2009, MRID 48194902 and Scott-Dupree, 2009, MRID 48191904) endpoints were not expressed in µg a.i./bee; therefore, these values are not represented in **Figure 5-1** below.

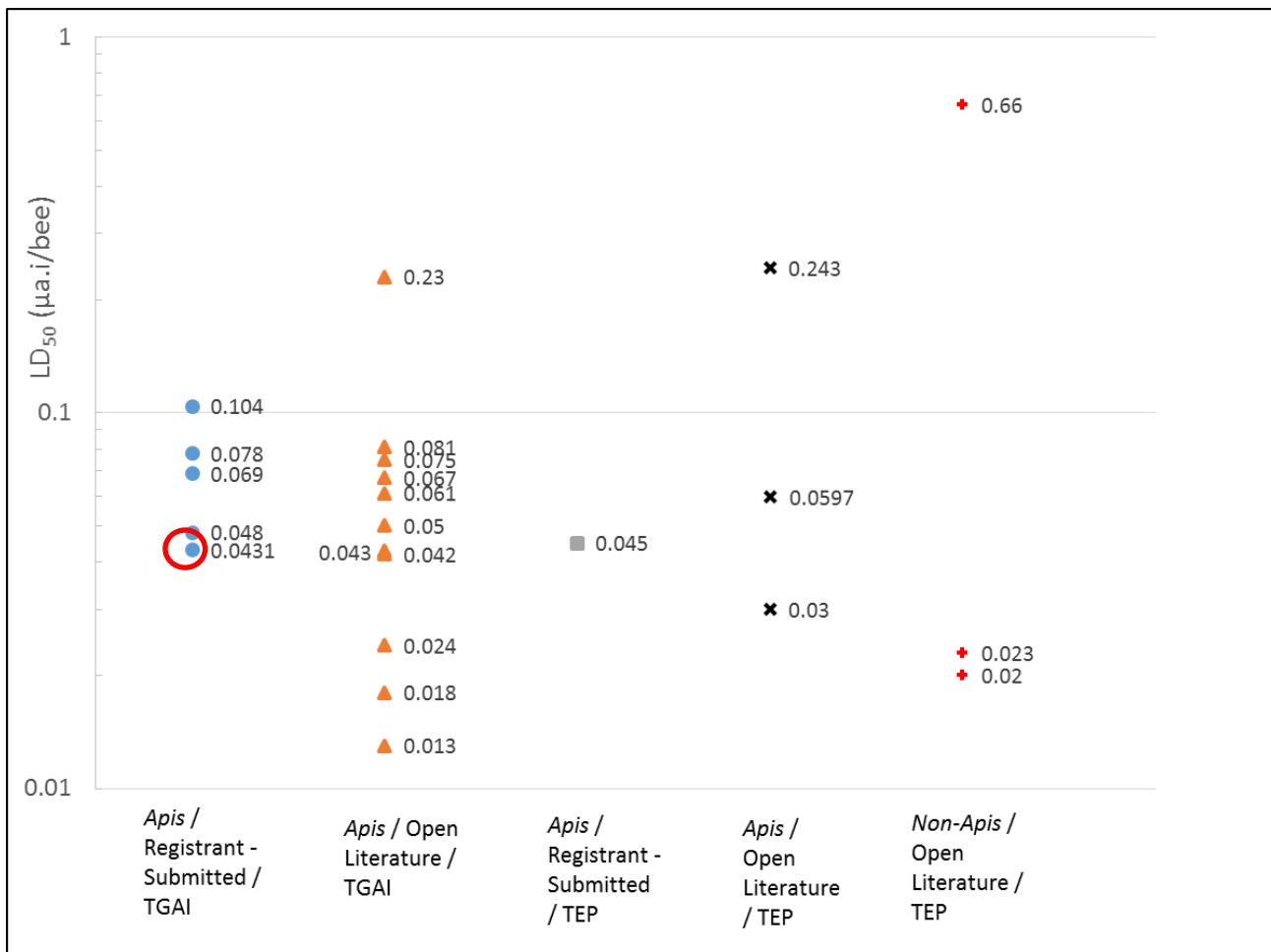


Figure 5-1. Scatterplot of adult acute contact LD₅₀ (48-96 hr) of *Apis* and non-*Apis* bees from registrant-submitted and open literature sources conducted with technical grade active ingredient (TGAI) and formulated typical end product (TEP) imidacloprid. Each point is a separate study and the red circle denotes the endpoint used for Tier I risk estimation purposes.

As depicted in the scatterplot above, the acute contact LD₅₀ values span over an order of magnitude (inclusive of all studies). The most sensitive (*i.e.* lowest) acute contact toxicity LD₅₀ value originating from a registrant-submitted study (allowing for an independent verification of the statistical analysis based on the raw data) is 0.043 µg a.i./bee. The duration of *Apis* studies conducted with TGAI (registrant submitted and open literature sources) range from 24 hours to 96 hours and the LD₅₀ values range from 0.013 – 0.104 µg a.i./bee, with a median LD₅₀ of 0.061 µg a.i./bee and a mean LD₅₀ of 0.068 µg a.i./bee. The duration of *Apis* studies conducted with TEP (registrant submitted and open literature) range from 48 – 96 hours and the LD₅₀ values range from 0.030 – 0.243 µg a.i./bee, with a median LD₅₀ of 0.052 and a mean LD₅₀ of 0.094 µg a.i./bee. It is noted that these ranges do not include endpoints that were non-definitive, nor does Figure 5-1 depict endpoints that were non-definitive.

5.1.4. Adult Acute Oral Exposure

5.1.4.1. Apis – Registrant-Submitted Studies

There are nine available acute studies to characterize the oral toxicity of imidacloprid to adult honey bees with TGAI (purities range from 98.6 - 99.8%) and one study conducted with a formulated TEP (200 g/L, 20% a.i., assuming density of 1 g/L; **Table 5-6**). These studies were generally in line with OECD TG 213 and LD₅₀ values ranged from 0.0039 µg a.i./bee – 0.151 µg a.i./bee. Clinical signs of toxicity were noted in most tests that included observation of bees being incapacitated and/or uncoordinated activity/movements and were similar to those reported for the acute contact toxicity tests. Summaries of each study are provided in **Appendix E**. From the suite of registrant-submitted Tier I adult acute contact toxicity studies (from which raw data were provided), the most sensitive *Apis* acute oral toxicity endpoint was 0.0039 µg a.i./bee (MRID 42273003 study).

Table 5-6. Summary of registrant submitted adult acute oral toxicity studies (Note: All studies tested *Apis mellifera*).

| Test Substance (% a.i) | Study Duration | Endpoint (95% CI) (expressed in terms of µg a.i/bee) | Comments | Classification (Reference, MRID) |
|------------------------|----------------|--|---|----------------------------------|
| TGAI (99.8) | 48-hr | LD ₅₀ : 0.0039 (0.0027 – 0.0054) | -- | Acceptable (42273003) |
| TGAI (98.0) | 48-hr | LD ₅₀ : >0.036 (NA) | - Clinical signs of toxicity included coordination problems, lethargy, and agitation were observed in the four highest treatment concentrations | Acceptable (49766202) |
| TGAI (98.6) | 48-hr | LD ₅₀ : >0.020 (NA) | - Clinical signs of toxicity included paralysis and spasm observed in bees at the four highest treatment groups | Acceptable (49766205) |
| TGAI (98.6) | 48-hr | LD ₅₀ : >0.045 (NA) | - Clinical signs of toxicity include bees observed being incapacitated or loss of coordination in the 3 highest treatment groups | Acceptable (49602716) |
| TGAI (98.6) | 48-hr | LD ₅₀ : >0.070 (NA) | - Clinical signs of toxicity included lethargy, loss of coordination, and immobility in the two highest treatment groups | Acceptable (49602714) |
| TGAI (98.6) | 96-hr | LD ₅₀ : >0.035 (NA) | - incapacitated/loss of coordination reported at the highest test concentration - Percent food uptake decreased in a dose dependent manner as concentration increased. | Acceptable (49602717) |
| TGAI (99.4) | 96-hr | LD ₅₀ : 0.151 (0.078 – 1.86) | - Clinical signs of toxicity included loss of coordination, lethargy, agitation, and incapacitation were observed in all but the lowest treatment groups | Supplemental (49766203) |

| Test Substance (% a.i.) | Study Duration | Endpoint (95% CI) (expressed in terms of µg a.i./bee) | Comments | Classification (Reference, MRID) |
|---|----------------|--|--|----------------------------------|
| TGAI (99.4) | 96-hr | LD ₅₀ : 0.041 (13.5 - 3980173) | - Clinical signs of toxicity included lethargy, loss of coordination problems, agitation, and inactivity were observed in the five highest treatment groups. | Supplemental (49766204) |
| TEP (200 g/L, 20% purity assuming product density of 1 g/L) | 96-hr | LD ₅₀ : 0.053 (0.038 – 0.074) 0.290 µg product/bee | - Clinical signs of toxicity that were noted were uncoordinated movement in the 2 highest treatment groups | Acceptable (49602707) |

NA: not available; TGAI: technical grade active ingredient; TEP: typical end use product

Bolded value represents endpoint to be used risk estimation

5.1.4.2. *Apis* - Open Literature Studies

Discussed below are those studies from the open literature that investigated the toxic effects to honey bees following oral exposure. All studies discussed below are a single oral exposure to 5 or more concentrations followed by a 48-96 hour observations period that generally follow OECD TG 213 with the exception of the study reported by Ramirez-Romero *et al.*, 2005 (MRID 47796305), which exposed bees to only a single concentration. As a result, this study did not estimate an endpoint (*i.e.* an LD₅₀) and does not appear in **Table 5-7** summarizing the adult acute oral exposure studies from the open literature (study summary provided in **Appendix E**). It is noted that for some studies, multiple trials were conducted, yielding several estimates of toxicity within the same study (*e.g.* Schmuck 2001 [MRID 47812303] and Schmuck 2003 [MRID 47796304]).

Table 5-7. Summary of adult acute oral toxicity studies for *Apis* bees evaluated from the open literature

| Test Species | Test Substance (% a.i.) | Duration | Endpoint (95% CI) (expressed in terms of µg a.i./bee) | Comments | Classification (Reference, MRID) |
|-------------------------------|-------------------------|----------|---|--|--------------------------------------|
| <i>Apis mellifera carnica</i> | TGAI (>98) | 48-hr | LD ₅₀ : 0.0037 (0.0027 – 0.0053) | - There was no mention of whether a dose response was present. | Qualitative (Schmuck 2001, 47812303) |
| | | | LD ₅₀ : >0.021 (NA) | | |
| | | | LD ₅₀ : 0.041 (NA) | | |
| | TEP (as WG 70) (70) | | LD ₅₀ : 0.012 (0.007 – 0.018) | | |
| | TEP (SC 200) (200 g/L) | | LD ₅₀ : 0.021 (0.015 – 0.030) | | |
| <i>Apis mellifera carnica</i> | TGAI (>98) | 48-hr | LD ₅₀ : 0.041 (NA) | - There was no mention of whether a dose response was present. | Qualitative (Schmuck 2003, |
| | | | LD ₅₀ : >0.020 (NA) | | |
| | | | LD ₅₀ : >0.081 (NA) | | |
| | | | LD ₅₀ : >0.081 (NA) | | |

| Test Species | Test Substance (% a.i) | Duration | Endpoint (95% CI) (expressed in terms of µg a.i/bee) | Comments | Classification (Reference, MRID) |
|---------------------------------|------------------------|----------|--|---|---|
| | | | LD ₅₀ >0.081 (NA) | | 47796304) |
| | | | LD ₅₀ : >0.081 (NA) | | |
| | | | LD ₅₀ : >0.081 (NA) | | |
| <i>Apis mellifera mellifera</i> | TGAI (98) | 48-hr | LD ₅₀ : 0.0048 (0.0045 – 0.0051) | - Analytical confirmation of imidacloprid in the treatment concentrations was not conducted | <i>Qualitative</i> (Suchail 2000 47800513) |
| <i>Apis mellifera caucasia</i> | | | LD ₅₀ 0.0065 (0.0047 – 0.0083) | | |
| <i>Apis mellifera</i> | TGAI (97) | 96-hr | LD ₅₀ : 0.037 (NA) | - Analytical confirmation of imidacloprid in the treatment concentrations was not conducted - No mention of whether a dose response was present | <i>Qualitative</i> (Suchail 2001, 47523402) |
| <i>Apis mellifera</i> | TGAI (99.9) | 48-hr | LD ₅₀ : 0.536 (0.339 – 1.18) | - Also tested myclobutanil, propiconazole, flusilazole, and tebuconazole in separate combinations with imidacloprid (no endpoint significantly lower than imidacloprid alone) - No mention of any presence of control mortality | <i>Qualitative</i> (Thompson 2014a, 49750606) |
| <i>Apis mellifera</i> | TEP (Confidor – 17.8%) | 72-hr | LD ₅₀ : 0.194 (NA) | - Study states that 42% of the data presented is from another source making this study both a primary source and review (secondary source) article (no way of discriminating the primary and secondary source data from the available information in the study) - The number of exposed bees per treatment group is not specified. - There was no mention of whether a dose response was present. | <i>Qualitative</i> (Laurino 2013, 49719620) |
| <i>Apis mellifera ligustica</i> | | | LD ₅₀ : 0.030 (NA) | | |
| | | | LD ₅₀ : 0.065 (NA) | | |
| | | | LD ₅₀ : 0.025 (NA) | | |
| | | | LD ₅₀ : 0.035 (NA) | | |

NA: not available; TGAI: technical grade active ingredient; TEP: typical end use product

5.1.4.3. Non-Apis – Registrant Submitted Studies

In an acute oral study, 30 bumble bees (*Bombus terrestris*) per group were exposed to nominal concentrations of TGAI (98.6%) imidacloprid at 0.110, 0.330, 0.530, 0.720, and 0.960 µg a.i./bee (including a negative control). Clinical signs of toxicity included paralysis, and spasms at all treatment concentrations. It was reported that most of the bumble bees that ingested 0.330 µg a.i./bee or more died within 24 hours. The 72-hour LD₅₀ was determined to be 0.170 µg a.i./bee; the study is classified as acceptable.

5.1.4.4. Non-Apis – Open Literature Studies

In Marletto, 2013 (MRID 47796306, discussed above regarding adult acute contact toxicity results), 5 bumble bee (*B. terrestris*) workers were placed in each cage, although it is not known how many replicates per treatment group were used. Additionally, the actual test concentrations to which the bees were exposed was not reported. The 72-hour oral LD₅₀ was determined to be 0.02 µg a.i./bee (95% confidence intervals not available). Limitations in addition to those listed above include the purity of imidacloprid not being provided, no information on the performance of the control available, and no analytical verification of the test substance in the provided sucrose.

In a study by Thompson *et al.* 2014b (MRID 49719632), TGAI (>99% purity) was administered to bumble bees (*B. terrestris*) in a 30% sucrose solution at nominal imidacloprid concentrations of 0 (control), 1.0, 10, and 100 µg a.i./L. After 3 days of exposure, mortality was 15, 5, 15, and 15% for the control, 1.0, 10, and 100 µg a.i./L groups, respectively. Additionally, it was reported that a significantly (statistical results not provided) lower spiked sucrose was consumed in the 10 and 100 µg a.i./L groups. Limitations in this study include that the discussion of certain results are not present. For example, mortality data were excluded if 100% mortality was reached before the end of the experimental period. Without raw data to confirm any of the statistical findings, the results of this study are uncertain. Also, despite concentrations spanning two orders of magnitude, mortality did not show evidence of a dose response.

*5.1.4.5. Summary of Adult Acute Oral Exposure Route to *Apis* and non-*Apis* Bees*

In total, there were 15 studies (from both registrant-submitted and open literature sources) that tested the acute oral toxicity of imidacloprid to adult honey bees, inclusive of studies indicating *A. mellifera* as the test species as well as studies testing two subspecies (*A. mellifera caucasia* and *A. mellifera carnica*). Similar to the dataset for the acute contact toxicity to adult bees, the available studies do not show a clear trend in differential sensitivity of one subspecies of *A. mellifera* as compared to others, nor do the data allow for making inferences of changes in toxicity associated with duration of the post-exposure observation period. Of the 15 acute oral studies for adult honey bees that tested TGAI (inclusive of both registrant-submitted and open literature sources), less than half (47%) yielded endpoints that were definitive LD₅₀ values. The non-definitive endpoints were not plotted in **Figure 5-2** depicting registrant and evaluated open literature *Apis* and non-*Apis* studies conducted with TGAI and formulated TEP of imidacloprid.



Figure 5-2. Scatterplot of adult acute oral toxicity of *Apis* and non-*Apis* bees from registrant-submitted and open literature sources conducted with technical grade active ingredient (TGAI) and formulated typical end product (TEP) imidacloprid. Red circle denotes endpoint used for Tier I risk estimation purposes.

As depicted above, the acute oral LD₅₀ values span over two orders of magnitude, ranging from 0.0039 – 0.536 μg a.i./bee (inclusive of registrant-submitted and open literature studies testing TGAI imidacloprid, observations periods of 48 – 96 hours). From the suite of Tier I registrant-submitted studies, the most sensitive *Apis* adult acute oral toxicity endpoint conducted was a 48-hour LD₅₀ value of 0.0039 μg a.i./bee (MRID 42273013). The mean and median for TGAI studies (registrant-submitted and open literature) are 0.087 and 0.039 μg a.i./bee, respectively, and for formulated TEP imidacloprid studies are 0.054 and 0.033 μg a.i./bee, respectively. It is noted that these measures of central tendency do not include endpoints that were non-definitive.

5.1.5. Adult Chronic Oral Toxicity (*Apis* and non-*Apis*)

There are 5 studies available from combined registrant-submitted and open literature sources that examine the chronic toxicity of imidacloprid through dietary exposure for honey bee and bumble bee adults (results combined into one summary table and discussion due to low number of studies relative to the acute data). These effects are summarized in the **Table 5-8** below. Where available, the no observed adverse effect concentration (NOAEC) and the lowest observed adverse effect concentration (LOAEC) are provided; otherwise, a description of the report's effects is tabulated. Summaries of each study, including methods and full findings, are provided in **Appendix E**.

5.1.5.1. *Apis* – Registrant-Submitted Studies

Table 5-8. Summary of registrant-submitted and evaluated open literature studies assessing the chronic oral toxicity of imidacloprid to *Apis* and non-*Apis* adults.

| Test Species | Test Substance (% purity) | Exposure Period | Exposure concentrations | Reported Effects | Comments | Classification (Reference / MRID) |
|-----------------------|---------------------------|-----------------|--|---|---|-----------------------------------|
| <i>Apis mellifera</i> | TGAI (99.4%) | 10 days | 0 (control), 10, 20, 50, and 100 µg a.i./L | NOAEC/LOAEC (mortality): 100/>100 µg a.i/bee NOAEC/LOAEC (food consumption: <10/10 µg a.i./L (equivalent to <0.0039 µg a.i/bee)) | - Concentrations in terms of mean intake over study course (excluding control) were 0.0039, 0.0063, 0.016, and 0.028 µg a.i/bee) - No definitive NOAEC established based on food consumption | Supplemental (49511703) |
| <i>Apis mellifera</i> | TGAI (99.4%) | 10 days | 0 (control), 1.1, 1.8, 3.3, 5.0, 8.4, and 14 ng a.i./bee/day | NOAEL/LOAEL (mortality): 0.0018/0.0033 µg a.i/bee/day NOAEL/LOAEL (food consumption: 0.0011/0.0018 µg a.i/bee/day) | - No deviations from OECD draft (2016) guideline: Chronic Oral Toxicity Test - Signs of toxicity included moribund appearance observed at ≥ | Acceptable (50399101) |

| Test Species | Test Substance (% purity) | Exposure Period | Exposure concentrations | Reported Effects | Comments | Classification (Reference / MRID) |
|--------------------------|---|-----------------|---|--|---|--|
| | | | | | 8.4 ng ai/bee/day | |
| <i>Apis mellifera</i> | Admire 240 (24.0% a.i assuming a product density of 1 g/L) | 10 days | 0 (control), 0.08, 0.16, 0.24, and 0.30 ng a.i/bee | NOAEC/LOAEC (mortality and body weight): 0.16/0.24 ng a.i/bee (0.00016/0.00024 µg a.i/bee) | - Test conducted with formulated product (Admire 240F) but concentrations provided in terms of active ingredient - No analytical verification of test solutions - No estimation of daily syrup consumption - Clinical signs of toxicity included tumbling and trembling at all doses | <i>Qualitative</i> (Boily 2013, 49750601) |
| <i>Apis mellifera</i> | Imidacloprid (purity not clear from citation but stated to be obtained from Cluzeau (Analytical Chemistry Materials Provider, France) | 10 days | 0 (control), 0.70, 7.0, 70 µg/L | Mortality: 5.6, 10.4, 16.3, and 17.4%, respectively | - Mortality for all treatment groups was significantly increased from control ($p<0.05$) - No significant effects reported for food consumption ($p>0.05$) | <i>Qualitative</i> (Alaux 2010, 48077922) |
| <i>Apis mellifera</i> | Analytical standard (exact purity not provided) ¹ | 6 days | 0 (control), 0.08, 0.2, 0.51, 1.3, 3.2, 8.0, 20, 50, and 125 µg a.i/L | No reported effects up to and including the highest concentration | - Mortality, locomotory activity, and food consumption were assessed - Results not reported as percent | <i>Qualitative</i> (Cresswell 2012, 497196610) |
| <i>Bombus terrestris</i> | Analytical standard (exact | | | 38% reduction in food consumption when ingesting 4.9 | | |

| Test Species | Test Substance (% purity) | Exposure Period | Exposure concentrations | Reported Effects | Comments | Classification (Reference / MRID) |
|--------------------------|--|--|--|---|---|--|
| | purity not provided) ¹ | | | ng a.i./bee (0.0049 µg a.i./bee) (percent effects reported only for certain concentrations) | difference from control | |
| <i>Apis mellifera</i> | Analytical standard (exact purity not provided) ¹ | 3 day exposure (followed by 5 days of untreated sucrose), or 8 day continuous exposure (treated sucrose) | 0 (control) and 125 µg a.i./L (0.0022 µg a.i./bee/day) | No reported effects in 3-day and 8-day exposures | - Food consumption and locomotory activity were measured | <i>Qualitative</i> (Cresswell 2013, 49719611) |
| <i>Bombus terrestris</i> | Analytical standard (exact purity not provided) ¹ | | | Significant reductions from control ($p<0.05$) in food consumption and locomotion | - Bumble bees on 3 days exposure showed recovery of these effects | |

¹As confirmed by study author, email communication 03/16/15

Bolded value represents endpoint to be used risk estimation

5.1.6. Larval Acute Oral Toxicity

5.1.6.1. Apis - Registrant Submitted Studies

There are no registrant-submitted studies or studies that were surveyed as part of the open literature effort that concern the acute oral exposure to honey bee larvae.

5.1.6.2. Non-Apis – Open Literature Studies

In a study conducted by Tomé *et al.* (2012), the larvae of the stingless bee *Melipona quadrifasciata anthidioides* were exposed to varying concentrations of imidacloprid TEP (reported as 700 g a.i./L, 70% purity assuming product density of 1 g/L), for up to 5 days, depending on when adults emerged. Observations were made for mortality, body mass, and developmental time. Colonies were collected in the field and maintained in an experimental apiary within a laboratory at Federal University, Vicoso, Brazil. Brood chambers containing eggs were removed from the hives and transferred to artificial cells containing larval diet (also obtained from the field) that was either untreated or spiked with 18 varying concentrations of imidacloprid ranging from 0.0056 to 56 µg a.i./bee. Upon emergence, the adult workers were marked with different colors to facilitate age monitoring and were fed with untreated honey and pollen syrup (not further described in the article). For each treatment concentration, there were five replicates of 24 larvae each. There was 97% control survival and survival was above 50% only at the lowest treatment concentration (0.0056 µg a.i./bee). There was a negative correlation between

imidacloprid dose and median survival time (TL_{50}). According to the study authors, body mass and development time, by contrast, were not significantly affected; however, statistical results were not provided. The authors noted that stingless bee larvae ingested the entire dose, irrespective of the treatment concentration. While a definitive endpoint was unclear from the study, none of the larvae reached pupation at treatment concentrations higher than 0.28 µg a.i./bee. Limitations from the study include no analytical verification of the concentrations of imidacloprid in the treatment groups and the fact that no explicitly stated endpoint was available from the study. Additionally, it is noted that the bees were wild collected as well as their diet and it is an uncertainty of the prior exposure to pesticides. Finally, it is noted that the geographic distribution of this species of stingless bee does not extend into North America, and it is unclear to what extent this species is representative of other species of stingless bees.

5.1.7. Larval Chronic Oral Toxicity

5.1.7.1. Apis – Registrant-Submitted Studies

In a chronic toxicity test, a repeated dose of TGAI (99.4%) was administered to honey bee larvae which were then monitored through pupation and emergence over the course of the 21-day study (MRID 49090506). This study followed the test protocol recommendations of Aupinel *et al.* (2009)²⁵ with modifications. Four independent test runs were conducted. At day +1 (Day 0 was the anticipated day of larval hatching), first instar bee larvae (*A. mellifera carnica*) were transferred from their bee hive into an artificial *in vitro* testing system. The bee larvae were fed with standardized amounts of untreated artificial diet at Day +1 and Day +3. On Day +4, +5 and +6, the bee larvae in the test item treatment groups were fed with standardized amounts of diet spiked with imidacloprid. Additionally, beginning on Day +4, the bee larvae in the reference item treatment group were fed with standardized amounts of diet spiked with dimethoate TGAI (98.5%) at 3.0 µg a.i./larva. Concurrently, the bee larvae in the control group (on Days +4, +5 and +6) and in the reference item group (on Days +5 and +6) received untreated standardized diet, respectively. The nominal concentrations of imidacloprid of treatment groups in the diet was 5, 10, 20 and 40 µg a.i./kg diet. Percent recovery of imidacloprid in the treatment concentrations was determined to be 98-115% of the nominal concentrations.

The study authors set a control mortality validity criterion of Day 0 to Day 22 mortality of equal to or less than 30%. In runs 2, 3, and 4 of the definitive test, this criterion was met with control mortality ranging from 15 – 19%. The first run yielded a control mortality of 37% by Day 22 of the study. Consequently, the combined results of runs 2, 3, and 4 (yielding a Day 22 mean control mortality of 16.7%) were used to verify the results of the study. There was generally no dose response observed either in each individual trial or when the results of the trials were combined. Specifically, in runs 2 and 3, the percent mortality in the highest treatment concentration (40 µg a.i./kg diet) was lower than that of the lowest treatment concentration (5 µg a.i./kg diet). In run 4, although the percent morality in the highest

²⁵ Aupinel, P., Fortini, D., Michaud, B., Medrzycki, P., Padovani, E., Przygoda,D., Maus, Ch., Charriere, J.D., Kilchenmann, V., Riessberger-Galle, U., Vollmann, J.J., Jeker, L., Janke, M., Odoux, J.F., Tasei, J.N. 2009. Honey bee brood ring-test: method for testing pesticide toxicity on honey bee brood in laboratory conditions; published in: Hazards of pesticides to bees: 10th International Symposium of the ICPBR Bee Protection Group, Bucharest (Romania), October 8-10, 2008. Julius-Kühn Archive 423: 96-102

treatment concentration exceeded that of the lowest concentration, percent mortality at the two middle treatment concentrations (10 and 20 µg a.i./kg diet) was roughly half of that observed at the lowest and highest concentrations. The percent mortality of runs 2, 3, and 4 combined were 16.7, 25.4, 10.0, 24.6, and 16.7 for the control, 5, 10, 20, and 40 µg a.i./kg diet groups, respectively. Due to the variability in the response across runs, as well as the absence of a monotonic dose response in the study, there is uncertainty in the NOAEC derived from this study. However, as the control mortality criterion was met for 75% of the runs tested and the study generally followed the protocol recommendations described above, this study is classified as supplemental and suitable for quantitative risk assessment purposes. The NOAEC and LOAEC for this study were determined to be 40 and >40 µg a.i./kg diet, respectively or 0.00183 and >0.00183, respectively when expressed on a µg a.i./bee basis.

5.1.7.2. Non-*Apis* – Open Literature Studies

In a study by Abbott *et al.* (2008, MRID 47812301), the eggs of blue orchard bees (*Osmia lignaria*) were exposed to varying concentrations of TGAI (97.5% purity) into microwell plates and until adulthood, representing a duration of approximately 30-40 days (**Table 5-9**). The bees were obtained as over-wintering adults in cocoons and kept in storage until the start of the experiment. Parameters that were assessed included the timing and completion of larval development, the number of days between the egg stage and the beginning of each larval stage, and the start of cocoon formation and its completion, including darkening. Time was also recorded from the date of first observation (egg stage) to the date each larva finished spinning a thin white cocoon around itself, and to the date the darkened cocoon was completed. Confirmation of the concentrations of the final pollen provisions were performed by Bayer CropScience and yielded levels for the low, medium, and high treatments of 2.7, 35, and 276 µg/L, respectively for imidacloprid.

Further details on the method and limitations of this study are provided in **Appendix E**.

Table 5-9. Summary of results from Abbott *et al.*, 2008 examining the effects of imidacloprid TGAI on larval development of blue orchard bees (*Osmia lignaria*).¹ (Note: Study classified as qualitative)

| Response variable | 3 µg/L | 30 µg/L | 300 µg/L |
|--|-------------------------|-------------------------|-------------------------|
| Lab Component – Own Pollen | | | |
| Time to reach last larval stage (days) | NS | NS | NS |
| Time to spin a cocoon (days) | NS | NS | NS |
| Time to finish darkening a cocoon (days) | NS | NS | Males: NS Females: ↓ |
| Time to emerge from cocoons (days) | NS | NS | NS |
| Weight of bees after emergence from cocoon (grams) | Males: ↑ Females: NS | Males: ↑ Females: NS | Males: ↑ Females: NS |
| Lab Component – New Pollen | | | |
| Time to reach last larval stage (days) | NS | NS | NS |
| Time to spin a cocoon (days) | NS | NS | NS |
| Time to finish darkening a cocoon (days) | NS | NS | NS |
| Time to emerge from cocoons (days) | NS | NS | Males: NS Females: ↓ |
| Weight of bees after emergence from cocoon (grams) | NS | NS | NS |
| Field Component | | | |
| Time to reach last larval stage (days) | NS | Males: NS | Males: ↑ |

| Response variable | 3 µg/L | 30 µg/L | 300 µg/L |
|--|--------|-------------------------|-------------------------|
| | | Females: ↑ | Females: NS |
| Time to spin a cocoon (days) | NS | Males: ↑ Females: NS | NS |
| Time to finish darkening a cocoon (days) | NS | Males: ↑ Females: ↑ | Males: ↑ Females: NS |
| Time to emerge from cocoons (days) | NS | NS | NS |
| Weight of bees after emergence from cocoon (grams) | NS | NS | NS |

¹ Means not presented. Arrow up or down denotes significant ($p<0.05$) increase or decrease from control, respectively; NS = not significant ($p>0.05$)

5.1.8. Acute and Chronic Toxicity of the Degradation Products of Imidacloprid

As discussed in **Section 4**, imidacloprid can degrade into various products both within the plant as well as in the soil. Specifically, imidacloprid is metabolized within the plant to IMI-4,5-OH, which then degrades to IMI-5-OH, and subsequently to IMI-olefin. In the aerobic soil metabolism pathway, the olefin-IMI metabolite is formed at a minor (*i.e.* less than 10% of the applied residues) rate.

While there are no registrant-submitted studies to characterize the toxicity of these metabolites, there are studies available from the open literature that investigated the acute and chronic oral toxicity of these metabolites to adult honey bees. As described in **Section 4**, parent imidacloprid undergoes metabolism to several degradates that include IMI-olefin, IMI-5-OH, IMI-4,5-OH, desnitro-IMI, 6-CNA, and a urea metabolite. **Table 5-10** below summarizes the studies assessing the acute oral toxicity of the various degradation products of imidacloprid. It is important to note here that although there is some chronic data for degradates, no chronic data is available for the degradates known to have some acute toxicity to bees and the chronic data available for some degradates suggest a similar lack of toxicity as those degradates exhibit on an acute basis. Also, this risk assessment uses a total toxic residue (TTR) approach including parent, olefin and hydroxy degradates to evaluate risk. On an acute basis, this approach is conservative given that parent imidacloprid is observed to be the most toxic. On a chronic basis, there is some uncertainty over the conservatism of this approach given the lack of chronic data for those two degradates.

There are registrant-submitted and open literature studies available to characterize the acute and chronic toxicity of the various degradation products of imidacloprid. The registrant-submitted studies primarily concern the chronic oral toxicity to honey bee adults of the urea metabolite and 6-CNA metabolites. Additionally, there are two studies from the open literature that assess the acute oral toxicity to honey bee adults to several degradates including IMI-olefin, IMI-5-OH, IMI-4,5-OH, desnitro-IMI, 6-CNA, and the urea metabolite.

Table 5-10. Summary of acute oral toxicity studies testing the degradates of imidacloprid in the open literature

| Species | Test Substance (% a.i.) | Duration | Endpoint ¹ | Comments | Classification (Reference, MRID) |
|-----------------------|-------------------------|----------|---|---|-----------------------------------|
| <i>Apis mellifera</i> | IMI-olefin (>98) | 72-hr | LD ₅₀ : >0.036 µg a.i/bee (NA) | - No mention of whether dose response was present | Qualitative |

| Species | Test Substance (% a.i) | Duration | Endpoint ¹ | Comments | Classification (Reference, MRID) |
|-----------------------|-----------------------------|----------|---|---|--------------------------------------|
| <i>Apis mellifera</i> | IMI-5-OH (>98) | 96-hr | LD ₅₀ : 0.159 µg a.i/bee (NA) | <ul style="list-style-type: none"> - Unclear from methods section whether analytical confirmation of the test substance in the treatment groups was conducted - Failure to capture sufficient dose response to enable calculation of LD₅₀ values | (Schmuck 2003, 47800520) |
| | 4,5-OH imidacloprid (>98) | | LD ₅₀ : >0.049 µg a.i/bee (NA) | | |
| | 6-CNA (>98) | | LD ₅₀ : >121 µg a.i/bee (NA) | | |
| | Urea metabolite (>98) | | LD ₅₀ : >99.5 µg a.i/bee (NA) | | |
| <i>Apis mellifera</i> | IMI-olefin (>97) | 96-hr | LD ₅₀ : 0.023 µg a.i/bee (NA) | <ul style="list-style-type: none"> - Analytical confirmation of imidacloprid in the treatment groups was not conducted - No mention of whether a dose response was present | Qualitative (Suchail 2001, 47523402) |
| | IMI-5-OH (>97) | | LD ₅₀ : 0.222 µg a.i/bee (NA) | | |
| | 4,5-OH imidacloprid (>97) | | LD ₅₀ >1 µg a.i/bee (NA) | | |
| | Desnitro-imidacloprid (>97) | | LD ₅₀ >1 µg a.i/bee (NA) | | |
| | 6-CNA (>97) | | LD ₅₀ >1 µg a.i/bee (NA) | | |
| | Urea metabolite (>97) | | LD ₅₀ >1 µg a.i/bee (NA) | | |

¹Numbers in parentheses for acute endpoints refer to 95% confidence intervals, listed as NA if not available

The available suite of chronic oral studies assessing the toxicity of the urea metabolite and 6-CNA, indicate that that these two degradates do not elicit a lethal effect significantly increased from that of controls up to and including a dietary concentration of 10 µg a.i/L. The test designs of all studies were generally the same although one key difference was the level of control mortality across studies, which ranged from 0 – 44% for the chronic urea metabolite studies and from 0 – 54% for the 6-CNA studies. While there is, at present, no formal guideline for a chronic adult 10-day oral toxicity test with honey bees, a control mortality level of above 20% suggests that husbandry conditions or general procedures in conducting the test may not have been optimal and therefore the ability to discern a true treatment-related effect may be compromised. As a result, the studies with greater than 20% mortality are not tabulated below.

As the study designs were so similar, the major elements of each study are summarized in **Table 5-11** below as opposed to a summary discussion of each study. All studies were conducted with *A. mellifera*, were 10 days in duration (*i.e.*, 10 days of exposure), and tested either the urea metabolite or 6-CNA at concentrations of 0.1, 1.0, and 10 µg a.i/L in the diet (sucrose solution). Additionally, there was generally no evidence of analytical verification of the concentrations of the urea metabolite and 6-CNA

in the treatment solutions. Finally, there were generally no observations of clinical signs of toxicity recorded for these studies (*i.e.* studies did not report whether such effects were examined).

The results for the urea metabolite studies indicate that concentrations up to and including 10 µg a.i/L do not have an increased mortality effect to adult honey bees as compared to the control group. Two studies (MRIDs 49602711 and 49602713) also included food consumption as a response variable, but this endpoint was not subjected to statistical analysis by the study authors.

Similarly, the results of the studies conducted with 6-CNA generally indicate (when not confounded by excessive control mortality; these studies not tabulated below) that concentrations up to and including 10 µg a.i/L do not result in an increased level of mortality when compared to controls after a 10-day exposure. As with the urea metabolite studies, for certain tests (MRIDs 49602710 49602720), food consumption was included as a response variable, although not statistically analyzed in the original study reports.

Interestingly, for MRID 49602711 (urea metabolite study), the bees that were reported to be older (*i.e.* 22-45 days) had a 3-fold higher level of control mortality than the same study that included a component that tested 12 to 17 day-old bees (results not tabulated below for this component). Additionally, while the age of the bees was not reported, MRIDs 49602713 and 49602710 tested bees characterized as “house” bees and “field” bees that showed markedly different rates of control mortality despite both cohorts being subjected to the same methodology within each test (results not tabulated below for this component). It is an uncertainty whether the age of the test bees had an effect on the results of these studies.

Table 5-11. Summary of chronic adult oral toxicity studies with urea metabolite and 6-CNA (all studies conducted with *Apis mellifera*)

| Experimental Design | Results (presented for the control, 0.1, 1.0, and 10 µg a.i/L in ascending order) | Comments | Classification (MRID) |
|--|--|--|--|
| Urea metabolite (99.4% purity for all studies) | | | |
| 3 reps/trt, 10 bees/rep | Mortality: 10, 37, 3, and 63% Food Consumption (per 10 bees): Mean food uptake was 4.87, 4.64, 3.93, and 3.57 g | - Bees were 12-17 days old - Statistical analysis of data not conducted by study authors | <i>Acceptable</i> (49602711) ¹ |
| 5 reps/trt, 10 bees/rep | Mortality: 4, 10, 8, and 12% Food Consumption (per 10 bees): 7.30, 7.27, 7.27, and 7.54 g | - Test bees characterized as “house” bees, with no age reported - No significant differences in mortality, food consumption not statistically analyzed by study authors | <i>Acceptable</i> (49602713) ² |
| | Mortality: 0, 8, 6, and 0% | - Statistical analysis of the data not conducted by the study authors - Age of bees up to 5 days old (post-emergence). | <i>Acceptable</i> (49602721) ¹ |
| 6-CNA (99.6% purity for all studies except MRID 49602720 where purity not reported) | | | |

| Experimental Design | Results (presented for the control, 0.1, 1.0, and 10 µg a.i/L in ascending order) | Comments | Classification (MRID) |
|--|--|--|--|
| | Mortality: 4, 10, 4 and 6% Food Consumption (per 10 bees): 7.29, 7.24, 7.34, and 7.19 g | - Test bees characterized as "house" bees, with no age reported - No significant differences in mortality, food consumption not statistically analyzed by study authors | <i>Acceptable</i> (49602710) ² |
| 3 reps/trt, 10 bees/rep | Mortality: 7, 10, 7, and 7% Food consumption (per 10 bees): 5.94, 5.87, 5.50, and 5.8 | - Test bees were 12-17 days old - Statistical analysis of data not conducted by study authors | <i>Acceptable</i> (49602720) ¹ |
| 5 reps/trt, unspecified number of bees/rep | Mortality: 0, 2, 4, and 0% | - Age of test reported to be up to 5 days old | <i>Acceptable</i> (49602722) ³ |

¹Results are the same as those provided in Schmuck 2004 ("Germany II" testing facility)

²Results are the same as those provided in Schmuck 2004 ("Germany III" testing facility)

³Results are the same as those provided in Schmuck 2004 ("Germany I" testing facility)

5.2. Tier II Studies

As discussed in the Pollinator Risk Assessment Guidance (USEPA *et al.* 2014), Tier II encompasses studies that characterize effects at the colony level. The need for these studies depends on whether Tier I LOCs are exceeded, the availability of data, and the nature of uncertainties that warrant further testing. Tier II studies can include those characterized as "semi-field" studies where small colonies are enclosed in tunnels, along with pesticide-treated crops. Additionally, these studies may be a feeding study design in which whole colonies are provided pesticide-treated sucrose or pollen and the colonies are not confined to enclosures (*i.e.*, the bees are free-foraging). Typically, semi-field studies are conducted under conditions that represent the worst-case exposure scenario of proposed uses to the entire colony or designed to address specific uncertainties with respect to the effects of the colony. Tier II study designs may be amenable to additional treatment levels and replication, this facilitating quantification of an application rate-response (semi-field tunnel study) or dose-response (feeding study) relationship at the colony level and determination of a NOAEC.

For imidacloprid, both registrant-submitted and open literature Tier II-type studies are available. The registrant-submitted Tier II study (MRID 49510001) employed a feeding design in which 84 hives were provided either untreated sucrose solution within the hives or sucrose spiked with one of 5 concentrations of imidacloprid. Additionally, there are a number of Tier II-type studies (inclusive of tunnel and feeding study designs) that were evaluated by EPA, Health Canada's Pest Management Regulatory Agency (PMRA), and the California Department of Pesticide Regulation (CDPR) (referred to as "tri-Agency") open literature review effort. While the registrant-submitted study exposed honey bee colonies to varying concentrations of imidacloprid spiked in sucrose solutions, the suite of open literature studies concern both *Apis* and non-*Apis* species (*B. terrestris* and *B. impatiens*) exposed to imidacloprid through diet (*i.e.*, both spiked sucrose and spiked pollen).

5.2.1. Registrant-Submitted

5.2.1.1. Colony Feeding Study

The registrant-submitted colony feeding study was conducted with honey bees to assess the potential for long-term effects, including colony overwintering survival, resulting from exposure to imidacloprid. The study was conducted in 12 test areas (Apiaries A – L) reported to be of low agricultural cultivation in North Carolina from June 21, 2013 to March 24, 2014. Eighty-four hives were divided according to hive strength (number of brood frames) with the strongest 7 hives assigned to Apiary A and the weakest 7 hives assigned to Apiary L (*i.e.*, the study design was stratified to account for differences in colony strength). Within each apiary, the 7 hives were randomly assigned to treatment groups. At each apiary, five test hives were artificially fed with 50% sugar solution spiked with imidacloprid at 12.5, 25, 50, 100 or 200 µg a.i./L for six weeks continuously in the field, with two hives at each apiary serving as controls. The 8th colony at each apiary served as a monitoring hive to characterize the alternative sources of forage (pollen/nectar) of the test colonies as well as to monitor for the potential contamination with other pesticides. The nominal test concentrations of 12.5, 25, 50, 100, and 200 µg/L were measured in the feeding solution over the study period for mean measured concentrations of 11.0, 23.3, 46.7, 96.3, and 189.6 µg/kg, respectively. Eight Colony Condition Assessments (CCAs) were conducted during the study. Three CCAs (CCA1 - 3) were conducted prior to feeding (*i.e.*, pre-exposure phase) to determine hive strength (number of adult and developing bees) and initial hive conditions. A CCA was conducted during exposure with another one conducted one week after termination of exposure (CCA4 and CCA5, respectively) which characterize hive condition during exposure (*i.e.*, exposure phase). Two more CCAs were conducted at 5 and 10 weeks after exposure (CCA6 and CCA7, respectively) to assess the chronic effect following exposure to imidacloprid and to characterize pre-overwintering hive conditions (post-exposure phase). A final CCA was conducted after overwintering in March 2014 (CCA8) to assess potential exposure impact on survival and chronic colony-level effects. Multiple parameters, such as hive weight, number of individuals at different life stages in the hive, hive honey and pollen stores, and hive overwintering survival, were measured during the course of the study.

A joint review effort of this study was conducted by the United States Environmental Protection Agency (EPA), Canada's Pest Management Regulatory Agency (PMRA), and the State of California Department of Pesticide Regulation (CDPR). As part of that effort, a separate statistical analysis was conducted by each regulatory entity as an independent verification of the results from the analysis provided by the registrant. These analyses were distinct in approach but generally yielded similar statistical results. It is noted here that when weighing the statistical results as well as biological concerns, particularly as they relate to honey bee biology at the colony level, EPA, PMRA, and CDPR arrived at the same overall conclusion and are therefore harmonized in terms of the determination of an overall NOAEC and LOAEC yielded by this study. For further details on the methodology and a more detailed discussion of the results of this study, please refer to **Appendix H**.

Colony Feeding Study Endpoints

While there were uncertainties that were generally related to inherent aspects of any semi-field or full field study design (such as dilution of the test chemical through alternative sources of forage, detection of other chemicals in the monitoring hives), this study still provides information on a number of colony condition parameters about the long-term effects (including overwintering) from dietary exposure to imidacloprid at the colony level.

As indicated in the results section above, the PMRA, EPA, and CDPR analyses determined significant effects (at both the 0.05 and 0.1 alpha levels) in the 47, 96, and 190 µg/L groups across multiple CCAs for the majority of response variables. Specifically, for the 96 and 190 µg/L treatment groups, significant effects ($p<0.05$) were determined for every response variable and persisted across at least 2 CCAs, along with very high overwintering mortality. While the 47 µg/L group had overwintering mortality similar to the controls, colony condition effects were different from controls with an early onset of effects which tended to persist, and notably poorer colony condition in surviving hives after overwintering in comparison to controls.

Conversely, there was not a strong indication from the PMRA, EPA, and CDPR analyses of an impact at the colony level at the 11 and 23 µg/L treatment groups. This is evidenced not only by a general lack of statistical findings ($p>0.1$) at these treatment levels but in cases where significant effects were determined, they either did not show strong dose-responsiveness, did not persist across multiple CCAs, or were considered potential transient effects (e.g., at CCA6) which did not persist after overwintering. This latter point was the case for the total life stage and pupal cell findings in which the PMRA analysis determined significant effects at all treatment levels at CCA6 (EPA also determined a significant reduction in pupal cells at the lowest treatment group of 11 µg/L at CCA6). As well at CCA6, PMRA determined significant effects on the proportion of eggs and larvae at 23 µg/L treatment (but not at the 47 µg/L). For these two lowest treatment groups (11 and 23 µg/L), the colony condition of surviving hives at CCA8 following overwintering was similar to controls, indicating the effects observed at CCA6 were likely transient and the colony was able to compensate for these effects.

When examining the effects on food stores (pollen and nectar), the PMRA, EPA, and CDPR analyses did not determine any consistent and significant reductions in pollen and nectar stores at the 11 and 23 µg/L treatment groups. This is distinguished from the 47 µg/L group where effects on nectar in particular were apparent when compared alongside the response of the control in terms of the level of nectar buildup before hive preparation for overwintering at CCA7. This finding was also confirmed statistically in all three agency analyses with significant reductions in honey stores at CCAs 6, 7, and 8 (CCA8 data excluded from the EPA analysis for the 96 and 190 µg/L groups). Significant ($p<0.05$) reductions in pollen stores were also confirmed at CCAs 4 and 5 at the 47 µg/L treatment during the exposure phase.

Specifically, when considering the adult and honey and pollen stores response variables, the differences from control were apparent both visually and statistically, particularly in the three highest treatment groups. For the proportion of adults, the onset of a decline in numbers occurred one CCA earlier in

these groups than in the control, 11 and 23 µg/L treatment groups. For honey stores, the buildup that occurred starting at CCA5 in the 50 µg/L treatment group, reached only half the level reached in the control, 11 and 23 µg/L treatment groups by CCA7. Pollen stores were also reduced at CCA4 and CCA5 compared to controls for the three highest treatment groups, as well as at CCA6 and CCA7 at the highest treatment group. These effects were statistically significant ($p<0.05$) and indicate that the 47 µg/L treatment group was associated with trends and proportions of abundance for life stages and food stores not observed in the control, 11 and 23 µg/L treatment groups.

Therefore, when weighing biological significance and the natural seasonal changes of honey bees colonies, as well as supporting conclusions from the statistical approaches used in PMRA, EPA, and CDPR, the NOAEC and LOAEC for this study is determined to be 23 and 47 µg/L, respectively.

Study Strengths and limitations

It is important to recognize the inherent strengths and limitations of this study as results are considered in this risk assessment.

In the context of available field studies involving honey bees and imidacloprid, this study contains a number of strengths including:

- Use of a high degree of replication ($n=12$) to achieve a reasonable level of statistical power;
- Demonstration of a generalized concentration-response relationship with respect to the concentration of imidacloprid in sucrose solution and the magnitude and duration of adverse effects;
- Quantification of exposure to parent (imidacloprid) and toxicologically-relevant metabolites in diet and in hive matrices (uncapped nectar, pollen, honey, bee bread);
- Use of a 6-week exposure duration to represent a “high end” exposure scenario;
- Inclusion of multiple colony-level endpoints reflecting hive strength, brood development and food stores;
- Detailed quality assurance/quality control (QA/QC) regarding quantification of chemical residues in various matrices; and,
- Availability of raw data for conducting/verifying statistical analysis.

A number of limitations are also noted with this study, including:

- Exposure of bees through nectar (sucrose) alone, whereas bees in the field are likely exposed through both pollen and nectar routes. While exclusion of the pollen route is expected to reduce overall exposure, the impact of this exclusion on the study results is uncertain and will likely depend on the life stage/caste of bee.
- Imidacloprid was found in both hive nectar and hive pollen (beebread), at concentrations lower than the feeding solutions. Dilution compared to the treatment feeding solution is expected since bees could also forage on outside nectar and pollen sources. As well, hive pollen contains only some hive nectar, thus would not be expected to have a concentration equivalent to nectar alone, and it is mixed with pollen which comes from outside [untreated] sources. Therefore,

exposure through both hive pollen and nectar occurred via exposure to the sucrose feeding solution, but how this compares to exposure through contaminated pollen directly is not known. It is also noted that nectar is considered the dominant exposure route for forager bees; other hive bees and larvae consume both nectar and pollen.

- The quantity of nectar provided to hives (2 L per week per hive) likely did not fulfill the complete carbohydrate needs of the colony, as indicated by colony bioenergetics and the lack of remaining sucrose solution upon their renewal. This suggests that bees could be exposed to a greater dose of imidacloprid in nectar had a greater volume of spiked sucrose been provided. Although the dosing regimen may have underestimated exposure through sucrose relative to 100% contaminated diet, it is noted that bees had to supplement their spiked sucrose by foraging on their own for other sources of nectar.
- Overwintering success of controls was impacted (36% hive mortality). This may have reduced the ability to detect adverse effects related to hive loss following overwintering. Although comparable to overwintering losses of commercial beekeepers (32% based on a 5-yr average²⁶), it is possible that elements of the study design may have contributed to this loss (e.g., lack of supers to allow for colony growth, delayed supplemental feeding during fall).
- Hive contamination with pesticides from food sources other than the artificial feeding was detected during the exposure period and post-exposure periods through collection of pollen from pollen traps. Although the study was deliberately conducted in an area where minimal potential for pesticide contamination from other sources was expected, the bees still appeared to be foraging on contaminated pollen and possibly nectar. During both exposure and post-exposure periods, multiple pesticides such as spiromesifen (maximum at 961 µg/L) and piperonyl butoxide (maximum at 591 µg/L) that may cause concern for bees were detected in most monitoring hives. Trace amounts of other bee-toxic pesticides, such as chlorpyifos (LOD = 1.0 µg/L) and malathion (LOD = 4.0 µg/L) were also detected. The test chemical imidacloprid was found at 12.1 µg/L in pollen from one (apiary L) of the total of six sites analyzed.
- Residues of imidacloprid in uncapped nectar and bee bread within the hives at CCAs 4, 5, and 8 represent a single sample per hive on a single frame rather than a composite sample from multiple portions of the comb within a hive. This means that residue results may reflect “hit or miss” scenario with respect to detecting residues in nectar laid down from spiked sucrose diets (fed) vs. outside sources.
- The exposure, based on residues measured in the hive (hive nectar and hive pollen) indicated that, overall, higher measured hive residues correlated with higher nominal residues in feeding solutions. However, individual hive residue values varied, and there was some overlap in measured values, particularly among the three lowest doses. Given the limited spatial and

²⁶ White House. 2015. National Strategy to Promote the Health of Honey Bees and Other Pollinators. Pollinator Health Task Force. May 19, 2015.

<https://www.whitehouse.gov/sites/default/files/microsites/ostp/Pollinator%20Health%20Strategy%202015.pdf>

temporal sampling methodology (as mentioned above), there is uncertainty in whether these residues represent actual in hive residues across all portions of the frame. Specifically, one sample of one area of the comb on one side of the frame to represent the nectar or pollen residues of an entire hive may not reflect the true nature of the residues across all portions of a given hive.

In addition to the colony feeding study, there are several registrant-submitted Tier II studies employing a tunnel design that were previously mentioned in **Section 4** regarding their residue information. These studies generally involved exposure to honey bee colonies foraging on seed-treated corn, canola, or sunflower within a netted enclosure (*i.e.* tunnel). These studies, while serving as a line of evidence in terms of the residue information provided, have several deficiencies that limit their utility from an effects standpoint. The limitations associated with each study can be found in **Appendix A**.

5.2.2. Open Literature Studies

This section summarizes the available Tier II (*i.e.*, tunnel and feeding study design) studies that were evaluated from the open literature as part of the aforementioned joint review between EPA, PMRA, and CDPR. At the Tier II (and Tier III) levels, effects on the colony as a whole are assessed as distinguished from Tier I studies that characterize the effects of imidacloprid at the individual bee level. Where sufficient information is available, a table summarizing the results is provided within the discussion of each study. Additionally, the limitations of each study are provided within each summary. It is noted here that all studies are determined to be of qualitative utility for characterization purposes in this assessment. As with the Tier I data, this is primarily due to the fact that raw data were not available to allow for an independent verification of the statistical results but, as will be discussed, other uncertainties contribute to this classification of utility.

5.2.2.1. Apis

Summary of Tier II Apis Studies from the Open Literature

While many of the evaluated studies from the open literature do not have a robust experimental design (*i.e.*, lack of replication of colonies or plots within treatment groups), lack of an overwintering component to provide insight on the long-term effects of imidacloprid at the colony level, and only one treatment concentration, these studies provide several additional endpoints not captured in the registrant-submitted colony feeding study. For example, foraging observations dealing with behavior and success are examined in the majority (90%) of the higher-tier *Apis* studies. Additionally, several higher-tier studies were evaluated that investigate the colony-level effects of imidacloprid on bumble bees and, as will be discussed, the concentrations in pollen and nectar at which effects are observed vary from that of *Apis* colonies.

A total of 6 Tier II studies (all feeding design; 4 with spiked sucrose, 2 with spiked pollen) were evaluated from the open literature to characterize the colony-level effects of imidacloprid to honey bees. These

studies employed study design elements that were akin to the registrant-submitted colony feeding study discussed above such as replication of hives among treatment groups, monitoring for pests and pathogens, multiple colony condition assessments to monitor the hives during and after exposure, and an overwintering component to assess the long-term effects of colony health as a result chronic exposure to imidacloprid. There were an additional 4 studies (Bortolotti 2003, Eiri and Nieh 20120, Schneider 2012, and Tan 2014), that exposed honey bees to a single oral dose, but examined endpoints that could potentially lead to colony-level impacts. These studies, while not traditional colony-level feeding study designs, provide information on foraging behavior and success endpoints not provided in other studies that were evaluated in the open literature. Besides being differentiated by the other colony feeding studies in their exposure duration, they are also distinct in that they do not include other measures of colony health such as information on mortality, proportions of various life stages, and overwintering survival. As noted in the Problem Formulation, while these studies do not provide information on regulatory endpoints by themselves, they provide additional information when characterizing the potential impact on the hive by measures of foraging success and behavior.

Table 5-12 below summarizes key elements and findings from the *Apis* high-tier studies that were evaluated from the open literature. While the studies were varied in their exposure duration, concentrations tested, and endpoints assessed, the following is a discussion of each subset of endpoints that aims to put into context the results of these studies with those of the registrant-submitted Tier II colony feeding study described above. Summaries of each of these studies including the methods and full results are provided in **Appendix E**. There are several points worth noting with regards to this discussion:

1. While the registrant-submitted colony feeding study had raw data provided to allow for an independent verification of the statistical results, only two higher tier studies from the open literature had this information available. For some studies, the responses of certain endpoints were estimated from the graphs provided in the original article and are therefore not without some uncertainty in their precision. For other studies, the means of the responses were not provided, but rather only the direction of the effect as compared to the control and whether or not the results were statistically significant.
2. The studies evaluated from the open literature do not demonstrate exposure to the extent provided in the registrant-submitted colony feeding study. Specifically, this refers to a general lack of information regarding analytical confirmation of imidacloprid in treatment solutions, as well as a general lack of in-hive residue data for stored pollen, honey, and honey bee samples.
3. While the registrant submitted study assessed numerous colony condition parameters, it did not include any response variables regarding foraging behavior or success. By contrast, a number of the Tier II studies from the open literature include some measure of foraging behavior or success as a response variable.
4. Only 5 of the 10 available Tier II studies included an overwintering component. This design element is critical in evaluating the long-term success of a colony following exposure to

imidacloprid since, as was suggested by the results of the registrant-submitted colony feeding study, the honey bee colony can be a resilient entity that is capable of recovery of certain effects when exposure ceases.

Table 5-12. Summary of semi-field (feeding) studies available from the open literature (*Apis*)¹

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur.) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects ² (all comparisons made relative to the study's control) | Limitations ² | Classification Citation (MRID Number) |
|---|--------------------------------------|--|---|--|--|--|--|
| Confidor - not reported (<i>Apis mellifera</i>) | Sucrose (0, 100, 500, and 1000 µg/L) | Not reported – although assumed to be single dose given that observations were made at given intervals after exposure study duration was 24 hours (24 hours) | - Single colony isolated from other colonies and bees trained to forage on feeder for observations | Percentage of bees returning to hive after treatment, percentage of bees returning to feeding sites -- (No) | <u>Return to hive:</u> ↓25% (100 µg/L, 0-2 hours post-exposure), ↓31% (100 µg/L, 4-5 hours post exposure), ↓5.1% (100 µg/L, 24 hours post exposure) <u>Return to feeder:</u> ↓90% (100 µg/L, 0-2 hours and 4-5 post exposure) | - Purity of test substance not reported - Bees in 500 and 1000 µg/L appeared to avoid feeders and were not observed for the duration of the test; - One hive per group precluded statistical analysis; - Unknown impact of these effects to other colony health parameters; - Unknown amount of time that the bees spent at the feeders. | Qualitative Bortolotti, 2003 ⁴ 47800505 |
| IMI - not reported (<i>Apis cerana</i>) | Sucrose (0, 10, 20, and 40 µg/L) | Single dose (not reported) | - 90 bees per group in feeder component - 21 bees per group in nectar collection component - 20 bees per group for predator avoidance component | Proportion of bees returning to feeder, average volume of nectar collected, predator avoidance -- (Yes) | Proportion of bees returned to feeder: ↓23% (40 µg/L)†; average volume of nectar collected: ↓46% (20 µg/L)†, ↓63% (40 µg/L)†; | - Majority of the sugar solution was stated by the study authors as having been regurgitated suggesting an unknown dose level the bees were exposed to. - The purity of imidacloprid was not stated - Test species (<i>Apis cerana</i>) is not distributed in North America. | Qualitative Tan, 2014 ⁴ 49719631 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations² | Classification |
|---|---|------------------------------------|---|--|--|--|--|
| IMI - technical ³ <i>(Apis mellifera)</i> | Sucrose (0, 0.15, 1.5, 3.0, and 6 ng a.i/bee) | Single dose (48 hours) | - Subset of bees from a colony were fitted with RFID tags to monitor foraging behavior after single oral dose - 12 bees per dose group - 2 identical trials conducted consecutively | -- (Yes) | Number of feeder visits: ↓47% (1.5 ng) [†] , ↓98% (3 ng) [†] Length of foraging trip: ↑50% (1.5 ng) [†] , ↑130% (3 ng) [†] Time to feeder: ↑65% (1.5 ng) [†] , ↑241% (3 ng) [†] Time at feeder: ↑25% (1.5 ng) [†] , ↑46% (3 ng) [†] Time to hive: ↑20% (1.5 ng) [†] , ↑210% (3 ng) [†] Interval between trips: ↑33% (1.5 ng) [†] , ↑993% (3 ng) [†] Time inside hive (1 st stay): ↑972% (3 ng) [†] Time inside hive (2 nd stay): ↑33% (1.5 ng) [†] , ↑1077 (3 ng) [†] | - 12 bees per group and two total trials results in limited sample size from which results are based. - High variability for certain endpoints that is likely the result of limited sample size and replication. - Unknown impact of these effects to other colony health parameters particularly since these effects were noted to have been observed immediately after treatment were not present 24 and 48 hours after dose administration. | Qualitative Schneider, 2012 ⁴ 49719629 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations² | Classification |
|---|--|---|---|--|--|---|---|
| IMI – technical (<i>Apis mellifera ligustica</i>) | Sucrose (0, 24, and 241 µg/L for sucrose response; 0 and 24 µg/L for dancing behavior) | Single dose (1 hour for SRT, 24 hours for dancing behavior) | - 314 nectar foragers and 209 pollen foragers used for SRT component - 65 bees used for dancing behavior component | - SRT (lowest sucrose concentration that bees would elicit complete PER) -Dancing behavior (number of dance circuits) -- (Yes) | Nectar forager SRT: ↑78% (24 µg/L)†, ↑81% (241 µg/L)† Pollen forager SRT: ↑206% (241 µg/L)† | - It was unclear whether the entire dose was consumed; - Mean % sucrose response threshold (minimum percent sucrose to elicit a proboscis extension response) noted to be highly variable with %CV values of 143% and 224% for control nectar and pollen foragers, respectively. - Although the authors state that the objective of the dancing behavior component was to examine the effects of imidacloprid metabolites, residues are not identified and/or measured. - Unknown impact of these effects to other colony health parameters. | <i>Qualitative</i> Eiri and Nieh ⁴ , 2012 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations² | Classification |
|--|---|--|--|---|---|--|--|
| IMI - not reported (<i>Apis mellifera mellifera</i>) | Sucrose (0-unfed, 0-fed), 0.5, and 5 µg/L | 34 days (7 months, including overwinter) | - Unfed control group relied exclusively on forage - 8 colonies/trt - 7 colony condition assessments | Mortality, egg laying, activity index(bees per min entering hive), capped brood area, hive weight, adult population, disease and parasite incidence -- (Yes) | Number of frames of capped brood area : ↑14% (0.5 µg/L)†; ↓34% (5 µg/L)† | - Purity of imidacloprid not reported - Results refer to after overwintering period and comparisons made to fed (sucrose) control (not clear from study whether different from unfed control) | <i>Qualitative</i> Faucon, 2005 47523406 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations² | Classification Citation (MRID Number) |
|---|---|--|--|---|---|--|--|
| AdmirePro – not reported (not reported) | Pollen (0, 5, and 20 µg/L) | 12 weeks (5 months from exposure start to last CCA (mid-October, colonies were then over-wintered) | - 10 replicate colonies per group - October 15 was last CCA - Limited space in nucleus hives and supplemental feeding was not provided | Egg-laying activity, larvae development, food consumption, amount of pollen collected, total foragers returning to hive, percentage of foragers with pollen pellets, nectar station visits -- (Yes) | Nectar station visits: ↓35.7% (5 µg/L)†, ↑13.1% (20 µg/L) | - Unknown confounding effect of queen replacement and food/brood removal frame removal - For the foraging trials, numbers of marked bees are provided but this represents a small (approximately 2-4% of the total numbers exposed) - No way to confirm the lack of potential for exposure to other sources of imidacloprid or neonicotinoids in the surrounding area or where the imidacloprid in the control colonies came from. The study area was noted to have been surrounded by corn that may have been seed treated with neonicotinoids. | <i>Qualitative</i> Dively, 2009 (47775502) |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations² | Classification Citation (MRID Number) |
|---|---|---|---|--|--|---|--|
| Admire Pro – 42.8% (not reported) | Pollen (0, 5, 20, and 100 µg/L) | 12 weeks (10 months from exposure start to last CCA (mid-March) | - 10 replicate colonies per group, each blocked in groups of 2 across 5 apiary locations - Pollen traps installed at each entrance to direct bees to feed on spiked pollen patties -Residue analysis conducted confirmed presence in pollen patties (5.5, 19.8, and 97.5 µg/kg for the 5, 20, and 100 µg/kg groups, respectively) | Queen event (manual replacement or natural supersedure), disease presence and incidence (<i>Varroa</i> and <i>Nosema</i>), mean colony size, mean amount of pollen collected, percentage of total frame covered for bees, capped brood cells, capped honey, bee bread, drawn out cells (defined by study as empty, cleaned out cells), overwintering survival -- (Yes) | 2009 Trial: Overwintering survival: ↓25% (100 µg/kg)† Percentage of total frame coverage by capped honey: ↑65% (100 µg/kg) 2010 Trial: Percentage of total frame coverage by capped honey: ↑125% (100 µg/kg) | - In the 2009 trial, mean <i>Varroa</i> mite levels were 7.1, 8.8, 6.6, and 13.3 mites per 100 bees in the control, 5, 20, and 100 µg/L treatment groups, respectively but there was no mention of treatment. It is noted however that overwintering success in this trial was 100% in the control group. - In the 2010 trial, queen events were collapsed for the control and 5 µg/L levels in one metric and for the 20 and 100 µg/L groups in another. It is unclear if more queen events occurred in the control or 5 µg/L group. - Control overwintering survival in the 2010 trial was 57% which renders results from this trial uncertain in discriminating treatment related effects - Survival data were pooled in the 2009 and 2010 trial despite 100% control survival in 2009 and 57% in 2010. | Qualitative Dively, 2015 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations² | Classification Citation (MRID Number) |
|--|--|---|--|---|--|---|--|
| IMI technical – not reported (Not reported) | Sucrose (2014 0, 5, and 100 µg/L 2015 0, 5, 20, and 100 µg/L) | 6 weeks (2014: 11 months 2015: 4 months) | - 4 colonies per treatment group - Site 1 2014 and 2015, Site 2 and 3 2015 only -Residue analysis conducted for IMI residue in hive matrices | Site 1: Adult bee population, capped brood area, frame weight, hive weight, temperature, varroa fall Site 2: Capped brood area, frame weight, hive weight Site 3: Capped brood area, frame spaces, varroa density (No) | Site 1 Capped brood ↓ (100 µg/L) Adult bee population ↓ (100 µg/L) Site 2 No differences Site 3 Capped brood ↓ (5 µg/L) | - Purity of imidacloprid not reported - Overwintering not observed in 2015 - Different methods, observations, and statistics conducted between years and sites. - Limited number of replicate colonies per treatment group | <i>Qualitative</i> Meikle, 2016 |
| IMI technical – 98.7 % (<i>Apis mellifera carnica</i>) | Sucrose (1000, 200, 50, and 0 µg/L) | 5 days (2 months) | - 9 colonies per treatment group - Observation of 3 colonies per group at 3 apiaries - Samples taken 21 and 64 days post exposure | Number of bees, capped brood, honey and pollen Secondary endpoints of genetic expression and body morphology (Yes) | Adult bee population ↓ in autumn Honey stores ↓ in summer Adult bee population ↓ after overwintering (50µg/L) | - No information on pathogen prevalence was provided -Limited exposure duration (5 days) -Limited statistical information given for effects found | <i>Qualitative</i> Wegener, 2016 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations² | Classification Citation (MRID Number) |
|--|---|------------------------------------|--|---|---|---|--|
| IMI technical – 99.5 % (<i>Apis mellifera</i>) | Sucrose (0, 10, 20, 50, and 100 µg/L) | 3 weeks (3 weeks) | - three or four replicate studies each year over three years (2012–2014) - hive sizes of 1500, 3000, or 7000 worker bees per exposure | Queen behavior/egg laying rate, foraging activity, brood (number of eggs, larvae, or pupae), food stores, number of adults (Yes) | Egg laying rate ↓ (10 µg/L) Foraging behavior ↓ (10 µg/L) Number of eggs ↓ (10 µg/L) Pollen stores ↓ (10 µg/L) | - No information on pathogen prevalence or treatment was provided - It is not known the extent to which measurements made on observation hives would differ from typical hives used in beekeeping - The period of observation was limited to the end of exposure (Day 23) therefore it is not known if exposure would result in sustained impacts to colonies health - Unknown relevance of the observed effects to larger colonies (i.e. > 20,000 bees) | <i>Qualitative</i> Wu-Smart, 2016 |

IMI: imidacloprid; PER: Proboscis extension response; RFID: radiofrequency identification; CCA: colony condition assessment, SRT: sucrose response threshold

¹Indicates effect was statistically significant (p<0.05).

¹Most studies not associated with NOAEC/LOAEC values. Reported is the most sensitive statistically derived or otherwise observed difference relative to the control.

²Only subset of limitations are listed here. Others associated with this study can be found with the study summaries in **Appendix E**.

³Although not explicitly stated in the article, personal communication with the author (email dated 01/29/15) indicates that imidacloprid was of technical grade.

⁴These studies, while assessing endpoints that could potentially impact colonies, are not of a feeding design in the traditional sense in that bees are exposed to a single dose

Mortality (inclusive of worker/forager and colony overwintering):

There were 3 studies which included either worker or colony mortality (or survival) as a response variable. With these studies, exposure to imidacloprid through spiked nectar, pollen, or following seed treatment applications generally did not appear to have an overall impact on worker or overall colony survival when compared to the control with the exception of colonies provided imidacloprid in spiked pollen at 100 µg/kg (Dively 2015). The registrant-submitted colony feeding study (technical imidacloprid, 6 week exposure, 12.5, 25, 50, 100, and 200 µg a.i/L groups, overwintering component) showed an erratic dose response (18, 9, 36, 91, and 82% overwintering mortality for the treatment groups, respectively) for overwintering mortality and when compared to 36% overwintering mortality in the control group, inferences made about treatment-related overwintering mortality at the lower groups (12.5, 25, and 50) are uncertain.

In Faucon, 2005, (sucrose feeding study design, 0.5, and 5 µg/L treatment groups, 34-day exposure, overwintering component), the study authors did not subject the mortality data to statistical analysis as it was stated that daily mean mortality was low with means of 3.1, 4.4, 4.3, and 3.3 for the unfed control group, untreated sucrose control, 0.5 and 5 µg/L imidacloprid groups, respectively. These data corresponded to a period that included the entire 34-day exposure phase as well as the 16-day interval just after exposure ended. For overwintering success, colonies were scored by the number of frames with brood combined with frames of adults. The colonies were scored the March after exposure began (previous July) and there were no significant differences ($p>0.05$) in the treated groups from that of both control groups.

Dively, 2015 (formulated imidacloprid, pollen feeding study design, 5, 20, and 100 µg/L treatment groups, 12-week exposure period, overwintering component) included two years of feeding study trials (2009 and 2010) with separate colonies and exposures taking place each year. In the 2009 trial, there was a significant ($p<0.05$) reduction at the 100 µg /kg [spiked pollen] group (mortality in 2/8 colonies as compared to 0/10 colonies in the control (two colonies in the 100 µg/kg group were terminated in early September by the study authors after the colonies underwent natural supersEDURE (queen replacement) and the researcher determined that the colonies were no longer healthy enough to survive overwintering). In the 2010 trial, there were no treatment-related effects on colony overwintering but it is noted the control group for this trial had 57% survival.

Effects on presence of various life stages:

The same 3 studies discussed above for mortality also assessed the impact of imidacloprid exposure to the presence of various life stages within the hive. Four additional studies also examined the presence of various life stages within the hive. While not every study examined the same life stages and route of exposure, in four of the seven studies there was generally no impact on the presence of different life stages up to and including the highest treatment concentrations assessed (20 µg a.i/L in sucrose, 100 µg/kg in pollen). However, the three relevant studies evaluated since the publication of the preliminary bee assessment found effects at some level.

The registrant-submitted colony feeding study determined significant reductions in the numbers (as percentage of frame coverage within the hive) of adults, eggs, and capped brood (pupae) at the three highest treatment groups (50, 100 and 200 µg a.i./L). These effects were usually observed following exposure and sustained through the duration of the study including after overwintering (100 and 200 µg a.i./L groups) but other effects were determined during exposure, showed recovery to the level of the control group following exposure, but were again reduced after the overwintering period (50 µg a.i./L group).

Faucon, 2005 did not determine significant effects ($p>0.05$) to percent frame coverage of adults and eggs up to and including the highest treatment group (5 µg/L in sucrose). The capped brood (pupae) coverage response changed depending on the interval considered. When considering the exposure duration interval as well as exposure phase plus 3 weeks post-exposure phase, there were no significant effects determined ($p>0.05$). However, after the overwintering period, there were significant effects on the number of frames with capped brood area ($p<0.05$) although these effects were not dose-responsive (14% increase at 0.5 µg/L group, 34% decrease in the 5 µg/L group). While the route of exposure was distinct from Schmuck, 2001 and Faucon, 2005, there were no significant effects ($p>0.05$) determined in both Dively, 2009 and Dively, 2015 on percent frame coverage of adults, eggs, and capped brood (pupae). While there was a dose-responsive increase of 27, 35, and 51% (for the 5, 20, and 100 µg/kg treatment groups, respectively, the different treatments were not statistically significant, $p>0.05$) in the coverage of capped brood cells in the 2010 trial of Dively, 2015 for observations made at a mid-August CCA. In the subsequent early October CCA, these observations did not indicate a treatment-related effect ($\uparrow 8\%$, $\downarrow 15\%$, no change, for the 5, 20, and 100 µg/L groups, respectively).

Wu-Smart (2016) investigated the effects on very small colonies (1,500, 3000, and 7,000 bees in size) over a 3-week period and noted a number of effects resulting from exposure to imidacloprid. Specifically, there were reductions ($p<0.05$) in the number of eggs laid at the lowest treatment level (10 µg/L in sucrose). In contrast, Wegener (2016) and Meikle (2016) examined full honey bee colonies and found reductions in capped brood and adult bee populations. Wegener found reductions in adult bee populations ($p<0.05$) after overwintering at the lowest tested concentration (50 µg/L in sucrose). By contrast, the study by Meikle determined effects to capped brood and adult bee populations at one site at concentrations of 100 µg/L in sucrose and effects to only capped brood at another location at the 5 µg/L level.

Foraging behavior/foraging success observations:

As noted previously, the majority of the available Tier II open literature studies with *Apis* include some measure of foraging behavior (numbers of foraging trips, time spent on trips, durations of trips) and success (amount of pollen and nectar collected). While some studies include foraging measurements with other colony health parameters in an attempt to link these effects to short- or long-term colony success, other studies assess foraging endpoints only. With the latter case, there is uncertainty in the impact of these effects on the success of the colony. As mentioned previously, the registrant-submitted colony feeding study did not include foraging endpoints.

It was previously mentioned that a subset of the studies examining foraging endpoints involved a single oral exposure for individual bees as opposed to a sustained exposure to colonies with spiked sucrose or spiked pollen provisions. While Bortolotti (2003) does not specify the duration of exposure, as the study was 24 hours in duration with endpoints made in pre-defined intervals after exposure, it was assumed to be a single oral dose.

In Bortolotti, 2003 (formulated imidacloprid, 100, 500, and 1000 µg/L treatment groups, duration of exposure not reported), there were decreases ranging from 25-31% of bees returning to the hive from directly after exposure to 5 hours post exposure in the 100 µg/L group. After 24 hours, this effect was reduced to 5.1%, suggesting a recovery of orientation after imidacloprid exposure ceases. Reductions to the number of bees returning to a sucrose feeder were observed to be 90% as compared to the control group at both the 0-2 and 4-5 hours after exposure intervals (no statistical analysis conducted on the results). There was no 24-hour post-exposure observation for this endpoint. Bees in the 500 and 1000 µg/L groups were not seen returning to the hive or feeder and therefore no further data were collected. It is noted that 500 and 1000 µg/L are markedly high concentrations that for a study investigating sublethal effects on foraging behavior and success. Tan, 2014 (spiked sucrose, 10, 20, and 40 µg/L treatment groups, single oral exposure) similarly investigated the numbers of bees returning to a feeder provided in the field. There was a 23% reduction ($p<0.05$) in the number of bees returning to the feeder at the 40 µg/L group. Additionally, the mean amount of nectar collected was significantly decreased ($p<0.05$) from the level of the control in the 20 and 40 µg/L treatment groups ($\downarrow 46\%$ and $\downarrow 63\%$, respectively). Schneider, 2012 (technical imidacloprid, 0.15, 1.5, 3, and 6 ng a.i./bee, RFID tagging) determined significant reductions ($p<0.05$) in number of feeder visits ($\downarrow 47 - 98\%$), and significant increases ($p<0.05$) in length of foraging trips ($\uparrow 50 - 130\%$), time to feeder ($\uparrow 65 - 241\%$), time at feeder ($\uparrow 25 - 46\%$), time to hive ($\uparrow 20 - 210\%$), and interval between trips ($\uparrow 33 - 993\%$). It is noted that these effects were observed immediately after treatment and were not observed 24 and 48 hours after treatment which corroborate to some extent the results of Bortolotti (2003). In Eiri and Nieh (2012), individual honey bees that were exposed to a single oral dose of either 24 or 241 µg/L in sucrose and subsequently assessed in a sucrose response threshold, which is defined as the lowest concentration of sucrose which will elicit a proboscis extension response (PER) in honey bees. The results indicated that there was a dose-responsive increase in the sucrose response threshold with increasing dose, indicating higher concentrations were needed to elicit a PER. No other response variables were assessed in this study. Finally, in Wu-smart, 2016 (treatment concentrations of control, 10, 20, 50, and 100 µg/L, mini colonies, 23-day exposure) foraging behavior was measured as number of foragers entering and exiting the colony. Foraging behavior was decreased ($p<0.05$) in the imidacloprid treated colonies relative to the control at the lowest treatment tested (10 µg/L). Additionally, pollen stores in treated colonies were significantly ($p<0.05$) less than in controls at the same treatment level (10 µg/L) suggesting the decrease in foraging behavior also resulted in a decrease in foraging efficiency.

Several studies also examined the amount of nectar and pollen collected. In the Dively studies (2009 and 2015) that had a pollen feeding study design, a variety of foraging endpoints were assessed. In Dively (2009), while there were no significant effects ($p>0.05$) on the amount of pollen collected and percentage of foragers with pollen pellets, there was a significant ($p<0.05$) reduction from control in the number of nectar station visits at the 5 µg/L group, although this response was a non-significant

increase of 13.1% at the 20 µg/L group. In Dively (2015), there were no effects on the amount of pollen collected (increases from control ranged from 14 – 32% but were not significant and not dose-responsive).

Summary:

This discussion illustrates that for the available set of higher-tier studies from the open literature, effects on colony health parameters such as overwintering survival, worker/forager mortality, and presence of various life stages (as percentage of frame coverage within the hive), were not determined at levels in spiked sucrose up to and including 40 µg/L, and in levels of pollen up to and including 20 µg/L. The latter statement is based only on two available pollen exposure studies (Dively, 2009 and Dively, 2015), but there was a significant reduction in overwintering survival at the 100 µg/L group in one of the two trial years.

For foraging measurements in which a single oral dose was administered to individual bees (Bortolotti 2003; Eiri and Nieh 2012; Schneider 2012, and Tan 2014), significant effects on orientation (bees returning to feeder, time to and at feeder, length of foraging trips) were observed at concentrations in sucrose as low as 1.5 ng a.i./bee. These effects were noted immediately following oral exposure and were not observed 24 hours after exposure. For the colony-level feeding studies, there were no effects up to and including 5 µg/L in sucrose and 20 µg/L in pollen. For effects on pollen and nectar collection, there were no effects in spiked sucrose feeding studies up to and including 10 µg/L and up to and including 100 µg/L in spiked pollen.

This summary is based on the results of a small number of studies and therefore there is uncertainty as to whether levels of imidacloprid in nectar and pollen above or below the concentrations described above could potentially impact the overall health of a colony following continuous exposure. There are no data at this time to link impaired foraging behavior of individual bees as a result of acute exposure to relatively low doses of imidacloprid to impaired colony condition.

5.2.2.2. *Bombus*

Summary of Tier II *Bombus* Studies from the Open Literature

A total of 2 Tier II studies (tunnel design, one of which also had a full-field Tier III component) and 8 feeding design studies were available to characterize the colony-level effects on bumble bees (*i.e.* various species of *Bombus*). Two of the Tier II feeding design studies originate from the same dataset (*i.e.* Gill 2012 and Gill and Raine 2014), with Gill and Raine 2014 re-analyzing a subset of the 2012 data (foraging measurements). As with the higher-tier *Apis* open literature studies, exposure duration, concentrations tested, and endpoints assessed varied across the 10 studies.

Several notable aspects of these studies include:

1. While workers and the queen bee undergo overwintering in honey bee colonies, and subsequently build up again the following spring, only the *Bombus* queen overwinters. Therefore, there was no overwintering component included in any of the open literature *Bombus* studies as distinguished from *Apis*.
2. Colonies of *Bombus* are much smaller than those of *Apis* and typically range from several dozen to several hundred bees at most. In contrast, *Apis* colonies consist of thousands of bees and can reach sizes up to several tens of thousands. It is therefore expected to some extent that *Apis* colonies are able to compensate for greater losses of their adult population before colony failure as compared to *Bombus*.
3. Some *Bombus* studies are conducted with microcolonies. Microcolonies are queen-less units of a few worker bumble bees where one individual eventually becomes dominant and starts laying unfertilized eggs that will eventually become drones (males).

Table 5-13 below summarizes key elements and findings from the *Bombus* higher tier studies that were evaluated from the open literature.

Table 5-13. Summary of semi-field (Tunnel) studies available from the open literature (*Bombus*)

| Test Substance Purity (Test species) | Crop (App. Rate) | Exp. Dur. (Observ. Dura) | Design Elements | Endpoints Assessed (Statistics analysis conducted? – Yes/No) | Effects ² (all comparisons made relative to the study's control) | Limitations ³ | Classification Citation (MRID Number) |
|--|---|--------------------------|--|--|---|---|--|
| Gaucho – not reported (<i>Bombus terrestris</i>) | Sunflower (0.7 mg a.i./seed) | 4 days (4 days) | - One tunnel /treatment - 75 total workers observed for foraging measurements | Number of workers visiting blooming heads, number of workers with 'short' foraging trips, number of bees with 'long' foraging trips ¹ (Yes) | Numbers of visits: ↑36%, Workers with 'long' foraging trips: ↑60% | - Insufficient demonstration of exposure as study authors cite unpublished data from nectar samples of sunflowers in greenhouse. - Small sample sizes for foraging data. - Minimal information on the husbandry the bees used. | Qualitative Tasei 2001 (47800503) |
| Merit 0.5 G – not reported (<i>Bombus impatiens</i>) | Turf + white clover, 25-50% bloom (0.4 lbs a.i/A) | | - 5 plots (3m x 5m per group - 1 colony per plot | Colony weight, worker weight, queen weight, number of workers, number of brood chambers, | # of workers: ↓26%, Time to initial defense response: ↓76%, Number of brood chambers: ↑75% | - Method used for defense response has not been formally standardized to determine its sensitivity - High variability for some endpoints, which could explain the statistical methods failing to detect high (over 70%) response vs control. | |
| Merit 75 WP – not reported (<i>Bombus impatiens</i>) | Turf + white clover, 25-50% bloom (0.3 lbs a.i/A) | 28 days (28 days) | - 5 plots (3m x 5m per group (control, spray w/ irrigation, spray w/ no irrigation) - 1 colony per plot | number of honey pots, time to initial defense response, duration of defense response, number of bees responding -- (Yes) | Colony weight (↓54%)†, worker weight (↓56%)†, # of workers (↓60%)†, # of brood chambers (↓87%)†, # of honey pot (↓72%)†, time to initial defense response (↓67%)†, duration of defense response (↓73%)†, # of bees responding (↓77%)† | - 28 day exposure period in a flight cage is longer than the 10-14 days recommended by OECD semi field tests for honey bees. It is unknown how adaptable bumble bees are to this length of confinement. | Qualitative Gels, 2002 47796308 |

¹Indicates effect was statistically significant (p<0.05).

²'Short' trips defined by study author to be 1-50 seconds and 'long' trips defined to be >50 seconds

³Not all studies were associated with NOAEC/LOAEC values. Reported is the most sensitive statistically derived or otherwise observed difference vs control.

³Limitations considered to be major listed here. Others associated with this study can be found with the study summaries in Appendix E.

Table 5-14. Summary of semi-field (feeding) studies available from the open literature (*Bombus*)

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects ² (all comparisons made relative to the study's control) | Limitations ³ | Classification Citation (MRID Number) |
|--|--|---|--|--|--|---|---|
| Confidor – 20% (<i>Bombus terrestris</i>) | Sucrose – component 1 and 2 (0, 10, 20, 200, 20000, and 200000 µg/L; component 3 (0, 2, 10, and 20 µg/L) | <u>Component 1 and 2:</u> - microcolony (4 colonies with 5 workers each) housed in cages for 11-week exposure <u>Component 3:</u> - 2 weeks (11 weeks and 2 weeks, respectively) | <u>Components 1 and 2:</u> - microcolony (4 colonies with 5 workers each) housed in cages for 11-week exposure <u>Component 3:</u> - queen right colonies (25 bees per colony, 1 per group) in 2-week greenhouse exposure | <u>Component 1:</u> Mortality: 100% in 200, 2000, 20000, and 200000 µg/L†; Reproduction: no reproduction at these doses† <u>Component 2:</u> Mortality: 50% in 20 µg/L, 100% in 200, 2000, 20000, and 200000 µg/L† <u>Component 3:</u> mortality, reproduction, and foraging behavior -- (Yes) | <u>Component 1:</u> Mortality: 100% in 200, 2000, 20000, and 200000 µg/L†; Reproduction: no reproduction at these doses† <u>Component 2:</u> Mortality: 50% in 20 µg/L, 100% in 200, 2000, 20000, and 200000 µg/L† <u>Component 3:</u> mortality, reproduction, and foraging behavior -- (Yes) | - There was no analytical confirmation of imidacloprid in the treatment solutions - Control performance was not reported in component 1 and component 2 of the study | <i>Qualitative</i> Mommaerts, 2010 48151502 |
| IMI – technical grade (<i>Bombus terrestris</i>) | Sucrose (0 and 10 µg a.i/L) | 4 weeks (4 weeks) | - 10 colonies per group of control, IMI, λ-cyhalothrin (spray treatment), and mix of two | Mean worker mortality, % workers getting lost, % worker loss + mortality, % sucrose consumption, pollen foraging size, number of workers/colony, number of foragers/colony, number of foragers/colony, | %workers getting lost (↑50%)†, %worker loss + mortality (↑37%), number of workers/colony (↓27%)†, number of foragers/colony (↑150%)†, brood | - Vulnerability of small size colonies may differ from that of larger colonies; - The protozoan <i>Critchidia bombi</i> was found in 55% | <i>Qualitative</i> Gill, 2012 49719618 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations³ | Classification Citation (MRID Number) |
|--|---|------------------------------------|--|---|--|---|--|
| | | | <ul style="list-style-type: none"> - Colonies housed in laboratory but allowed to freely forage outside through connecting tube - Foraging observations recorded with RFID tags | <p>brood production, queen loss, nest structure mass, colony failure, number of foraging bouts/colony, pollen load score/foraging worker, pollen load score/foraging bout, % foraging bouts/forager that returned with pollen, duration of pollen bouts</p> <p>-- (Yes)</p> | <p>production/colony ($\downarrow 22\%$)†, pollen load score/foraging worker ($\downarrow 31\%$)†, %foraging bouts/forager that returned with pollen ($\downarrow 28\%$)†, duration of pollen bouts ($\uparrow 18\%$)†</p> | <p>of the colonies although there was no treatment-related effect in the incidence of the disease among the bumble bees.</p> <ul style="list-style-type: none"> - No analytical confirmation of treatment concentrations | |
| IMI – technical grade (<i>Bombus terrestris</i>) | Sucrose (0, 0.08, 0.20, 0.51, 1.28, 3.20, 8.0, 20.0, 50.0, and 125.0 µg a.i./L) | 13 days (14 days) | <ul style="list-style-type: none"> - Micro-colonies (4-5 workers, no queen) established to examine effects on ovary development and reproduction - Varying number of replicates for each concentration | <p>Fecundity (number of eggs and larvae produced), food consumption, and oocyte development</p> <p>-- (Yes)</p> | <p>Fecundity: $\downarrow 42\%$ at 1 µg a.i./L.</p> | <ul style="list-style-type: none"> - Unknown relevance of reproductive effects on workers for effects to colony health given that worker production of males is generally much less of the colony male output and workers cannot produce new workers or new queens - No analytical confirmation of treatment concentrations | <i>Qualitative</i> Laycock, 2012 49719622 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations³ | Classification Citation (MRID Number) |
|--|---|---|---|---|--|---|---|
| IMI – technical grade (<i>Bombus terrestris</i>) | Sucrose (of 0, 0.06, 0.16, 0.40, 1.0, 2.5, 6.3, 16, 39, and 98 µg/L | 14 days or 28 days (14 days or 28 days) | <ul style="list-style-type: none"> - 3 queenright colonies (1 queen, 4 workers) per group for 14-days on dose + 14-days off dose (unspiked syrup) - Results from two trials pooled - Continuous exposure of 1 group (5 colonies) to 98 µg/L for 28 days (7 colonies for control) | <p>Brood production, time to first oviposition, pollen consumption, sucrose consumption</p> <p>-- (Yes)</p> | <p>Brood production: 14-day on-dose EC₅₀: 1.44 µg/L, 28-day (on/off dose) EC₅₀: >98 µg/L</p> <p>Pollen consumption: 14-day on-dose EC₅₀: 4.4 µg/L, 28-day (on/off dose) EC₅₀: 44 µg/L</p> | <p>- Long-term impacts of decreased brood production on other colony health parameters like queen loss and worker mortality were not investigated</p> | <i>Qualitative</i> Laycock and Cresswell, 2013 49719621 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations³ | Classification Citation (MRID Number) |
|--|---|------------------------------------|---|--|---|---|--|
| IMI – technical grade (<i>Bombus terrestris</i>) | Sucrose (0 and 10 µg a.i/L) | 6 weeks (6 weeks) | <ul style="list-style-type: none"> - 8 queen-right colonies in each group - Colonies were kept in cages within the laboratory for the entire duration of the study - Data informed the Sublethal Stress Model development (developed by the study authors) | <p>Mortality, brood production -- (No)</p> | <p>Mortality (day 0-42) (↓2.56%), birth rate (day 0-42) (↓71.3%)</p> | <p>- Control mortality differed substantially between the 8 colonies, ranging from 9-38%, and above 25% in 5 of 8 colonies. As this study was conducted in the laboratory, this is suggestive of general husbandry issues;</p> <p>- Although there appeared to be sufficient replication among the treatment groups, the results were not subjected to statistical analysis by the study authors.</p> <p>- No analytical confirmation of treatment concentrations</p> | <i>Qualitative</i> Bryden, 2013 49719607 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations³ | Classification Citation (MRID Number) |
|--|---|------------------------------------|---|--|---|---|--|
| IMI – technical grade (<i>Bombus terrestris</i>) | Sucrose (0 and 10 µg a.i./L) | 4 weeks (4 weeks) | - Same methodology used in Gill 2012 - Temporal analysis of the foraging data of Gill 2012 assessing week-by-week results. | Number of foragers, foraging bouts, foraging bout duration, pollen load size from all foraging bouts, pollen load size from successful foraging bouts, successful pollen foraging bout duration -- (Yes) | Number of foragers (↑ for all intervals/sampling times)†, foraging bouts (↓ - week 2 only)†, pollen load size from all foraging bouts (↓ - week 4 only)†, successful pollen foraging bout duration (↑ - week 4 only)† | Same limitations as those identified in Gill 2012 | <i>Qualitative</i> Gill and Raine, 2014 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations³ | Classification Citation (MRID Number) |
|--|---|------------------------------------|---|---|--|--|--|
| IMI – technical grade (<i>Bombus terrestris</i>) | Sucrose (0, 0.7, and 1.4 µg/L – ‘low group’); Pollen (0, 6, and 12 µg/L – ‘high group’) | 14 days – lab (6 weeks in field) | <ul style="list-style-type: none"> - 25 colonies per group (mean 15 bees per colony) - Colonies provided spiked sucrose and spiked pollen simultaneously in lab for 2 weeks - Moved to field (with mixed farmland) for 6-week observation period | <p>Colony weight, mean numbers of life stages (workers, males, pupae, and empty pupal cells), mean number of queens produced</p> <p>--</p> <p>(Yes)</p> | <p>Colony weight: ↓8% ('low group')†, ↓12% ('high group')†, Number of queens produced: ↓85% ('low group')†, ↓90% ('high group')†</p> | <ul style="list-style-type: none"> - No analytical verification of imidacloprid in nectar and pollen - It would have been informative to have a measure of food consumption or whether the pollen and nectar stores had to be replenished at any time during the 14-day exposure - Although the authors suggest that imidacloprid may have reduced foraging efficiency in the treated colonies, this study did not include any response variables to evaluate foraging efficiency | <i>Qualitative</i> Whitehorn, 2012 49719634 |

| Test Substance – Purity (Test species) | Exposure Matrix (Exposure Level) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations³ | Classification Citation (MRID Number) |
|---|---|------------------------------------|--|---|---|--|---|
| IMI – not reported (<i>Bombus terrestris</i>) | Sucrose: (0, 0.7 µg/L); Pollen: (0 and 6 µg/L) | 14 days – lab (4 weeks in field) | - 3 colonies per group (65 bees per colony) - Colonies observed after exposure in area described as urban garden area with nearest farmed area 0.5 miles away | Colony survival, weight of nectar collected/foraging bout, nectar foraging efficiency, weight of pollen collected, pollen foraging efficiency -- (Yes) | Weight of pollen collected: ↓28%†, pollen foraging efficiency: ↓31%† | - Purity of imidacloprid not reported - Analytical verification of imidacloprid in spiked pollen and nectar was not conducted | <i>Qualitative</i> Feltham, 2014 49719617 |

IMI = imidacloprid; RFID = radiofrequency identification;

[†]Indicates effect was statistically significant (p<0.05).

²Not all studies were associated with NOAEC/LOAEC values. This column will report the most sensitive statistically derived or otherwise observed difference from that of the control.

³Limitations considered to be major listed here. Others associated with this study can be found in the study summaries in **Appendix E**.

There were 4 feeding design studies that assessed worker bumble bee mortality. Mommaerts, 2010 (formulated imidacloprid, spiked sucrose) tested both microcolonies (5 bees) and queen-right colonies (25 bees) for 11 week and 2-week exposure durations, respectively. In one microcolony trial, there was 100% mortality in the 200, 2000, 20000, and 200000 µg/L treatment groups while mortality was not significantly reduced (maximum reduction of 15% from control) at the 10 and 20 µg/L groups. In a second trial with the same treatment groups but an additional experimental chamber to evaluate foraging, there was again 100% mortality in the top 4 groups with 50% mortality in the 20 µg/L. For queen-right colonies (2, 10, and 20 µg/L treatment groups), mortality was significantly increased over the control at the 10 and 20 µg/L groups (\uparrow 62 – 92%, respectively). It is not clear why the queen-right colonies were determined to be more sensitive to lower concentrations and for shorter durations as compared to the queenless microcolonies. In Gill, 2012 (technical imidacloprid, spiked sucrose, 10 µg a.i./L, 4-week exposure), there was no significant ($p>0.05$) impact on worker mortality determined. Bryden, 2013 (technical imidacloprid, spiked sucrose, 10 µg a.i./L, 6-week exposure period) observed a 2.6% reduction in survival (no statistical analysis conducted) from the control. In Feltham, 2014 (spiked sucrose – 0.7 µg/L, and spiked pollen – 6 µg/L, 14-day exposure), 92% of exposed colonies in the treatment group (both food provisions available simultaneously) survived until the end of the 4-week post-exposure observation period in the field.

Effects on numbers of various life stages:

There was one semi-field tunnel design study and 2 semi-field feeding design studies that investigated effects on various life stages of bumble bees. In Gels, 2002 (formulated imidacloprid, 28-day exposure period in flight cage) bumble bee colonies were placed in flight cages following either granular or spray application to turf. For the granular application (0.4 lbs a.i/A of Merit® 0.5 G), there were no significant effects ($p>0.05$) determined although the number of workers decreased by 26% and the number of brood chambers increased by 75% relative to the control. There was high variability in the responses for this component of the study with statistical methods used failing to identify percent differences of 70% and above. In the spray application component (0.3 lbs a.i/A Merit® 75 WP), there were significant ($p<0.05$) decreases in the numbers of workers (\downarrow 60%) as well as the number of brood chambers (\downarrow 72%). Interestingly, these differences were identified when spray applications were not followed by irrigation; however, when irrigation was administered, there were no significant differences from the control group. In Gill, 2012, there was a significant reduction ($p<0.05$) in the number of workers per colony (\downarrow 27%) following a week exposure to 10 µg a.i./L. Finally, Whitehorn, 2012 (technical imidacloprid, spiked sucrose – 0.7 and 1.4 and spiked pollen – 6 and 12 µg/L co-exposure, 14-day exposure period) did not identify significant effects ($p>0.05$) on the numbers of workers, males, and pupae.

Effects on reproduction (brood and queen production)

There were 6 feeding design studies (4 spiked sucrose studies, 2 with co-exposure of spiked sucrose and spiked pollen) and one full-field study that assessed endpoints related to reproduction. In Mommaerts, 2010 in addition to no reproduction at the concentrations which elicited 100% mortality in the microcolony trials, there was no reproduction in the 10 and 20 µg/L groups for the queen-right colony

trial. Reproduction was not significantly impacted ($p>0.05$) at 2 µg/L. Gill, 2010 found a significant ($p<0.05$) 22% reduction in brood production as compared to the control group. Laycock, 2012 (technical imidacloprid, spiked sucrose, concentrations ranging from 0.08 – 125 µg a.i./L, 13-day exposure period) tested microcolonies (4-5 workers each) and determined a 42% reduction in fecundity at a concentration of 1 µg a.i./L. Whitehorn 2012 exposed queen-right colonies (25 per treatment) for 14 days in the laboratory followed by a 6-week observation period in the field. The number of queens produced was significantly reduced by 85 and 90%, for the “low” (6 µg/L/0.7 µg/L pollen/sucrose) and “high” (12 µg/L/1.2 µg/L pollen/sucrose) fed groups, respectively. As shown in **Figure 5-3**, it is evident that queen production is highly variable in the control *B. terrestris* colonies, with the bulk of new queens coming from 5 colonies. These same 5 control colonies were also the largest in terms of overall weight (data not shown), which supports the hypothesis that queen production is dependent on colony size of *B. terrestris*. It is also noteworthy that 48% of the control colonies did not produce queens whereas 88% and 68% of the low and high exposure groups, respectively, did not produce queens. It is not known whether the failure of 48% of the control hives to produce new queens reflects “normal” development and queen production in natural *B. terrestris* colonies in the field. Nevertheless, it is evident that colonies failed to produce large number of queens in the low and high exposed treatments, relative to controls.

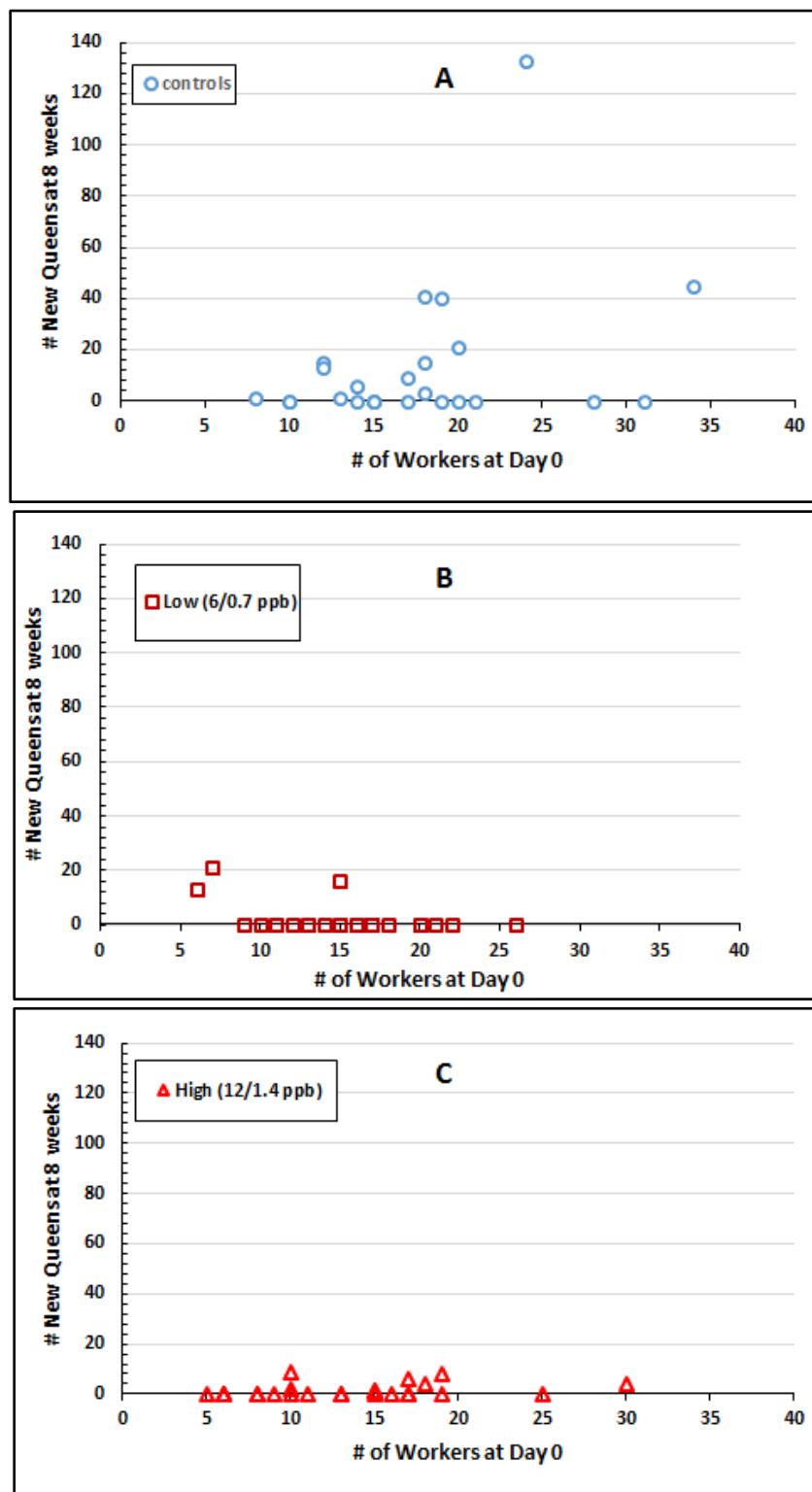


Figure 5-3. Queen Production Data from Whitehorn et al (2012) in Controls (A), Low (B) and High Exposure Treatments (C). Legend numbers indicate the concentration in pollen and nectar, respectively.

In Bryden, 2013, there was a 71% reduction in brood production the sole treatment group of 10 µg a.i./L (statistical analysis not conducted). In Laycock and Cresswell, 2013 (technical imidacloprid, spiked sucrose, concentrations ranging from 0.06 – 98 µg a.i./L), queen-right colonies (1 queen, 4 workers) were exposed to imidacloprid spiked sucrose for 14 days followed by 14 days of observation while colonies were fed untreated sucrose. When assessing the exposure only interval, the EC₅₀ for brood production was 1.44 µg a.i./L, a similar finding of Laycock 2012. When assessing the entire 28-day duration (including the 14-day ‘off dose’ period) the EC₅₀ was determined to be >98 µg/L, suggesting a recovery in brood production after exposure to imidacloprid ceases. Finally, in Tasei, 2001, there were 17 and 24 queens per colony in the control and treatment fields, respectively, and the difference was not statistically significant ($p>0.05$).

Foraging behavior/foraging success observations:

There was one semi-field tunnel design study and 3 semi-field feeding design studies evaluated for *Bombus* that assessed endpoints related to foraging behavior and success. In Tasei, 2001 (0.7 mg a.i./sunflower seed), while the effects were not statistically significant ($p>0.05$) there were increases in the number of workers visiting blooming heads of seed treated sunflowers ($\uparrow 36\%$), and the number of ‘long’ foraging trips (characterized by the study authors as being longer than 50 seconds). In Gill, 2012 (sucrose exposure to 10 µg a.i./L), the study authors used radio frequency identification (RFID) tags to obtain various measures of foraging behavior and success. There were significant increases ($p<0.05$) in the numbers of foragers per colony ($\uparrow 150\%$) and the duration of pollen foraging trips ($\uparrow 18\%$), as well as significant decreases ($p<0.05$) in pollen load score (amount of pollen collected relative to the size of the worker) ($\downarrow 31\%$), and the number of foraging trips that returned with pollen ($\downarrow 28\%$). The results of this study were collected over a 4-week exposure duration. In follow up work by Gill and Raine, 2014, the foraging data were analyzed more temporally (*i.e.* week-by-week) as opposed to collapsing the entire 4-week study duration. While means of the response variables were not provided, there were significant ($p<0.05$) increases in the number of foragers (all intervals assessed), and the duration of pollen foraging trips (week 4 only) at the sole treatment concentration of 10 µg a.i./L. Additionally, there were significant decreases ($p<0.05$) in the number of foraging trips (week 2 only), and the pollen load size from all foraging trips (week 4 only). Finally, in Feltham, 2014, colonies were evaluated for the weight of nectar and pollen collected as well as efficiency (weight collected per hour). While there were no significant effects on nectar variables, the weight and foraging efficiency for pollen were significantly decreased ($p<0.05$), $\downarrow 28\%$ and 31%, respectively at the sole treatment group of 0.7 µg/L in nectar and 6 µg/L in pollen.

Summary:

The suite of evaluated higher-tier studies with the *Bombus* suggest that impacts to reproductive endpoints and measures of foraging behavior and success occur at lower concentrations in sucrose and pollen than those that elicit effects on mortality (as supported by Gill, 2012, Mommaerts, 2010, Laycock, 2012, Laycock and Cresswell, 2013, Whitehorn, 2012, and Bryden, 2013). In these studies, effects to reproduction (inclusive of worker and queen production) occurred at sucrose levels as low as 0.7 µg/L and pollen levels as low as 1.4 µg/L. Interestingly, queen-right colonies of bees exposed for 2 weeks appeared more sensitive to effects on mortality (62 and 92% reductions at concentrations of 10 and 20

$\mu\text{g}/\text{L}$) compared with 11-week exposure periods with queenless microcolonies (0 and 15% mortality in 10 and 20 $\mu\text{g}/\text{L}$; 0 and 50% mortality in 10 and 20 $\mu\text{g}/\text{L}$ for two trials, respectively). However, the effects on fecundity when microcolonies and queen-right colonies exposed to similar concentrations of imidacloprid appear to be similar as suggested by work by Laycock (2012 and 2013) with microcolonies showing a 42% reduction in fecundity at 1 $\mu\text{g}/\text{L}$ while queen-right colonies showed a 50% decrease in brood production at 1.44 $\mu\text{g}/\text{L}$.

The impact at 1.44 $\mu\text{g a.i./L}$ identified by Laycock and Cresswell (2013) was determined after a 14-day exposure period. These colonies were subsequently observed a further 14 days feeding on untreated syrup and when the entire 28-day study duration interval is considered, there were no significant effects on brood production up to and including the highest dose (98 $\mu\text{g}/\text{L}$). This suggestion of a recuperation from significant effects when imidacloprid exposure ceases is also suggested in other work by Cresswell on individual bumble bees. As discussed previously, bumble bees exposed to 125 $\mu\text{g a.i./L}$ for 3 days were observed to consume less food and exhibit less locomotor activity ($p < 0.05$). When switched to untreated sucrose, bumble bee workers were significantly more active after 3 days, and feeding rates were at levels similar to control after 8 days. While these results suggest that colonies and individuals can recover from short-term exposures to imidacloprid, it is noted that even in crops with short blooming periods that are highly synchronous (e.g. canola), the fate of colony could still potentially be impacted as foragers would be expected to bring nectar back to the hive, process it, and store it for potentially long periods of time.

The results of these studies also indicate that imidacloprid exposure ranging from 2 – 6 weeks, could potentially lead to a greater recruitment of foragers that is hypothesized to be due to more frequent and less efficient foraging trips in collecting pollen. These effects were determined in one study (Gill and Raine 2014) to occur immediately following exposure (increased numbers of foragers) or appear after several weeks of exposure (decreased pollen load size, increased pollen foraging trip duration). It is noted here that pollen is a vital food source for the colony (both for *Bombus* and *Apis* species), not only promoting the development of the queen's ovaries, but also serving as the primary food for the *Bombus* larvae. While the studies indicating increased foraging numbers, and decreased foraging efficiency also indicated that these colonies did not fail (at 4 weeks exposure, 10 $\mu\text{g a.i./L}$), the impact to colonies under conditions different from those tested in these studies is uncertain.

5.3. Tier III Studies

Tier III represents the highest level of refinement for pollinator studies since they are intended to characterize the potential effects of a pesticide on bee colonies under actual use conditions. These studies are organized by source (*i.e.*, registrant submitted vs. open literature) and are discussed below.

5.3.1. Registrant Submitted

Since the publication of the preliminary risk assessment, the registrant submitted two full field studies to evaluate the colony level risk associated with agricultural field applications to cotton and pumpkin

fields. The experimental design, conclusions, and strengths and limitations of each study are further described below.

5.3.1.1. Full field study with Cotton

A full field study was conducted to evaluate the potential long-term effects of imidacloprid exposure to honey bee hives, which were placed within or at the edge of treated and untreated (reference) cotton fields in the California Central Valley during the summer of 2015 (MRID 50206701). The study contained 4 imidacloprid-treatment sites and 4 reference sites ($n=4$) near agricultural cropping areas where there was documented pesticide use. Each site was at least 12 ha (29.6 acres), and each was 3 miles apart. One reference field was discontinued during the middle of study due to the severe adverse effects of other pesticides. Two additional treated field sites were prepared but data were excluded from the data analysis due to the deviation of imidacloprid treatments according to the study protocol. Multiple pesticides were applied to all test sites for crop production purposes during the study. Imidacloprid-treated cotton fields received various combinations with imidacloprid treatment, imidacloprid-treated seed, in-furrow application, and one or two foliar applications prior to the exposure period. The total imidacloprid application rates ranged 0.06-0.45 lb a.i/A (0.07- 0.50 kg/ha) and the days between the last imidacloprid applications to initiation of hive exposure varied between 18-30 days.

Eight experimental study hives and one monitoring hive were selected and randomly assigned in a stratified manner to either imidacloprid-treated cotton field sites or reference cotton field sites. The study hives were placed in their assigned fields at the beginning of the cotton blooming period and remained at the cotton fields for exposure for 6 weeks. Thereafter, hives were relocated to a post-exposure apiary near Lost Hills, CA. Two collections of non-*Apis* bees were conducted during the mid- and late-exposure periods, using bee bowl traps containing soapy water. Pesticides residues were measured from various matrices (soil, plants and hives) and time points. The hive conditions were assessed multiple times during and after the exposure period. There were two colony condition assessments (CCAs) conducting after the overwintering period to measure overwintering success. During the study, all test hives were treated with an additional pesticide for the control of varroa mites and were fed with supplemental sugar for the entire period after exposure. Two treatment sites received imidacloprid applications in error and were considered for removal from the study. Site NT003 was intended to be a reference site but received imidacloprid applications at similar rates to the treatment sites and site NT008 received almost double the rate of imidacloprid as the other treatment sites and represents an off-label application.

Multiple pesticides other than imidacloprid were applied to the test fields during the study in accordance with agricultural practice. Several additional chemicals were found in pollen and nectar of reference and treatment hives. **Table 5-15** below shows the chemicals found in nectar and pollen collected from bee hives in the study and the associated acute oral RQ calculated from those residue values.

Table 5-15. Measured residues and associated RQs for chemicals found in the cotton field study hives (MRID 50206701)

| Chemical residue found | Max residue in nectar ppb | Max residue in pollen ppb | Acute oral RQ from measured residues | Bee caste or task |
|-------------------------------------|---------------------------|---------------------------|--------------------------------------|-------------------|
| 2,4 Dimethylphenyl formamide (DMPF) | 10 | 285 | 0.07 | Nurse bee |
| Acephate* | 27.9 | | NA | |
| Acetamiprid | 308 | | 10 | Nectar forager |
| Bifenthrin* | 16.3 | 122 | NA | |
| Carbaryl | | 114 | 4.7 | Nurse bee |
| Chlorpyrifos | | 9.9 | 95 | Nurse bee |
| Cyhalothrin total* | | 4.2 | 0.08 | Nurse bee |
| Cypermethrin* | | 34.2 | 1.9 | Nurse bee |
| Etoxazole* | 5.9 | 79.2 | 0.01 | |
| Flonicamid* | 511 | 78.6 | 2.5 | Nectar forager |
| Fluvalinate | 2.5 | | NA | |
| Methamidophos | 4.7 | | NA | |
| Methoxyfenozide | | 155 | 0.01 | |
| Pendimethalin | | 142 | 0.01 | |
| Pyraclostrobin | | 183 | 0.02 | |
| Pyrimethanil | | 85.1 | 0.01 | |

*Chemical sprayed on cotton fields during study

NA oral ingestion toxicity information not available for this chemical

Conclusions

Imidacloprid was detected in plant pollen, nectar and leaves during the entire 6-week exposure period in both reference and treatment sites. However, the magnitude of the total imidacloprid (parent + 2 degradates of concern) in the treated sites were marginally greater than that in the reference (approximately 2-3×). The averages of total imidacloprid in the 6-week exposure period in the reference and treatment site respectively were: 4.4 and 12.9 µg/L in intra-floral nectar, 2.8 and 7.7 µg/L in extra-floral nectar, and 1.9 and 3.5 µg/L in pollen, and 7.3 and 7.2 µg/L in leaves. The average of total imidacloprid detected in experimental hives in the reference and treatment sites were 1.15 µg/L and 4.03 µg/L respectively in hive nectar, and 1.94 and 2.97 µg/L, respectively, in hive bee bread.

It was reported that there were no significant treatment-related differences in capped brood, pollen frame coverage, and overwintering survival between the hives that were adjacent to untreated and imidacloprid-treated cotton fields. The adult bee counts differed between imidacloprid-treated and reference plots at two CCAs: at CCA 4, hives at imidacloprid-treated sites had higher adult bee counts, while at CCA 6, hives from reference-treated sites had higher adult bee counts. However, at the end of the study (*i.e.* post overwintering) there were no significant differences between treatment groups and reference for this response variable. To compare the mortality in treatment and reference, when two sites (NT003 and NT008) were excluded from the study, the hive mortality was 12.5% (3 out of 24 hives)

in the reference and 22.6% (7 out of 31 hives) in the treatment. When site NT003 was considered to be a treatment site (similar imidacloprid application rate as other treatment sites) and site NT008 was excluded due to the overdosing, the hive morality was 12.5% (3 out of 24 hives) in the reference and 23.1% (9 out of 39 hives) in the treatment.

The results of this study indicate that imidacloprid exposure from field applications to cotton at the label permitted rate do not show impact on capped brood, pollen frame coverage, or adult bee counts. There was some indication of differences in overwintering hive mortality between the reference and treatment fields. However due to the many limitations of the study, these conclusions are highly uncertain. The primary limitations include the use of many other toxic to bee chemicals (further supported by their observation in hive residues), the variable nature of the imidacloprid applications, and imidacloprid contamination in reference and monitoring sites. Therefore, the results of Tier III study are not considered informative as a line of evidence for risk assessment.

Strengths and Limitations

It is important to recognize the inherent strengths and limitations of this study as results are considered in this risk assessment. In the context of available field studies involving imidacloprid, this study contains a number of strengths including:

- Quantification of exposure to imidacloprid and toxicologically-relevant metabolites directly in plants (pollen and intra- and extra-floral nectar) and in hive matrices (uncapped nectar, trapped pollen, honey, bee bread)
- Use of a 6-week exposure duration to represent a reasonably conservative exposure scenario.
- Measurement at multiple time points with multiple colony-level endpoints reflecting hive strength, brood development and overwintering success and recovery
- Analysis of multiple pesticide residues in monitoring hives to consider potential cross-contamination of other pesticides to the treatments
- Analysis of pollen species (palynology) to consider the extent of test bees foraging on the test plants (cotton) and other plants.
- Measurement of non-*Apis* bee species richness and abundance.

A number of limitations/uncertainties were also noted with this study, including:

- The study was conducted in agricultural areas with intensive pesticide use. Multiple pesticides, including those that are highly toxic to bees, were detected at high concentrations in monitoring hives. Impact of other pesticides to the capability of the study in detection of any imidacloprid treatment effects was unknown, but likely was reduced.
- Multiple pesticides other than imidacloprid were applied to the test fields during the study. There is uncertainty in associating the study results to imidacloprid treatment only. The honey bee colony effects observed during the study might result from the combination effect of imidacloprid and other pesticides by considering high magnitude of other pesticides and relatively low magnitude of imidacloprid detected in the

- monitoring hive. In fact, hives at site TN002 had to be discontinued due to the concerns with exposure to other toxic pesticides.
- Imidacloprid contamination in the reference sites, wintering apiary after exposure and after overwintering was commonly detected throughout the entire test period. These imidacloprid contaminations are expected to undermine the detection of imidacloprid treatment effects of the study.
 - The level of exposure of imidacloprid to honey bee colonies was low in the study. Compared to the level of contaminated imidacloprid in cotton plants and test hives in the reference sites, imidacloprid in the treatment sites was approximately 2-3 times greater than that in the reference, which is expected to further complicate the detection of treatment effects considering both the reference contamination and small difference in the treatment and reference.
 - There were low numbers of study replicates (*i.e.* fields). The study was initially designed with five replicates. However, there were only two reference sites and four treatment sites due to various issues that occurred during study. Two sites were removed due to the use of imidacloprid and other pesticides, and one additional site was artificially removed due to the concern of exposure to other highly toxic pesticides. The reduced number of replicates decreases the statistical power in determining a chemically-mediated effect.

5.3.1.2. Full Field study with Pumpkin

A full-field study was conducted to evaluate the potential long-term effects of imidacloprid exposure to honey bee colonies and other non-*Apis* bees. The study was conducted in pumpkin fields (all with soils characterized as clay) in central South Dakota in 2015-2016 (MRID 50263601). The fields were approximately 40 acres each and located in areas for which grassland/pasture and wheat fields were the predominant land use. Imidacloprid was applied as sub-surface side dress at 0.38 lb/acre (the maximum labeled single application rate; 0.43 kg/ha) once pumpkins had reached the six true leaf stage (BBCH16). Nine honey bee colonies were placed in each of the pumpkin fields during flowering period. Additional honey bee colonies were placed in each of the fields to monitor other non-imidacloprid pesticide exposure to the test hives. There were five replicate sites for each treated and untreated field. The hives remained in the pumpkin fields for exposure for 6 weeks and were then relocated to a post-exposure apiary near Durand, WI.

Conclusions

In the reference fields, the total imidacloprid (parent + 2 degradates of concern) was not detected in plant nectar but was detected at 2.0-7.9 µg/L in plant pollen (5 out of 15 samples, in 3 out of 5 reference sites for at least one-time point). The total imidacloprid in treated sites was detected at 1.1-5.1 µg/L in plant nectar (13 out of 15 samples), and 2.1-15.8 µg/L in the plant pollen (14 out of 15 samples).

The data indicated that there was imidacloprid contamination in plant pollen in the reference fields, and the maximum detections in plant pollen were about two times greater in the treatment than that in the reference, and the frequency of detection was lower in the references than in the treatments. Test hives

had a low level of background contamination with imidacloprid. Prior to the exposure (CCA 2), low levels of imidacloprid contamination were detected in hive nectar and bee bread. Hives in the treatment sites had slightly increased levels of imidacloprid exposure compared to reference during exposure period (during exposure (CCA 3) and at the end of the exposure (CCA 4)). Compared to the reference, the concentration of total imidacloprid detected in uncapped nectar in treated hives appeared to be similar (range 1-2.6 µg/L), but the detection frequency was slightly increased from 2/45 hives in the reference to 7 out 45 hives in the treatment. In bee bread, the concentration and the frequency of detection of total imidacloprid in treated hives appeared to be greater than those in the reference. In CCA 3 and CCA 4, the range of the imidacloprid concentrations was 1.7-4.5 µg/L detected in 2-8 out of 45 hives in the reference and increased to 1.7-17.9 µg/L detected in 14-30 out of 43 hives in the treatments. Imidacloprid was not detected in capped honey after overwintering in any hives.

For honey bees, no treatment related adverse colony effects were detected in terms of colony conditions, hive weight, overwintering hive survival, queen conditions, and Nosema and varroa infestation in the study. For other non-*Apis* bees, data indicated that there was a high degree of variability in the abundance of non-*Apis* bees among the study pumpkin fields, regardless of the use of imidacloprid. However, no adverse impact was detected on non-*Apis* species diversity and abundance due to imidacloprid use in the pumpkin fields. Multiple bee species were found in both reference and treatment fields.

Strengths and Limitations:

It is important to recognize the inherent strengths and limitations of this study as results are considered in this risk assessment. In the context of available field studies involving imidacloprid, this study contains a number of strengths including:

- Quantification of exposure to imidacloprid and toxicologically-relevant metabolites directly in plants (pollen and nectar) and in hive matrices (uncapped nectar, trapped pollen, honey, bee bread)
- Use of a 6-week exposure duration to represent a reasonably conservative exposure scenario.
- Measurement at multiple time points of multiple colony-level endpoints reflecting hive strength, brood development and overwintering success and recovery. Analysis of multiple pesticide residues to consider the potential cross-contamination of other pesticides to the treatments.
- Analysis of multiple pesticide residues to consider the potential cross-contamination of other pesticides to the treatments.
- Analysis of pollen species (palynology) to consider the extent of test bees foraging on the test plants (pumpkins) and other plants.
- Measurement of species richness and abundances of non-*Apis* bees.

A number of limitations are also noted with this study, including:

- The level of exposure to test plants (pumpkins) was low relative to levels reported from other studies of cucurbit crops treated with soil application of neonicotinoids.

- With regards the residues, the detected maximum total imidacloprid in the treatment was 5.1 µg/L in plant nectar, 15.8 µg/L in plant pollen, 2.6 µg/L in hive honey, and 17.9 µg/L in hive bee bread in the treatment, which were approximately two times greater than that in the reference. In the reference the detected maximum total imidacloprid were <LOD in plant nectar, 7.9 µg/L in plant pollen, 2.6 µg/L in hive honey, and 4.5 in hive beebread.). The frequency of detection of imidacloprid in the references was lower than in the treatment.
- In addition, pumpkin pollen was rarely found in pollen collected by honey bees, indicating that test honey bees were foraging on food sources, at least pollen, mainly from other plants. Information on whether bees collected pumpkin nectar was not collected. This low level of exposure may be due to the inherent inferior attractiveness of pumpkins to honey bees. However, it may also be related to the availability of other more attractive flowering plants in and nearby the test area. Therefore, there may be uncertainties in extrapolating these pumpkin study results to other more attractive plants.
- The hive colony mortality after overwintering was high in both reference and treatment, approximately 40%. This high mortality was similar to the overall US national mortality in the study year. The high background mortality during the study period in the study area may compromise the sensitivity of the study to detect treatment effects.
- Other pesticides were detected in monitoring hives after the exposure period; impact of other pesticides to the treatment is unknown.
- Study was conducted in predominantly heavy (clay) soils, which have been shown to limit the uptake of imidacloprid residues when applied as a soil treatment. Other growing areas with higher proportions of loam and sand in the soil may have higher residues in pollen and nectar.
- Detailed effect data on bumble bee colonies were not provided. Bumble bee colonies were reported to perform poorly in both control and treatment fields.

5.3.2. Open Literature

There are two *Apis* and one *Bombus* full field studies that were evaluated in the open literature which are summarized below with further details on the methods provided in **Appendix E**.

5.3.2.1. *Apis*

In Pohorecka, 2013 (formulated imidacloprid, seed-treated corn full-field design, 21-day exposure period, overwintering observation in one trial year) reported the number of dead honey bees in the 2011 trial was not significantly different from control ($p>0.05$) throughout the exposure period and up until the last colony visit in mid-October (141 dead bees/colony in treatment group compared to 132 dead bees/colony in control; **Table 5-16**). In 2012, while the observation period for mortality was a month and a half shorter (last assessment made in late August) there was no treatment-related effect on mortality ($p>0.05$, 22 dead bees/colony in treatment group compared to 30 dead bees/colony in the control). All colonies (control and treatment) were stated to have overwintered successfully for the

2011 trial (no further information given, similar information not provided for the 2012 trial). The analysis of the pollen collected by bees indicated only 3% was from the treated crop.

Stadler, 2003 (formulated imidacloprid, seed-treated sunflower full-field design, 10-day exposure period, overwintering component) reported that there were no significant ($p>0.05$) effects on mortality. It is noted however that this determination appeared to only be from the exposure phase of the study and there was no indication of mortality results for the rest of the 216-day observation period, including after the overwintering period (**Table 5-16**).

In both the Pohorecka and Stadler studies, there were significant ($p<0.05$) increases in the percent frame coverage of brood area for the treatment groups compared to controls in multiple CCAs. In Pohorecka, these increases (relative to controls) were 44% and 87% in the mid-September and early October CCAs, respectively, although it was noted in the study report that these numbers were typical for the time of season. It is noted that despite these increases, the study authors stated that all control and treatment group colonies overwintered successfully. Similarly, while Stadler identified significant increases in brood area coverage, it was not clear from the study article the actual magnitude of these effects as means were not presented and indications of statistical significance were not uniform in their use within the article.

Table 5-16. Summary of Tier III (full field) studies available from the open literature for *Apis* bees

| Test Substance – Purity (Test species) | Crop (App. Rate) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted? – Yes/No) | Effects ² (all comparisons made relative to the study's control) | Limitations ³ | Qualitative Citation (MRID Number) |
|---|--------------------------|-----------------------------|--|---|---|---|--|
| Gaucho® 600 FS - 60% ¹ (<i>Apis mellifera</i>) | Corn (83.3 mL/50k seeds) | 21 days (approx. 3 months) | - One control plot (unknown size), one treatment plot (89 acres) - Colonies assessed every 3-4 weeks during observation period) | Mortality, number of combs covered by bees, brood area -- (Yes) | Brood area: ↑44% (mid-September CCA)†, ↑87% (early October CCA)† | - Pollen analysis indicated 3% or less of pollen collected originating from treated crop; - Two fungicides (metalaxyll and fludioxonil) were seed treated along with imidacloprid. Metalaxyll is known to be systemic in plants and would be expected to be available in pollen and nectar but no information is available for residues in pollen from this study. | Qualitative Pohorecka, 2013 (49719625) |
| Course® 350 FS - 35% ¹ (<i>Apis mellifera</i>) | Corn (150 mL/50k seeds) | | - One control plot (unknown size), one treatment plot (74 acres) - Colonies assessed every 3-4 weeks during observation period) | | Brood area: ↑16% in 1 colony assessments | | |

| Test Substance – Purity (Test species) | Crop (App. Rate) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted? – Yes/No) | Effects² (all comparisons made relative to the study's control) | Limitations³ | Qualitative Citation (MRID Number) |
|--|--------------------------|--|---|---|--|---|--|
| Gaucho® 600FS - 60% ¹ (<i>Apis mellifera</i>) | Sunflower (0.24 mg/seed) | 10 days (216 days, including overwinter) | - One control plot, one treatment plot (each 60 acres) - Hives acclimated for 35 days then moved to fields for 10 days | Hive weight, percent cells occupied with honey and nectar, percent cells occupied with pollen, percent cells occupied with worker brood, percent empty cells, foraging activity, mortality -- (Yes) | ↑ in hive weight†, ↑ in percentage of cells occupied with pollen†, worker brood†, and empty cells† | - Means for each response variable not reported, only direction of effect and indication of statistical significance are reported; - Although foraging activity and mortality were assessed, the summary table differs from the text in reporting of effects in the study article. - Lack of pollen, nectar, and soil residue analysis to confirm exposure. | Qualitative Stadler, 2003 47796301 |

¹Indicates effect was statistically significant (p<0.05).

¹Purity not reported but assumed to be percentage indicated assuming a product density of 1 g/L

²Not all studies were associated with NOAEC/LOAEC values. This column will report the most sensitive statistically derived or otherwise observed difference from that of the control.

³Limitations considered to be major listed here. Others associated with this study can be found in with the study summaries in **Appendix E**.

5.3.2.2. *Bombus*

In a study by Tasei (2001), a full-field design component was initiated with two sunflower fields (located in France), one each serving as a control and the other with seed-treated sunflower (Gaucho[®] - purity not provided - 0.7 mg a.i./seed; **Table 5-17**). Colonies of bumble bees (10 per field in the control and treatment plots) were exposed to untreated and seed-treated sunflower, respectively, for a 9-day exposure period. After this exposure period, the colonies were brought into the laboratory, where they were fed with untreated syrup and pollen paste. After 26 days, the study authors recorded the number of marked bees (with colored spot on thorax to delineate exposure) to estimate their homing rate during the field period and the growth rate of each colony. At the conclusion of the colony life cycle, emerged queens were captured, recorded, and housed in cages along with male bees for mating purposes.

When considering the exposure phase duration (Day 0 to Day 9), the mean loss of marked workers per colony was 33.5% in the treated group as compared to 23.1% in the control group, a difference that was not significant ($p>0.05$). The mean population increase, which was assessed 26 days after the introduction of the hives into the fields, was 86.5 and 78.1 workers/colony in control and treated fields, respectively. This difference was not significant ($p>0.05$). New queens were produced by 8 colonies out of 10 in each field. There were 17 and 24 queens/colony in hives of the control and treated fields, respectively, a difference that was not significant ($p>0.05$). While this study investigated individual and colony-level effects with bumble bees resulting from exposure to seed-treated sunflower, there are uncertainties as to what extent the bumble bees were exposed. Despite the finding that nectar foragers and pollen foragers had 98 and 25% of their respective loads originating from sunflowers, there were no confirmatory measurements in either the semi-field or field components to indicate that imidacloprid was present in the nectar or pollen collected from the bumble bees. Further details on this as well as additional information on the methods and results are provided in **Appendix E**.

Table 5-17. Summary of Tier III (full field) studies available from the open literature for *Bombus* bees.

| Test Substance – Purity (Test species) | Crop (App. Rate) | Exposure Dur. (Observ. Dur) | Design Elements | Endpoints Assessed -- (Statistical analysis conducted? – Yes/No) | Effects ¹ (all comparisons made relative to the study's control) | Limitations ² | Qualitative Citation (MRID Number) |
|---|------------------------------|-----------------------------|---|---|---|--|---|
| Gaucho® – not reported (<i>Bombus terrestris</i>) | Sunflower (0.7 mg a.i./seed) | 9 days (days) | - One control field (44 acres) and one treated field (40 acres); - 10 colonies introduced in each field when sunflowers began blooming, removed after 9 days; - Control and treated field were 12 miles away. | Mean loss of marked workers/colony, colony population (Day 0-26), mean number of new queens. (Yes) | Colony population (Day 0-26) (↓8.65%); mean number of new queens (↑41.2%) | - There were no pollen, nectar, bee, or other samples taken to demonstrate exposure to imidacloprid. Only soil samples were taken in which imidacloprid was not detected (LOD = 5 µg/L), and study authors cite previous work in same field to state that bees were exposed. - Minimal information on the husbandry of the bees and overall health at study initiation. | Qualitative Tasei, 2001 (47800503) |

¹Indicates effect was statistically significant (p<0.05).

²Not all studies were associated with NOAEC/LOAEC values. This column will report the most sensitive statistically derived or otherwise observed difference from that of the control.

³Limitations considered to be major listed here. Others associated with this study can be found in with the study summaries in Appendix E.

5.4. Reported Bee Incident Information

The Office of Pesticide Programs (OPP) maintains a database called the Incident Database System (IDS) in which wildlife incidents reported to the Agency from a variety of sources are maintained.

Additionally, the Environmental Fate and Effects Division (EFED) within OPP maintains an incident database called the Environmental Information Incident System (EIIS). There is some overlap with the information housed in these databases, but generally a more detailed narrative of an incident is contained in an EIIS report such as magnitude of the number of organisms impacted, location, date, product used, use pattern, whether the use was a registered use, and any confirmatory residue analysis if available. The sources of information for incidents include, registrant reports submitted under the Federal Insecticides, Fungicides, and Rodenticides Act (FIFRA) §6(a)(2) reporting requirement, as well as reports from local, state, national and international level government reports on bee kill incidents, news articles, and correspondence made to EFED by phone or via email (through beekill@epa.gov) generally reported by homeowners and beekeepers.

It is noted that not all reported incidents are associated with narrative or analytical information that definitively links imidacloprid exposure to the bee kill event. Analytical information can include residue analysis of dead bees observed at a site or within hive residues of pollen and nectar that confirm imidacloprid was present. Even in those cases, many incident reports are associated with findings of other pesticides, of which the interactions with imidacloprid in contributing to potentially enhanced toxicity to bees are not fully understood. In other instances, imidacloprid was only suspected to be the cause of bee kill events based on observational accounts between beekeepers in a given area. This, as indicated by the summaries below, is not always supported by a confirmatory residue analysis or apiary inspector examination of colony health. Typically, the reported wildlife incidents serve as a line of evidence in determining the potential effects of imidacloprid, as the reports are useful in understanding how its use may impact pollinators under the actual use conditions. As evidenced in the incident summaries below, much of the incident information made through phone and email correspondence to EFED does not usually include a thorough investigation of the incident or provide any confirmatory residue data to link a chemical with a particular incident. Rather, much of these reports are anecdotal in nature.

5.4.1. U.S. Reported Incidents

Over half (14/19) of the incidents summarized in **Table 5-18** below either included a follow-up investigation that confirmed through residue analysis the presence of imidacloprid in at least one matrix (dead bees, floral pollen, nectar) or were submitted by the registrant under FIFRA 6(a)(2). Ten of these incidents originated from an agricultural use while others were mainly from residential and commercial use on ornamentals. In some of these instances, other chemicals (including other neonicotinoid chemicals) were also detected. For others, the incident was determined to originate from a misuse of imidacloprid.

Of the ten incidences reported on agricultural crops half were from soil applications and half were from seed treatment applications. The soil applications four reported dead honey bees near citrus and

soybean fields while one was for bumble bees in greenhouse tomatoes. The majority of non-agricultural incidences (7/9) were applications to ornamental tree species; linden, arbutus, and laurel.

Several other incident reports were more anecdotal in the narrative they provided without a confirmatory residue analysis such as news reports and beekeeper organization newsletters (these incidents are tabulated along with those below in **Appendix G**). Of the incidents that provided a residue analysis, imidacloprid concentrations of dead bee samples were quantified as high as 2456 µg/L. It is important to note incident information serve as one line of evidence and that the absence of reports does not indicate an absence of pollinator losses due to pesticides.

Table 5-18. Summary of reported pollinator incident reports that are either associated with confirmatory residue analysis or registrant submitted

| Incident Record | Date | Use Pattern | Product | Location | Legality | App. Method | Comments |
|-----------------------------|---------|---------------------|---------------|----------|----------------|----------------|---|
| I020700-001 | 06-2008 | Non-Ag (Ornamental) | Merit 2F | DE | Registered use | Soil injection | Submitted under FIFRA 6(a)(2). Linden trees (<i>Tilia cordata</i>) on a commercial golf course were treated for Japanese beetle control using Merit 2F soil injection treatment. It was stated in the report that some months after treatment, the trees bloomed, and dead bumble bees (<i>Bombus</i>) and carpenter bees (<i>Xylocopa</i>) were found at the base of the tree. It was estimated that 2000-4000 individuals were affected (11 trees treated). A follow up residue analysis (August 2008) conducted by Bayer confirmed imidacloprid presence in the leaves of parent imidacloprid (ranging from 2.6 – 11.7 mg/L), IMI-5-OH (1.6 – 2.2 mg/L), and IMI-olefin (0.59 – 1.8 mg/L). Residues of these products in dead bee samples were 0.146, 0.016, 0.138 mg/L, respectively (composite samples). |
| I021017-001 | 03-2009 | Ornamental | Xytect 75 WSP | PA | Undetermined | NR | Submitted under FIFRA 6(a)(2). Product applied to control aphids in 6 linden trees that were reported to 8-10 inches. The application took place March 30, 2009. During blooming, it was discovered that an unspecified number of bees were killed and that the bee deaths ceased when blooming ended. It was unspecified of what species of bee was affected. |
| I025610-001; I025610-002 | 05-2013 | Non-Ag (Ornamental) | Quali-Pro | OR | Misuse | Soil drench | Submitted under FIFRA § 6(a)(2) by Makhteshim Agan of North America (MANA) involving soil drench of linden trees at a golf club in Portland, Oregon that resulted in an unspecified number of dead bumble bees. Oregon Department of Agriculture investigated and conducted residue analysis and determined presence of imidacloprid but there were no residues presented in the report. It was reported that while this use represented one that was permitted by the label, the pest control operator (PCO) did not have the necessary licenses to make this application. |
| I026301-001 | 08-2013 | Non-Ag (Ornamental) | Merit 2F | CA | Undetermined | Tree injection | Submitted as part of FIFRA 6(a)(2) by Bayer Crop Science. A pest control operator (PCO) applied Merit® 2F (imidacloprid) as tree injection to Arbutus and Laurel trees on residential property. The observation of dead bees (number not specified) occurred shortly after the trees were treated. No other confirmatory residue analysis provided in the report. |

| Incident Record | Date | Use Pattern | Product | Location | Legality | App. Method | Comments |
|-----------------|---------|----------------------|------------------|----------|----------------|----------------|--|
| I026563-001 | 06-2014 | Non-Ag (Ornamental) | NR | OR | Misuse | NR | Sidewalks were reported to be littered with dead and dying bumble bees in Eugene, Oregon. The bees were collected the following day by the Oregon Department of Agriculture for testing. Imidacloprid and acephate were detected at 0.05 and 0.30 µg a.i/bee, respectively. An investigation prompted a suspension of the pest control operator company who sprayed linden trees while in bloom, which is a violation of the label restrictions. |
| I026593-001 | 06-2014 | Non-Ag (Ornamental) | Ima-Jeet | OR | Registered Use | Tree injection | Beaverton, OR incident involving bumble bees and honey bees being discovered underneath linden trees in a neighborhood. The trees were treated to control aphids. An investigation led to the discovery that the same pesticides (imidacloprid, dinotefuran) were used here as in a related incident involving linden trees in a parking lot (I025610-001). Follow on investigation took bee, flower, and leaf samples where analysis determined residue levels of 0.050 µg a.i/bee, 0.49 mg/L, and 2.2 mg/L, respectively. |
| I027663-001 | 05-2014 | Non-Ag (Ornamental) | Criterion 75 WSP | MO | Undetermined | NR | Report from the curator of the GT Butterfly House and Bug Zoo in Michigan. The facility inquired about neonicotinoid use on the commercial flowering plant they wanted to purchase in time for their butterflies to arrive in early spring. They settled on Beroske Farms in Ohio that confirmed that no neonicotinoids were used on their flowering plants. After delivery of the plants, subsequent planting, and the beginning of the observation of the foraging of the butterflies on the flowers, it was discovered that 4 nectar feeding butterflies appeared comatose and then later died. No deaths were reported among the fruit eating butterflies. A call with Beroske farms confirmed that the product Criterion® 75 WSP (75% imidacloprid) was used among 6 other pesticides on the flowering plants before delivery to the zoo. It was later confirmed that application to commercial flowering plants represented an off-label use of this product. A follow-up report (I027748) summarized the residue analysis results for imidacloprid for geranium (<LOQ), butterfly bush (1.5 µg/L), coneflowers (<LOQ), livewire grass inside butterfly area (0.51 µg/L), and potting medium (0.12 µg/L); no analysis conducted of dead butterflies. |

| Incident Record | Date | Use Pattern | Product | Location | Legality | App. Method | Comments |
|-----------------------------|---------|-----------------------|---------|----------|--------------|----------------|---|
| I028034-001; I028034-002 | 06-2015 | Urban | NR | OR | NR | Soil drench | Reported by Oregon Department of Agriculture (ODA) to have occurred near Portland State University in Portland, Oregon. According to ODA, the preliminary investigation revealed that the linden trees in the reported incident location had been treated with imidacloprid via soil drench in 2013 and with clothianidin via soil drench in 2014 to control for aphids. Samples of dead bumble bees, linden flowers and leaves were collected for residue analyses and indicate residues of imidacloprid, its degradates (IMI-5-OH, desnitro and IMI-olefin) and chlorothalonil in leaves and flowers, while the samples of dead bumble bees contained the parent imidacloprid (0.0009 µg a.i/bee) and chlorothalonil (0.029 µg a.i/bee) alone. Update: These were the same trees involved in a previous incident (I025610-002). Residues of imidacloprid (0.0095 µg a.i/bee), IMI-olefin (0.0010 µg a.i/bee), desnitroimidacloprid HCl (0.0037 µg a.i/bee) and clothianidin (0.0026 µg a.i/bee) were detected in bumble bee samples and in linden leaves, while linden flowers contained both parent imidacloprid (0.028 mg/L) and clothianidin (0.065 mg/L) alone. It was confirmed by ODA that these trees were the same as those involved in an earlier incident (I025610-002) |
| I029512-010 | 08-2016 | NR | NR | NC | NR | NR | A bee kill incident was reported where a private resident indicated that 3 of his 4 hives had lost some, if not all, of their foraging bee force. Apiary Inspection Services provided further investigation and determined it was obvious the bees had been exposed to some pesticide due to the spinning and shaking symptoms they exhibited. Two samples of dead bees were collected as well as a sample of pollen, Lab analysis confirmed the presence of imidacloprid, bifenthrin, and diethyltoluamide, although the level detected were not provided in the report. After interviewing neighbors and more follow-on investigations, the source of these pesticides could not be located. |
| I023702-001 | 2006 | Ag (Canola, rapeseed) | Gaucho | ND | Undetermined | Seed treatment | Part of an April 2009 report from the Nebraska Beekeepers Association. Seven beekeepers in North Dakota and Minnesota initiated legal action against Bayer Crop Science when they suspected Gaucho (used as a seed treatment on neighboring canola fields) were responsible for their bee losses. Laboratory analysis of the wax comb and honey found imidacloprid in all |

| Incident Record | Date | Use Pattern | Product | Location | Legality | App. Method | Comments |
|-----------------|---------|--------------|--------------|----------|--------------|----------------|---|
| | | | | | | | samples with residues ranging from 22 – 671 µg/L. Carbofuran, dichlotvos, and coumaphos were also screened for (no results provided). |
| I023702-005 | 2007 | Ag (Citrus) | Admire | FL | Undetermined | Soil | Part of an April 2009 report from the Nebraska Beekeepers Association. A beekeeper maintaining 7500 hives for honey production and crop pollination provided 18 hives to a research project organized by Penn State that would monitor the hives to investigate causes for mortality. The beekeeper stated that while he provided 18 hives for the study, he only received 4 back with only 1 hives in a state sufficient to produce honey. The first samples taken were from when the bees were pollinating Florida citrus where imidacloprid residues ranging from 14-17 µg/L were detected in the pollen. Follow up with the grove manager revealed that Admire Pro had been used as a ground application as the trees began to bloom. |
| I022340-001 | 04-2010 | Ag (Corn) | NR | IN | Undetermined | Seed treatment | Summary report from bee kill incidents at the Purdue University Department of Entomology. There were reports of hives with dead bees out in front with observations of seed treated corn being planted in the fields adjacent to the university lab. A residue analysis determined that sampled pollen from affected hives (composite sample) had imidacloprid at levels of 2.8 µg/L. All other sampled matrices (live and dead bees) did not return any detectable residues (LOD and LOQ not reported). Clothianidin was detected in pollen at 21 µg/L. |
| I025512-001 | 08-2013 | Ag (Soybean) | Leverage 360 | MO | Undetermined | Ground | Submitted by Bayer Crop Science under FIFRA 6(a)(2). A soybean farm was being sprayed by Leverage 360 (imidacloprid and beta-cyfluthrin) which was adjacent to neighbor who had 11 honey bee hives. The neighbor had reported that he had “piles of dead honey bees,” back on his property. There was no further confirmatory residue information provided in the report. |

| Incident Record | Date | Use Pattern | Product | Location | Legality | App. Method | Comments |
|-----------------|---------|-------------------|--------------|----------------|----------------|----------------|---|
| I025980-001 | 12-2013 | Ag (Citrus) | Admire Pro | FL | Undetermined | Surface | Submitted by Bayer Crop Science as part of FIFRA §6(a)(2). Admire® Pro application was made on orange tree orchard in which bees had been placed. The hive yards ranged from 1550 – 5500 feet away from the treated grove. The application method was described as “surface” application. A follow-up investigation conducted by Bayer found that the apiaries had small hive beetle in some hives, no varroa present, small amount of early stage European foulbrood, adequate honey stores, and all stages of brood present in the queen yard (1550 yards from grove). In the apiary 5500 yards from grove, there were fewer dead bees than in the yard used for queen breeding and evidence of hive robbing and heavily infested with all stages of small hive beetle larvae. Residue analysis of dead bees from the various yards returned total residues of imidacloprid (parent + IMI-olefin+ IMI-5-OH) yielded results of 2.5–2456 µg/L. Live bee residue analysis had total residues ranging from 1.1 – 5.1 µg/L. |
| I026789-001 | 08-2014 | Ag (Soybean) | Leverage 360 | IL | Registered Use | Ground | Submitted by Bayer Crop Science under FIFRA 6(a)(2). Four hives adjacent to soybean fields were reported to be implicated, with at least 300 dead bees in one hive and 100 dead bees from the other 3 hives. The bees were within ½ mile from the field which had been reported to have made applications of Leverage® (imidacloprid, <i>beta</i> -cyfluthrin) and Stratego® (trifloxystrobin, propiconazole). There was no residue analysis of the bee or any other in hive matrices to confirm exposure to imidacloprid or any other pesticide applied. |
| I026904-001 | 08-2014 | Ag (Oilseed rape) | NR | United Kingdom | Undetermined | Seed treatment | From news article from Smallholder (United Kingdom-based news service). The incident was reported to have occurred in Havering, East London, next to a field of oilseed rape that was thought to have been planted with imidacloprid-treated seeds the previous fall. Hundreds of dead bees were scattered all over the ground with queens from at least 3 species being identified among dead bees. Results of residue analysis of the dead bees determined imidacloprid at levels of 6 µg/L as well as two fungicides (one being flusilazole, the other not being reported). |

| Incident Record | Date | Use Pattern | Product | Location | Legality | App. Method | Comments |
|-----------------|---------|---------------|--------------|----------|----------------|----------------|--|
| I028123-002 | 06-2015 | Ag (Corn) | NR | IN | NR | Seed treatment | In June 2015, a private resident contacted the Office of Indiana State Chemist to report a bee kill to his hives. He estimated a total of 1500 individual bee deaths and suspected the cause of a neighboring farmer applying a seed treated corn application and the resulting dust. A follow-on investigation indicated no agricultural fields immediately within the area of the hives but some were further away nearby. No odd behavior from the bees reported prior to death. Apivar was used as in hive treatment for Varroa. Observance of only hundreds of dead bees instead of the reported 1500. Chemical residue analysis showed all nitro and cyano substituted neonicotinoid insecticides as well as fipronil were below the detectable limit. |
| I028798-001 | 04-2016 | Ag (Tomatoes) | Admire Pro | NJ | Registered Use | | Two bumble bee box hives were placed within a 1500 ft ² greenhouse with potted tomatoes beginning to flower. An application of Admire Pro through drip was made 2-3 weeks before placement of the hives within the greenhouse. There were approximately 12-15 bees dead on the ground of the greenhouse and a few dead bees dead within each hive. |
| I029385-001 | 05-2016 | Ag (Soybean) | Acceleron IX | IN | Registered Use | Seed Treatment | A complaint from a private resident in May, 2016 about a bee kill on her hives prompted an investigation of the Office of the State Chemist in Indiana. The resident suspected pesticides were applied in a neighboring farm field. Investigator interview nearby farmers about planting and pesticide operations. Soybean applications were made around time of bee death but grower indicated he did not use chemicals. Grower provided seed package label to investigator and report indicated seed were previously treated with imidacloprid formulation. An analysis of the dead bees and nearby vegetation and hive sites for multiple neonicotinoid insecticides indicated imidacloprid and other neonics below the level of detections. |

NR: Not reported

5.4.2. Incidents Outside the U.S.

For two incidents (I023737-005 and I24127), the reports concerned broad studies/investigations that detailed bee losses in Italy and Austria, respectively. Full details and methods are described in **Appendix G**. The Italian report details colony losses thought to be due to dust dispersion from the sowing of imidacloprid-treated seed. The Austrian report is similar in nature but generally indicated less frequency of detection (3-11% in samples, depending on the matrix) as compared to 25.7% of dead bees showing imidacloprid residues in the Italian report.

In a report from Health Canada's PMRA entitled "*Update on Neonicotinoid Pesticides and Bee Health (2014)*", incident reports were compiled in collaboration with the Regions and Programs Bureau of Health Canada that included information on residue analysis of samples and planting practices surrounding the affected apiaries. These reports were from 2012 – 2014. The PMRA concluded that neonicotinoids (imidacloprid, thiamethoxam, and clothianidin) present in dust generated during planting of treated corn and soybean seeds contributed to the reported bee mortalities in 2012 and 2013, that were described either as dead bee (*i.e* forager loss) or colony losses. Analytical results and evaluation of the 2014 data are still pending. The report stated that 70% of dead bees collected during the corn and soybean planting period in 2012 and 2013 had neonicotinoid residues present; whereas, the majority of the live bees sampled did not have such residues present. Additionally, it was reported that the 2012 incidents primarily identified high numbers of dead bees and symptoms of pesticide poisoning, while the 2013 reports involved lower number of dead bees but increased incidence of colony-level effects such as lack of foragers, and loss of honey production especially in the later months of the beekeeping season. The latter was also reported in 2014. It is noted that the report states that unclear how widespread the colony losses are as in 2014, three beekeepers accounted for over 72% of the reported incidents.

In 2012, a total of 278 bee yards from all participating provinces (Ontario, Québec, Alberta, Saskatchewan, Manitoba, and Nova Scotia) reported bee loss incidents that represented 53 beekeepers. A follow-up investigation revealed that 86% of these incidents were associated with corn and soybean planting. The number of reported incidents increased in 2013 and 2014 to 420 and 343, respectively, but the causality assessment of these incidents is still pending. Of these incidents, the majority (>85%) originated in Ontario where corn in particular is intensively cultivated. The analysis also found that the majority of the incidents were reported at the time of seed-treated corn and soybean planting, suggesting exposure to abraded treated-seed coatings (dust off) during planting. Interestingly, the corn growing areas of Québec and Manitoba are not associated with a similar frequency of incident reports, and the Western Canadian provinces where the majority of canola seed is treated with neonicotinoids are also not associated with reported incident information. This report does not provide the breakdown of the number of incidents associated with a particular chemical, and therefore it is unknown what percentage of the reported incidents are the results of seed treated imidacloprid. Also, PMRA responded to these incidents by requiring in 2014 a dust-reducing seed flow lubricant when planting neonicotinoid treated seeds using pneumatic planting equipment. Additionally, PMRA updated the best management practices (BMPs) for the responsible use of treated seed as well as enhanced warnings of pesticide labels and seed package labels for directions on how to protect bees were published.

While the reports detailed above pertain to wildlife incidents originating in foreign countries, where the registered use patterns and associated application methods and rates may be different relative to registered labels in the United States, they are still considered informative as a line of evidence as they collectively demonstrate that honey bee losses may occur even when imidacloprid is used as registered.

6. RISK CHARACTERIZATION

Estimating risks to bees associated with the registered uses of imidacloprid follows OPP's published guidance entitled: "*Guidance for Assessing Pesticide Risks to Bees*"²⁷. This guidance presents an iterative, tiered process for assessing risks that considers multiple lines of evidence related to exposure and effects of pesticides to bees.

6.1. Tier I Risk Assessment

As described in Section 4, the Tier I method is intended to generate "reasonably conservative" estimates of honey bee contact and oral exposure to pesticides for determining the need for additional refinement of exposure estimates (e.g. measured residues in pollen and nectar). As such, exposure estimates are determined using high-end values predicted from the Bee-Rex model (v.1.0). What follows is a summarization of RQs for each route of exposure (contact vs oral) separated by application type (foliar, soil, and seed treatment) and whether the on-field or off-field risks (foliar applications only) are estimated. As described earlier in Section 5.1 apis bees are a good surrogate for other non apis bees at the tier I level as many bee species have similar toxicity endpoints. Therefore, conclusions at this level would be protective of other non apis bee species.

For crop uses where an exposure potential of bees is identified the next step in the risk assessment process is to conduct a Tier I risk assessment. By design, the Tier I assessment relies on conservative (high end) estimates of exposure via contact and oral routes. For contact exposure, only the adult (forager) life stage is considered since this is the relevant life stage of honey bees for contact exposure. Effects are defined by laboratory exposures to groups of individual bees. As described in **Section 4**, the endpoint selected for acute contact toxicity for adult honey bees is a 96-hour LD₅₀ of 0.043 µg a.i./bee.

6.1.1. Acute Contact Risk (On-Field, Screening)

Table 6-1 summarizes the screening-level acute contact RQ values for adult honey bees that are assumed to be foraging on treated crop during pesticide application. As such, **Table 6-1** includes only those crops that are considered bee attractive or for which no data are available on bee attractiveness (as a conservative assumption). As the Tier I screening-level for acute contact exposure utilizes the maximum single application rate and a standard contact dose rate of 2.7 µg a.i./bee per 1 lbs. a.i/A, registered use patterns with the same maximum single application rate are grouped together in **Table 6-1**. For all foliar uses assessed, acute contact RQ values range from 2.5 (legumes, peanut, herbs) to 15.7 (citrus and pome fruits) and exceed the Agency's acute risk LOC of 0.4. The estimate of contact exposure is considered conservative (although not impossible) since it is determined using a high-end estimate of forager bees exposure to spray droplets.

²⁷ http://www2.epa.gov/sites/production/files/2014-06/documents/pollinator_risk_assessment_guidance_06_19_14.pdf

Table 6-1. Summary of Tier I screening-level RQs for contact exposure resulting from foliar uses of imidacloprid (screening-level contact on-field)

| Use pattern | Max. Single Appl. Rate (lbs a.i./A) | Dose (μg a.i./bee per 1 lbs. a.i./A) ¹ | Imidacloprid Contact Dose (μg a.i./bee) | Acute Contact RQ ^{1,2} |
|--|--|--|--|------------------------------------|
| Tuberous and corm vegetables, Legume vegetables (except soybean), Peanut, Herbs | 0.04 | 2.7 | 0.108 | 2.5 |
| Potato, Soybean, Strawberry | 0.05 | 2.7 | 0.135 | 3.1 |
| Cotton | 0.06 | 2.7 | 0.162 | 3.8 |
| Fruiting vegetables | 0.08 | 2.7 | 0.216 | 5.0 |
| Stone fruit, Caneberry, Bushberry, Grape, Tree nuts, Banana and plantain, Pomegranate, Tropical fruit, Coffee, Hops, Non ag forestry | 0.10 | 2.7 | 0.27 | 6.3 |
| Citrus, Pome fruit | 0.25 | 2.7 | 0.675 | 15.7 |
| Ornamental uses | 0.4 | 2.7 | 1.08 | 25 |
| Turf | 0.5 | 2.7 | 1.35 | 31 |

¹ Based on a 96-h acute contact LD₅₀ of 0.043 μg a.i./bee for imidacloprid (MRID 49602717)

² **Bolded** value exceeds the acute risk LOC of 0.4.

6.1.2. Acute Oral Risk (On-Field, Screening)

For oral (dietary) exposure, the Tier I assessment initially considers just the caste of bees with the greatest oral exposure (foraging adults). If risks are identified, then other factors are considered for refining the default Tier I risk estimates. These factors include other castes of bees and available information on residues in pollen and nectar which are deemed applicable to the crops of interest. Oral exposure through the consumption of imidacloprid-contaminated pollen is considered for on-field and off-field scenarios resulting from foliar applications. For soil and seed-treatment applications, where no spray drift is expected, oral exposure is assessed for the on-field scenario only.

For foliar applications, the Bee-REX model uses a standard dose of 32 μg a.i./bee per 1 lbs. a.i./A for adults and 13.6 μg a.i./bee per 1 lbs. a.i./A for larvae that are based off of consumption rates for these life stages. This dose is multiplied by the application rate to yield an oral dose, one each for adults and larvae. For imidacloprid, this dose is compared against the most sensitive quantitative acute oral LD₅₀ value of 0.0039 μg a.i./bee for adult acute exposure and the NOAEC of 0.0011 μg a.i./bee/day for adult chronic exposure. For larvae, there are no acute oral toxicity studies for imidacloprid and therefore these cells are shaded in Table 6-2 below. For chronic toxicity, the NOAEC was determined to be 0.0018 μg a.i./larva/day.

For soil applications, the oral exposure estimate for adults and larvae are determined using Briggs model estimates (based off application rate, the log K_{ow}, and organic carbon partition coefficient K_{OC} of imidacloprid) multiplied by the consumption rates of 0.292 g/day for adults and 0.124 g/day for larvae. The exposure estimates are compared against the same endpoints as described above.

Finally, for seed treatment applications, the exposure estimate is assumed to be 1 µg a.i/g for all uses regardless of the application rate. This is multiplied by the consumption rates of 0.292 g/day for adults and 0.124 g/day for larvae (as with soil applications) to yield the oral dose that is compared to the Tier I toxicity endpoints described previously.

6.1.2.1. Foliar applications

Table 6-2 summarizes the on-field acute and chronic oral RQs resulting from the foliar applications of imidacloprid. The acute and chronic RQs for adult bees exceed the LOCs of 0.4 and 1, respectively, for all use patterns assessed (adult acute RQs ranged from 329 – 2059, and adult chronic RQs ranged from 321 – 7301). As noted previously, there are no acute oral toxicity studies to honey bee larvae available for imidacloprid; therefore, these cells are shaded in **Table 6-2**. For chronic larval toxicity, RQ values exceed the LOC of 1 for all use patterns assessed, with RQs ranging from 321 – 2008.

Table 6-2. Summary of Tier I screening-level RQs for oral exposure resulting from foliar uses of imidacloprid (based on model-generated exposure values on-field).⁴

| Use pattern | Max. Single Appl. Rate (lbs a.i/A) | Bee Life Stage | Dose (µg a.i./bee per 1 lbs. a.i./A) ¹ | Imidacloprid Oral Dose (µg a.i/bee) | Acute RQ ² | Chronic RQ ³ |
|--|------------------------------------|----------------|---|-------------------------------------|-----------------------|-------------------------|
| Tuberous and corm vegetables, Legume vegetables (except soybean), Peanut, Herbs | 0.04 | Adult | 32 | 1.2850 | 329 | 1168 |
| | | Larval | 13.6 | 0.5878 | | 321 |
| Potato, Soybean, Strawberry | 0.05 | Adult | 32 | 1.6062 | 412 | 1460 |
| | | Larval | 13.6 | 0.7348 | | 402 |
| Cotton | 0.06 | Adult | 32 | 1.9275 | 494 | 1752 |
| | | Larval | 13.6 | 0.8818 | | 482 |
| Fruiting vegetables | 0.08 | Adult | 32 | 2.5700 | 659 | 2336 |
| | | Larval | 13.6 | 1.1757 | | 642 |
| Stone fruit, Caneberry, Bushberry, Grape, Tree nuts, Banana and plantain, Pomegranate, Tropical fruit, Coffee, Hops, Non ag forestry | 0.10 | Adult | 32 | 3.2125 | 824 | 2920 |
| | | Larval | 13.6 | 1.4696 | | 803 |
| | | Larval | 13.6 | 1.8517 | | 1012 |
| Citrus , Pome fruit | 0.25 | Adult | 32 | 8.0311 | 2059 | 7301 |
| | | Larval | 13.6 | 3.674 | | 2008 |
| Ornamental uses | 0.4 | Adult | 32 | 12.8498 | 3295 | 11682 |
| | | Larval | 13.6 | 5.8784 | | 3212 |
| Turf | 0.5 | Adult | 32 | 16.0623 | 4119 | 14602 |
| | | Larval | 13.6 | 7.348 | | 4015 |

¹ Source: USEPA et al. 2014. *Guidance for Assessing Pesticide Risks to Bees*.

² Based on a 48-h acute oral LD₅₀ of 0.0039 ug a.i/bee for imidacloprid (MRID 42273003)

³Based on adult 10-day chronic NOAEC of 0.0011 µg a.i/bee/day (MRID 50399101) and larval 21-day chronic NOAEC of 0.0018 µg a.i/larva (MRID 49090506).

⁴**Bolded** value exceeds the acute risk LOC of 0.4 or chronic LOC of 1.

6.1.2.2. Soil applications

Table 6-3 summarizes the on-field acute and chronic oral RQs resulting from the soil applications of imidacloprid. The acute RQs for adult bees exceeded the LOCs of 0.4 for all use patterns assessed except tobacco (adult acute RQs ranged from 0.32 – 4.0). The chronic RQs for adult bees exceeded the LOC of 1, for all use patterns assessed (adult chronic RQs ranged from 1.1 – 14). For chronic larval toxicity, the LOC of 1 was exceeded for all use patterns assessed except tobacco (0.04 lbs a.i/A), with RQs ranging from 0.29 – 3.7.

Table 6-3. Summary of Tier I screening-level RQs for oral exposure⁵ resulting from soil uses of imidacloprid (based on model-generated exposure values on-field).⁴

| Use pattern | Max. Single Appl. Rate (lbs a.i/A) | Bee Life Stage | Imidacloprid Oral Dose (μg a.i/bee) ¹ | Acute RQ ² | Chronic RQ ³ |
|---|------------------------------------|----------------|--|-----------------------|-------------------------|
| Tobacco | 0.04 | Adult | 0.0018 | 0.32 | 1.1 |
| | | Larval | 0.0008 | | 0.29 |
| Sugar beet | 0.18 | Adult | 0.0082 | 1.4 | 5.1 |
| | | Larval | 0.0037 | | 1.3 |
| Hops | 0.3 | Adult | 0.0136 | 2.4 | 8.5 |
| | | Larval | 0.0062 | | 2.2 |
| Potato | 0.31 | Adult | 0.0141 | 2.5 | 8.8 |
| | | Larval | 0.0064 | | 2.3 |
| Cotton | 0.33 | Adult | 0.0150 | 2.6 | 9.3 |
| | | Larval | 0.0069 | | 2.4 |
| Root vegetables, Tuberous and corm vegetables, Legume vegetables (except soybean), Cucurbit vegetables, Pome fruit, Stone fruit, Peanut, Strawberry (perennial and post-harvest), Herbs | 0.38 | Adult | 0.0173 | 3.0 | 11 |
| | | Larval | 0.0079 | | 2.8 |
| Ornamental uses | 0.4 | Adult | 0.0124 | 3.2 | 11 |
| | | Larval | 0.0057 | | 3.1 |
| Fruiting vegetables, Citrus, Caneberry, Bushberry, Cranberry, Grape, Tree nuts, Banana and plantain, Pomegranate, Strawberry (annual and perennial), Tropical fruit, Coffee, Turf, Forestry | 0.50 | Adult | 0.0227 | 4.0 | 14 |
| | | Larval | 0.0104 | | 3.7 |

¹Briggs EEC (derived from Bee-REX) * consumption rate for life stages (0.292g/day for adults; 0.124 g/day for brood)

² Based on a 48-h acute oral LD₅₀ of 0.0039 ug a.i/bee for imidacloprid (MRID 42273003)

³Based on adult 10-day chronic NOAEC of 0.0011 μg a.i/bee/day (MRID 50399101) and larval 21-day chronic NOAEC of 0.0018 μg a.i/larva (MRID 49090506).

⁴**Bolded** value exceeds the acute risk LOC of 0.4 or chronic LOC of 1.

⁵Bee-REX run for soil application used Log Kow of 0.568 and Koc of 266

6.1.2.3. Seed treatment applications

As indicated previously, the Bee-REX model assumes all seed treatment applications to have an EEC in pollen and nectar of 1 mg a.i/kg regardless of the application rate. This is multiplied by the consumption rate factors for adults and brood (0.292 and 0.124 g/day, respectively) and then compared to the Tier I toxicity endpoints previously discussed. All RQs (adult acute oral, adult chronic oral, larval chronic oral) exceed the acute and chronic LOCs of 0.4 and 1, respectively (**Table 6-4**).

Table 6-4. Summary of labeled use information for seed treatment applications of imidacloprid (screening-level oral on-field)⁴

| Use pattern | Bee Life Stage | EEC in pollen and nectar | Imidacloprid Oral Dose (µg a.i/bee) ¹ | Acute RQ ² | Chronic RQ ³ |
|--|----------------|---|--|-----------------------|-------------------------|
| All registered seed treatment use patterns | Adult | 1 mg a.i/kg (screening-level value for all seed treatment uses) | 0.2920 | 74.9 | 265 |
| | Larval | | 0.1336 | | 73 |

¹ Source: USEPA et al. 2014. *Guidance for Assessing Pesticide Risks to Bees*.

² Based on a 48-h acute oral LD₅₀ of 0.0039 ug a.i/bee for imidacloprid (MRID 42273003)

³ Based on adult 10-day chronic NOAEC of 0.0011 µg a.i/bee/day (MRID 50399101) and larval 21-day chronic NOAEC of 0.0018 µg a.i/larva (MRID 49090506).

⁴ **Bolded** value exceeds the acute risk LOC of 0.4 or chronic LOC of 1.

6.1.3. Acute Oral Risk (Off-Field, Screening)

As described in **Section 3**, imidacloprid products may be applied to crops via foliar spray applications. Consistent with the Agency's risk assessment process for bees and other taxa, exposure beyond the treated field is expected to occur as a result of spray drift. This so-called "off-field" exposure is assessed here for honey bees that are assumed to be foraging adjacent to treated fields. The AgDRIFT model (v. 2.1.1²⁸) is used here to estimate the fraction of the foliarly-applied application rate at various distances beyond the treated field. The AgDRIFT model accounts for multiple factors that affect the distance and amount of spray drift (and consequently the associated risk) of a single spray application. These include factors such as wind speed, spray nozzle type, release height, application volume and label restrictions pertaining to spray drift mitigation. **Table 6-5** below summarizes various aspects of label restrictions applicable to foliar spray applications of imidacloprid using the Admire® Pro label as an example (EPA Reg No. 264-827).

Table 6-5. Imidacloprid Use Patterns for Crops with or without Specific Application Restrictions

| Use pattern | Max. Single Appl. Rate (lbs a.i./A) | Restrictions |
|---|-------------------------------------|-----------------|
| Tuberous and corm vegetables, Legume vegetables (except soybean), Peanut, Herbs | 0.04 | No restrictions |
| Leafy green vegetables, Brassica (Cole) Leafy vegetables | 0.046 | No restrictions |
| Strawberry | 0.047 | No restrictions |

²⁸ Available at <http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment#atmospheric> (accessed 11/8/15).

| Use pattern | Max. Single Appl. Rate (lbs a.i./A) | Restrictions |
|---|-------------------------------------|---|
| Potato, Soybean, Tobacco | 0.05 | No restrictions |
| Cotton | 0.06 | No restrictions |
| Fruiting vegetables | 0.08 | No restrictions |
| Caneberry, Banana and plantain, Pomegranate, Tropical fruit, Coffee, Hops | 0.10 | No restrictions; For tree crops, a minimum of 5 gal/A is recommended. |
| Bushberry | 0.10 | For ground applications use 20 gal/A and for aerial applications use 50 gal/A. |
| Grape | 0.10 | Only ground applications are allowed. |
| Stone fruit, Tree nuts | 0.10 | For ground applications use 25 gal/A and for aerial applications use 50 gal/A. |
| Globe artichoke | 0.126 | No restrictions |
| Citrus, Pome fruit | 0.25 | For tree crops, a minimum of 5 gal/A is recommended. |
| Poultry house treatment | 0.132 & 0.771 | Assumes treated poultry litter is applied to bee-attractive agricultural crops at the rate used to fertilize field corn |

As shown in **Table 6-5** certain crops have limits related to the spray volume. It is expected that higher spray volumes will result in lower drift. There are no restrictions related to boom height, droplet size or wind speed; however, all these factors are also expected to affect drift levels. Spray drift is expected to increase with higher boom heights, smaller droplets, and higher wind speeds. Based on the information provided in **Table 6-5**, nine AgDRIFT scenarios were modeled that span the range of foliar spray application rates and conditions that favor higher and lower drift estimates in order to bracket the potential for off-field risks. In addition, the Tier I acute and chronic toxicity endpoints for the honey bee summarized in **Table 5.1** were used to determine the distance required to achieve the applicable acute LOC (0.4) and chronic LOC (1.0). These distances can be interpreted as the distance from the edge of the treated field beyond which the acute and chronic LOC values would not be exceeded. In modeling using AgDRIFT, default conditions were used, except for the variations mentioned in the following paragraphs and/or in the tables and footnotes.

6.1.3.1. Citrus and Pome Fruit

Airblast Application

Citrus and pome fruits have the highest single application rate among all crops for foliar sprays. The only label restriction identified is a minimum of 5 gal/A for tree crops. Ground applications are usually through airblast methods for citrus and pome fruits. Spray drift was modeled using AgDRIFT (Tier I Orchard/Airblast mode of AgDRIFT) with two options: sparse (default) and orchard (**Table 6-6**). RQ values for contact indicate the acute risk LOC for honey bees is exceeded out to 62 and 66 ft from treated field edge for the sparse and orchard scenarios, respectively. Using screening-level oral exposure estimates, dietary-based RQ values exceed the acute or chronic risk LOC values from 455 to >1000 ft (the limit of model estimation).

Table 6-6. Distance from the edge of the field associated with LOC exceedance, for citrus and pome fruits, calculated using AgDRIFT v.1.1.1, the Tier I Orchard/Airblast module, and app rate of 0.25 lbs. a.i./A.

| Application selection | Distance from the field and point estimate of application rate (lbs./A) | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|--------------------------------------|---|--------|--------|--------|--------|--|--|--|--|
| | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| Sparse (young, dormant) ¹ | 0.0571 | 0.0252 | 0.0093 | 0.0026 | 0.0011 | 62 | 581 | >1000 | 455 |
| Orchard ² | 0.027 | 0.0126 | 0.0052 | 0.0018 | 0.001 | 66 | >1000 | >1000 | 963 |

¹The “sparse” orchard spray drift curve is based on deposition data for small grapefruit and dormant apple orchards

²The “orchard” spray drift curve is based on deposition data for all orchard trees

Aerial Application

Aerial applications to citrus and pome fruit were modeled using AgDRIFT in Tier II Aerial mode with wind speeds of 10 mph and 15 mph (default) and a range of droplet sizes (fine to medium, medium, medium to coarse), respectively. In the absence of additional label restrictions, the default droplet size utilized in risk assessments is fine to medium. Results indicate that contact RQ values exceed the acute risk LOC from 184 to 318 ft beyond the treated field assuming a wind speed of 15 mph (Table 6-7) and from 141 to 269 ft beyond the treated field assuming a wind speed of 10 mph (Table 6-8). With aerial application, which results in greater amounts of spray drift compared to airblast, acute and chronic Tier I dietary-based RQ values exceed their respective LOCs for more than 1000 ft from the edge of the treated field.

Table 6-7. Citrus and Pome Fruits: Tier II aerial applications, boom height 10 ft, wind speed 15 mph (label required), non-volatile rate 0.25 lbs./A, spray volume 5 gal/A

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|-------------------------|--|--------|--------|--------|--------|--|--|--|--|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| F to M | 255 | 0.1408 | 0.0832 | 0.0519 | 0.0305 | 0.0189 | 318 | >1000 | >1000 | >1000 |
| M | 294 | 0.1207 | 0.0705 | 0.0435 | 0.0249 | 0.0148 | 269 | >1000 | >1000 | >1000 |
| M to C | 341 | 0.1014 | 0.0575 | 0.0244 | 0.0187 | 0.0107 | 213 | >1000 | >1000 | >1000 |
| C | 385 | 0.0872 | 0.049 | 0.0291 | 0.0152 | 0.0088 | 184 | >1000 | >1000 | >1000 |

In the Tier II mode, there are additional droplet size options: fine (F) to medium (M; default), medium, and medium to coarse (C; among others).

Table 6-8. Citrus and Pome Fruits: Tier II aerial applications, boom height 10 ft, wind speed 10 mph (label required), non-volatile rate 0.25 lbs./A, spray volume 5 gal/A

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|---------------|--|--------|--------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| F to M | 255 | 0.0783 | 0.0506 | 0.0389 | 0.021 | 0.0128 | 269 | >1000 | >1000 | >1000 |
| M | 294 | 0.0682 | 0.0429 | 0.0319 | 0.0165 | 0.01 | 223 | >1000 | >1000 | >1000 |
| M to C | 341 | 0.0573 | 0.0347 | 0.025 | 0.012 | 0.0071 | 167 | >1000 | >1000 | >1000 |
| C | 385 | 0.0496 | 0.0303 | 0.0205 | 0.0098 | 0.0058 | 141 | >1000 | >1000 | >1000 |

In the Tier II mode, there are additional droplet size options: fine (F) to medium (M; default), medium, and medium to course (C; among others).

6.1.3.2. *Globe Artichoke*

Globe artichoke represents the second highest foliar spray application rate at 0.126 lbs a.i./A. Only ground applications are allowed according to the label. Two options were modeled using AgDRIFT in the Tier I mode: a high boom height (50 inches; default) and a low boom height (20 inches); and two droplet sizes: very fine to fine and fine to medium/coarse. Results indicate that the contact-based RQ values exceed the acute risk LOC from 10 to 52 ft beyond the treated field assuming a high boom height (**Table 6-9**) and from 7 to 20 ft beyond the treated field assuming a low boom height (**Table 6-10**). With the exception of fine to medium/coarse droplet size using a high boom, and very fine to fine, and fine to medium/coarse droplet size using a low boom height for larval chronic oral risk, the acute and chronic Tier I dietary-based RQ values exceed their respective LOCs for more than 1000 ft from the treated field.

Table 6-9. Globe artichoke (only ground apps allowed): Tier I ground applications, high boom height (50 inches), application rate 0.126 lbs. a.i./A, 90th percentile results

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate (lbs./A) | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|---------------|---|--------|--------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| VF to F | 175 | 0.0327 | 0.0131 | 0.0063 | 0.0031 | 0.0021 | 52 | >1000 | >1000 | >1000 |
| F to M/C | 341 | 0.0058 | 0.0026 | 0.0015 | 0.0009 | 0.0006 | 10 | >1000 | >1000 | 771 |

For ground applications, there are two droplet size options: very fine (VF) to fine (F), and medium (M)/course (C).

Table 6-10. Globe artichoke (only ground apps allowed): Tier I ground applications, low boom height (20 inches), application rate 0.126 lbs. a.i./A, 90th percentile results

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate (lbs./A) | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|----------------------------|---|--------|--------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| VF to F | 175 | 0.0116 | 0.0044 | 0.0022 | 0.0012 | 0.0008 | 20 | >1000 | >1000 | 932 |
| F to M/C | 341 | 0.0035 | 0.0016 | 0.0009 | 0.0006 | 0.0004 | 7 | >1000 | >1000 | 587 |

For ground applications, there are two droplet size options: very fine (VF) to fine (F), and medium (M)/course (C).

6.1.3.3. Stone Fruit and Tree Nuts

Stone fruit and tree nuts are examples of crops with label restrictions regarding application volumes for ground and aerial applications. Since the spray volume is not an option in AgDRIFT modeling for ground applications, only aerial applications were modeled assuming wind speeds of 15 mph and 10 mph. Results indicate that the contact-based RQ values exceed the acute risk LOC from 92 to 161 ft beyond the treated field assuming a wind speed of 15 mph (**Table 6-11**) and from 66 to 115 ft beyond the treated field assuming a wind speed of 10 mph (**Table 6-12**). All of the Tier I dietary-based RQ values exceed the acute oral and chronic risk LOCs more than 1000 ft from the treated field.

Table 6-11. Stone fruit, Tree nuts: Tier II aerial applications, boom height 10 ft, wind speed 15 mph (label required), non-volatile rate 0.10 lbs./A, spray volume 25 gal/A (label required for these crops)

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|----------------------------|--|--------|--------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| F to M | 255 | 0.0553 | 0.0324 | 0.02 | 0.0116 | 0.007 | 161 | >1000 | >1000 | >1000 |
| M | 294 | 0.0476 | 0.0276 | 0.0168 | 0.0095 | 0.0055 | 138 | >1000 | >1000 | >1000 |
| M to C | 341 | 0.0401 | 0.0226 | 0.0136 | 0.0072 | 0.004 | 115 | >1000 | >1000 | >1000 |
| C | 385 | 0.0344 | 0.0192 | 0.0113 | 0.0058 | 0.0033 | 92 | >1000 | >1000 | 974 |

In the Tier II mode, there are additional droplet size options: fine (F) to medium (M; default), medium, and medium to course (C; among others).

Table 6-12. Stone fruit, Tree nuts: Tier II aerial applications, boom height 10 ft, wind speed 10 mph, non-volatile rate 0.10 lbs./A, spray volume 25 gal/A (label required for these crops)

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|----------------------------|--|--------|--------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| F to M | 255 | 0.0303 | 0.0192 | 0.0146 | 0.0076 | 0.0045 | 115 | >1000 | >1000 | >1000 |
| M | 294 | 0.0265 | 0.0164 | 0.0121 | 0.006 | 0.0035 | 95 | >1000 | >1000 | >1000 |

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|----------------------------|--|--------|--------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| M to C | 341 | 0.0224 | 0.0134 | 0.0095 | 0.0044 | 0.0025 | 75 | >1000 | >1000 | >1000 |
| C | 385 | 0.0194 | 0.0117 | 0.0078 | 0.0036 | 0.002 | 66 | >1000 | >1000 | >1000 |

In the Tier II mode, there are additional droplet size options: fine (F) to medium (M; default), medium, and medium to course (C; among others).

6.1.3.4. Tuberous and Corm Vegetables

To model a range of application rates, tuberous and corm vegetables, which represent the lowest single application rate for foliar sprays with imidacloprid (0.04 lbs. a.i./A), were also modeled. Aerial applications were modeled using various droplet sizes, and assumed boom height of 10 ft, a spray volume of 5 gal/A, and wind speeds of 15 and 10 mph. Results indicate that the acute contact-based RQ values exceed the acute risk LOC from 36-69 ft beyond the treated field assuming a wind speed of 15 mph (**Table 6-13**) and from 16 to 43 ft beyond the treated field assuming a wind speed of 10 mph (**Table 6-14**). With the exception of coarse and medium to coarse droplet sizes for larval chronic oral risk, all of the acute and chronic Tier I dietary-based RQ values exceed their respective LOCs more than 1000 ft from the treated field.

Table 6-13. Tuberous & Corm Vegetables and Certain Other Crops: Tier II aerial applications, boom height 10 ft, wind speed 15 mph (label required), non-volatile rate 0.04 lbs./A, spray volume 5 gal/A

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|----------------------------|--|--------|--------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| F to M | 255 | 0.0222 | 0.013 | 0.008 | 0.0047 | 0.0028 | 69 | >1000 | >1000 | >1000 |
| M | 294 | 0.019 | 0.011 | 0.0067 | 0.0038 | 0.0022 | 56 | >1000 | >1000 | 860 |
| M to C | 341 | 0.016 | 0.009 | 0.0055 | 0.0029 | 0.0016 | 43 | >1000 | >1000 | 591 |
| C | 385 | 0.0138 | 0.0077 | 0.0045 | 0.0023 | 0.0013 | 36 | >1000 | >1000 | 534 |

In the Tier II mode, there are additional droplet size options: fine (F) to medium (M; default), medium, and medium to course (C; among others).

Table 6-14. Tuberous & Corm Vegetables and Certain Other Crops: Tier II aerial applications, boom height 10 ft, wind speed 10 mph, non-volatile rate 0.04 lbs./A, spray volume 5 gal/A

| Droplets | Dv0.5 (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|----------------------------|--|-------|-------|--------|--------|--|---|---|---|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| F to M | 255 | 0.0122 | 0.008 | 0.006 | 0.0031 | 0.0018 | 43 | >1000 | >1000 | >1000 |
| M | 294 | 0.0107 | 0.007 | 0.005 | 0.0024 | 0.0014 | 30 | >1000 | >1000 | >1000 |

| Droplets | D _{v0.5} (μm) | Distance from the field and point estimate of application rate | | | | | App rate lbs./A at ea. LOC and distance associated to app rate | | | |
|----------|---------------------------|--|-------|-------|--------|--------|--|--|--|--|
| | | 10 ft | 25 ft | 50 ft | 100 ft | 150 ft | Acute Contact (0.00637) | Adult Acute Oral (4.86×10^{-5}) | Adult Chronic Oral (4.98×10^{-6}) | Larval Chronic (1.32×10^{-4}) |
| M to C | 341 | 0.009 | 0.005 | 0.004 | 0.0018 | 0.001 | 20 | >1000 | >1000 | 673 |
| C | 385 | 0.0078 | 0.005 | 0.003 | 0.0015 | 0.0008 | 16 | >1000 | >1000 | 551 |

In the Tier II mode, there are additional droplet size options: fine (F) to medium (M; default), medium, and medium to course (C; among others).

6.1.3.5. Applications of Poultry Litter from Treated Broiler Houses

For poultry house use, chicken litter waste collected from a broiler house could potentially be disposed of as a soil amendment after it has been treated with imidacloprid. To assess the impacts of imidacloprid-treated poultry litter used as soil amendments, EFED modeled the amount of imidacloprid predicted to be in the poultry litter, as if it were applied to a corn field prior to planting. The poultry house use pattern evaluated by EFED represents an upper-end use pattern for products applied to poultry houses. The primary pest targeted by these products is the darkling beetle, which is mostly found on the perimeter portions of floors and lower walls, near feeders and water lines. While only portions of a poultry house may need to be treated, this is not explicitly stated or restricted on the product label. For modeling the highest exposure scenario, EFED conservatively assumed that the whole poultry house was treated each time a treatment is made. Treatments are made prior to a new flock occupying the poultry house, and it is assumed that annually, six broiler flocks will occupy a house. Although treatments are made, removal of the litter from the house may not occur, and fresh litter will be placed on top of existing litter. For broilers, this means that six whole house treatments will occur prior to an annual litter clean out, with multiple layers of treated litter possible. An application rate for imidacloprid-treated manure on a corn field was developed using information found in Shamblen and Judkins, 2012 and fully described in **Appendix K**.

Application rate used in modeling depends on how many tons of litter is applied to the corn field and the expected amount of imidacloprid it contains full details are discussed in **Appendix K**. The range of application rates assessed for soil applications of imidacloprid in treated poultry litter was 0.032 – 0.756 lb a.i./A. Based on the maximum rate, RQs calculated using Bee-REX range 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).

Table 6-15 summarizes the on-field acute and chronic oral RQs resulting from the soil incorporated poultry litter application of imidacloprid. The acute and chronic RQs for adult bees exceed the LOCs of 0.4 and 1, respectively, when the litter application exceeded 0.052 lb a.i./A of imidacloprid. As noted previously, there are no acute oral toxicity studies to honey bee larvae available for imidacloprid; therefore, these cells are shaded in **Table 6-15**. For chronic larval toxicity, RQ values exceed the LOC of 1 for 5 of the 13 use rates assessed, with RQs ranging from 0.23-5.5.

Table 6-15. Summary of Tier I screening-level RQs for oral exposure resulting from soil incorporated poultry littler applications of imidacloprid (based on model-generated exposure values on-field).⁴

| Use pattern | Max. Single Appl. Rate (lbs a.i/A) | Bee Life Stage | Dose (μ g a.i./bee per 1 lbs. a.i./A) ¹ | Imidacloprid Oral Dose (μ g a.i./bee) | Acute RQ ² | Chronic RQ ³ |
|---------------|------------------------------------|----------------|---|--|-----------------------|-------------------------|
| Run 13 (BEAD) | 0.032 | Adult | 32 | 0.0010 | 0.26 | 0.91 |
| | | Larval | 13.6 | 0.0004 | | 0.23 |
| Run 12 | 0.033 | Adult | 32 | 0.0010 | 0.26 | 0.93 |
| | | Larval | 13.6 | 0.0004 | | 0.24 |
| Run 8 | 0.04 | Adult | 32 | 0.0012 | 0.32 | 1.13 |
| | | Larval | 13.6 | 0.0005 | | 0.29 |
| Run 11 | 0.052 | Adult | 32 | 0.0016 | 0.41 | 1.47 |
| | | Larval | 13.6 | 0.0007 | | 0.38 |
| Run 6 | 0.083 | Adult | 32 | 0.0026 | 0.66 | 2.35 |
| | | Larval | 13.6 | 0.0011 | | 0.61 |
| Run 10 | 0.101 | Adult | 32 | 0.0031 | 0.81 | 2.86 |
| | | Larval | 13.6 | 0.0013 | | 0.74 |
| Run 2 | 0.121 | Adult | 32 | 0.0038 | 0.97 | 3.42 |
| | | Larval | 13.6 | 0.0016 | | 0.89 |
| Run 5 | 0.13 | Adult | 32 | 0.0040 | 1.04 | 3.68 |
| | | Larval | 13.6 | 0.0017 | | 0.95 |
| Run 9 | 0.206 | Adult | 32 | 0.0064 | 1.64 | 5.83 |
| | | Larval | 13.6 | 0.0027 | | 1.51 |
| Run 4 | 0.253 | Adult | 32 | 0.0079 | 2.02 | 7.16 |
| | | Larval | 13.6 | 0.0033 | | 1.85 |
| Run 7 | 0.304 | Adult | 32 | 0.0095 | 2.42 | 8.60 |
| | | Larval | 13.6 | 0.0040 | | 2.22 |
| Run 3 | 0.326 | Adult | 32 | 0.0101 | 2.60 | 9.22 |
| | | Larval | 13.6 | 0.0043 | | 2.38 |
| Run 1 | 0.756 | Adult | 32 | 0.0235 | 6.03 | 21.38 |
| | | Larval | 13.6 | 0.0100 | | 5.53 |

¹ Source: USEPA et al. 2014. *Guidance for Assessing Pesticide Risks to Bees*.

² Based on a 48-h acute oral LD₅₀ of 0.0039 ug a.i./bee for imidacloprid (MRID 42273003)

³ Based on adult 10-day chronic NOAEC of 0.0011 μ g a.i./bee/day (MRID 50399101) and larval 21-day chronic NOAEC of 0.0018 μ g a.i./larva (MRID 49090506).

⁴ **Bolded** value exceeds the acute risk LOC of 0.4 or chronic LOC of 1.

⁵ Bee-REX run for soil application used Log Kow of 0.568 and Koc of 266

Additional Considerations

Poultry litter is commonly used as a fertilizer supplement on pastures, forages, and agronomic crops such as cotton and corn. In the case of corn, which typically receives the highest rates of litter application other than pastures and some vegetable production (USEPA, 2017b), the corn crop only produces honey bee attractive pollen. Therefore, if treated poultry litter were restricted to application to corn where bee exposures would be restricted to only pollen, the resulting acute and chronic RQs would be below the LOCs (Bee-REX screening level acute and chronic dietary RQs of 0.01 and 0.10, respectively).

6.1.4. Refined Acute Oral Risk (On-field)

As distinguished from the default Tier I assessment, in cases where residue information in pollen and nectar are available, these data can be used to refine the estimates of oral exposure as well as further characterize the level of risk for other castes of bees using their food consumption rates. These refined exposure estimates in pollen and nectar are then compared to the Tier I (*i.e.* individual level) toxicity endpoints in a manner similar to that for the model-generated or default Tier I exposure estimates. Rather than reporting the highest exposure estimates for contact and/or dietary exposure routes (as with the default Tier assessment), the Bee-REX model also calculates dietary exposure values and associated RQs for larvae of different ages, adult workers with different tasks (and associated energy requirements) and the queen using the various aforementioned consumption rates.

6.1.4.1. Foliar and Soil Applications

To refine default Tier I risk estimates, available measured residue data in pollen and nectar are used to evaluate oral exposure (contact exposure not considered in refined estimates) and further characterize risk for other castes of bees using their food consumption rates. These refined exposure estimates in pollen and nectar are then compared to the Tier I (*i.e.* individual level) toxicity endpoints analogous to that for the model-generated or default Tier I exposure estimates. While RQs presented in the default Tier I assessment are based on highest exposure estimates for contact and/or dietary exposure routes (*i.e.* exposure to workers foraging for nectar and 5-day old larvae), the Bee-REX model also calculates dietary exposure values and associated RQs for larvae of different ages, adult workers with different tasks (and associated energy requirements) and the queen using those different food consumption rates. Consequently, a potential spectrum of risk estimates is available for multiple castes and life-stages of honeybees. As described earlier in Section 5.1 honey bees are a good surrogate for other non apis bees and at the refined tier I level conclusions should also be protective of non apis bees.

Presented below (**Table 6-16**) is a summary of RQs resulting from using available measured residues in pollen and/or nectar for use patterns of imidacloprid. For the purposes of this assessment, the refined Tier I RQs presented below are the maximum. The range of RQs calculated by Bee-REX are presented in **Appendix J**. This was done because any exceedance of the LOCs for dietary exposure at the Refined Tier 1 level was considered to warrant an evaluation of risks at the colony level where available residue data exists. For adult acute oral RQs, the acute EECs (maximum measured concentration among all individual replicates following application) and the chronic EECs (maximum average concentration among all individual sampling events following application) will be compared against the same acute and chronic toxicity endpoints used in the default Tier I assessment using imidacloprid toxicity endpoints. Imidacloprid does not have an available study for acute larval toxicity, and therefore, that endpoint is not included in the analysis. Although Bee-REX includes consumption rates for royal jelly, residue information for this matrix is not available from any residue study for imidacloprid. As royal jelly constitutes the exclusive diet of the larval and adult queen and for 1 to 3 day-old worker larvae, refined Tier I oral RQs are not available for the queen (larval and adult) or 1 to 3 day-old worker larvae.

This Tier I refinement also considers the RQ exceedances at different times based on measured residues at distinct time points. The RQs are based on residues of both pollen and nectar where data are available and may reflect time points over the course of a single season or multiple seasons, depending on study design. Due to differences in study designs (*i.e.*, if residues were measured over the course of the season or once yearly), estimates for how long an RQ exceeds the LOC are not available for every study/crop where empirical residue values are available. This information is summarized in **Table 6-16** below, and the graphical representation of all crops (where available) is in **Appendix J**.

Table 6-16. Summary of Refined Tier I Risk Conclusions

| Group # | Crop Group | Appl. Method | Crop Residue Data Used | EECs (Nectar/Pollen µg/L) | | Adult RQs Endpoint ⁽¹⁾ | | Larval RQs Endpoints ⁽²⁾ | % RQs Exceeding over time | |
|---------|-----------------------|---------------|------------------------------|------------------------------|-----------|--------------------------------------|------------|--|---------------------------|--------|
| | | | | Acute | Chronic | Acute | Chronic | Chronic | Adult | Larval |
| 6 | Legume Vegetables | Foliar | Soybean | 2.5/5.2 | 1.25/2.7 | 0.19 | 0.33 | 0.1 | 0% | 0% |
| | | Seed | Soybean | 1.5/4.2 | 0.92/2.5 | 0.11 | 0.24 | 0.07 | 0% | 0% |
| 8 | Fruiting Vegetables | Soil | Tomato | --/242 | --/198 | 0.60 | 1.7 | 0.39 | 9% | 0% |
| | | Foliar + Soil | Tomato | --/1763 | --/1268 | 15.4 | 11 | 2.5 | 57% | 13% |
| 9 | Cucurbit Vegetables | Soil | Melon, watermelon* | 11/53 | 11/41 | 0.82 | 2.9 | 0.87 | 35% | 0% |
| 10 | Citrus Fruits | Foliar | Orange | 430/4100 | 324/3300 | 32 | 86 | 30 | 100% | 100% |
| | | Soil | Orange*, grapefruit* | 35.5/10.2 | 23.8/9.4 | 2.7 | 6.3 | 1.7 | 98% | 44% |
| 11 | Pome Fruits | Foliar + Soil | Apple | 36.3/103 | 36.3/81 | 2.7 | 9.7 | 2.8 | 18% | 5.9% |
| 12 | Stone Fruits | Foliar | Cherry | 10/1000 | 5.6/545 | 2.8 | 5.5 | 1.5 | 38% | 8% |
| | | Foliar + Soil | Cherry, plum, apricot, peach | 33.6/341 | 32.8/237 | 2.5 | 8.7 | 2.8 | 33% | 11% |
| 13 | Berry and Small Fruit | Soil | Blueberry*, strawberry | 16/42 | 8.8/16.5 | 1.2 | 2.3 | 0.66 | 12% | 0% |
| 15 | Cereal Grains | Seed | Corn | --/39.7 | --/22.3 | 0.10 | 0.19 | 0.04 | 0% | 0% |
| 20 | Oilseed | Foliar | Cotton | 66/-- | 56/-- | 4.9 | 15 | 4 | 100% | 100% |
| | | Soil | Cotton | 127/43.4 | 83.1/41.1 | 9.5 | 22 | 6 | 67% | 47% |
| | | Foliar + Soil | Cotton | 2775/2906 | 1952/2316 | 208 | 518 | 146 | 100% | 88% |
| | | Foliar + Seed | Cotton | 39.5/56.7 | 29/25.2 | 3 | 7.7 | 2.1 | 70% | 12% |
| NA | Non-agricultural uses | Soil | Ornamental | 1682/-- | 845/-- | 126 | 224 | 60 | NA | |
| | | Forestry | Woody ornamental | 975/-- | 467/-- | 73 | 124 | 33 | | |

¹ Based on a 48-h acute oral LD₅₀ of 0.0039 µg a.i./bee for imidacloprid (MRID 42273003) and a 10-d adult chronic NOAEC of 0.0011 µg a.i./bee (MRID 50399101)

² Based on and larval 21-day chronic NOAEC of 0.0018 µg a.i./larva (MRID 49090506).

* denotes crop with highest residues used for RQ calculation when data for more than one crop is available

Bolded value exceeds the acute risk LOC of 0.4 or chronic risk LOC of 1.

6.1.4.2. Seed Treatment Applications

As discussed in the use characterization, imidacloprid is registered for use as a seed treatment on a wide variety of use patterns. The Tier I RQs using the Bee-REX default exposure assessment for seed treatments resulted in RQs that exceeded LOCs. Therefore, a refined approach is considered here.

Crops that are not bee attractive

Table 6-17 lists the crops that are registered for seed treatments of imidacloprid but are not attractive to honey bees (according to USDA 2017). **Table 6-18** lists that registered crops that are harvested prior to bloom. Given the lack of potential exposure, a low risk call is made for seed treatment uses that are either not attractive to honey bees or are harvested prior to the bloom period.

Table 6-17. Seed treatment uses that are not attractive to honey bees

| Crop | Rate (mg a.i./seed) |
|-----------|---------------------|
| Barley | 0.05 |
| Oat | 0.03 |
| Rye | 0.02 |
| Triticale | 0.03 |
| Wheat | 0.05 |

Table 6-18. Seed treatment uses that are harvested prior to bloom

| Crop | Rate (mg a.i./seed) |
|------------|---------------------|
| Broccoli | 0.39 |
| Carrot | 0.01 |
| Mustard | 0.05 |
| Onion | 0.06 |
| Sugar Beet | 1.3 |

Refined Tier I RQs for crops with potential exposure

As discussed in **Attachment 4**, residue data are available for pollen and nectar from several crops (*i.e.*, corn, soybean, canola and cotton) that received seed treatments. This attachment recommends refined exposure values for Tier I and II (if needed) assessments. For imidacloprid, those exposure recommendations are provided in **Table 6-19**.

Table 6-19. Tier I recommendations for imidacloprid residues in pollen and nectar

| Crop | Maximum seed treatment rate (mg a.i./seed) | Matrix | Tier I (acute) Concentration (ng a.i./g) | Tier I (chronic) Concentration (ng a.i./g) |
|-----------------------------------|---|--------|--|--|
| Corn | 1.3 | Pollen | 33 | 9.0 |
| | | Nectar | 0 | 0 |
| Cotton | 0.33 | Pollen | 0 | 0 |
| | | Nectar | 3.0 | 1.7 |
| Soybean | 0.16 | Pollen | 23.8 | 12.8 |
| | | Nectar | 17.7 | 6.8 |
| Canola | 0.015 | Pollen | 21.7 | 16.3 |
| | | Nectar | 5.7 | 4.0 |
| All other crops (may increase) | 0.1 (note: this is not the max rate for other crops) | Pollen | 3.2 | 1.8 |
| | | Nectar | 7.6 | 4.5 |

Table 6-20 includes the refined RQs for imidacloprid for adult honey bees. RQs were not generated for larvae because of their lower RQs relative to adults and therefore, it was assumed that adult bees would be protective of larvae. Several of the refined RQs are below the acute and chronic RQs (buckwheat, corn, millet and sorghum), suggesting low risk from these seed treatments. For crops with residues that result in RQs above the LOC, a Tier II assessment was conducted.

Table 6-20. Refined RQs (for adult honey bees) for crops with potential exposure from imidacloprid seed treatments

| Crop (or group) | Rate | Acute RQ | Chronic RQ | Pass Tier I? | Risk conclusion |
|-----------------|------|----------|------------|--------------|--------------------|
| Beans | 0.54 | 0.32 | 4.63 | No | Proceed to Tier II |
| Buckwheat | 0.01 | 0.01 | 0.09 | Yes | LOW |
| Canola | 0.05 | 0.43 | 7.30 | No | Proceed to Tier II |
| Corn (field) | 1.41 | 0.08 | 0.54 | Yes | LOW |
| Corn (pop) | 0.83 | 0.05 | 0.32 | Yes | LOW |
| Corn (sweet) | 0.63 | 0.04 | 0.24 | Yes | LOW |
| Cotton | 0.51 | 0.22 | 3.10 | No | Proceed to Tier II |
| Millet | 0.01 | 0.01 | 0.09 | Yes | LOW |
| Peanuts | 0.61 | 0.36 | 5.23 | No | Proceed to Tier II |
| Peas | 0.43 | 0.25 | 3.69 | No | Proceed to Tier II |
| Safflower | 0.3 | 0.18 | 2.57 | No | Proceed to Tier II |
| Sorghum | 0.06 | 0.04 | 0.51 | Yes | LOW |
| Soybeans | 0.38 | 1.33 | 12.41 | No | Proceed to Tier II |
| Sunflower | 0.32 | 0.19 | 2.74 | No | Proceed to Tier II |

6.1.5. Uncertainties In Tier 1 Risk Assessment

There are several sources of uncertainty at the screening-level and refined Tier I level associated primarily with the screening-level exposure estimates and use of residue data, respectively. What follows are the uncertainties associated with each point:

Uncertainties in the screening-level exposure estimates include:

- The extent to which the amount of food consumed by bees for the Tier I exposure estimate represent pesticide concentration in food sources.
- The extent that residues on leaves and even soil may be available for bee uptake
- For soil applications, there are three notable limitations to the modified Briggs' model approach that include:
 - This methodology is based on one species of plant (barley)
 - The dataset used to derive elements of the model is based on a limited number of chemicals that represent only two classes of pesticides that do not include the neonicotinoid insecticides
 - The model is based upon data on pesticide concentrations in vegetative plant matrix (*i.e.*, shoots) as a surrogate for nectar and pollen
- For seed treatment applications, the screening-level assumption of exposure within Bee-REX is 1 mg/kg (1 mg/L). This is based in the Internal Commission for Plant-Bee Relationships' 1 mg a.i/kg to represent an upper bound concentration in pollen and nectar. This assumption of exposure is independent of application rate (*i.e.*, mass of chemical applied to the seed but is considered to be protective of the varying rates currently being used for seed treatments).
- Bee-REX assumes exposures through consumption of nectar and pollen are conservative representations of potential exposures through consumption of honey and bee bread, respectively. This approach is likely to be conservative because it assumes that pesticides do not degrade while honey and bee bread are stored in the hive. For bees that consume honey, it is assumed that the estimated pesticide exposures can be related back to the original concentration in nectar by accounting for the amount of sugar consumed by bees. It is also assumed that pollen and nectar consumption rates and resulting exposures are protective of exposures of bees to pesticides through consumption of royal jelly and brood food.
- The screening-level exposure assumption in Bee-REX assumes pesticide concentrations in pollen and nectar are equivalent (*i.e.* effectively one EEC for bee food). As was shown in the suite of available residue studies, pollen and nectar residue values can vary markedly depending on the use pattern and application method. For example, maximum residues in pollen in the foliar applied cherry study were 100-fold higher than maximum residues in nectar. Conversely, extra-floral nectar residues were over 8-fold higher than pollen residues in the soil + foliar-applied cotton study.

- For estimating off-field RQ values, several conservative assumptions are made which may overestimate exposure and risk:
 - Parameterization of AgDRIFT is representative of common application and environmental conditions;
 - Estimated spray drift via AgDRIFT deposit on bee-attractive vegetation adjacent to the treated field;
 - Vegetation is in bloom at the time of application;
 - Bees are actively foraging adjacent to the treated field at the time of application; and
 - Bees get all of their pollen and nectar from the contaminated vegetation.

Notable uncertainties in the use of pollen and nectar residue data for tier I risk estimation include:

- The limited quantity of residue data for several crop/application method scenarios;
- The extent to which these data represent the wide range of conditions across the U.S. which could affect residues in pollen and nectar;
- Representing Tier 1 EECs by the maximum residue values for the initial RQ calculation²⁹ which could over estimate exposure particularly in cases where residue data are abundant for a given crop/application scenario.

6.2. Higher Tier Risk Assessment for *Apis* Bees

For those uses indicating risk based on the Tier 1 assessment, a higher tier risk assessment is conducted. The higher tier risk assessment is based on colony-level effects on honey bees combined with estimates of exposure derived from higher tier field residue studies (**Section 4.6**). At the Tier II level, a NOAEC and LOAEC of 23 and 47 µg/L of total imidacloprid in sucrose was determined from the registrant-submitted colony feeding study (MRID 49501001). The NOAEC and LOAEC of 23 and 47 µg/L, respectively, are based on reductions in several colony-level apical endpoints including numbers of adults, number of pupae, pollen stores, and honey stores that persisted across multiple assessments of the colonies throughout the course of the study.

At this time, the registrant-submitted colony feeding study is considered the most comprehensive and robust Tier II study available from which to characterize the colony-level effects of imidacloprid to honey bees. Specifically, this study:

- Contains a high degree of replication and adequate statistical power,
- Demonstrates a robust dose-response relationship between sucrose residues and colony-level apical endpoints,
- Examined a 6-week exposure period that is commensurate with relatively long-term exposures expected for some crop use scenarios,
- Provides raw data that enabled an independent statistical evaluation of the responses,
- Was conducted according to Good Laboratory Practice specifications, and

²⁹ It is noted that refine Tier 1 RQ estimates were conducted using all of the residue data within each crop/application scenario when RQ values calculated with the maximum values exceeded the LOCs.

- Included an evaluation of over-wintering colony survival.

In addition, Tier III (full field) studies are considered in the higher tier risk assessment where available (e.g., cucurbits, cotton).

A major emphasis of the higher tier risk assessment for honey bees is the application and interpretation of the higher-tier residue data. Specifically, a new method has been developed to integrate exposure from both pollen and nectar for assessing risk at the Tier II (colony) level. In contrast to assessing nectar and pollen exposure separately in the 2016 Preliminary Bee Risk Assessment for Imidacloprid, both matrices are now combined for a total diet (nectar equivalents) approach for estimating oral exposure at the colony level (**Attachment 1**). In addition, a comprehensive residue bridging analysis was conducted to support extrapolations of residue data among various chemicals, crops, and matrices (**Attachments 2, 3 and 4**). Finally, risk assessment determinations at the higher tier were made by evaluating multiple lines of evidence and the strength of evidence supporting each risk determination was explicitly characterized. Additional information of these elements of the higher tier risk characterization is described in the subsequent sections.

6.2.1. Method to Assess Combined Pollen and Nectar Exposure

Incorporation of oral exposure of honey bees to residues in both pollen and nectar is explicitly addressed in the Tier I risk assessment methodology. However, there is also need to consider both pollen and nectar exposure for interpreting risks using the Tier II colony feeding study. To assess exposure from total food at the colony level, a method has been developed that considers both the amount of each matrix consumed on a daily basis, as well as potential differences in toxicity to the colony that may be the result of different matrices. Summarized below this “total food” method is a weight of evidence approach based on colony biology and comparisons of available colony level toxicity studies from sucrose and pollen patties. Since the sucrose-based colony feeding study is considered more robust than the available pollen-based feeding studies, the exposure values are converted to a “total nectar equivalent” concentration ($C_{total-t}$; ng a.i./g; Equation 1). $C_{total-t}$ is the sum of the concentration in nectar (at a given time), i.e., $C_{nectar-t}$ (ng a.i./g), and the concentration in pollen at the same time divided by a factor of 20, i.e., $C_{pollen-t}$ (ng a.i./g)/20. Details on the derivation of the weighting factor for pollen are provided in **Attachment 1**.

$$\text{Equation 1. } C_{total-t} = C_{nectar-t} + \frac{C_{pollen-t}}{20}$$

6.2.2. Residue Bridging Strategy

To account for gaps in the knowledgebase of residue data, a residue bridging strategy was developed to support the extrapolation of residues in pollen and nectar among neonicotinoids, crops and plant matrices when necessary. Details and analysis of the available residue data for supporting the residue bridging strategy for all four neonicotinoids are provided in **Attachment 2** (for foliar and soil applications to agricultural crops), **Attachment 3** (for foliar and soil applications to non-agricultural crops), and **Attachment 4** (for seed treatment applications). A summary of the analysis for foliar and soil application to agricultural crops is provided below, since the seed treatment and non-agricultural uses required much less characterization at the Tier II level.

Approximately 80 residue studies were considered in the residue bridging analysis, most of which had protocols submitted and reviewed by EPA prior to being conducted. The vast majority of residue studies were submitted by the registrants in accordance with Good Laboratory Practices (GLP) defined under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). The design of these residue studies varied considerably, in part due to the lack of standardized test guidelines for conducting field residue studies relevant to bees. In addition, regulatory objectives differed among the regulatory authorities involved in the generation of these data.

The bridging analysis focused on a subset of factors that are believed to influence residues in pollen and nectar which could be quantified and evaluated with the submitted data. The factors included:

- Chemical;
- Crop;
- Plant matrix (pollen, nectar, flower);
- Season of application;
- Application site;
- Application method; and,
- Application timing.

The overall methodology underlying the residue bridging analysis involved controlling for as many of the potentially confounding variables as possible (*e.g.*, application rate, application method, time between application and residue measurement, crop, *etc.*) and conducting appropriate comparisons when sufficient data were available. In most cases, the sample size was insufficient to conduct robust statistical analysis. In these cases, other approaches were used such as comparisons of the 95% confidence intervals or frequency distributions associated with differences (ratios) among residue measurements associated with different factors.

Based on the results summarized in **Attachment 2**, the following general conclusions are made regarding the neonicotinoid residue data:

1. Influence of Application Method. The type of application method (foliar spray vs. soil application) has a major influence on the magnitude and duration of neonicotinoid residues in pollen and nectar. Specifically, residues from foliar applications made prior to bloom are typically one to several orders of magnitude greater than those resulting from soil application. Furthermore, residues resulting from foliar applications made pre-bloom tend to show consistent declining trends with increasing time after application. Residues from soil applications tend to remain relatively stable or show varying trends over time. These findings support the recommendation that residues from foliar application be considered separately from those associated with soil application.

2. Influence of Application Rate. The results from the residue bridging analysis support the hypothesis that residues in pollen and nectar scale in approximate proportion to application rate. This finding supports the normalization of residue values by application rate for bridging and risk characterization purposes.

3. Influence of Application Timing. For perennial crops (*i.e.*, within orchard and berry groups), foliar applications made within several weeks prior to bloom resulted in residues in pollen and nectar up to

several orders of magnitude greater than those made after bloom (and measured during the following season). This finding supports the separate characterization of exposure from pre-bloom vs. post-bloom foliar spray applications for perennial crops. With soil applications, the impact of application timing is less pronounced and more variable compared to foliar applications.

4. Influence of Matrix. Residues of the neonicotinoids in pollen tend to be at least an order of magnitude greater than those found in floral nectar measured near the same time. Residues in extrafloral nectar in cotton are substantially greater than those in floral nectar (*i.e.*, 10X or more) for dinotefuran, clothianidin and thiamethoxam, but not for imidacloprid.

5. Influence of Site and Season. Residues in pollen and nectar typically vary by up to an order of magnitude when measured at different sites for the same crop and neonicotinoid. Occasionally, residues vary up to two orders of magnitude among sites. Within a residue trial, residues at one site often differ by a greater magnitude compared to those from the other sites in the trial. Similarly, residues measured at the same site but from trials conducted over multiple seasons typically vary up to 10-fold. It is noted that differences among sites incorporate multiple factors that could influence residues including weather, soil characteristics, hydrology, agronomic practices and crop variety. These findings support considering the number of sites upon which a risk finding is based as a line of evidence for characterizing the robustness of risk assessment conclusions.

6. Influence of Crop and Chemical. With a few exceptions, the variation in residues observed in pollen and nectar from different crops and neonicotinoids is comparable to that observed between different sites for the same chemical and crop. Exceptions occurred for cotton and berries/small vine crops. It is noted that since residue trials involving different chemicals and crops were nearly always distributed among different sites, the influence of site could not be distinguished from that of chemical or crop.

7. Differences in Residues from Different Matrices. The relationship of neonicotinoid residues among different plant matrices was investigated in order to support the use of surrogate plant matrices (*e.g.*, anther, flower) when the data for the target matrix was missing. As a result of the variability observed in the relationship between residues in different plant tissues, central tendency (50th percentile) and upper bound (90th percentile) estimates of extrapolation factors were derived for various plant tissues. These factors are summarized in **Table 6-21**.

Table 6-21. Recommended Extrapolation Factors for Converting Neonicotinoid Residues from Surrogate to Target Plant Matrices

| Matrix Extrapolation | Application Method | Extrapolation Factor ¹ | |
|----------------------|--------------------|---|--|
| | | Central Tendency (50 th Percentile) | Upper Bound (90 th Percentile) |
| Anther to Pollen | Foliar & Soil | 1 | 5 |
| Flower to Nectar | Foliar & Soil | 0.3 | 1 |
| Flower to Pollen | Foliar | 0.8 | 5 |
| | Soil | 0.5 | 3 |

8. Residue Decline Curves. For pre-bloom foliar applications orchard crops, berries, cucurbits and cotton, the underlying residue data supported the development of residue-decline curves using an analysis of residue kinetic parameters. Through the use of Monte Carlo modeling, a subset of these

residue-decline curves was generated to represent the 50th, 70th and 90th percentiles of residue decline curves that would be expected among multiple fields and conditions. These modeled residue-decline curves are recommended for use as an additional line of evidence for characterizing the oral risk of neonicotinoids to bees because they enable estimation of risk at time points where measured residue data are not available. These residue-decline curves also incorporate variability in residue data such that modeled residue estimates may extend beyond the limits of the observed data.

9. Final Residue Bridging Recommendations. Bridging recommendations for specific crop groups and application methods for agricultural uses are shown in **Table 6-22**. In general, bridging among chemicals and crops is recommended within a crop group. Bridging is not recommended between residue values representing foliar applications to perennial crops made pre- and post-bloom. For several crops or crop groups, little or no residue data were available; in these situations, bridging from a broader range of crops (e.g., all herbaceous crops) is recommended based on considerations of crop physiology, agronomy and taxonomy.

Table 6-22. Crop-group specific recommendations for bridging neonicotinoid residue data resulting from foliar and soil applications.

| Crop Group | Method | Recommended Bridging Option: | | | |
|-----------------------|-----------------|-------------------------------------|-----------------------------------|-----------------------------|-------------------------------------|
| | | Across Chemical? | Across Crop? | Across Pre- vs. Post-Bloom? | Use Modeled Residue Decline Curves? |
| Orchards ¹ | Foliar | Yes | Yes | No | Yes (pre-bloom only) |
| | Soil | Yes | Yes | Yes | No |
| Berries/Small Vines | Foliar | Yes | Yes, except grape | No | Yes (pre-bloom only) |
| | Soil | Yes ² | Yes, except grape | No ² | No |
| Oilseed (Cotton) | Foliar | No (Imi, Dino) Yes (Cloth, Thia) | NA | NA | Yes |
| | Soil | NA | NA | | No |
| Cucurbits | Foliar | Yes | Yes | NA | Yes |
| | Soil | Yes | Yes | | No |
| Root/Tuber | Foliar & Soil | Yes ² | Yes (all herbaceous) | NA | No |
| Legumes | Foliar | Yes ² | Yes (Imi only) ³ | | No |
| | Soil | NA ⁴ | Yes (all herbaceous) | NA | No |
| Fruiting Veg. | Foliar & Soil | Yes | Yes | NA | No |
| Hops & peanut | Foliar and Soil | Yes ² | Yes (fruiting veg.) ⁵ | NA | No |
| Herbs/Spices | Foliar and Soil | Yes ² | Yes (all herbaceous) ⁵ | NA | No |

NA= not applicable; Imi = imidacloprid, Cloth = clothianidin; Dino = dinotefuran; Thia = thiamethoxam; “all herbaceous” indicates bridging with residue data from all herbaceous crops.

¹ Includes pome fruit, stone fruit, citrus, tree nuts and tropical fruits

² Bridging recommendation based on limited data and supported by lines of evidence from other crop groups.

³ Clothianidin and thiamethoxam are only registered for foliar applications to soybean in the legume crop group whereas imidacloprid is registered for multiple legume crops.

⁴ Soil applications to legumes are only registered for imidacloprid

⁵ Bridging recommendation based on similarity on taxonomy/biology due to lack of residue data to conclude otherwise.

6.2.3. Drawing Higher Tier Risk Conclusions

The potential for colony-level risks from registered imidacloprid uses considered multiple lines of evidence within each crop group. Within the context of the Tier II assessment and residue data, these lines of evidence include:

- The quantity and quality of available chemical-specific residue data,
- Available residue data for other neonicotinoid chemicals (when bridging was conducted),
- The magnitude by which maximum measured (and modeled) residue values exceeded the NOAEC and LOAEC,
- The frequency that daily mean-measured residue values exceed the NOAEC and LOAEC,
- The duration after application that daily mean-measured residue values exceed the NOAEC and LOAEC,
- The number of sites and/or crops with exceedances of the NOAEC and LOAEC,
- The number of days required for modeled residues to fall below the NOAEC and LOAEC (based on 50th, 70th, and 90th percentile estimates),
- The percentage of honey bee diet from the treated field that would be required to meet the NOAEC and LOAEC at the maximum measured or modeled residue value, and
- Qualitative consideration of other residue data that were not sufficiently robust for quantitative use in risk assessment.

Aside from comparisons of residue data with the Tier II colony level endpoints, other lines of evidence considered in this risk characterization include:

- Reported ecological incidents with bees associated with the application method and crop group
- Spatial extant of potential exposures based on usage information
- Agronomic practices
- Results from Tier III field studies

In cases where residues are below the colony-level effects endpoints (i.e., NOAECs and LOAECs), and no other evidence is available to suggest that there are risk concerns, a “low risk” conclusion is made for honey bee colonies. If residue values exceed the colony-level endpoints, then a colony level “risk” conclusion is made.

In addition, the relative strength of the evidence associated with this colony-level risk conclusion is characterized. This assessment employs three categories (“strongest,” “moderate” and “weakest”) to convey the strength associated with the weight of evidence for a crop with risk concerns for colony level effects from clothianidin or thiamethoxam.

The “strongest” evidence of risk is represented by cases where assumptions related to exposure and effects are not expected to have a major influence on risk conclusions and there are multiple lines of evidence indicating the potential for effects to honey bee colonies. A strong evidence of risk may be represented by a case where a high frequency of measured residues for the crop of interest exceed both the colony level LOAEC and NOAEC for a long duration (*e.g.*, several weeks); residues that are an order

of magnitude above colony-level endpoints (indicating that only a small fraction of the honey bee colony's nectar and pollen need to be from treated fields); and the observation that multiple locations in the residue trials and/or multiple crops within the crop group yielded residues above CFS endpoints. In addition, incident reports of bee kills may provide additional lines of evidence for a strong evidence of risk conclusion.

The "moderate" evidence of risk category is represented by cases where some lines of evidence indicate risk concerns; however, not all lines of evidence suggest risk, or there are some uncertainties associated with the data that can influence the risk conclusion. An example of moderate evidence of risk may be a case where only a small proportion of residues (from a small proportion of sites) exceed CFS endpoints for a short period of time (*e.g.*, days). In this case, there is some uncertainty whether effects will occur because residues from some sites do not exceed CFS endpoints and because the relatively short exposure duration may not be sufficient to elicit effects (*i.e.*, in the available CFS studies, after 3 and 6 weeks of constant exposure, effects were observed to colonies).

The "weakest" evidence of risk category is represented by cases where there is evidence to suggest colony level effects; however, it is not well supported by measured residue data for the chemical of interest. For example, this may be the case when only a few residues are above the CFS NOAEC but not the LOAEC and those residues only exceed for a few days and sites. Another example may be when 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 (*e.g.*, bridging residue data derived from seed treatment applications to turmeric seed piece treatments).

6.2.4. Higher Tier Uncertainties

Uncertainties at the Tier II level originating directly from the registrant-submitted Tier II colony feeding study are described in **Section 5.2**. Aside from these uncertainties, interpreting risk based on the Tier II colony feeding study also involves various assumptions and uncertainties. Specifically, it is assumed that bees forage on the treated crop nearly 100% of the time to represent the nectar needs of the colony. In the field, bees may forage for significantly shorter periods of time particularly for crops such as cherries and blueberries that have a 2-3 weeks blooming duration. Bees may also forage on alternative (untreated) plants which would have the effect of "diluting" the exposure from the treated field. Conversely, bees associated with migratory pollination services may feed on treated crops for similar or longer periods of time over the course of a growing season.

Additionally, the 6-week duration of the exposure phase in the available colony feeding study may be an under or overestimation of the duration of exposure that is potential for bees in a given area. For example, citrus fruit trees and cotton are noted to have a bloom duration of at least 6 weeks, consistent with the colony feeding study exposure phase, while stone fruit trees have a shorter bloom duration of 2-3 weeks.

Finally, there is uncertainty in the lack of a quantitative assessment of effects at the colony level resulting from the pollen route of exposure. This stems primarily from the fact that the available colony

feeding study assessed spiked sucrose. In effort to reduce this uncertainty, EPA has attempted to assess the pollen route of exposure through summing pollen and nectar residues and dividing the pollen concentration by a factor of 20, as explained in **Attachment 1**. There are assumptions and uncertainties with this methodology including no degradation of clothianidin or thiamethoxam in the bee bread (or its components), the bee bread is at a constant ratio, for which the ratio is based on two plant species.

Although assessing risk at the Tier III level incorporates the greatest environmental realism, it also contains important assumptions and uncertainties that impact the interpretation of risk. For example, practical constraints often limit the size of Tier III field studies to a fraction of the foraging area of honey bees. This limitation may under estimate exposure in large, agriculturally dominated landscapes where treated crops may constitute a much greater portion of the foraging area of honey bees. Furthermore, the extent to which bees actually forage on the treated crop in the Tier III studies often varies widely. For imidacloprid, only a small percentage of pollen was obtained from the treated field in the cotton and pumpkin Tier III studies. This may under estimate exposure in situations where bees are feeding mostly on treated crops. Lastly, the extent to which Tier III studies represent “high end” exposures is often difficult to establish, given site and region-specific factors that affect pollen and nectar residues and the amount of time bees forage on the treated site.

6.2.5. Crop group 20 – Oilseed

The oilseed crop group includes, among other members, cotton, flax, sunflower, and rapeseed (canola). Foliar and soil applications are allowed on cotton only whereas seed treatments are registered for multiple oil seed crops. For foliar applications, the single maximum application is 0.06 lb a.i./A with five applications allowed per season. Soil applications are registered with a maximum annual application rate of 0.33 lb a.i./A. Combined foliar and soil applications are allowed with a maximum seasonal application rate of 0.5 lb a.i./A. Seed treatment application rates vary from 0.02 – 0.175 lbs a.i./A calculated from a.i. per seed and seeding rate.

Specific to the usage of imidacloprid on oilseed, cotton is the only crop represented by usage information, with 50,000 lbs a.i./yr for each of foliar/soil and seed treatment uses (**Table 3-4**). Cotton is noted to have nectar that is attractive to honey bees while the pollen is not considered to be attractive to honey bees (USDA 2017). Cotton is associated with a blooming duration of at least 6 weeks. The sequence of bloom is known as vertical flowering, whereby flowers bloom in a distinct, upward spiral among branches over time. Once bloom begins, each flower lasts only for 1 day. This differs from other crops (e.g., stone fruit) where all blossoms develop and bloom at a similar time. Additionally, cotton is known to produce extrafloral nectar which may be attractive to honey bees. However, the extent to which honey bees utilize extrafloral nectar as a food source from cotton (or other crops) is currently uncertain. Therefore, this risk characterization for honey bees considers both floral nectar and extrafloral nectar, but not exposure to residues in pollen.

A summary of the lines of evidence considered in the characterization of risk to honey bees from foliar and soil applications of imidacloprid to cotton is shown below in **Table 6-23**. For foliar applications of imidacloprid to cotton, a moderate strength of evidence indicates a potential for colony-level risk to

honey bees foraging on fields treated at the maximum labeled rates. Specifically, measured residues of total imidacloprid in floral nectar exceed the colony-level NOAEC by a maximum of **1.1X** for up to 20 days after the last foliar application (MRID 49511702), although most residue values do not exceed the colony-level NOAEC. While the magnitude by which residues in floral nectar exceed the NOAEC is small, residue values from this study likely underestimates exposure since measurements were taken no sooner than 2 weeks after the last application. The imidacloprid label permits application during bloom. Therefore, bees may be exposed immediately after application to substantially higher residues. Modeled residues of total imidacloprid in floral nectar one day after application exceed the NOAEC and LOAEC by up to **6.3X** and **3.1X**, respectively, based on the 90th percentile decline curve. Residues of total imidacloprid in extrafloral nectar are about half those in floral nectar, and modeled residues (90th percentile) exceed the colony-level NOAEC for up to 8 days. A supplemental study of imidacloprid in cotton floral nectar (MRID 49103301) supports the modeled residue findings of NOAEC exceedances shortly after bloom (6 days), as do cotton nectar residue profiles measured for other neonicotinoids (**Attachment 2**). No ecological incidents have been reported involving foliar applications of imidacloprid to cotton. The strength of evidence is considered “moderate” primarily due to:

1. the small magnitude of NOAEC exceedances by measured residues ($\leq 1.1X$),
2. the relatively limited duration that modeled residues exceed the NOAEC (8-15 days) and LOAEC (3-8 days), and
3. the fact that NOAEC exceedances are largely based on modeled 90th percentile residue values.

For soil applications of imidacloprid to cotton, moderate evidence of risk is indicated based on residues measured ≥ 70 days after soil applications. Residues in floral nectar exceed the colony-level NOAEC for up to two months by a maximum of **3.6X**. However, the NOAEC exceedances appear dependent on soil type, with risks being associated with sites containing coarser soils. Because the spatial scale of risks appears to be dependent on soil type, the strength of evidence is considered “moderate.”

With combined soil + foliar applications to cotton, the evidence of risk is considered “strong” as indicated by residues in floral and extrafloral nectar exceeding the colony level NOAEC by up to **7X** and **80X**, respectively, for a duration of up to 2 months. There was no evidence of a dependency of risk on soil type for combined soil + foliar applications. No ecological incidents have been reported involving foliar applications of imidacloprid to cotton. A tier III full field study which examined the effects of soil and foliar applications to cotton is considered invalid. The complete characterization of colony level risks based on comparison of available residue data and colony level effects studies for honey bees (Tier II semi-field and Tier III full field) is described in further detail below for each application method.

Table 6-23. Lines of evidence considered in characterizing colony-level risk to honey bees from foliar and soil applications of imidacloprid to oilseed crops

| Line of Evidence | | Foliar Applications (Moderate Evidence of Risk) | | Soil Applications (Moderate Evidence of Risk) | | | |
|---|---|--|-----------------------------------|---|----------------------------------|--|--|
| Imidacloprid-specific residue data | | Cotton | | Cotton | | | |
| Residue data for other chemicals | | Not Used | | NA | | | |
| Measured Data: (Imidacloprid) | Exceedance Attribute | NOAEC | LOAEC | NOAEC | LOAEC | | |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC | 2/43 (FN) 0/42 (XFN) | 0/43 (FN) 0/42 (XFN) | 5/17 (FN) 1/15 (XFN) | 3/17 (FN) 0/17 (XFN) | | |
| | Duration: Number of days > NOAEC & LOAEC | 20 (FN) 0 (XFN) | 0 (FN) 0 (XFN) | 90 (FN) 78 (XFN) | 78 (FN) 0 (XFN) | | |
| | Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 1.1X (90%) FN 0.6X (N.C.) XFN | 0.5X (N.C.) FN 0.3X (N.C.) XFN | 3.6X (28%) FN 1.6X (64%) XFN | 1.7X (58%) FN 0.7X (N.C.) XFN | | |
| Modeled Data: (90 th percentile) | Duration: Number of days > NOAEC & LOAEC | 15 (FN) 8 (XFN) | 8 (FN) 3 (XFN) | NA | | | |
| Modeled Data: (70 th percentile) | Magnitude: Ratio to Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 6.3X (16%) FN 2.9X (34%) XFN | 3.1X (33%) FN 1.4X (70%) XFN | | | | |
| Modeled Data: (70 th percentile) | Duration: Number of days > NOAEC & LOAEC | 11 (FN) 5 (XFN) | 3 (FN) 0 (XFN) | | | | |
| Modeled Data: (50 th percentile) | Magnitude: Ratio to Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 2.5X (40%) FN 1.7X (59%) XFN | 1.2X (83%) FN 0.8X (N.C.) XFN | | | | |
| Combined Soil + Foliar Applications | | Strongest Evidence of Risk: Residues in floral and extrafloral nectar from combined soil (0.32 lb a.i./A) and foliar (0.06 a.i./A x 3) application exceed the NOAEC by up to 7X and 85X , respectively, and for up to two weeks after the last application (MRID 49665202). | | | | | |
| Crop Attractiveness⁽²⁾ & Bloom Duration | | Attractive (floral nectar); Potentially attractive (extrafloral nectar); Not attractive (pollen); Long bloom duration (indeterminant bloom) | | | | | |
| Managed Pollinators | | Not Required, but cotton used for honey production by some commercial beekeepers | | | | | |
| Tier III (Full Field) Studies | | Cotton study (MRID 50206701) considered invalid for evaluating effects | | | | | |
| Ecological Incidents | | None for foliar or soil applications | | | | | |
| Spatial Extent of Risk (acres treated) | | 383,220 (Avg. annual); 766,440 (Max. annual) | | | | | |

| Line of Evidence | Foliar Applications (Moderate Evidence of Risk) | Soil Applications (Moderate Evidence of Risk) |
|-----------------------------|--|---|
| Other Considerations | For foliar applications, initial residue measurements were taken \geq 13 DALA. Since the label does not restrict application during bloom, these measured residues likely underestimate exposure and risk . Furthermore, a single foliar application of 0.06 lb a.i./A resulted in a maximum daily average residue in floral nectar of 2X the NOAEC (DALA = 6; MRID 49103301). | |

⁽¹⁾ Max. residue for foliar and soil applications corresponds to 14 days (MRID 49511702) and 78 days (MRID 49665202) after application, respectively

⁽²⁾ Based on USDA 2017; FN = floral nectar, XFN = extrafloral nectar, N.C. = not calculated because > 100% of the treated diet would be needed to reach the NOAEC; NA = data not available

6.2.5.1. Foliar application

Based on the results of the residue bridging analysis (**Attachment 2**), the dissipation rate of total imidacloprid (parent+ imidacloprid olefin+ 5-hydroxy imidacloprid) in floral and extrafloral nectar following foliar application to seed treated cotton (MRID 49511702) appears substantially slower than rates determined for clothianidin and dinotefuran. Therefore, only residue data for imidacloprid are used for comparison to the colony level NOAEC and LOAEC from the colony feeding study (MRID 49510001). While the available residue data for comparison come from a study that examined both seed treatment and foliar application to cotton, the expected contribution of seed treatment to imidacloprid residues is considered minor (e.g., 1-5 ppb) compared to that from foliar application alone.

The distribution of dissipation rate constants and concentrations of total imidacloprid (normalized to DALA 15) were used in a Monte Carlo analysis to describe the 50th, 70th and 90th percentiles of the modeled residue decline curves in cotton floral nectar (**Attachment 2**). The resulting modeled residue decline curves are shown in **Figure 6-1** along with residues of total imidacloprid measured in floral nectar (green diamonds). Residue values are normalized to the maximum seasonal foliar application rate of 0.31 lb a.i./A

With floral nectar, daily mean residues of total imidacloprid generally fall below the colony level NOAEC of 23 µg a.i./kg, except for slight exceedances on day 14 (26 µg a.i./kg) and day 21 (26 µg a.i./kg) from one trial in 2014. At the maximum daily mean residue of 26 µg a.i./kg, cotton floral nectar would have to represent 90% of the diet of a honey bee colony to exceed the NOAEC. Importantly, however, the imidacloprid residue data reflect measurements taken \geq 13 days after the last foliar application, which was made at the onset of bloom. Since there are no label restrictions precluding the foliar application of imidacloprid to cotton during bloom, it is reasonable to assume that bees may be exposed to imidacloprid residues in floral nectar shortly after application. In these cases, residues shortly following application would likely be substantially greater than residues measured 2 weeks after application in this study.

Based on the Monte Carlo modeling of imidacloprid residues and associated kinetic parameters, the predicted exceedance of the NOAEC ranges from 8 days (50th percentile) to 15 days (90th percentile; **Table 6-23**). Furthermore, 90th percentile modeled residues in floral nectar exceed the NOAEC and LOAEC by a maximum of **6.3X** and **3.1X**, respectively.

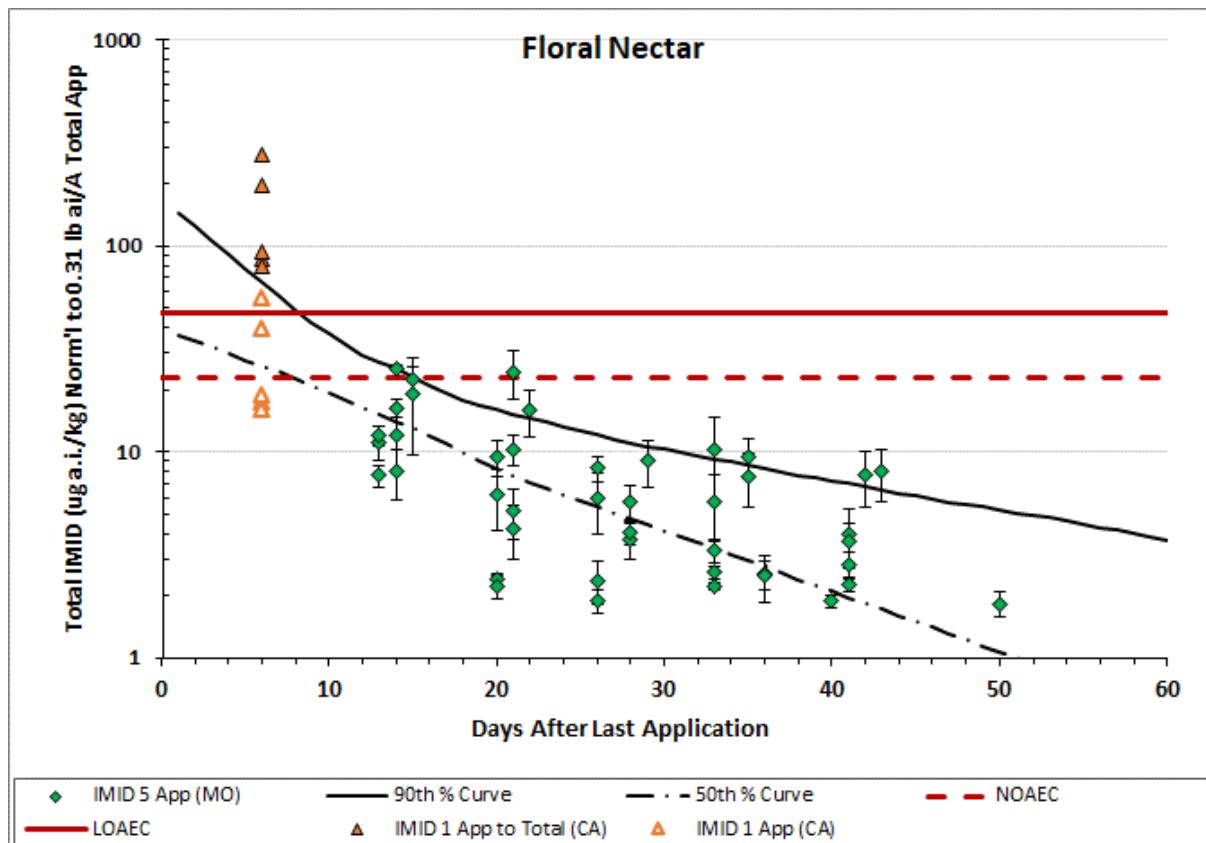


Figure 6-1. Daily mean concentration (+/- 95% CL) of total imidacloprid in cotton floral nectar (adjusted to the maximum seasonal foliar rate of 0.31 lb a.i./A) following seed + 5 foliar applications in 3 MO trials (MRID 49511702) and 1 foliar application in 5 CA trials (MRID 49103301, supplemental). Dashed and solid horizontal lines represent the colony level NOAEC and LOAEC, respectively.

Since residues were measured no sooner than 13 DALA in the MO cotton study, residue data from the CA cotton study (MRID 49103301) involving a single aerial application of 0.063 lb a.i./A were also included in **Figure 6-1** (orange triangles) because they were measured shortly after application (6 DALA). The CA cotton study is classified as supplemental because of limitations in its design and therefore was not used quantitatively in risk assessment (*i.e.*, it was excluded from Monte Carlo modeling and only used qualitatively as an additional line of evidence). Mean residues of total imidacloprid in nectar (unadjusted for application rate) varied from 16 to 56 ppb among the 5 California sites sampled (**1X to 2.5X** the NOAEC; **Figure 6-1**, open triangles). Since these residue values reflect only a single application rate, they likely underestimate exposure that would be associated with 5 applications at the maximum annual rate of 0.31 lb a.i./A (*e.g.*, 5 x 0.063 lb a.i./A @ 5-day intervals). When adjusted to the total application rate of 0.31 lb a.i./A, residue values range from 79 to 276 ppb, which exceed the NOAEC by **3X-11X** (**Figure 6-1**, solid triangles). Notably, this adjustment likely overestimates residue concentrations because some dissipation would be expected during the minimum 5-day application intervals. It is therefore likely that nectar residue values associated with 5 sequential foliar applications would fall in between the open and solid triangles of **Figure 6-1** and still exceed the NOAEC and LOAEC.

Although the CA cotton study was not considered suitable for quantitative use in risk assessment due its limitations, it clearly suggests higher residue values of imidacloprid occur had measurements been made sooner after application compared to the MO cotton study. Furthermore, the CA residue data suggest that the Monte Carlo-based decline curves are reasonable estimates of exposure prior to when measurements were taken in the MO study. Similar decline curves were observed for the other neonicotinoids (**Attachment 2**).

The same analysis conducted with residues in floral nectar was also performed using residues measured extrafloral nectar (**Figure 6-2**). Daily mean residues of total imidacloprid measured in cotton extrafloral nectar do not exceed the colony-level NOAEC or LOAEC. Again, however, the imidacloprid residue data reflect measurements taken \geq 13 days after the last foliar application. Since there are no label restrictions precluding the foliar application of imidacloprid to cotton during bloom, it is reasonable to assume that bees may be exposed to greater concentrations of imidacloprid residues in extrafloral nectar sooner after application. Based on the Monte Carlo analysis of imidacloprid residues and associated kinetic parameters, the predicted exceedance of the NOAEC ranges from 2 days (50th percentile) to 8 days (90th percentile; **Table 6-23**). The modeled 90th percentile residues in extrafloral nectar exceed the NOAEC and LOAEC by a maximum of **2.9X** and **1.2X**, respectively. No additional data on imidacloprid residues in extrafloral nectar are available for comparison (*i.e.*, the CA cotton study did not measure residues in extrafloral nectar).

The strength of evidence associated with colony-level risks from foliar applications of imidacloprid to cotton are considered “moderate” due to the small magnitude of NOAEC exceedances by measured residues (\leq 1.1X), the limited duration that modeled residues exceed the NOAEC (8-15 days) and LOAEC (3-8 days), and the fact that NOAEC exceedances are largely based on modeled 90th percentile residue values, which may be more uncertain compared to measured residue values.

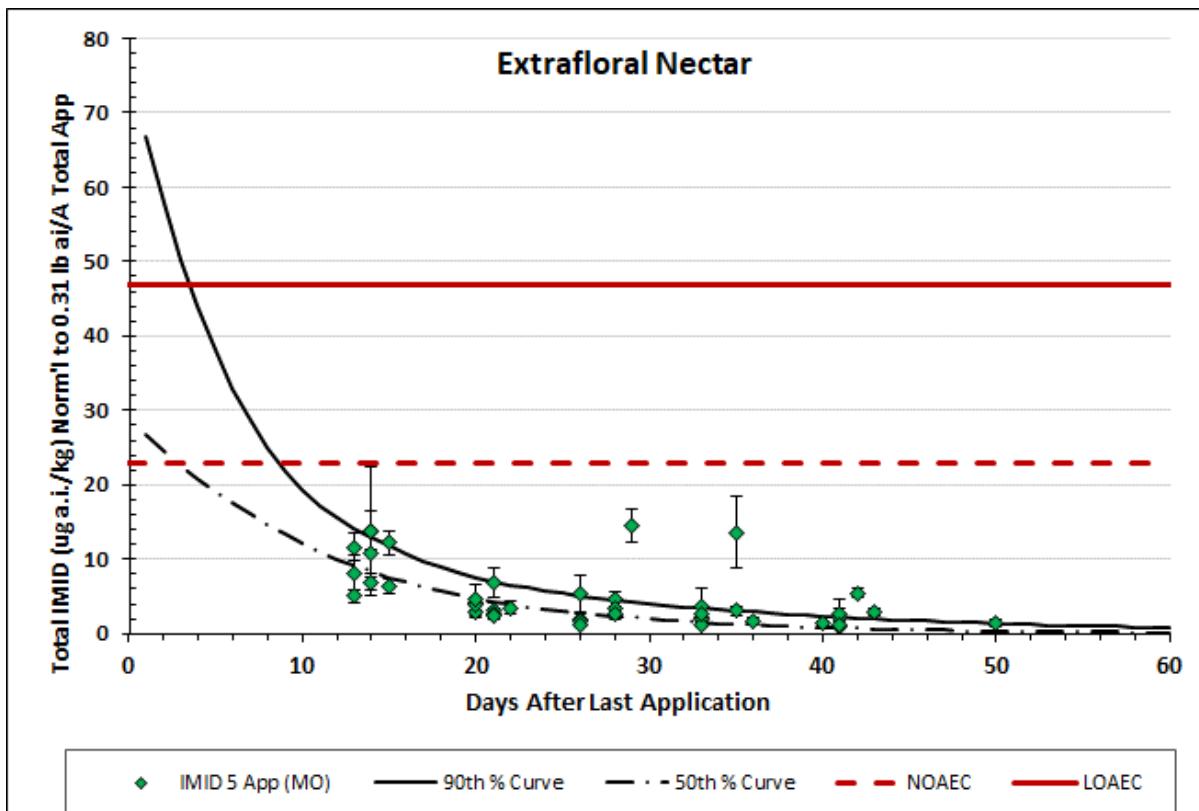


Figure 6-2. Mean concentration (+/- 95% CL) of total imidacloprid in cotton extrafloral nectar (adjusted to the maximum seasonal foliar rate of 0.31 lb a.i./A) following seed + foliar application in 3 MO trials (MRID 49511702). Dashed and solid horizontal lines represent the colony level NOAEC and LOAEC, respectively.

6.2.5.2. *Soil Applications to Cotton*

Unlike the other neonicotinoids, imidacloprid is registered for soil applications to cotton. One study is available to evaluate the magnitude of residues following soil applications to cotton (MRID 49665202). This study also evaluated residues from the combined soil and foliar applications to cotton (described later in the “Combined Applications to Cotton” section). A total of nine (9) field trials were conducted, with 3 trials having one year of data and 6 trials having two years of data. Soil types ranged from light to heavy. Soil application rates varied from 0.33 to 0.34 lb a.i./A at planting and samples were taken only at one time point after soil application (70-95 days after application). Residues of total imidacloprid in cotton floral nectar are shown in **Figure 6-3** and those for extrafloral nectar are shown in **Figure 6-4**.

Depending on the site and year, mean daily residues in floral and extrafloral nectar exceed the colony-level NOAEC of 23 µg/L nearly 80 days following application. With floral nectar, 3 values also exceed the LOAEC of 47 µg/L. This suggests a potential for colony-level effects from soil application of imidacloprid to cotton, at least with some sites. These residues are higher than those for foliar applications which could be due to the higher application rate and therefore possible increased uptake for soil applications.

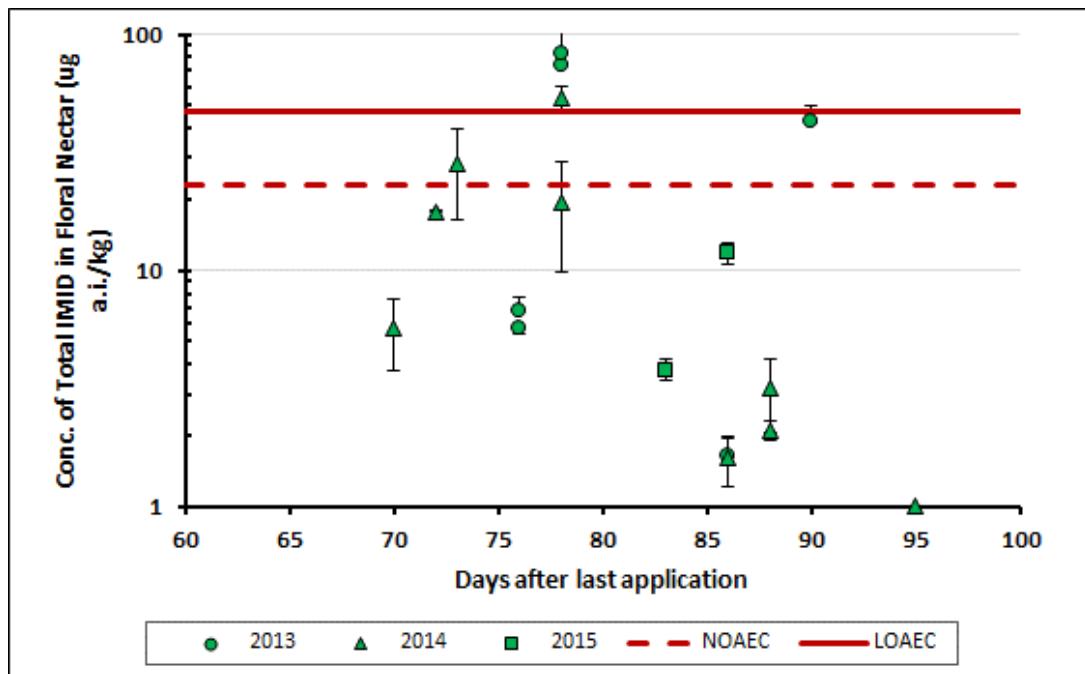


Figure 6-3. Mean daily concentrations of total imidacloprid in cotton floral nectar following soil application of 0.33 lb a.i./A at 9 sites in California over 2 years (MRID 49665202)

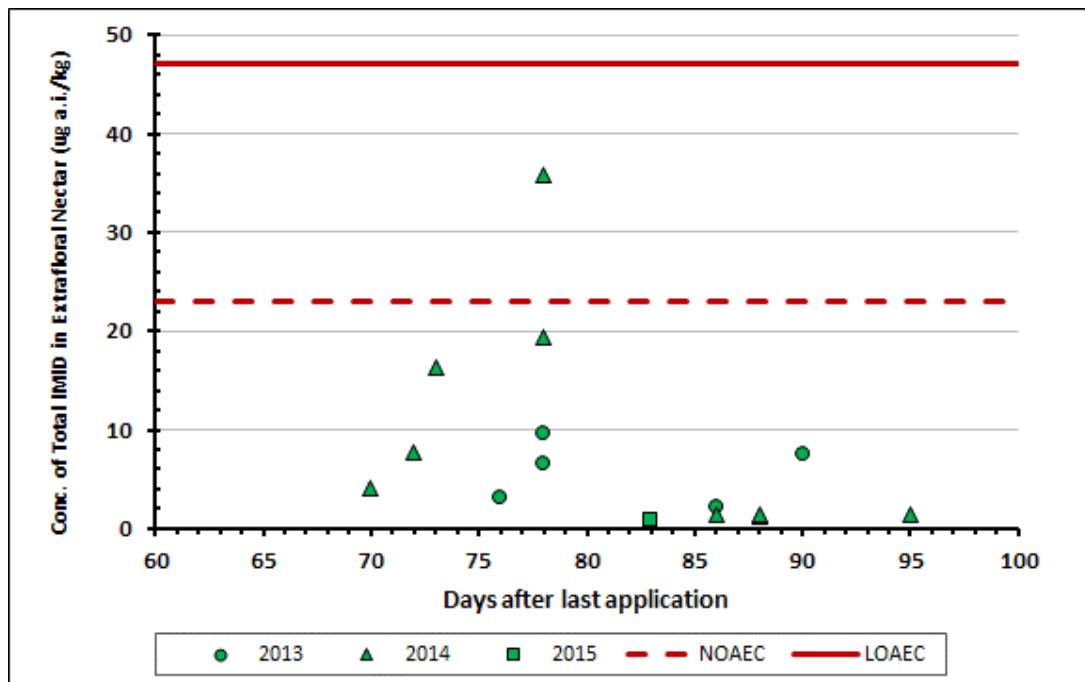


Figure 6-4. Mean daily concentrations of total imidacloprid in cotton extrafloral nectar following soil application of 0.33 lb a.i./A at 9 sites in California over 2 years (MRID 49665202)

Further investigation of the sites suggests that residues are correlated with the soil type (**Figure 6-5**). Specifically, sites with $\geq 70\%$ sand and $\leq 0.5\%$ soil organic matter have the greatest concentrations of imidacloprid in floral nectar. This suggests that the spatial scale of risks associated with soil applications of imidacloprid in accordance with the label may depend on soil type and may be limited to sites with coarser soils. Therefore, the strength of evidence associated with colony-level risks from soil applications of imidacloprid to cotton is considered “moderate” due the apparent dependence of risk on soil types. It is noted, however, that the residue data used in assessing risk of soil applications to cotton are limited to California sites. Therefore, there exists some uncertainty in the current risk findings for imidacloprid to the extent that residues in pollen and nectar vary across the U.S. sites due to regional differences such as weather, hydrology or agronomic practices.

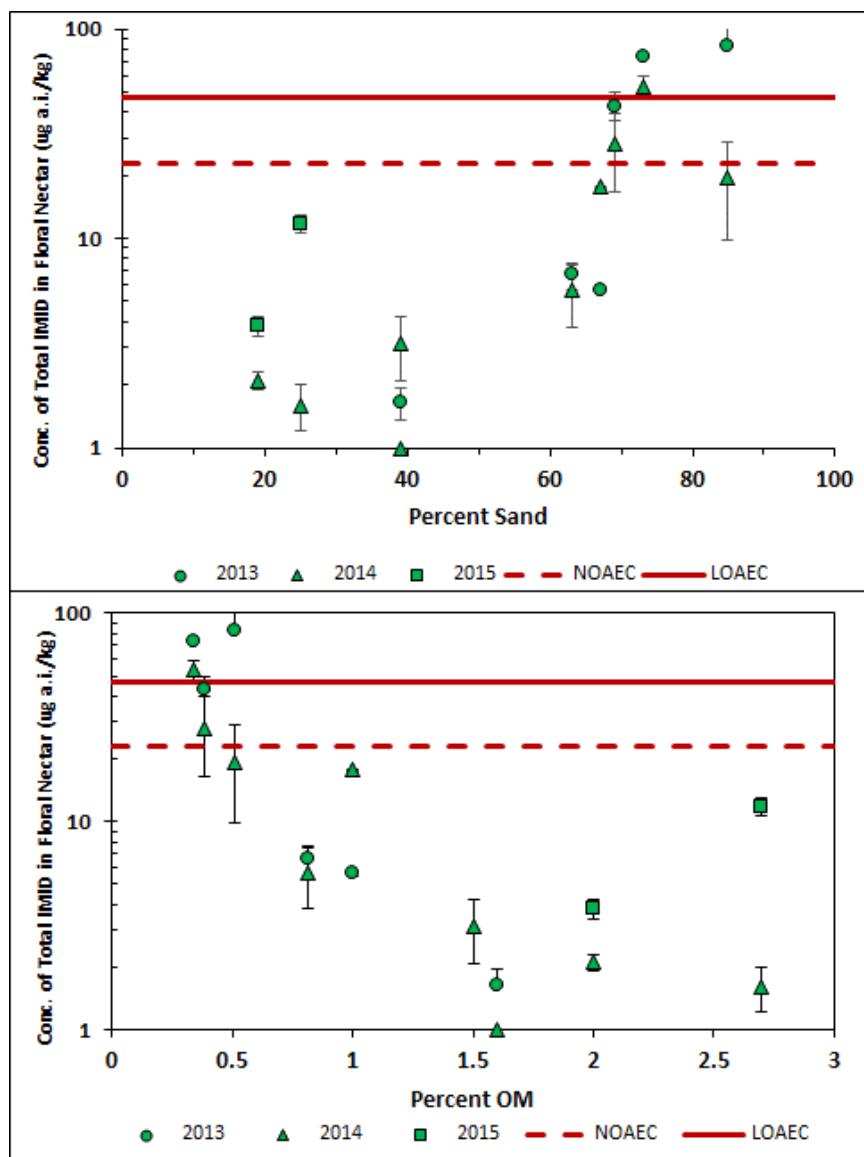


Figure 6-5. Mean daily concentrations of total imidacloprid in cotton floral nectar following soil application of 0.33 lb a.i./A at 9 sites in California vs. % sand and % organic matter (MRID 49665202)

6.2.5.3. Combined Soil and Foliar Application to Cotton

Current label language for imidacloprid allows a combined soil application to cotton at a maximum single application rate of 0.33 lbs a.i./A and 3 foliar applications of 0.06 lb a.i./A with no specific restrictions to honey bees or other pollinators. The previous study of soil applications to cotton (MRID MRID 49665202) also included residue measurements subsequent to the soil application and 3 successive foliar applications of 0.06 lb a.i./A to cotton during bloom at the same sites (0.5 lb a.i./A total application). Residues of total imidacloprid were measured between 4 and 14 days after the last foliar application.

For floral nectar, residues exceed the colony-level NOAEC and LOAEC with the majority measurements made at each time points following application (**Figure 6-6, Panel A**). The NOAEC was exceeded by **6.7X** (DALA 4-5) and **5X** (DALA 10-15). This corresponds to the NOAEC being exceeded if honey bees were obtaining 15% or 20% of the diet was composed of treated cotton, respectively, based on the maximum mean residues. A general decline in residues is seen from the first to the second sampling periods (DALA 4-5 vs. DALA 10-15).

Much higher concentrations of total imidacloprid are seen in extrafloral nectar during the first sampling period (DALA 4-5) compared to floral nectar (**Figure 6-6, Panel B**). Maximum daily average concentrations in extrafloral nectar reach 1,630 ug ai/kg, which is **85X** the colony-level NOAEC of 23 ug/L. By 10-15 days after the last foliar application, concentrations of total imidacloprid in extrafloral nectar decline to 110 ug/L or less, which is within 4X of the NOAEC.

Unlike results with soil only application, no trend was observed between the magnitude of imidacloprid residues in floral nectar and % sand or % OM following soil + foliar applications (**Figure 6-7**). This suggests that residues following soil + foliar applications to cotton are not nearly as dependent on soil type compared to those resulting from soil only application. This finding is reasonable considering that residues in pollen and nectar following foliar applications do not require translocation from soil through the roots (as required for soil applications) but instead depend on translocation within the plant itself. The strength of evidence associated with colony-level risks from combined soil+foliar applications of imidacloprid to cotton is considered “strongest” based on the duration, magnitude and frequency that residues exceed the colony-level endpoints.

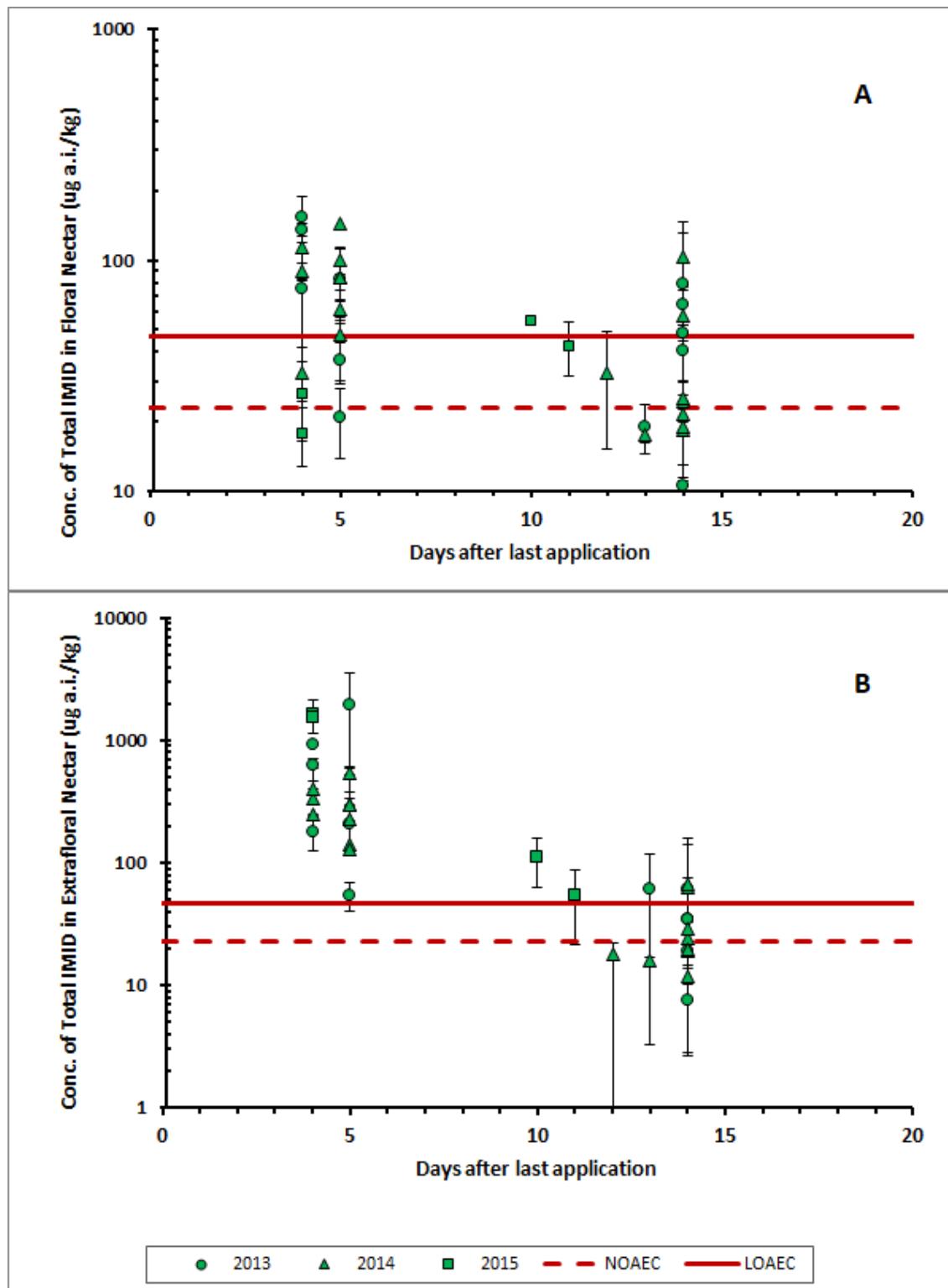


Figure 6-6. Concentrations of total imidacloprid in cotton floral nectar (A) and extrafloral nectar following one soil application of 0.33 lb a.i./A and three foliar applications of 0.06 lb a.i./A (MRID 49665202). Data represent 9 sites among 1-3 years.

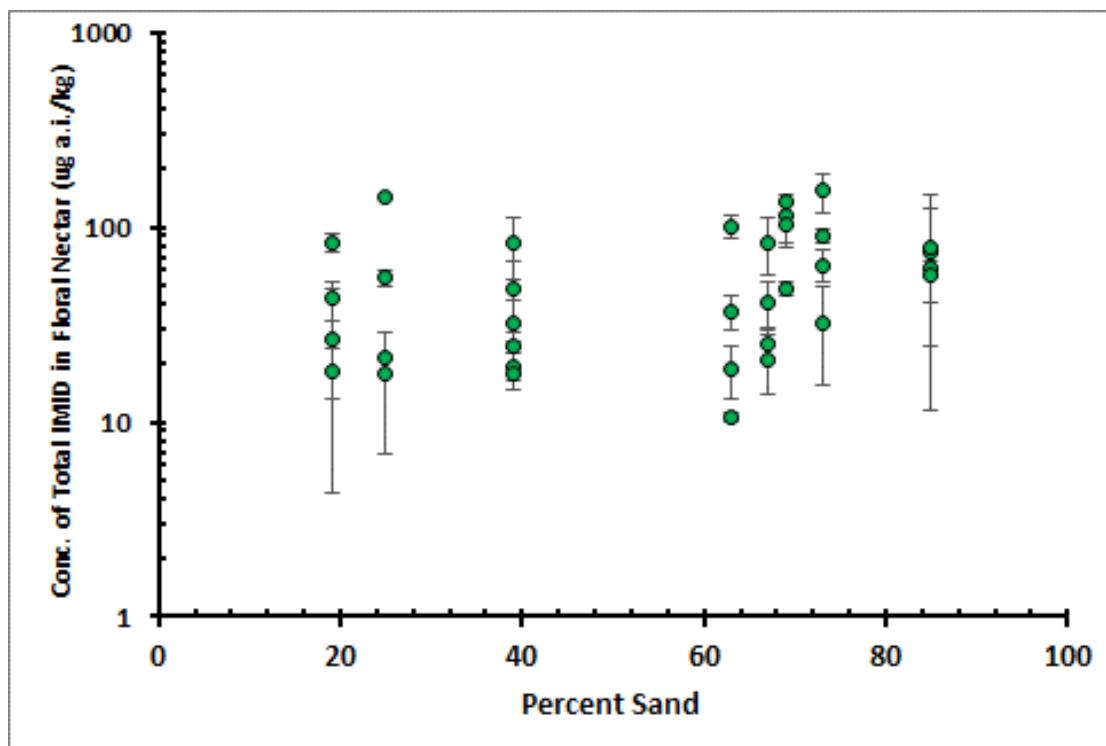


Figure 6-7. Concentrations of total imidacloprid in cotton floral nectar following one soil application of 0.33 lb a.i./A and three foliar applications of 0.06 lb a.i./A vs. % sand (MRID 49665202). Data represent 9 sites among 1-3 years.

6.2.5.4. Seed treatment

Attachment 4 provides recommendations for residues for a Tier II assessment of seed treatments as was needed for the oilseed crop group. **Table 6-24** includes the crop-specific recommended values (based on treatment rate and crop) for imidacloprid. The Tier II exposure values are compared to the imidacloprid CFS NOAEC (23 ng a.i./g). If the residue is below the NOAEC, a low risk call is made. This is the case for imidacloprid uses on canola, cotton, safflower, and sunflower.

Table 6-24. Tier II assessment for imidacloprid and oilseed crops

| Crop | Tier II concentration (nectar equivalents) | Above IMI CFS NOAEC (23)? | Risk conclusion |
|-----------|--|---------------------------|-----------------|
| Canola | 4.8 | No | LOW |
| Cotton | 2.1 | No | LOW |
| Safflower | 14 | No | LOW |
| Sunflower | 15 | No | LOW |

6.2.5.5. Additional Considerations

According to the SLUA, the average percentage of cotton acreage treated with imidacloprid is relatively low (10% for seed treatment and 5% for foliar/soil treatment). Based on approximately 7.6 million acres

of cotton grown in the U.S. (USDA 2017), the treated area associated with cotton approximates 760,000 acres for seed treatment and 380,000 acres for soil/foliar treatment. Given the apparent dependence of risk on soil type, the spatial footprint of risks associated with soil applications is not precisely known.

Other Tier II Semi-Field Studies

For canola/rapeseed, multiple semi-field studies (MRIDs 47699417, 47699422, 47699423, 47699425, 48699418, and 47699419) were conducted across a variety of locations (France, Sweden, Germany), all with imidacloprid applied with *beta*-cyfluthrin as a seed treatment. All studies examined either nectar alone or pollen and nectar from hand-collected, bee collected, and hive collected sources (depending on the study). All samples were reported to be either below LOD (either not reported or 1.5 µg/L, depending on the study) or <LOQ (either 5 or 10 µg/L, depending on the study). Additionally, in a full-field study (MRID 49073605), imidacloprid (co-formulated with *beta*-cyfluthrin) was applied as a seed treatment to canola with resulting residues in hand-collected and bee-collected nectar samples below the LOQ (10 µg/L). It is noted for the above studies that the sampling interval for these studies was reported with varying frequency with some studies noting a 55 day after application interval, others with a 59- to 69-day interval, and others not reporting this information.

For sunflower, semi-field studies (MRIDs 47699417, 47699422, 47699423, and 47699425) were all conducted in Germany with seed treated imidacloprid. All studies examined both hand and bee collected pollen and nectar data with some studies noting a 2 to 8-day interval and other studies not reporting this information. All hand-collected and bee-collected pollen and nectar data (sources of collection varied depending on study) were found to be below the LOD (1.5 µg/L in all studies). Additionally, in a full field study conducted with seed treated sunflower (Schmidt 1998, MRID 49766206), bee collected nectar after a 14-day duration in the treatment fields was below the LOQ (10 µg/L). Hand collected nectar residues were not available.

Stadler (2003; qualitative) investigated the colony-level effects of honey bees foraging on imidacloprid seed-treated sunflower (0.24 mg a.i./seed) in full-field design for a 10-day exposure period. Similar to Pohorecka (2013), there were no effects on mortality but an increase in the brood area coverage. It is noted however; the magnitude of this effect is uncertain as means were not presented in the article and indications of statistical significance were unclear.

Tier III Full Field Studies

For sunflower, two registrant-submitted full-field studies were previously classified as qualitative from an exposure standpoint but not suitable for risk assessment purposes with regards to effects due to major deficiencies in these studies. In Schmidt et al. (MRID 49766206), honey bee colonies were exposed for 14 days to seed-treated sunflower applied at 0.7 mg a.i./seed. The bee-collected nectar after the 14-day exposure period was determined to be below the LOQ, which was notably less sensitive at 10 µg/L as compared to other studies. In the full-field component of Schmuck 2001, seed-treated sunflower sampled 62 – 66 days after exposure yielded pollen and nectar residues below LOD (1.5 µg/L). It is noted that the seeds were also treated with carbendazim, metalaxyl and copper oxyquinolinate. Finally, in a study evaluated in the open literature (Laurent and Rathahao, 2003; MRID 48077902; full

details of methods provided in **Appendix B**), pollen residues from radiolabeled seed-treated sunflower (1 mg a.i./seed) averaged 13 µg/L with maximum residues in pollen of 36 µg/L. It was also noted from the analysis of radioactive residues that a maximum of 10% of the residues from the treated seed were taken up by the various plant parts.

As previously described in **Section 5.3.1**, an additional cotton Tier III field study was recently conducted to evaluate the potential long-term effects of imidacloprid exposure to honey bee hives, which were placed within or at the edge of treated and untreated commercial cotton fields in the California Central Valley during the summer of 2015 (MRID 50206701). The study contained 4 imidacloprid-treatment sites and 4 reference sites (n=4) near agricultural cropping areas where pesticides are traditionally used. One reference site was discontinued during the middle of study due to the severe adverse effects of other pesticides. Multiple pesticides were applied to all test sites for crop production during the study. Imidacloprid-treated cotton fields received various combinations with imidacloprid treatment, imidacloprid-treated seed, in-furrow application and one or two foliar applications prior to the exposure period. The total imidacloprid application rates ranged 0.06-0.45 lb/ac (0.07- 0.50 kg/ha) and the days between the last imidacloprid applications to initiation of hive exposure varied between 18-30 days.

Pesticides residues were measured from various matrices (soil, plants and hives) and time points (**Table 6-25**). The hive conditions were assessed multiple times during and after exposure periods. Hive success was assessed two times after overwintering. During the study, all test hives were treated with an additional pesticide for the control of varroa mites and were fed with supplemental sugar for the entire period after exposure for overwintering success. Imidacloprid was detected in plant pollen, nectar and leaves during the entire 6-week exposure period in both reference and treatment sites.

Table 6-25. Summary of imidacloprid residues in tier III cotton study (MRID 50206701)

| Matrix | Reference (mean ± 95% CL) in ppb | Treatment (mean ± 95% CL) in ppb |
|--------------------------|-------------------------------------|-------------------------------------|
| Plant Floral Nectar | 3.7 ± 1.4 | 13.7 ± 6.6 |
| Plant Extrafloral Nectar | 2.5 ± 2.2 /L | 7.1 ± 4.5 |
| Plant Pollen | 1.2 ± 0.8 /L | 3.1 ± 1.8 |
| Bee Nectar | 1.25* | 4.0* |
| Bee Pollen | 1.9* | 3.0 * |

* mean of detections only.

There were no significant treatment-related differences in capped brood, pollen counts, and overwinter survival between the hives that were placed at untreated and imidacloprid-treated cotton fields. The adult bee counts differed between imidacloprid-treated and reference plots at two CCAs: at CCA4 hives at imidacloprid-treated sites had higher adult bee counts, while at CCA6 hives from reference-treated sites had higher adult bee counts. However, at the end of the study there were no significant differences between treatment groups for this parameter.

It is important to recognize the inherent strengths and limitations of this study as results are considered in this risk assessment. As described previously, multiple pesticides other than imidacloprid were applied to both the reference and treated fields during the study which resulted in elevated residues being detected in various hive matrices. Therefore, it is uncertain to what extent exposure to other

pesticides confounded the interpretation of the results in this study. In addition, the average level of exposure of imidacloprid to test honey bees (as measured by nectar residues) was low in this study compared to the submitted cotton field residue studies. Compared to the level of contaminated imidacloprid in cotton plants and test hives in the reference sites, imidacloprid in the treatment sites was only 2-3 times greater than that in the reference. The similarity between residues in the reference and treatment sites may confound the detection of treatment effects considering the small difference in the treatment and reference site residues.

6.2.6. Crop group 9 – Cucurbit vegetables

The cucurbit vegetables crop group includes, among other members, cucumbers, muskmelon (inclusive of cantaloupe, honeydew and others) pumpkin, squash, and watermelons. Soil applications are registered with a maximum annual application rate of 0.38 lb a.i./A. Foliar applications to cucurbits are not currently registered. Cucurbits bloom indeterminately (6 weeks or longer) and, according to USDA (2017), produce pollen and nectar that is attractive to honey bees. Cucurbits also utilize managed pollination services.

Specific to the uses of imidacloprid, cantaloupes and watermelons are the dominant crops with an estimated usage of estimated 9,000 lbs/year each and an average of 40% of all cantaloupe nationwide treated with imidacloprid (**Table 6-26**). This is followed by cucumbers, honeydew, pumpkin, and squash with total poundage of roughly one third of that for cantaloupe and watermelon

For imidacloprid soil applications to the cucurbit group, the strength of evidence is considered strong in suggesting a colony-level risk to honey bee foraging on treated fields. Residue data for the other neonicotinoids (clothianidin, thiamethoxam, dinotefuran) scaled to the imidacloprid application rate indicate exceedances of the colony-level NOAEC up to two months after application. Maximum residues exceed the NOAEC and LOAEC by **3.3X** and **1.6X** respectively. No ecological incidents have been reported that associate imidacloprid applications to cucurbits with impacts on bees. Imidacloprid-specific residue data considered suitable for risk assessment are available for melon and watermelon (MRID 49090501 & 50357101). Based on these two imidacloprid studies, no exceedances of the colony-level NOAEC and LOAEC values are indicated. However, these studies have significant limitations which restrict their utility in risk assessment. A Tier III full field study (MRID 50263601) also indicates that residues of imidacloprid in pumpkin nectar and pollen 1-2 months after soil applications are below the colony-level NOAEC. Importantly, all three imidacloprid studies were conducted in medium to heavy soils with residues measured 1-3 months after application. These study attributes may have biased results towards lower residue values compared to cucurbits grown in lighter soils and/or applications applied closer to bloom. The strength of evidence associated with colony-level risks is considered “strongest” given the duration and magnitude of exceedance of the colony-level NOAEC and LOAEC values by the bridged residue data from 3 neonicotinoids, 5 species of cucurbits, and 6 sites. While imidacloprid-specific residue data did not exceed the colony-level endpoints, these data are very limited in scope (few sites, moderate to heavy soils only) and quality (supplemental) which renders these data less impactful on the strength of evidence finding.

Table 6-26. Lines of evidence considered in characterizing colony-level risk to honey bees from soil application of imidacloprid to cucurbits.

| Line of Evidence | | Soil Applications (Strongest Evidence of Risk) | |
|---|---|--|-------------------|
| Imidacloprid-specific residue data ⁽¹⁾ | | Melon and watermelon | |
| Residue data for other chemicals ⁽²⁾ | | Pumpkin (C, T, D), cucumber (C, T), cantaloupe (C), muskmelon (T), squash (C, T) | |
| Measured Data: (Imidacloprid) | Exceedance Attribute | NOAEC | LOAEC |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC | 0/16 | 0/16 |
| | Duration: Number of days > NOAEC & LOAEC | 0 | 0 |
| Measured Data (All Neonicotinoids) | Magnitude: Ratio of Max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC) | 0.9X (N.C.) | 0.4X (N.C.) |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC | 24/185 | 7/185 |
| | Duration: Number of days > NOAEC & LOAEC | 67 | 57 |
| Crop Attractiveness ⁽³⁾ & Bloom Duration | Magnitude: Ratio to Max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC) | 3.3X (30%) | 1.6X (63%) |
| | Highly attractive (nectar and pollen); long bloom duration (Indeterminate bloom) | | |
| | Required | | |
| Tier III (Full Field) Studies | | Application to pumpkin in heavy (clay) soils results in low exposure and no discernable effects on colonies relative to reference sites; study not representative of more vulnerable sites (medium to light soils). | |
| Ecological Incidents | | None | |
| Spatial Extent of Risk (acres treated) | | 54,511 (avg. annual); 102,856 (max. annual) | |
| Other Considerations | | Imidacloprid-specific melon study conducted in heavy soils; not considered representative of potential exposure and risk at sites with lighter soils. Imidacloprid watermelon study approach NOAEC Exceedance of NOAEC with all 3 other neonicotinoids for 5 crops across 6 sites. | |

⁽¹⁾ Imidacloprid residue data: melon (MRID 49090501); watermelon (MRID 50357101)

⁽²⁾ Clothianidin residue data: pumpkin (MRID 49705901, 49910601, 49602801); cucumber, squash, cantaloupe (MRID 49705901, 50154306); Thiamethoxam residue data: pumpkin, muskmelon, squash (MRID 50265501); cucumber (MRID 49550801); Dinotefuran residue data: pumpkin (MRID 49852701, 50145704).

⁽³⁾ Based on USDA 2017; N.C. = not calculated because > 100% of the treated diet would be needed to reach the NOAEC

6.2.6.1. Soil application

Two registrant-submitted imidacloprid studies examined residues of bee-collected nectar and pollen in soil treated watermelon and melon (cantaloupe). However, the watermelon study (MRID 50357101) involved only one site in Brazil and the melon study (MRID 49090501) only measured residues at 100 DALA. Based on the bridging analysis (**Attachment 2**), clothianidin, thiamethoxam and dinotefuran pumpkin, melon, squash and/or cucumber data are considered extrapolatable to imidacloprid and are used for assessing risk of imidacloprid soil applications to cucurbits.

While a Monte Carlo analysis involving residue data and dissipation rate constants was conducted for foliar applications to cucurbits for other neonicotinoid compounds (foliar applications on cucurbits are not registered for imidacloprid), this approach was not supported for soil applications due to the characteristics of the residue data (**Attachment 2**). Instead, the applicable measured residue data from soil applications for all the neonicotinoid compounds are compared directly to the NOAEC and LOAEC from the available CFS. Residue values were normalized to the maximum total (seasonal) application rate registered across the cucurbit crop group (i.e., 0.38 lb a.i./A).

Mean daily concentrations of total imidacloprid measured in cucurbits are shown in **Figure 6-8** in relation to the honey bee colony effect endpoints. Residues are expressed as nectar equivalent concentrations and normalized to the total maximum application rate (0.38 lb a.i./A). These residue data are derived from two studies of melon (cantaloupe) and watermelon. The cantaloupe study involved applications to 10 sites in California in medium to heavy soils with measurements taken approximately 100 days following application. Specific information on the study parameters were limited since the field portion of this study was non-GLP and consisted of grower reported information on application rates, timing, planting dates, etc. The watermelon study was conducted in Brazil at one site in medium soils (sandy clay loam) with bee-collected samples taken 32-44 days after application.

Although none of the normalized mean-measured imidacloprid data exceeds the colony effects endpoints, the highest daily mean nectar equivalent value (21 ng a.i./g at 37 DALA from the Brazilian watermelon study), approaches the colony level endpoint. Furthermore, some of the residue values from this study reflect sampling of one matrix (nectar or pollen) which likely underestimates total food exposure (nectar + pollen). Importantly both studies were conducted in medium to heavy soils which may result in lower residues in pollen and nectar if trials had included lighter (sandier) soils. Soil type has been identified as a factor potentially influencing pollen and nectar residues from other imidacloprid soil application residue studies with cotton. In addition, the timing of application relative to sample collection was relatively long (1-3 months). Therefore, results from these trials may not be representative of applications made sooner to the bloom periods. Finally, one of the three replicates for the maximum average concentration of 21 ng a.i./g consisted solely of nectar, with no pollen sample taken. Therefore, mean residues are reduced slightly compared to if a pollen sample had been available.

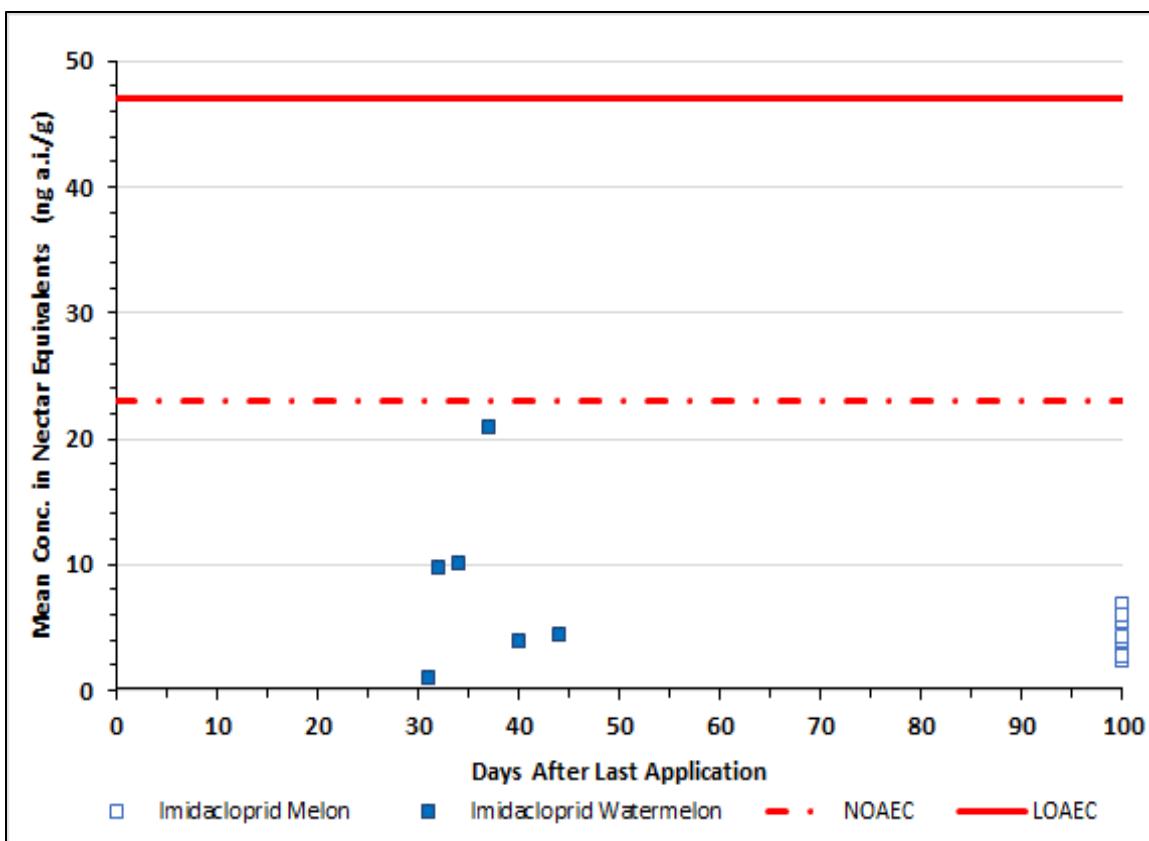


Figure 6-8. Measured imidacloprid residue data in nectar equivalents (normalized to 0.38 lb a.i./A total annual application) versus imidacloprid endpoints for the cucurbit crop group.

Based on the bridging analysis (**Attachment 2**), clothianidin, thiamethoxam and dinotefuran pumpkin, melon, squash and/or cucumber data were considered extrapolatable and are used as representative crops in the cucurbit crop group. **Figure 6-9** below depicts all the residue data (normalized to total seasonal application rate of 0.38 lb a.i./A) compared to the imidacloprid CFS NOAEC and LOAEC endpoints. Overall, 24/185 daily mean measured residues exceed the NOAEC (13%) and 7/185 exceed the LOAEC (4%) with a maximum mean concentration of 76 ng a.i./g

The contribution of pollen on the mean concentration in nectar equivalents ranges widely, from 1% to 99% (this excludes those samples where nectar and pollen were not collected at the same time). Approximately half the data available are for pumpkins, which generally appear to have lower residue concentrations than the other crops tested. Observations of mean (normalized to 0.38 lb a.i./A) samples exceeding the NOAEC no longer occur approximately 70 days after treatment. It is noted that the residue studies conducted with clothianidin, thiamethoxam and dinotefuran included sites with lighter (sandy) soils, which may have contributed to higher residues found in these studies.

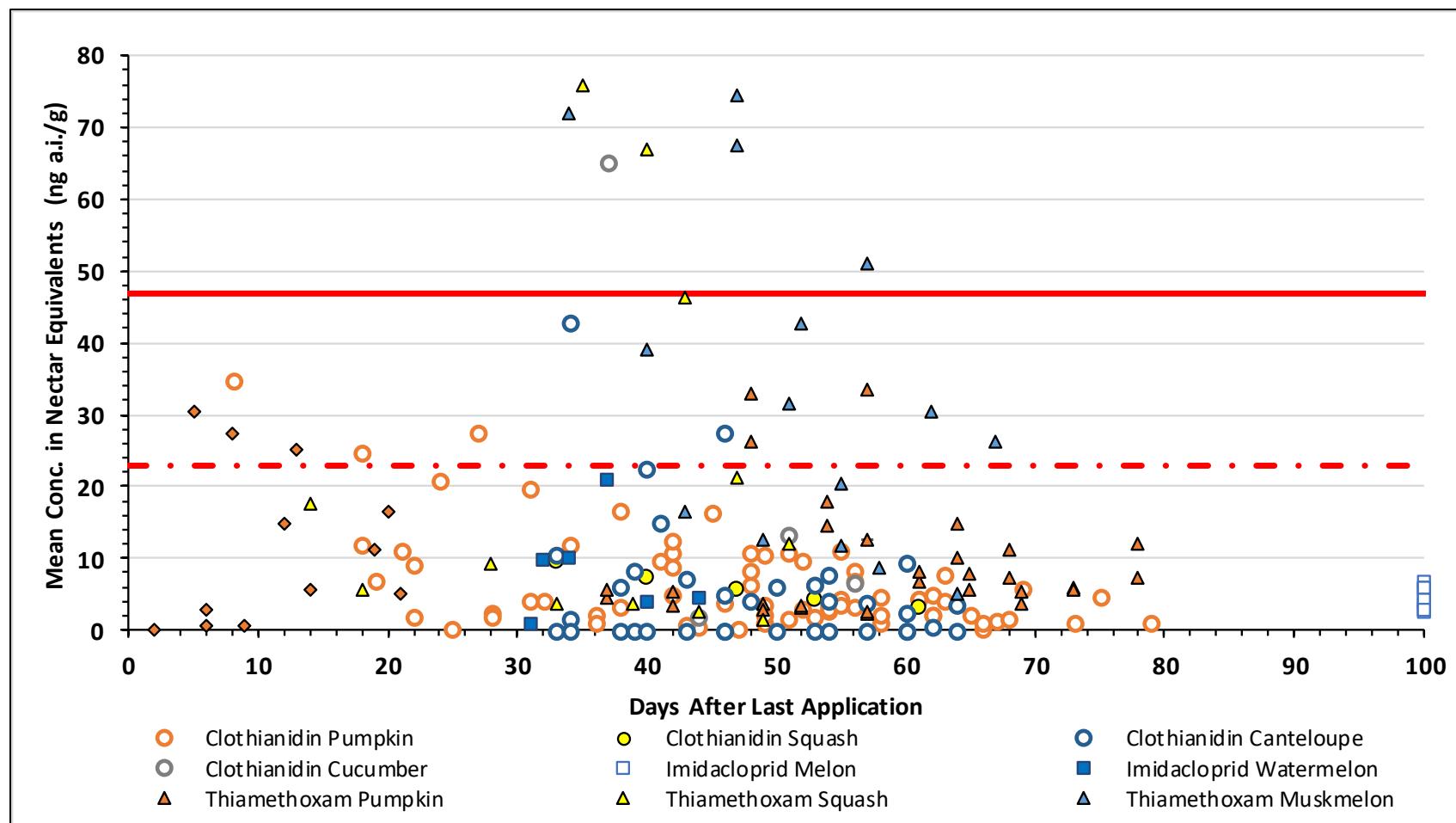


Figure 6-9. Measured imidacloprid, clothianidin, thiamethoxam, and dinotefuran residue data in nectar equivalents (normalized to 0.38 lb a.i./A total application) versus imidacloprid colony level endpoints

6.2.6.2. Additional Considerations

The analysis above used anther data quantitatively as a direct surrogate for pollen (as suggested by the residue bridging strategy in **Attachment 2**) when pollen data was not collected and only anther data was available. The residue bridging strategy also suggests characterizing the anther data qualitatively using a 3X factor as an upper bound conservative estimate. Generally, using this extrapolation would not change the overall conclusions as only two additional normalized daily sample means (dinotefuran treated cantaloupe at 8 DALA and dinotefuran treated cucumbers at 9 DALA), would exceed the imidacloprid NOAEC in this scenario. Overall, the available information suggests potential for risk concerns for soil applications of imidacloprid to cucurbit crops.

Open literature

There are two studies available from the open literature that investigate the residues of imidacloprid in pollen and nectar from soil-applications to cucurbit vegetables. In a study by Stoner and Eitzer (2012, MRID 49719616), imidacloprid (as Admire® Pro) was applied as a soil spray pre-planting at 0.32 lbs a.i/A 1 day before squash was planted. In a subsequent trial, the same application rate was used at a 5-day post-transplant via drip irrigation in a greenhouse. The residue values in pollen and nectar were pooled separately from the various trials and no information on the interval between application and sampling was available. Maximum and average values for pollen were 28 and 14 µg/kg, respectively, and were 14 and 10 µg/kg, respectively, for nectar. These translate to maximum and average nectar equivalents of 15.4 and 10.7 µg/kg using the methodology described earlier. While it is noted that the application rate is slightly below the maximum labeled single application rate 0.38 lbs a.i/A, adjustment to 0.38 lb a.i./A would still result in residue values that are below the colony-level NOAEC of 23 ppb.

In a study by Dively and Kamel (2012, MRID 49719612), several trials were conducted with various soil treatment regimens to pumpkins. Applications rates of Admire® Pro included bedding drench applications (0.027 lbs a.i/A, transplant water treatment (0.25 lbs a.i/A and 0.38 lbs a.i/A), and split application of 0.19 lbs a.i/A first as transplant water, then as drip irrigation (See **Appendix B** for further details). All treatment regimens utilized are permitted on the label for soil-applied cucurbit vegetables. Average pollen residue levels ranged 4.9– 80.2 µg/kg across all application methods and rates. Average nectar values ranged from 0.4 – 11.2 µg/kg, with the maximum nectar residue value was 13.7 µg/kg). This translates to maximum total food equivalents of 15.2 µg/kg which is below the colony-level NOAEC of 23 ppb. Soil type information was not available from this study.

Tier III Full Field Study

A field study was conducted to evaluate the potential long-term effects of imidacloprid exposure to honey bee colonies and other non-*Apis* bees (MRID 50263601). The study was conducted in pumpkin fields (6 sites; all clay soil) in central South Dakota in 2015-2016. Imidacloprid was applied as sub-surface side dress at 0.38 lb/acre (0.43 kg/ha) once pumpkins had attained the six true-leaf stage (BBCH16). Nine honey bee colonies were placed in each of the pumpkin fields during flowering period. Additional honey bee colonies were placed in each of the fields to monitor the pesticides exposure to hives.

The data indicated that there was imidacloprid contamination in plant pollen in the reference fields, and the maximum detections in plant pollen were about two times greater in the treatment than that in the reference, and the frequency of detection was lower in the references than in the treatments. There were no detections of imidacloprid in plant nectar from the reference fields. Test hives had a low level of background contamination with imidacloprid as well.

For honey bees, no treatment related adverse colony effects were detected in terms of colony conditions, hive weight, overwintering hive survival, queen conditions, and Nosema and varroa infestation in the study. Furthermore, residues in plant- and bee-collected pollen and nectar are below the colony level NOAEC and LOAEC for imidacloprid (**Table 6-27**). This study had a number of strengths including relatively high replication (n=5), reasonably long exposure duration of hives (6 weeks), measurement of residues in plant and hive matrices, use of palynology to estimate foraging on cucurbit crops, inclusion of overwintering, and assessment of native bee abundance. However, several limitations are also noted with this study which affect the degree to which results are considered representative of use on cucurbits as a whole. First, the level of exposure to test plants (pumpkins) was low with cucurbit pollen rarely collected by honey bees. The low residue levels may have been due to the heavy (clay) soils used in this study. Furthermore, a maximum of 4% of the trapped and bee-collected pollen originated from cucurbit crops, which indicates foraging (at least for pollen) occurred beyond the study sites. The hive colony mortality after overwintering was high in both reference and treatment, approximately 40%. This high mortality was similar to the overall US national mortality in the study year. The high background mortality during the study period in the study area may compromise the sensitivity of the study to detect treatment-related effects on overwintering. Thus, when the results of the Tier III field study are taken in context with the available residue data specific to imidacloprid, these data suggest that soil application of imidacloprid in medium to heavy soils does not result in colony-level risks to honey bees, when applied at a month or longer prior to bloom. However, these results cannot be used to extrapolate to sites where exposure to imidacloprid in pollen and nectar may be greater, due to lighter soils, applications made closer to the bloom period, or greater foraging on treated sites.

Table 6-27. Summary of total imidacloprid residues (µg a.i./kg) measured in the pumpkin tier III field study

| Matrix ¹ | Reference (µg a.i./kg) | Treatment (µg a.i./kg) |
|--|----------------------------|------------------------|
| Plant Nectar | <LOD (0/15 sites) | <LOD-5.1 µg/L (13/15) |
| Plant Pollen | <LOD-7.9 µg/L (5/15 sites) | <LOD-15.8 µg/L (14/15) |
| Total Nectar Equivalent Conc. ² | < LOD-0.7 µg/L | 0.5-5.9 µg/L |
| Bee Nectar | 1-2.6 µg/L (2/45) | 1-2.6 µg/L (7/45) |
| Bee Pollen | 1.7-4.5 µg/L (8/45) | 1.7-17.9 µg/L (30/45) |

¹ LOD for nectar, pollen and total nectar equivalents = 0.6, 1.3 and 1.0 ug/kg, respectively

² Nectar equivalent concentrations = nectar conc + pollen conc/20

Spatial Extent

Another consideration of the risk potential is the spatial extent of risk. As discussed previously, usage data are available for imidacloprid application to cucurbits. These data indicate that 27,000 lbs are applied per year across the crop group to 10-40% of the total acres in the US, depending on cucurbit crop. When considering the highest usage in watermelon (40%), and the total number of acres (*i.e.*, 123,000 acres of watermelon; from USDA 2017), this translates to an annual average of ~49,000 acres of watermelon treated with imidacloprid with a maximum of 74,000 acres. In contrast, for crops where imidacloprid is not as frequently used (*i.e.* pumpkin and squash at 10-15%) and considering the total number of acres (*i.e.* 92,000 acres of pumpkin and squash; USDA 2017), this translates to an annual average of 9,000-14,000 acres of pumpkin and squash treated with imidacloprid with a maximum of less than 30,000 acres. Similar estimate of acres of cantaloupe treated cannot be generated due to lack of crop extent for this crop.

6.2.7. *Crop group 10, 11, 12, 14, and others - Orchard crops*

Orchard crops include several crop groups, including pome fruit (*e.g.* pears and apples), stone fruit (*e.g.*, peaches, plums, cherries), tree nuts (*e.g.*, almonds, pecans), citrus (*e.g.*, oranges, lemons) and tropical fruit (*e.g.*, pomegranate). According to the USDA guidance on crops attractive to honey bees and other bees (USDA 2017), most orchard crops are considered attractive to bees. In addition, many orchard crops require managed pollinator services. Therefore, exposure to bees from orchard crops is considered potential in the neonicotinoid bee assessments for registered uses of these crops. Imidacloprid is registered for use on all orchard crop groups as well as members of the tropical fruit group including banana, plantains, and pomegranate. It may be applied via foliar or soil applications. For all orchard crops, pre-bloom applications are only allowed on citrus and banana/plantains. Labels prohibit applications during bloom.

Table 6-28 summarizes the foliar and soil applications for each crop group as well as available usage data for imidacloprid applied to orchard crops. Combined foliar and soil applications are allowed with a maximum seasonal application rate of 0.5 lb a.i./A.

Table 6-28. Use and Application information for imidacloprid use on orchard crops and tropical fruits

| Orchard crop group | Foliar, pre-bloom | Foliar, post-bloom | Soil, pre-bloom | Soil, post-bloom | Estimated lbs applied/year (based on SLUA) |
|--------------------|-------------------|--|-----------------|------------------|--|
| Pome fruit | NAL | 0.25 x 2 Pear 0.1 x 5 all other crops | NAL | 0.38 x 1 | 11,000 |
| Stone fruit | NAL | 0.1 x 3 ¹ 0.1 x 5 ² | NAL | 0.38 x 1 | 5,000-6,500 |
| Citrus | 0.25 x 2 | 0.25 x 2 | 0.5 lb/A x 1 | 0.5 x 1 | 77,000-77,500 |
| Tree nuts | NAL | 0.1 x 3 | NAL | 0.5 x 1 | 27,000-27,500 |
| Tropical fruits | NAL | 0.1 x 5 | NAL | 0.5 x 1 | 4,000-4,500 |

NAL = Not all labels. Some product labels restrict applications to post bloom.

¹ three applications allowed for apricot, nectarine, and peach

² five applications allowed for cherry, plum, plumcot, and prune

For imidacloprid applications to orchard crops, strongest evidence indicates that pre-bloom foliar and soil applications pose a risk to honey bee colonies foraging on treated fields. Based on the residue bridging analysis (**Attachment 2**), residues from other neonicotinoids (clothianidin, thiamethoxam, dinotefuran) are considered extrapolatable to imidacloprid. The available lines of evidence indicate that both empirical and estimated residues in pollen and nectar associated with pre-bloom applications exceed colony level NOAEC and LOAEC values for periods of time that range from days to weeks. Given the magnitude of residues, if ≥5% of food resource required by a colony is collected from pre-bloom treated fields, the resulting exposure is sufficient to exceed the colony level endpoints. This suggests that dilution of concentrations from other sources likely will not have a substantial influence on risk.

Potential colony level risk is also indicated for post-bloom foliar and soil applications of imidacloprid to orchard crops, but the strength of evidence is considered moderate to weak. Of the available residue data, very few foliar residues measured at times consistent with post bloom applications (e.g., > 120 DALA) exceed the colony-level NOAEC and none exceed the LOAEC. A summary of risk conclusions and lines of evidence considered for assessing colony-level risks to honey bees via applications to orchard crops is provided in **Table 6-29** (for foliar applications) and **Table 6-30** (for soil applications).

Table 6-29. Lines of evidence considered in characterizing colony-level risk to honey bees from foliar applications of imidacloprid to orchard crops

| Line of Evidence | | Foliar Pre-Bloom Applications ⁽⁴⁾ (Strongest Evidence of Risk, Citrus, Banana/Plantain) | | Foliar Post-Bloom Applications ⁽⁴⁾ (Weakest Evidence of Risk, Citrus, Stone, Pome, Tropical Fruit) | | Foliar Post-Bloom Applications ⁽⁴⁾ (Low Risk, Tree nut) | | | | | |
|--|---|--|------------|---|-------------|--|-------------|--|--|--|--|
| Imidacloprid-specific residue data | | Orange | | Cherry | | Cherry | | | | | |
| Residue data for other chemicals | | Apple and Orange (T) | | Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T) | | Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T) | | | | | |
| Measured Data: (Imidacloprid) | Exceedance Attribute | NOAEC | LOAEC | NOAEC | LOAEC | NOAEC | LOAEC | | | | |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC | 11/11 | 11/11 | 1/12 | 0/12 | 0/12 | 0/12 | | | | |
| | Duration: Number of days > NOAEC & LOAEC | 30+ | 30+ | 200+ | 0 | 0 | 0 | | | | |
| | Magnitude: Ratio of Max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 10X (10%) | 5X (20%) | 1.4X (72%) | 0.7X (N.C.) | 0.8X (N.C.) | 0.4X (N.C.) | | | | |
| Measured Data: (all Neonicotinoids) | Frequency: Number daily mean residue values > NOAEC & LOAEC | 23/47 | 21/47 | 4/71 | 0/71 | 0/71 | 0/71 | | | | |
| | Duration: Number of days > NOAEC & LOAEC | 34 | 34 | 300+ | 0 | 0 | 0 | | | | |
| | Magnitude: Ratio to Max to NOAEC & LOAEC ⁽²⁾ (% of diet required to reach NOAEC & LOAEC) | 166X (0.6%) | 81X (1.2%) | 1.5X (67%) | 0.7X (N.C.) | 0.9X (N.C.) | 0.4X (N.C.) | | | | |
| Modeled Data: (50 th percentile) | Duration: Number of days > NOAEC & LOAEC | 43 | 35 | NA | | | | | | | |
| | Magnitude: Ratio of Max (day 1) to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC) | 83X (1.2%) | 40X (2.5%) | | | | | | | | |
| Crop Attractiveness ⁽³⁾ & Bloom Duration | | Attractive or highly attractive. Bloom duration varies depending on crop/variety | | | | | | | | | |
| Managed Pollinators | | Yes, and used for honey production by some commercial beekeepers | | | | | | | | | |

| Line of Evidence | Foliar Pre-Bloom Applications ⁽⁴⁾ (Strongest Evidence of Risk, Citrus, Banana/Plantain) | Foliar Post-Bloom Applications ⁽⁴⁾ (Weakest Evidence of Risk, Citrus, Stone, Pome, Tropical Fruit) | Foliar Post-Bloom Applications ⁽⁴⁾ (Low Risk, Tree nut) |
|---|---|---|--|
| Tier III (Full Field) Studies | None | | |
| Ecological Incidents | 1 bee kill incident (with certainty of either possible or probable) has been reported in association with soil applications of imidacloprid to orchard crops (citrus). | | |
| Spatial Extent of Risk (acres treated) | Citrus: 193,765 (avg. ann'l); 323,770 (max. ann'l) Pome fruit: 101,060 (avg. ann'l); 155,670 (max. ann'l) Stone fruit: 39,199 (avg. ann'l); 87,520 (max. ann'l) Tree nuts: 54,350 (avg. ann'l); 101,000 (max. ann'l) | | |
| Other Considerations | 10-d pre-bloom interval for foliar applications to citrus. | | |

⁽¹⁾ Max. measured residues for foliar pre- and post-bloom applications of imidacloprid corresponds to 7 and 208 days after application, respectively (MRID 49521301, orange).

⁽²⁾ Max. measured residue for foliar pre- and post-bloom applications among all neonicotinoids corresponds to 5 and 221 days after application, respectively. Data include: imidacloprid (cherry; MRID 49535601), clothianidin (almond, apple, peach; MRID 50154302; 50154304; 50154303), thiamethoxam (cherry, peach, plum; MRID 49819501, 50096606) and dinotefuran (cherry, peach; MRID 50145706, 50456901).

⁽³⁾ Based on USDA 2017; N.C. = not calculated because > 100% of the treated diet would be needed to reach the NOAEC.

⁽⁴⁾ Post-bloom applications considered to be >120 days prior to bloom the following season and pre-bloom considered to be 120 days or less.

Table 6-30. Lines of evidence considered in characterizing colony-level honey bee risk from soil applications of imidacloprid to orchard crops

| Line of Evidence | | Soil Pre-Bloom Applications ⁽¹⁾ (Strongest Evidence of Risk, Citrus, Banana/Plantain) | | Soil Post-Bloom Applications ⁽¹⁾ (Moderate Evidence of Risk, Citrus, Tree nut) | | Soil Post-Bloom Applications ⁽¹⁾ (Weak Evidence of Risk, Stone, Pome, Tropical Fruit) | |
|---|---|---|------------|---|------------|--|------------|
| Imidacloprid-specific residue data | | None | | None | | None | |
| Residue data for other chemicals | | Apple and Orange (T) | | Lemon and Orange (C, T) | | Lemon and Orange (C, T) | |
| Measured Data: (all Neonics) | Exceedance Attribute | NOAEC | LOAEC | NOAEC | LOAEC | NOAEC | LOAEC |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC | 57/124 | 21/124 | 5/17 | 4/17 | 5/17 | 2/17 |
| | Duration: Number of days > NOAEC & LOAEC | 118 | 105 | 186 | 179 | 186 | 156 |
| | Magnitude: Ratio to Max to NOAEC & LOAEC ⁽²⁾ (% of diet required to reach NOAEC & LOAEC) | 19X (5.4%) | 8.9X (11%) | 4.8X (21%) | 2.3X (43%) | 3.6X (28%) | 1.8X (56%) |
| Combined soil + foliar (Stone & Pome, post-bloom) | | Only 1 exceedance of NOAEC with post-harvest application of 0.38 lb a.i./A (soil) + 0.18 lb a.i./A (foliar) for pome (apple) and stone (4 crops); no exceedance pre-harvest application (MRID 49819401; 49662101) | | | | | |
| Crop Attractiveness⁽³⁾ & Bloom Duration | | Attractive or highly attractive. Bloom duration varies depending on crop/variety) | | | | | |
| Managed Pollinators | | Yes and used for honey production by some commercial beekeepers | | | | | |
| Tier III (Full Field) Studies | | None | | | | | |
| Ecological Incidents | | 2 bee kill incidents (with certainty of either possible or probable) have been reported in association with imidacloprid applications to orchard crops. | | | | | |
| Spatial Extent of Risk (acres treated) | | Citrus: 193,765 (avg. ann'l); 323,770 (max. ann'l); Pome fruit: 101,060 (avg. ann'l); 155,670 (max. ann'l); Stone fruit: 39,199 (avg. ann'l); 87,520 (max. ann'l); Tree nuts: 54,350 (avg. ann'l); 101,000 (max. ann'l) | | | | | |
| Other Considerations | | 10-d pre-bloom interval for foliar applications to citrus. Nectar residues from post-bloom soil applications to citrus (orange, tangerine) resulted in nectar residues below NOAEC (DALA = 231) | | | | | |

⁽¹⁾ Post-bloom applications considered to be >120 days prior to bloom the following season and pre-bloom considered to be 120 days or less. Application rate for citrus, tree nut and tropical fruit = 0.5 lb ai/A and that for Stone and Pome = 0.38 lb ai/A. Residue data include: thiamethoxam (MRID 49881001, 49881002, 50131102); clothianidin (MRID 50478201)

⁽²⁾ Max. residue for pre-bloom & post-bloom soil applications corresponds to 16 and 156 days after application, respectively

⁽³⁾ Based on USDA 2017.

6.2.7.1. Foliar application

Based on the bridging analysis (**Attachment 2**), the available foliar residue data for pre-bloom applications to orchards are considered extrapolatable among orchard crops and neonicotinoids (imidacloprid, clothianidin, thiamethoxam and dinotefuran). Due to the obvious influence of application timing on the magnitude of residues in pollen and nectar, separate assessments of risk are made from pre-bloom and post-bloom applications. As discussed previously, imidacloprid is only registered for pre-bloom foliar applications to citrus at a maximum seasonal rate of 0.5 lb a.i./A. Post-bloom foliar applications are allowed on all other orchard crop groups at a maximum seasonal rate of 0.5 lb a.i./A, except tree nuts which have a maximum seasonal rate of 0.3 lb a.i./A. One imidacloprid residue study is available for pre-bloom, foliar applications to citrus (oranges) and one is available for post-bloom, foliar applications to stone fruit (cherries). As discussed in the bridging analysis (**Attachment 2**), the available residue data resulting from post-bloom foliar applications of neonicotinoids to orchard crops are also considered extrapolatable among crops and chemicals.

Pre-Bloom Applications

Figure 6-10 depicts the residues from nectar and pollen (expressed as nectar equivalents; details provided in **Attachment 1**) adjusted to the maximum seasonal rate allowed for pre-bloom foliar applications of imidacloprid on citrus (*i.e.*, 0.5 lb a.i./A). These data are based on foliar applications of imidacloprid and thiamethoxam to orange trees (MRID 49521301, 50425902) and thiamethoxam to apple trees (MRID 50265504). This figure also depicts the imidacloprid colony-level NOAEC and LOAEC (23 and 47 ng a.i./g, respectively). Twenty-two residues sampled within 34 days of application exceeded the imidacloprid LOAEC, with nectar-equivalent residues ranging from 57-3,820 ng a.i./g (*i.e.*, up to 80x the imidacloprid LOAEC). Twenty-three residue values exceed the imidacloprid NOAEC. **Figure 6-10** also depicts the median (50th percentile) residue decline curve that is estimated for nectar equivalent residues. Based on this decline curve, residues exceed the imidacloprid colony-level NOAEC and LOAEC for 43 and 35 days, respectively. Current labels for imidacloprid preclude foliar application to citrus within 10 days prior to bloom. However, it can be seen from **Figure 6-10** that both measured and modeled residues exceed the imidacloprid colony-level NOAEC for longer durations than this 10-d pre-bloom restriction (*e.g.*, 34 and 43 days, respectively). The strength of evidence associated with the pre-bloom, foliar application risk finding is considered strong for imidacloprid based on the magnitude, duration and frequency that residue values exceed the colony-level NOAEC.

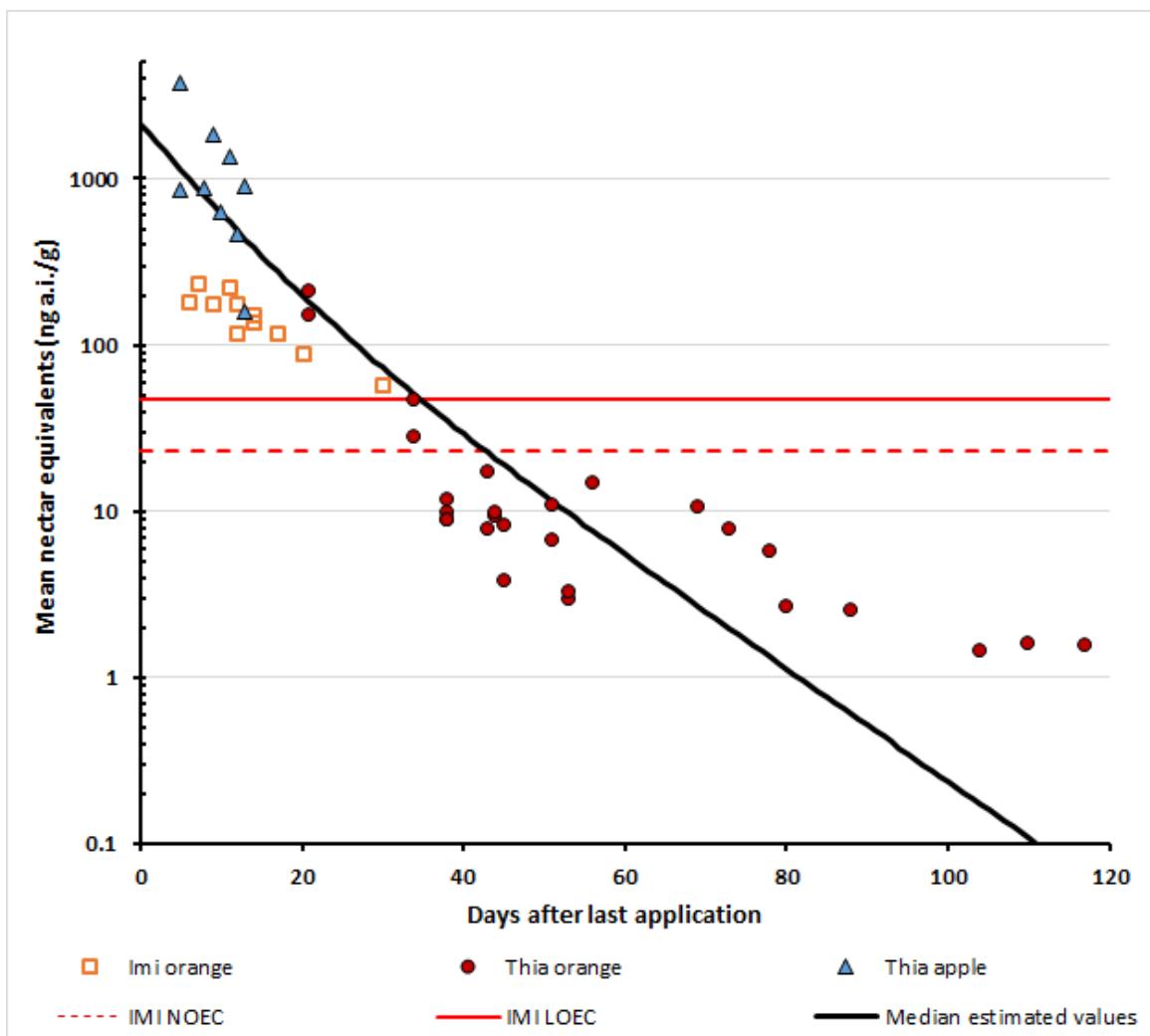


Figure 6-10. Mean-measured neonicotinoid residues (expressed as nectar equivalents) in orchard crops (normalized to 0.5 lb a.i./A) from pre-bloom, foliar applications relative to the imidacloprid colony level NOAEC and LOAEC.

Post-Bloom Applications

Mean nectar equivalent residues resulting from post-bloom foliar applications made at 0.5 lb a.i./A (all uses except tree nuts) and 0.3 lb a.i./A (tree nuts) are depicted in **Figure 6-11** and **Figure 6-12**, respectively. Residue data supporting these figures originate from imidacloprid (cherry; MRID 49535601), clothianidin (almond, apple, peach; MRID 50154302; 50154304; 50154303), thiamethoxam (cherry, peach, plum; MRID 49819501, 50096606) and dinotefuran (cherry, peach; MRID 50145706, 50456901). In these studies, applications were made between 140-324 d before bloom the following season. All residue values are well below the imidacloprid LOAEC. At the 0.5 lb a.i./A rate, while four residue values exceed the NOAEC. However, no residue values exceed the NOAEC for the 0.3 lb a.i./A rate. This indicates that post-bloom applications to tree nuts likely do not pose a colony-level risk to honey bees, while post-bloom applications to all other orchard crops potentially pose a risk. Notably, the imidacloprid cherry study evaluated two different application times: pre-harvest and post-harvest.

Applications made pre-harvest resulted in residues that are below the colony-level effect endpoints. Applications made post-harvest resulted in residues that were generally higher than those made prior to harvest and exceed the NOAEC in one trial. Similar findings were found with combined soil + foliar applications of imidacloprid to stone and pome fruits described in the combined application section below. Therefore, the timing of post bloom application relative to fruit harvest appears to be important with respect to the potential for colony level risks of imidacloprid to honey bees.

Overall, the strength of evidence supporting the colony-level risk from post-bloom, foliar applications of imidacloprid to citrus, stone, pome, and tropical fruits is considered “weakest” considering the limited magnitude and frequency of exceedance of the colony-level endpoints and apparent influence of application timing (pre- vs. -post harvest) on imidacloprid residues (**Figure 6-11**). Colony-level risks from post-bloom, foliar applications of imidacloprid to tree nuts is considered low given no exceedances of the colony-level NOAEC (**Figure 6-12**).

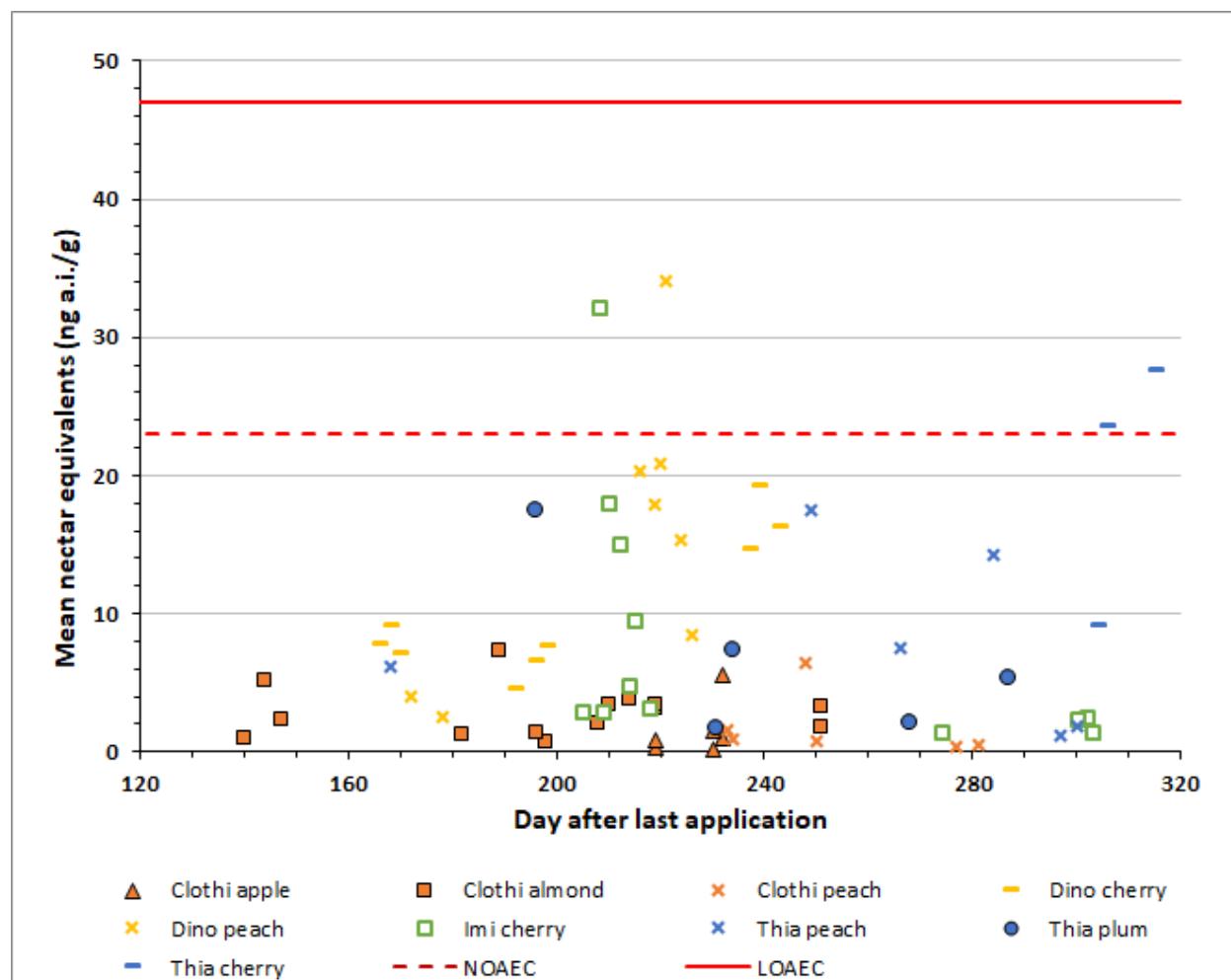


Figure 6-11. Mean measured neonicotinoid residues (expressed as nectar equivalents) in orchard crops (normalized to 0.5 lb a.i./A for orchard uses except tree nuts) from post-bloom, foliar applications relative to the imidacloprid colony level NOAEC and LOAEC.

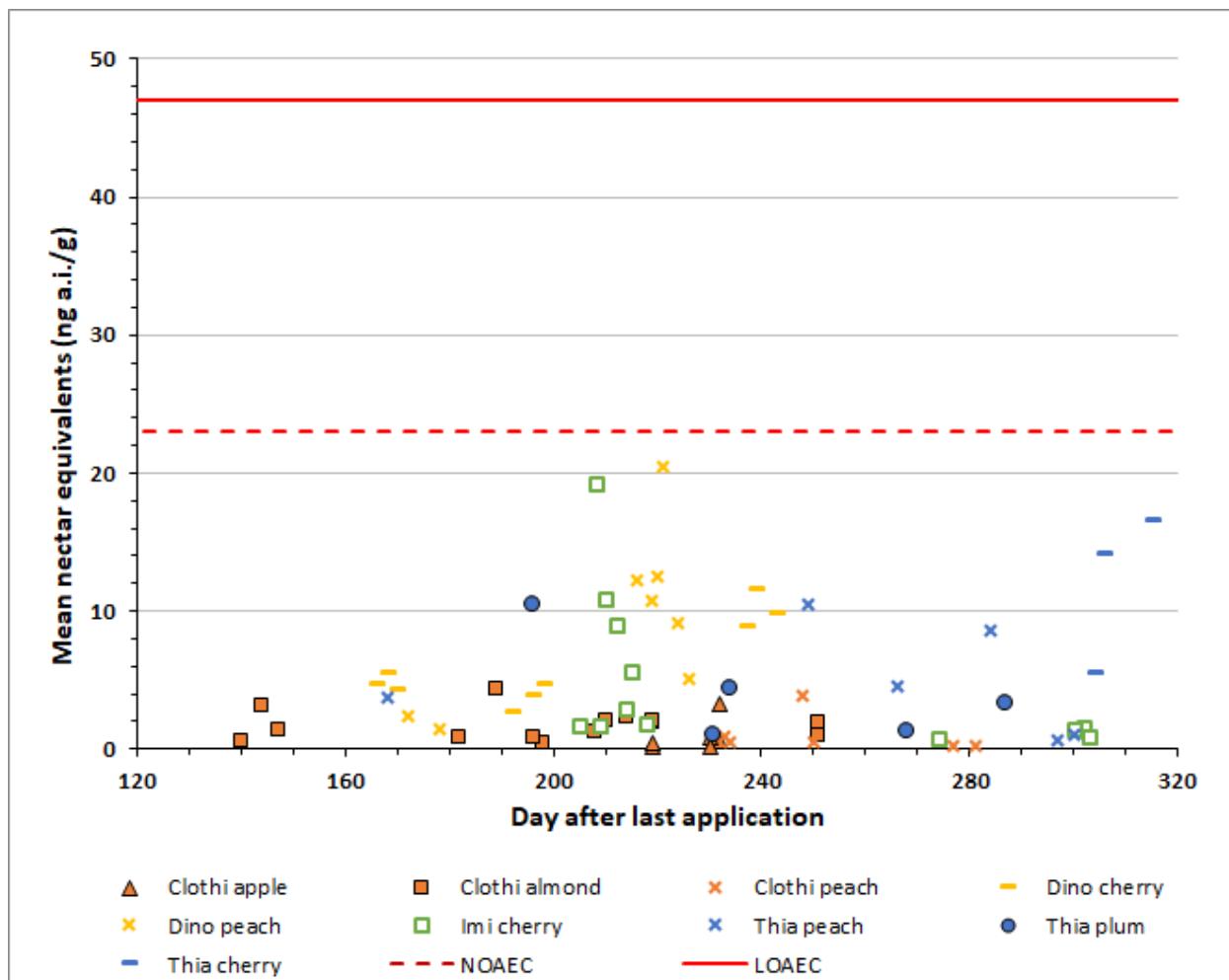


Figure 6-12. Mean measured neonicotinoid residues (expressed as nectar equivalents) in orchard crops (normalized to 0.3 lb a.i./A for tree nuts) from post-bloom, foliar applications relative to the imidacloprid colony level NOAEC and LOAEC

6.2.7.2. Soil application

Based on the residue bridging analysis (**Attachment 2**), the available orchard residue data are considered extrapolatable across orchard crops and the four neonicotinoids. As discussed above, pre-bloom, soil applications of imidacloprid are only registered for citrus crops at a maximum seasonal rate of 0.5 lb a.i./A. Imidacloprid is also registered for post-bloom soil applications to all orchard crops at a maximum seasonal rate of either 0.5 lb a.i./A (citrus, tree nuts, tropical fruits) or 0.38 lb a.i./A (pome and stone fruits).

Residue data specific to soil applications of imidacloprid to orchard crops are only available from one supplemental study with citrus (MRID 49090504). However, this study measured imidacloprid residues in nectar only from post-bloom applications to orange and lemon. Therefore, it is not used quantitatively for risk assessment. For the other neonicotinoids, residue data are available for oranges

and lemons treated with clothianidin and thiamethoxam. Since data are bridged across chemicals, the available residue data are also used to characterize risks of imidacloprid to honey bees.

Figure 6-13 depicts the nectar and pollen residues (expressed as nectar equivalents; details provided in **Attachment 1**) adjusted to the maximum soil application rate allowed for imidacloprid on citrus, tree nuts and tropical fruits (*i.e.*, 0.5 lb a.i./A). Similarly, **Figure 6-14** depicts the residues relevant to the maximum rate for pome and stone fruits (*i.e.*, 0.38 lb a.i./A). These figures also include the imidacloprid colony-level NOAEC and LOAEC. Residues from the imidacloprid soil/citrus study are not included in these figures since there is no way to express them as total food (nectar equivalents) because pollen residues were not measured. The following summarizes the residues that exceed the two endpoints.

For pre-bloom soil applications to citrus (0.5 lb a.i./A), 57 daily mean residue values (expressed as nectar equivalents) exceed the imidacloprid colony level NOAEC of 23 ng a.i./g and 21 exceed the LOAEC of 47 ng a.i./g. For the purposes of this assessment, post-bloom applications are assumed to represent residue measurements made 120 days and longer after application. Residue values exceed the NOAEC and LOAEC for over 100 days after application by factors of **19X** and **8.9X**, respectively. The magnitude, duration and frequency of exceedances of the colony-level endpoints by the residue data support a strength of evidence classification of “strongest.”

For post-bloom soil applications to citrus, tree nuts and tropical fruits (0.5 lb a.i./A), 5 daily mean residue values (expressed as nectar equivalents) exceed the imidacloprid colony level NOAEC of 23 ng a.i./g and 4 residue values exceed the LOAEC of 47 ng a.i./g. For the purposes of this assessment, pre-bloom applications are assumed to represent residue measurements made within 120 days after application. Residue values exceed the NOAEC and LOAEC by as much as 180 days after application by factors of **4.8X** and **2.3X**, respectively. The magnitude, duration and frequency of exceedances of the colony-level endpoints by the residue data support a strength of evidence classification of “moderate.”

For post-bloom soil applications to pome and stone fruits (0.38 lb a.i./A), 5 daily mean residue values (expressed as nectar equivalents) exceed the imidacloprid colony level NOAEC and 2 residue values exceed the LOAEC. Residue values exceed the NOAEC and LOAEC by as much as 186 ad 156 days, respectively, by factors of **3.6X** and **1.8X**, respectively. Importantly, imidacloprid-specific residue data for pome and stone fruits are available from combined foliar (0.38 lb a.i./A)+ soil applications (2 x 0.06 lb a.i./A (MRID 49819401). These data are discussed further in the “Combined Application” section below. However, since these data reflect the maximum soil application rate (in addition to foliar application), they are considered “conservative” estimates of residues associated with the maximum soil only application rate of 0.38 lb a.i./A. Imidacloprid residues (expressed as nectar equivalents) from this combined soil + foliar application to pome and stone fruits do not exceed the colony-level LOAEC, and only one value exceeds the NOAEC. Therefore, considering these data along with the bridged residue data, a “weakest” strength of evidence is indicated for colony-level risks from post-bloom soil applications to pome and stone fruit.

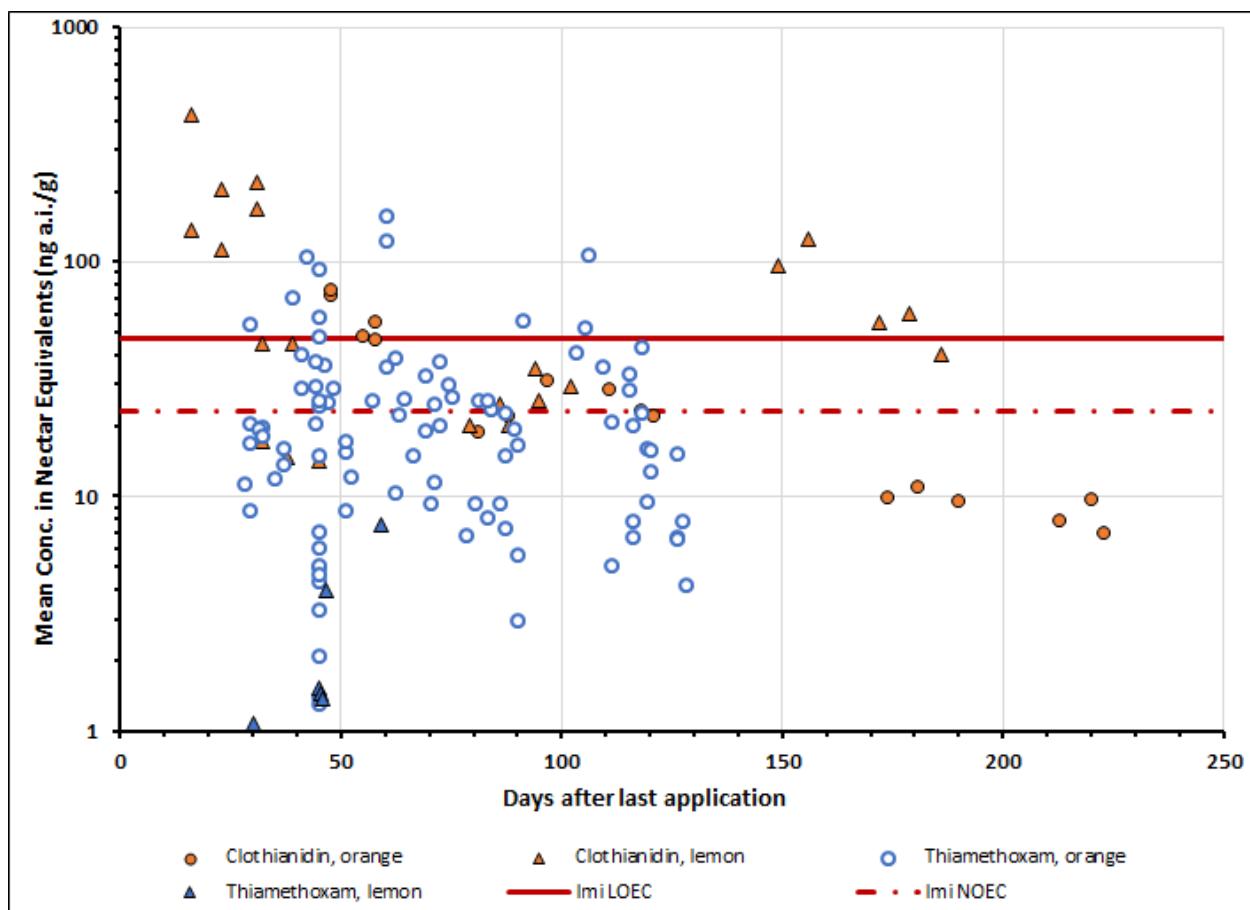


Figure 6-13. Mean measured neonicotinoid residues (expressed as nectar equivalents) in citrus (normalized to 0.5 lb a.i./A for citrus, tree nuts & tropical fruits) from soil applications relative to the imidacloprid colony-level NOAEC and LOAEC

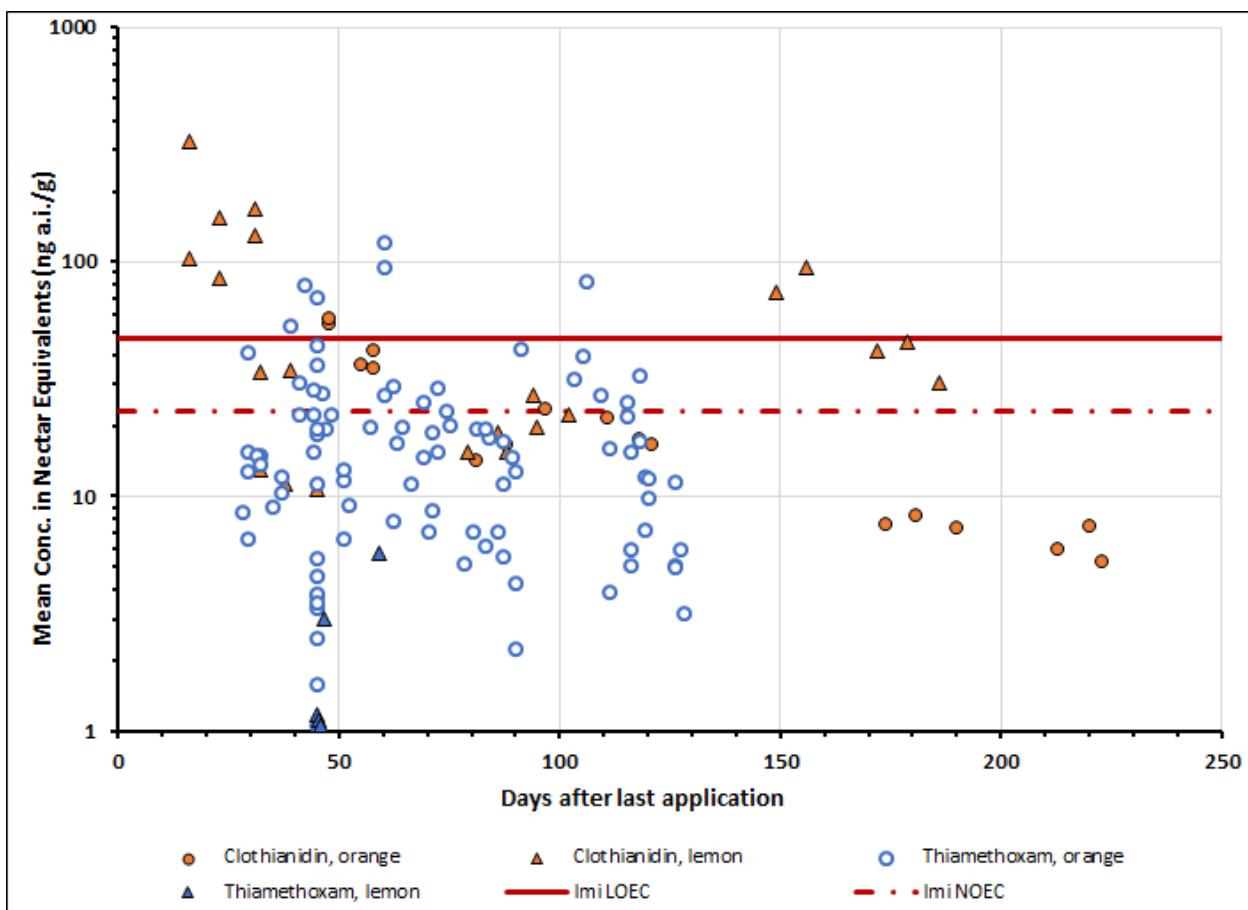


Figure 6-14. Mean measured neonicotinoid residues (expressed as nectar equivalents) in citrus (normalized to 0.38 lb a.i./A) for pome and stone fruits from soil applications relative to the imidacloprid colony-level NOAEC and LOAEC

6.2.7.3. Combined Application: Stone and Pome Fruits

Combined soil and foliar applications to pome and stone fruits are permitted for imidacloprid (post bloom only). Two residue studies were submitted that evaluated residues associated with the combined soil and foliar applications to stone and pome fruit (MRID 49819401; 49662101, respectively) each based on the maximum application rate for soil (0.38 lb a.i./A) plus two foliar applications of 0.06 lb a.i./A. As described in **Figure 6-15**, residue values (expressed as nectar equivalents) from the aforementioned combined application of imidacloprid to pome fruit fall below the colony level NOAEC of 23 µg/L except for one value. This value, however, is driven by a single nectar sample (36 µg/L) which is 4X greater than the sample from the same location/day for leaf and pollen residues. Since nectar residues of neonicotinoids are typically a fraction of those in pollen and leaf, this sample is considered suspect.

For combined application to stone fruits, one trial results in a single residue value that exceeds the colony-level NOAEC and another residue value which approaches the NOAEC (**Figure 6-16**). These residue values are considered reliable and consistent with residues measured in the other matrices.

Since these residue values reflect post-harvest application, they represent a shorter time period between application and residue measurement. It is not known the extent to which differences in residue values from pre- vs. post-harvest applications reflect the shorter time window prior to bloom or the effect of application prior to fruit set and harvest. Based on the limited magnitude and frequency of exceedance of the colony-level NOAEC, the strength of evidence associated with potential colony-level risk to honey bees associated with these combined (post-bloom) applications to pome and stone fruit is considered "weakest."

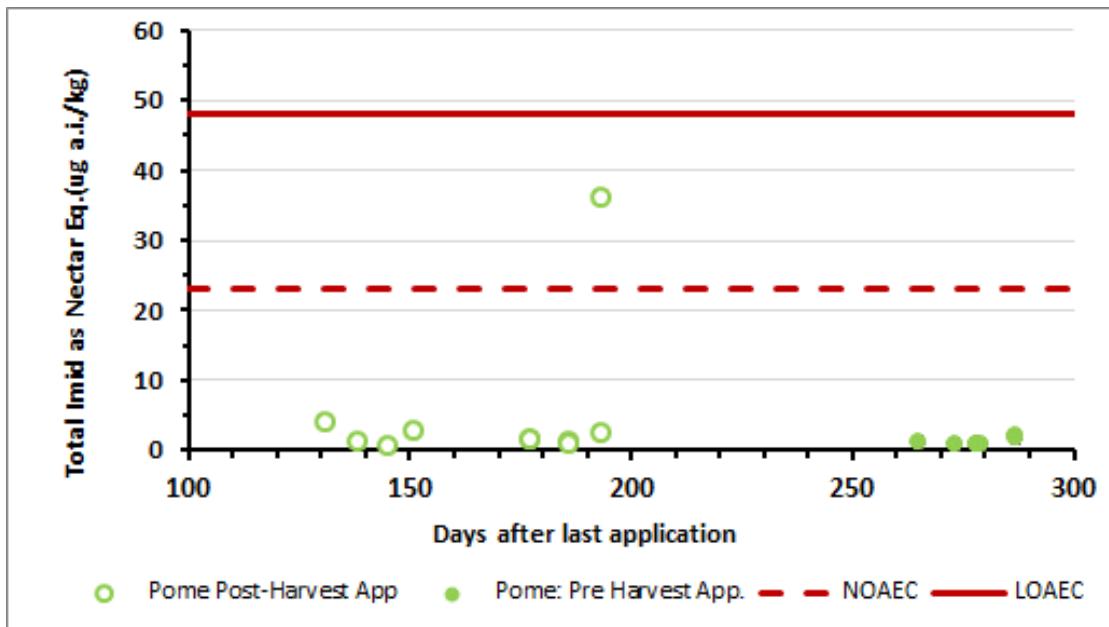


Figure 6-15. Mean concentration of total imidacloprid (expressed as nectar equivalents) in pome fruit (apples) following soil (0.38 lb ai/A) +foliar (2 x 0.06 lb ai/A) application pre- and post-harvest

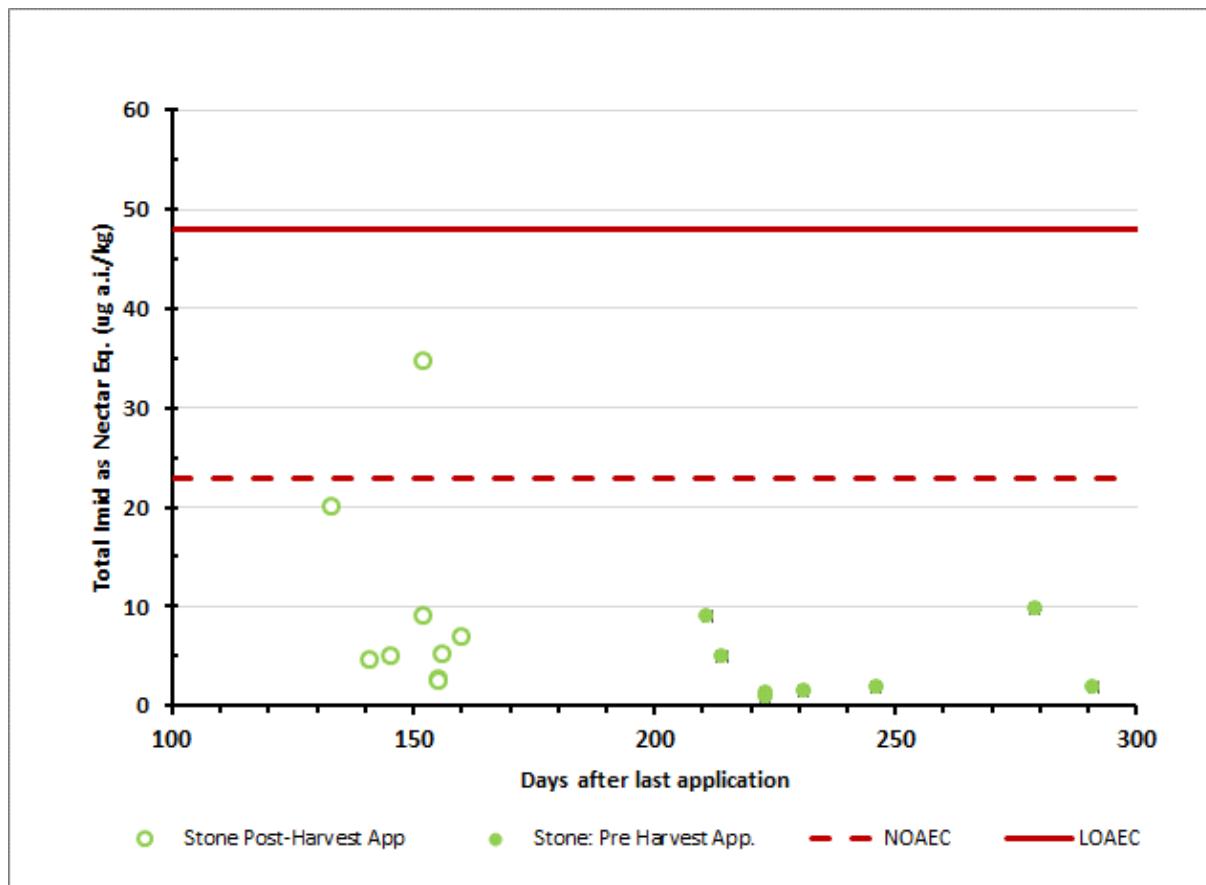


Figure 6-16. Mean concentration of imidacloprid (total nectar equivalents) in stone fruit (cherry, plum, apricot, peach) following soil (0.38 lb ai/A) +foliar (2 x 0.06 lb ai/A) application pre- and post-harvest

6.2.7.4. Additional Considerations/Conclusions

As discussed above, pre-bloom foliar and soil applications of imidacloprid are only allowed on citrus. For both types of applications, residues exceed the imidacloprid colony-level NOAEC and LOAEC. For foliar applications, residues exceed the NOAEC and LOAEC for applications made >1 month prior to bloom. For soil applications, residues exceed both endpoints for >5 months. Residue levels from pre-bloom applications are 1-2 orders of magnitude greater than colony-level endpoints.

When considering post-bloom applications, for foliar applications made several months prior to bloom, residues are below colony-level endpoints for the 0.38 lb a.i./A rate (relevant to pome and stone fruit); however, residues from the 0.5 lb a.i./A rate (relevant to citrus, tree nuts and tropical fruits) are above the NOAEC. This suggests that post-bloom foliar applications of imidacloprid to pome and stone fruit present a low risk to honey bee colonies, but there is risk from post-bloom foliar applications to citrus, tree nuts and tropical fruits. For post-bloom soil applications, residues exceed colony level endpoints for applications made up to six months prior to bloom.

When considering the risk potential, two major assumptions of this approach should be considered, *i.e.*, it is assumed that the nectar and pollen from treated crops are the only sources of imidacloprid exposure and that there is no dilution of exposure concentrations from food sources with lower concentrations. This dilution could come in the form of foraging on nectar and pollen from other orchards that are not treated or on other plants that are not treated. Given that residues (especially pre-bloom) are orders of magnitude higher than colony level endpoints, more than 90% dilution of nectar and pollen food would be required to lead to concentrations below the colony-level NOAEC. It seems likely that colonies will forage on treated orchards for 1-10% or more of their resources. Given that imidacloprid is registered on a wide variety of crops, it is possible that other plants within the foraging areas of honey bee colonies could also be treated with imidacloprid. So, the extent to which dilution of exposure may occur is unknown.

Another consideration of the risk potential is the spatial extent of risk. As discussed previously, usage data are available for imidacloprid applications to orchard crops. These data indicate that tens of thousands of lbs are applied per year to orchards in the US. When the total number of acres of bearing orchards is considered (**Table 6-29**), this translates to an annual average of approximately 400,000 acres of orchards treated with imidacloprid, with a maximum of 660,000. Approximately half of the treated acres are represented by citrus (which allows pre-bloom applications).

Therefore, honey bees could potentially be exposed to imidacloprid from pre-bloom applications to citrus on hundreds of thousands of acres in the US. If foliar applications of imidacloprid occur within 1.5 months of bloom, colonies could be exposed to levels of imidacloprid in nectar and pollen that could result in a colony level risk. Post-bloom foliar applications to pome and stone fruits pose a low risk to honey bee colonies; however, post-bloom foliar applications to citrus, tree nuts and tropical fruits pose a risk although the strength of evidence is considered “weakest.” Both pre- (citrus) and post-bloom (all other orchard crops) soil applications pose a risk to honey bee colonies with strength of evidence ranging from “strongest” (soil, pre-bloom) to “moderate” (soil, post-bloom citrus, tree nut, tropical fruit) to “weakest” (soil, post-bloom, stone & pome fruits).

6.2.8. *Crop group 13 – Berry and small fruit*

The berries crop group includes, among other members, blackberry, blueberry, and raspberry. This crop group also includes group 13-07 (small fruit and berries group), which itself encompasses 8 subgroups that contain other crops such as strawberry, cranberry, and grape. Imidacloprid is registered for use on caneberry and bushberry subgroups (13A and 13B), grape (small fruit vine climbing subgroup 13-07D), cranberry (13-07G, 13-07H), and strawberry (low growing berry subgroup 13-07H). For foliar applications, single maximum application rates range from 0.047 – 0.1 lb a.i./A, with two to five applications allowed per season. Soil applications have a maximum seasonal application rate of 0.5 lb a.i./A except perennial and post-harvest strawberries which have a rate of 0.38 lbs a.i./A.

Specific to the uses of imidacloprid, grapes are the dominant crop with an estimated usage of 60,000 lbs/year based on SLUA data described in Section 3. This is followed by strawberries and blueberries to a far lesser extent. According to USDA (2017), blueberries, blackberries, and raspberries require bee pollination blueberries uses managed sources of pollination. Although, bee pollination of strawberry is

not considered essential, it may be used to compliment wind pollination. Similarly, grapes are wind pollinated and therefore do not require honey bee pollination. Additionally, grapes do not produce nectar, although their pollen is noted to be attractive according to USDA (2017).

This section describes the lines of evidence associated with the assessment of risks of imidacloprid to honey bee colonies from foliar and soil applications to berry and small fruit crops. Specifically, the strength of evidence is considered “strongest” with respect to potential colony-level risks to honey bees associated with pre-bloom foliar and pre-bloom soil applications of imidacloprid to crops in the berries and small fruits group. One imidacloprid-specific residue study available for pre-bloom applications to strawberry, but it is not suitable for quantitatively use. Based on the residue bridging analysis (**Attachment 2**), the available residue data for pre-bloom applications to orchards are considered extrapolatable among berry crops and neonicotinoids. These residue data indicate that both empirical and estimated residues in pollen and nectar exceed colony level NOAEC and LOAEC values for periods of time that range from weeks to months. Given the magnitude of residues, if $\geq 5\%$ of food resource required by a colony is collected from pre-bloom treated berry fields, the resulting exposure is sufficient to exceed the colony level endpoints. No incidents have been reported in association with applications to berry and small fruit crops.

In contrast, the evidence for post-bloom foliar and soil applications of imidacloprid indicates a low potential for risk. Two residue studies conducted with berries support the risk call for post-bloom applications. One imidacloprid residue study is available for post bloom soil application to blueberries. This study does not indicate risk but samples were taken 200+ days after last application and may not be representative of all post-bloom applications. A full summary of the risk conclusions and lines of evidence considered with imidacloprid use on berries/small fruit crops is provided in **Table 6-31**.

Table 6-31. Lines of evidence considered in characterizing colony-level risk to honey bees for applications of imidacloprid to berry and small fruit.

| Line of evidence | | Foliar applications, pre-bloom (Strongest Evidence of Risk) | | Foliar applications, post-bloom (Low Risk) ⁽³⁾ | | Soil applications, pre-bloom (Strongest Evidence of Risk) | | Soil applications, post-bloom (Low risk) ⁽³⁾ | | | | | | | | | |
|--|--|--|----------------------|--|-------|--|---------------------|--|-------|--|--|--|--|--|--|--|--|
| Imidacloprid specific residue data | | No data | | No data | | No data | | Blueberry | | | | | | | | | |
| Residue data for other chemicals | | Blueberry (D, T), Cranberry (T, D), Strawberry (T) | | Grape (C) | | Grape (C), Strawberry (T) | | | | | | | | | | | |
| Measured data | Exceedance Attribute | NOAEC | LOAEC | NOAEC | LOAEC | NOAEC | LOAEC | NOAEC | LOAEC | | | | | | | | |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC (Imidacloprid) | NA | | NA | | NA | | 0/13 | 0/13 | | | | | | | | |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC (All Neonics) | 48 /54 | 44 /54 | 0/8 | 0/8 | 15 /26 | 14 /26 | 0/13 | 0/13 | | | | | | | | |
| | Duration: Number of days > NOAEC & LOAEC | 25 | 25 | NC | | 83 | 83 | NC | | | | | | | | | |
| | Magnitude: Ratio of max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 86X (1.2%) | 42X (2.4%) | NC | | 21X (4.9%) | 10X (10%) | NC | | | | | | | | | |
| Modeled data: 90 th percentile | Duration: Number of days > NOAEC & LOAEC | 33 | 26 | NA | | | | | | | | | | | | | |
| | Magnitude: Ratio of max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 200X (0.5%) | 97X (1.0%) | | | | | | | | | | | | | | |
| Modeled data: 70 th percentile | Duration: Number of days > NOAEC & LOAEC | 27 | 22 | | | | | | | | | | | | | | |
| | Magnitude: Ratio of max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 82X (1.2%) | 40X (2.5%) | | | | | | | | | | | | | | |
| Modeled data: 50 th percentile | Duration: Number of days > NOAEC & LOAEC | 23 | 19 | NA | | | | | | | | | | | | | |
| | Magnitude: Ratio of max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | 46X (2.2%) | 22X (4.5%) | | | | | | | | | | | | | | |
| Crop attractiveness ⁽²⁾ & Bloom Duration | | Blueberries, cranberries, raspberries, strawberries: Nectar and pollen are attractive to honey bees; Currants and gooseberries: Only nectar is attractive to honey bees; Grapes: Only pollen is attractive to honey bees. Bloom duration varies depending on crop/variety. | | | | | | | | | | | | | | | |
| Managed pollinators required ⁽²⁾ | | Yes | | | | | | | | | | | | | | | |
| Spatial extent of risk (acres treated) | | Other berries 13,275; Grapes 288,630 (Average annual) Other berries 28,594; Grapes 481,050 (Maximum annual) | | | | | | | | | | | | | | | |

⁽¹⁾ Max. residue for measured, pre-bloom foliar & soil apps. reflect 14 & 42 DALA, respectively. Max. residue for modeled residue data reflects 1 DALA.

⁽²⁾ Based on USDA 2017.

⁽³⁾ assuming post bloom applications made > 200 prior to bloom during the previous season.

N.C. = not calculated because > 100% of the treated diet would be needed to reach the NOAEC; NA = data not available

6.2.8.1. Foliar applications

For foliar applications to caneberry and bushberry, current label language restricts application to after bloom. Strawberries have applications during the pre-bloom window permitted but with a 10-day pre-bloom restriction. Finally, foliar applications to grapes make no restriction on application relative to the bloom period. However, grapes produce pollen only.

Pre-Bloom Foliar Application

Available residue data for pre-bloom foliar applications of neonicotinoids to the berry group are summarized in Error! Reference source not found. **Figure 6-17**. Imidacloprid specific data are not available for foliar applications. Based on the residue bridging analysis (**Attachment 2**), dinotefuran and thiamethoxam blueberry and cranberry data are considered extrapolatable and can be used to represent crops in the low growing berry subgroup (13-07H). Monte Carlo distributions representing the 50th and 90th percentiles of the data are also presented in **Figure 6-17**. Residue values are normalized to the maximum single application registered for imidacloprid across the low growing berry subgroup (i.e., 0.1 lb a.i./A).

Mean measured residues (expressed as nectar equivalents, **Attachment 1**) from pre-bloom foliar applications of neonicotinoids to berry and small fruit crops range from 3.6 to 1,973 ng a.i./g, with 89% of values above the NOAEC. The maximum magnitude by which the colony-level NOAEC and LOAEC are by mean measured residue values are **86X** and **42X**, respectively. Furthermore, the colony-level endpoints are exceeded for 25 days based on mean measured residue values.

Predicted residues based on the 50th and 90th percentile curve from the Monte Carlo analysis of residue decline curves exceeded the colony-level NOAEC and LOAEC by similar magnitudes and durations as the measured residue data taken on similar days after application. Depending on the percentile of the data used to generate the distribution, residues in low growing berry crops may remain above the NOAEC and LOAEC for up to 33 and 26 days after application, respectively. Strawberries are the only nectar-producing members of the group where foliar applications of imidacloprid are permitted prior to bloom (> 10 days prior to bloom). Based on the both the measured and modeled residue data for berries, this 10-day pre-bloom interval does not appear sufficient to reduce exposure to below the colony-level NOAEC and LOAEC for honey bees foraging on treated strawberries. Based on the magnitude and duration that residues in berry crops exceed the colony-level NOAEC and LOAEC, the strength of evidence associated with colony-level risk to honey bees from pre-bloom foliar applications is considered “strongest.”

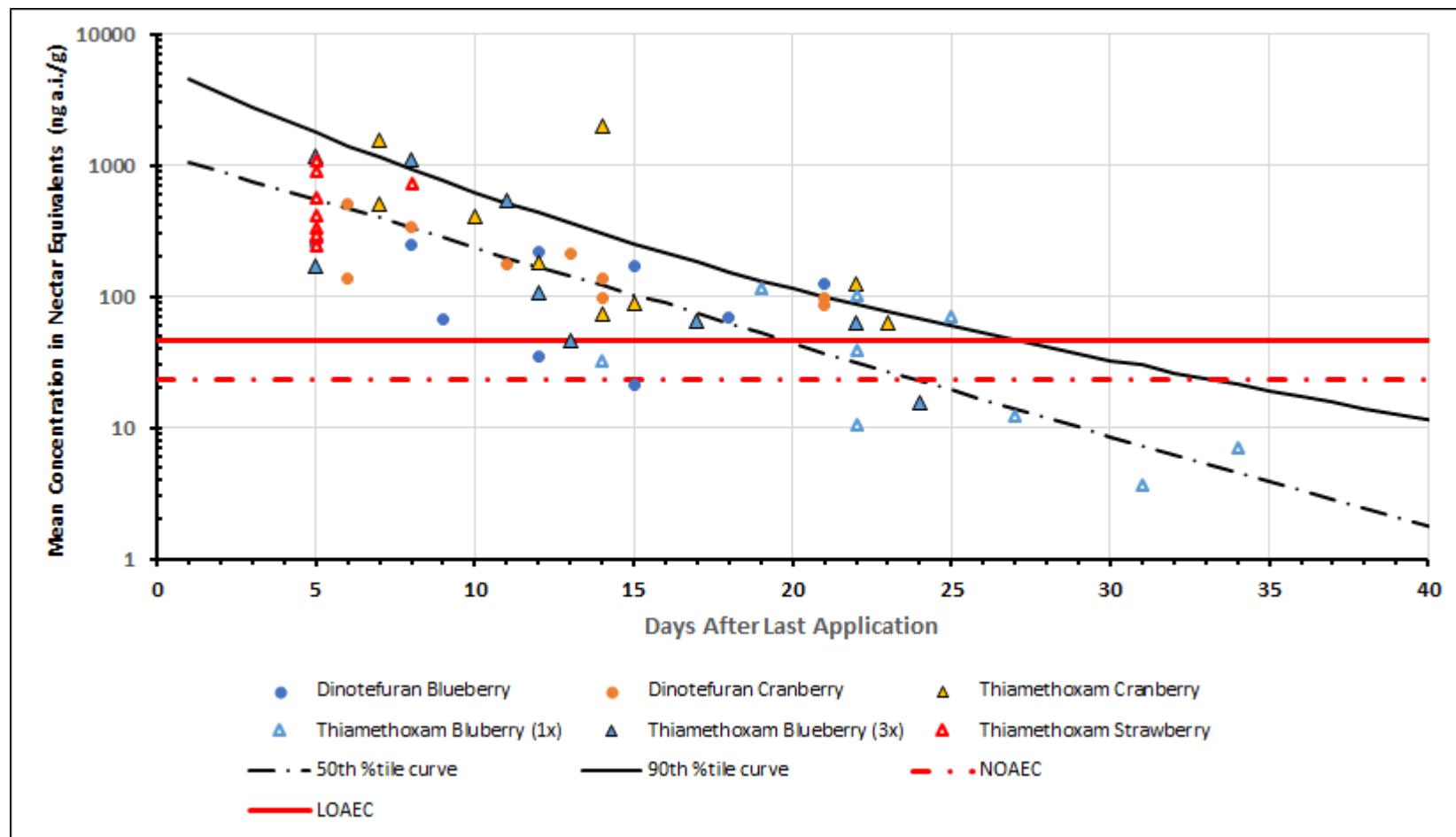


Figure 6-17. Mean-measured neonicotinoid residues (expressed as nectar equivalents) and modeled 50th and 90th percentiles for pre-bloom foliar applications (normalized to 0.1 lb a.i./A) of neonicotinoids to berry and small fruits. Dashed and solid horizontal lines represent the imidacloprid colony level NOAEC and LOAEC, respectively.

Post-Bloom Foliar Application

For post-bloom foliar residue data for the berries and small fruit crop group, only one clothianidin study conducted with grapes was available for consideration. **Figure 6-18** summarized residues in grape (expressed as nectar equivalents; **Attachment 1**) following post bloom application (residues collected the following year). All residue values are below the imidacloprid colony level NOAEC. Grape, however, is attractive to bees only through pollen and therefore, only pollen residue data were collected. As a result, there is uncertainty associated with these nectar equivalent residue values since they were based entirely on the conversion of pollen residues to nectar equivalents. Furthermore, the data for grape reflect measurements made nearly a year after application, which may not be representative of shorter post-bloom intervals of other berry crops. However, residues in berry crops from pre-bloom applications were modeled to drop below the imidacloprid colony NOAEC after two months. These lines of evidence suggest post bloom foliar applications to grapes have a low potential for colony-level risk to honey bees.

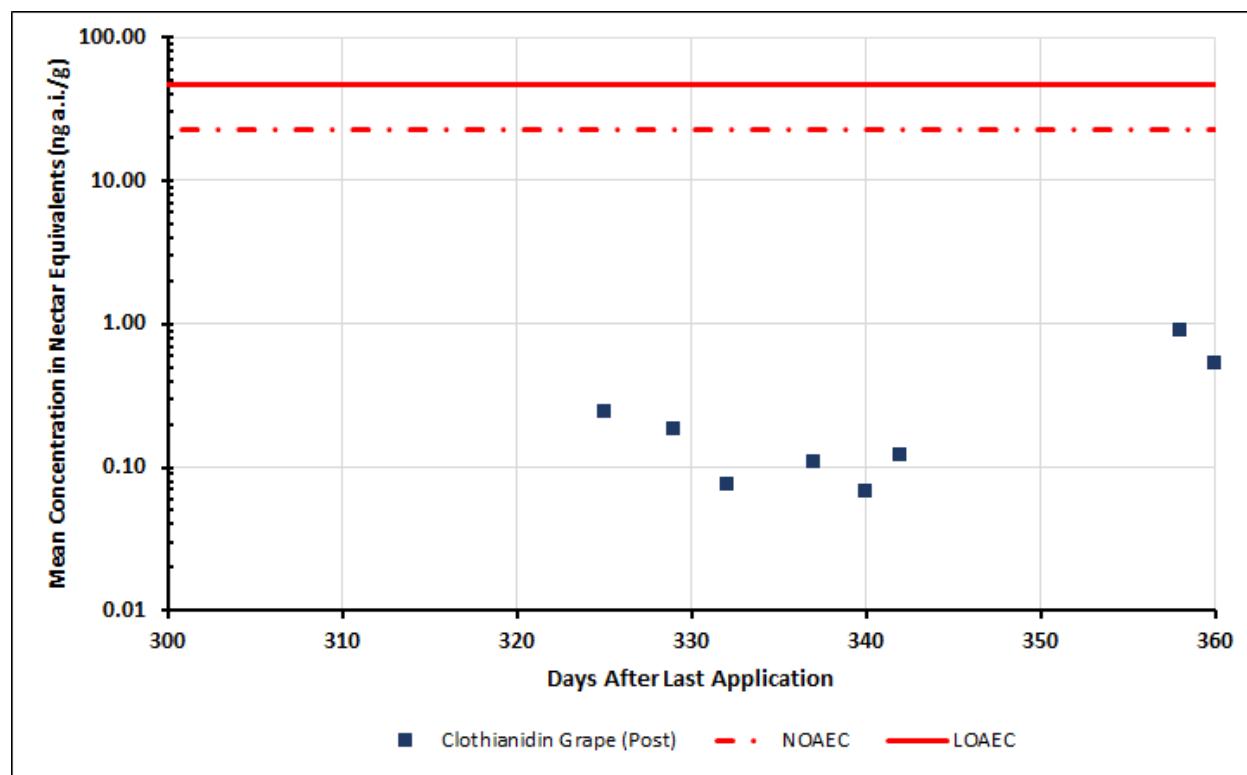


Figure 6-18. Measured neonicotinoid residues (expressed as nectar equivalents) normalized to 0.1 lb a.i./A for post-bloom foliar applications to the berry crop group in relation to and imidacloprid colony-level endpoints.

6.2.8.2. Soil application

Similar to the label instructions for foliar applications, there are no pre-bloom or during bloom soil applications of imidacloprid permitted for caneberry and bushberry. However, grape has no label restrictions on timing of application relative to the bloom period. For cranberry and annual and

perennial varieties of strawberries, applications are restricted during bloom and immediately prior to bud opening, which suggests a pre-bloom application prior to this window is permitted. Finally, a further application scenario for soil applications to strawberry includes a post-harvest application to perennial varieties.

There are two imidacloprid studies that examine the residues in pollen and nectar from soil treated blueberry (post bloom; MRID 49535602) and strawberry (MRID 49090502). While a Monte Carlo analysis involving residue data and dissipation rate constants was conducted for foliar applications to the small fruit and berry crop group, this approach was not supported for soil applications due to limitations in the dataset (**Attachment 2**).

Pre-Bloom Soil Applications

The imidacloprid strawberry study (MRID 49090502) did not provide information on when residues were sampled relative to the application rate; but it is presumed to reflect a pre-bloom soil application based on other information in the study. Residue measurements were made in flowers and pollen at 7 sites in California; three reflecting sandy soils and 4 reflection loam soils (**Figure 6-19**). Concentrations in nectar were estimated by multiplying blossom concentrations by 0.3 (**Attachment 2**). Nectar and pollen concentrations were combined and expressed as nectar equivalent concentrations as described previously. It appears from these limited data that soil type may influence residue concentrations, with mean residue values exceeding the NOAEC and LOAEC at sites in sandy soils while those in heavier soils were much lower and did not exceed the colony level endpoints. Since information was not available on the timing of residue measurements relative to application, the effect of soil type on these residue values are not considered conclusive.

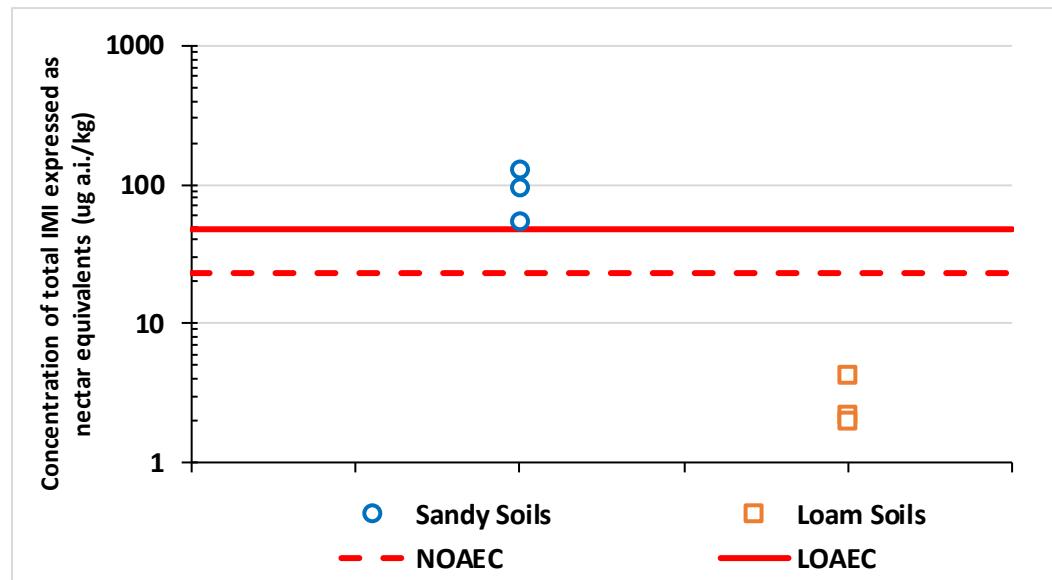


Figure 6-19. Mean residue concentrations of imidacloprid (expressed as nectar equivalents) in strawberries following pre-bloom soil application of 0.5 lb ai/A (MRID 49090502)

Data is available for other neonicotinoids for grape pollen, but it is uncertain how representative grape crops are for other berries and small fruit. Bridging in other crop groups and across chemicals was determined to be acceptable in most cases however with only one study on grapes its representativeness is less certain. In addition, as mentioned previously, several crops within the small fruit vine climbing subgroups also produce nectar (*e.g.*, gooseberries), so it is uncertain how representative residues in grape pollen are for other crops in the subgroups.

Only strawberries and grapes permit soil applications either just before the bloom (strawberries) or during the bloom period (grapes). All other members of the group prohibit soil applications pre or during bloom. **Figure 6-20** presents the mean measured residues from pre-bloom soil applications of other neonicotinoids to available strawberry and grape data, normalized to the maximum soil application rate for imidacloprid (0.5 lb a.i./A). Values for strawberries range from 0.7 to 474 ng a.i./g, with 15 values above the NOAEC and 14 above the LOAEC. Grape (which does not produce nectar that is attractive to honey bees) had residue values all below the colony level NOAEC. The contribution of pollen on the mean concentration in nectar equivalents ranges from 5 to 100%. Based on measured and modeled residue data, the strength of evidence is considered “strongest” regarding the potential for colony-level risks to honey bees foraging on berries (*i.e.*, strawberries) treated via soil application prior to bloom.

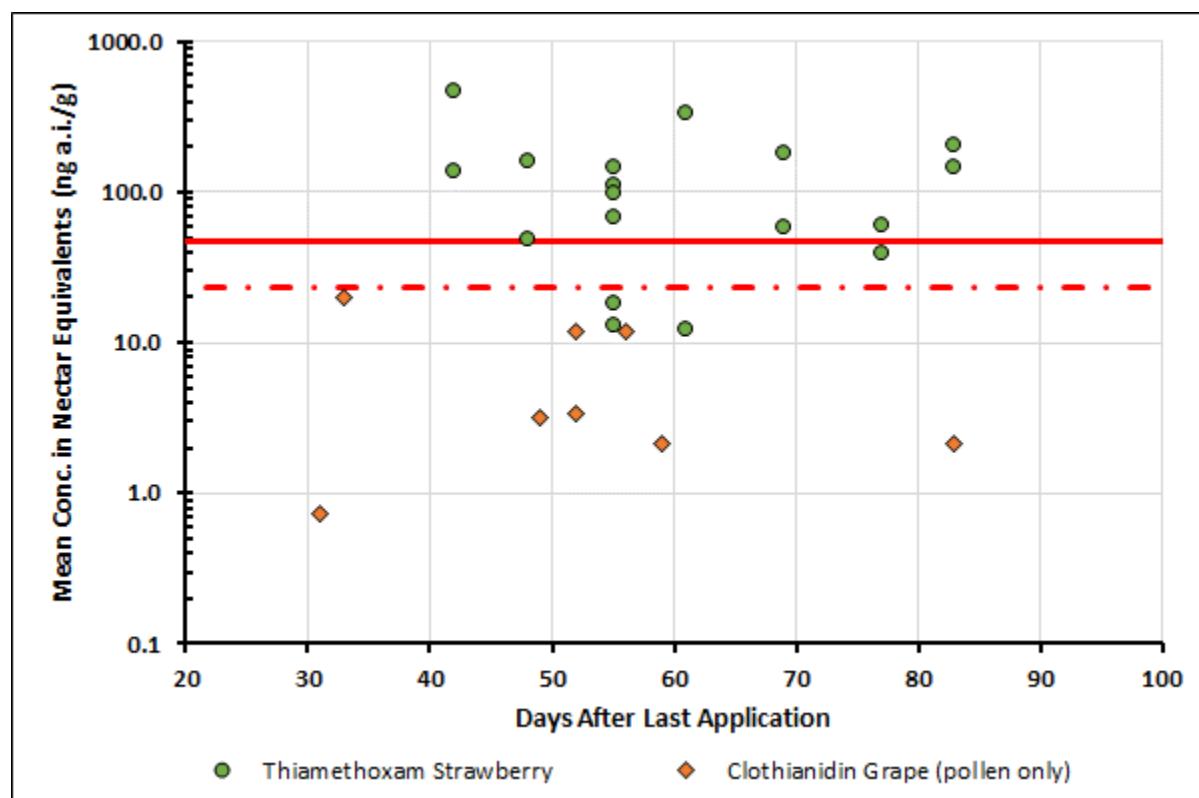


Figure 6-20. Measured neonicotinoid residue data (normalized to 0.5 lb a.i./A) versus imidacloprid endpoints for the low growing berry crop group subgroup (13-07H); Pre-bloom applications.

Post-Bloom Soil Applications

Most members of the small fruit and berry crop group are permitted as a post-bloom soil application only. One residue study is available for post-bloom, soil applications of imidacloprid to blueberry. These residues are plotted in **Figure 6-21** below and all residues are below the colony level NOAEC. Based on these data, a low potential for colony-level risk is indicated for post-bloom, soil applications of imidacloprid to berries.

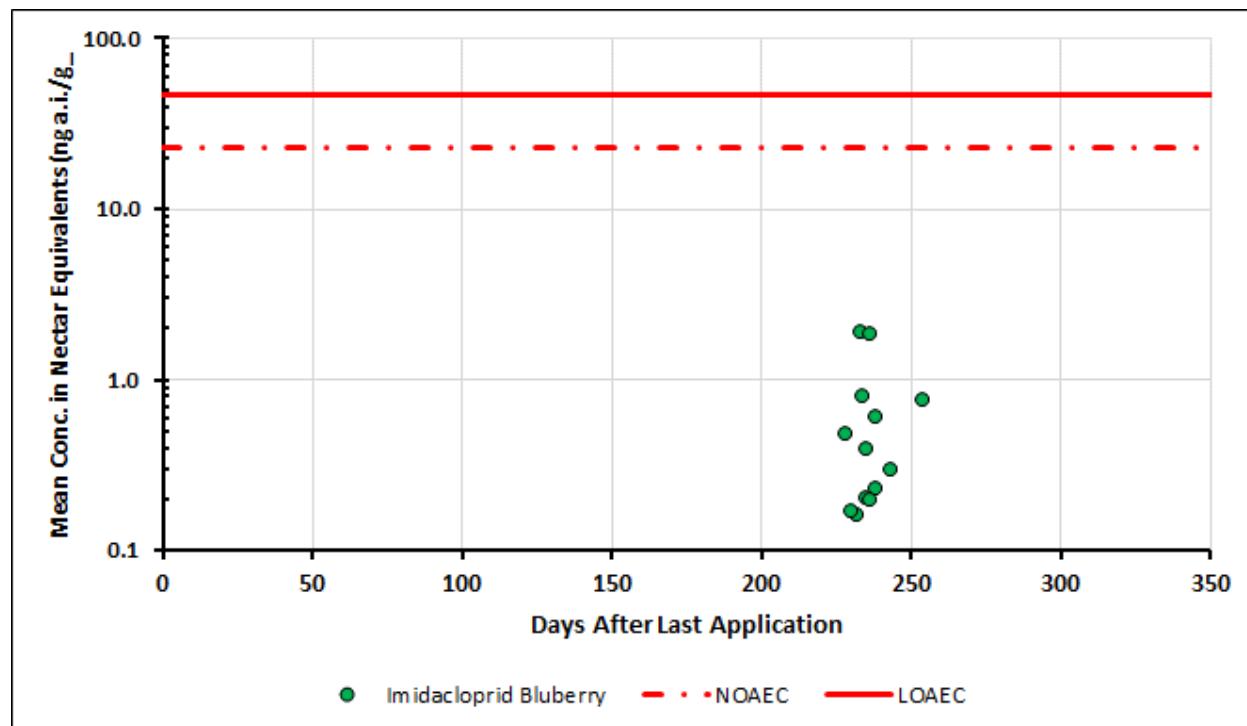


Figure 6-21. Mean measured imidacloprid residues (expressed as nectar equivalents) normalized to 0.5 lb a.i./A for post-bloom soil applications to blueberries in relation to imidacloprid colony-level endpoints

6.2.8.3. Additional Considerations/Conclusions

Based on the analysis above, residues in total nectar equivalents (nectar and adjusted pollen) for registered uses in the berry small fruit crop group do not exceed the imidacloprid NOAEC for post-bloom-bloom applications made via soil treatments (at the maximum permitted rates) beyond 200 DALA. Pre-bloom foliar and pre-bloom soil applications do result in risk based on exceedance of the colony level NOAEC (applicable to strawberries).

All members of the berry and small fruit group do not permit pre-bloom or during bloom foliar applications with the exception of strawberry, which has a 10-day pre-bloom interval. Strawberries are also associated with an extended (several week) bloom period.

Another consideration of the risk potential is the spatial extent of risk. As discussed previously, usage data are available for imidacloprid applications to caneberries (blackberry and raspberry), grapes, strawberries, and blueberries. These data indicate that approximately 63,000 lbs are applied per year to members of this group, with the overwhelming majority to grapes, which has an average of a 30% PCT. When made as a post-bloom foliar application or pre-bloom soil application, all residues in grapes were below the colony level of concern. As current labels do not restrict foliar or soil applications of imidacloprid to grapes relative to the bloom period, it is an uncertainty as to whether pre or during bloom foliar and soil applications pose a colony level risk, and the spatial extent to which applications to grapes are made in this way.

While the 10-day pre-bloom interval for foliar applications to strawberries does not appear to be protective of the potential for colony-level risks, imidacloprid applications (foliar and soil) total 2,000 lbs a year with an average PCT of 5%

Therefore, honey bees could potentially be exposed to imidacloprid from foliar pre-bloom applications strawberries. If applications of imidacloprid occur within a roughly a month and a half of bloom, colonies could be exposed to levels of imidacloprid in nectar and pollen that could result in a colony level risk. If soil applications are made at least 200 DALA post bloom, the risk is considered low.

6.2.9. Crop group 6 – Legumes

The legume crop group includes, among other members, beans, peas, soybeans, and various hybrids thereof. For foliar applications, the single maximum application is 0.05 lb a.i./A for soybeans and 0.04 for all other legume crops, with three applications allowed per season. Soil applications are registered with a maximum annual application rate of 0.38 lb a.i./A. Seed treatment application rates are 0.209 lbs a.i./A for soybean and 0.5 lbs a.i./A for other beans and peas calculated from a.i. per seed and seeding rate. Current label language for foliar imidacloprid applications to legumes does not specify restrictions pertaining to timing of application in relation to bloom period.

Specific to the soil and foliar applications of imidacloprid to legumes, soybeans are the dominant crop with an estimated usage of estimated 30,000 lbs/year. This is followed by beans and peas to a far lesser extent. According to USDA (2017), soybeans are considered attractive to bees; however, bees are not required for pollination. Some members of the legume crop group are considered highly attractive to bees and require bee pollination (*e.g.* broad beans). Consequently, there is the potential for exposure for bees on treated crops.

For imidacloprid applications to the legume group, foliar applications show low risk based on refined tier I data for soybeans. There is no data available for soil applications for imidacloprid or other neonicotinoid chemicals. Therefore, for soil applications to legumes extrapolation from risk conclusions for other herbaceous crops will be used as a surrogate. As seen in **Sections 6.2.6 and Section 6.2.10.2**, the risk conclusion for cucurbits and fruiting vegetables indicates tier II risk. The strength of evidence for this risk call is weakest as it is unclear to which degree other herbaceous crops can act as a surrogate for legumes.

Weak evidence indicates that seed treatment on beans poses a risk to honey bee colonies foraging on treated fields. There is not imidacloprid specific data available for seed treatment applications to beans but the bridged dataset is robust. Soybeans and peas have low risk while beans have risk because of higher application and seed planting rates. Additionally, the seed bridging analysis (**Attachment 4**) indicates that estimated residues in pollen and nectar exceed CFS NOAEC but not the LOAEC. A summary of the risk conclusions and lines of evidence considered with imidacloprid use on legume crops is provided in **Table 6-32**.

Table 6-32. Lines of evidence considered in characterizing colony-level risk to honey bees from imidacloprid application to legume crops

| Line of evidence | Foliar applications (Low Risk) | Soil Applications (Weakest Evidence of Risk) | Seed Treatment (Weakest Evidence of Risk) |
|--|---|--|--|
| Imidacloprid specific residue data | Soybean | NA | Soybean |
| Residue data for other chemicals | Soybean (T) | NA | Bridged from all seed data |
| Basis for risk call | Passed at refined tier I | Based on extrapolation from other herbaceous crops | Beans exceed NOAEC by 2 µg a.i./kg Other seed uses pass through bridge analysis |
| Crop attractiveness ⁽¹⁾ | Attractive for all crops | | |
| Managed pollinators ⁽¹⁾ | No | | |
| Ecological incidents | 3 bee kill incidents (with certainty of either possible or probable) have been reported in association with imidacloprid applications to soybean crops. | | |
| Spatial extent of risk (acres treated) | All: 1,933,623; Beans: 16,973 (Average annual) All: 1,937,483; Beans: 20,833 (Maximum annual) | | |

⁽¹⁾ Based on USDA 2017

6.2.9.1. *Soil application*

There are no neonicotinoid residue data available corresponding to soil application to legumes. Soybean is the only use pattern in the legume crop that is not currently registered for soil applications. Because of this lack of data, extrapolation from all other herbaceous crops will be used as a surrogate to make the risk call for this use pattern. As concluded in **Section 6.2.6.1** cucurbit vegetables have risk to honey bee colonies at the tier II level with several studies showing residue exceedances of the imidacloprid LOAEC and NOAEC for months after last application date. Additionally, as concluded in **Section 6.2.10.2** fruiting vegetables also have risk to honey bee colonies with studies showing exceedances of the imidacloprid LOAEC and NOAEC. These studies were conducted with tomato which produces pollen only and therefore could be an underestimation for exposure from nectar and pollen producing plants. Therefore, based on extrapolation from these other herbaceous crop groups it is expected that legume crops will have risk to honey bee colonies.

6.2.9.2. Seed treatment

Details of the bridging and risk recommendations for seed treatment with all four neonicotinoids are found in **Attachment 4**. Three members of the legume crop group resulted in residues that exceeded the refined Tier I levels of concern (soybean, peas and beans). Therefore, a Tier II analysis was conducted on these crops (**Table 6-33**). Concentrations, expressed on a nectar equivalent basis and scaled to the application rate specific to each crop, are below the honey bee colony-level NOAEC for soybean and peas. However, normalized concentrations in beans (25 µg a.i./kg slightly exceed) the colony level NOAEC of 23 µg a.i./kg. However, since the larger suite of seed treatment residue data for legumes was so limited, the residue data used in this Tier II assessment reflect a 90th percentile from all seed treatment uses across the neonicotinoids.

Table 6-33. Seed treatment Tier II assessment for imidacloprid and legume crops

| Crop | Tier II concentration (nectar equivalents) | Above IMI CFS NOAEC (23)? | Risk conclusion |
|---------|---|---------------------------|-----------------|
| Beans | 25 | Yes | Risk |
| Peas | 20 | No | Low Risk |
| Soybean | 7.5 | No | Low Risk |

6.2.9.3. Additional Considerations/Conclusions

In terms of the number of acres treated, foliar and seed treatment applications to soybean comprise the majority of the poundage of imidacloprid applied for this crop group. Specifically, seed treated soybeans account for 36% of the annual poundage of imidacloprid applied per year. Foliar applications to soybeans comprise 3% of the annual total, but the amount applied translates to a spatial scale of almost 2 million acres treated for foliar treatment considering the number of acres of soybean in the United States.

Residue data were available to refine foliar and seed treatment applications to soybean. While default Tier I RQs for soil exceeded the acute and chronic LOC, the lack of residue data above the colony level NOAEC from foliarly applied soybean suggests no exceedance of the colony level endpoint for soil given the general trend of higher residues from foliar applications relative to soil.

For seed treatment applications to beans, residue data marginally exceeded the colony level NOAEC (25 µg/L relative to 23 µg/L). Out of the roughly 77,000 acres of beans grown in the United States, it is not known to what extent this is treated as a seed treatment with imidacloprid. The colony level conclusion of risk from this use pattern is therefore uncertain.

6.2.10. Other herbaceous crops

This section considers members of herbaceous crop groups which display characteristics related to honey bee attractiveness that differ from the majority of members in their respective crop groups or for which no or limited residue data are available for any member. This includes:

- sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish (root/tuber)
- okra, roselle, chilis, pepper (fruiting vegetable)
- herbs and spices

Maximum label application rates for these three groups of hervaceous crops are shown in **Table 6-34**. Maximum single application rates for foliar applications vary from 0.04 to 0.08 lb a.i./A while those for soil applications vary from 0.38 to 0.5 lb a.i./A.

Table 6-34. Maximum application rates for registered uses of imidacloprid on attractive root and tubers, fruiting vegetables and herbs/spices.

| Application Method | Sweet Potatos (lb a.i./A, # apps, interval) | Okra, Roselle, Chilies & Peppers (lb a.i./A, # apps, interval) | Herbs and Spices (lb a.i./A, # apps, interval) |
|--------------------|--|---|---|
| Foliar | 0.05 x 4 @7d | 0.08 x 3 @ 5d | 0.04 x 3 @ 5d |
| Soil | 0.38 x 1 | 0.5 x 1 | 0.38 x 1 |

Due to the lack of residue data for most attractive members of these groups, residue data used for estimating tier II risks were bridged from other herbaceous crops (cucurbits, legumes, oilseed). For soil and foliar applications to sweet potatos and herbs/spices, there is a potential for colony-level risk to honey bees from registered foliar and soil uses of imidacloprid. However, the strength of evidence is considered “weakest” due to uncertainty associated with bridging residue data across crops and chemicals. For foliar and soil applications to attractive fruiting vegetables that produce pollen only (chilis and peppers), the potential for colony-level risks to honey bees is also indicated and the supporting lines of evidence are considered “strongest.” This risk finding is largely based on the residue data for other pollen-only producing fruiting vegetables (tomato, chili, bell pepper). For attractive fruiting vegetables that produce pollen and nectar (okra & roselle), “moderate” strength of evidence supports the finding of colony-level risk to honey bees. **Table 6-35** summarizes the basis of the risk characterization for attractive root and tubers and attractive herbs and spices and **Table 6-36** summarizes the risk characterization for attractive fruiting vegetables. Further description of the risk characterization is provided in the subsequent sections.

Table 6-35. Lines of evidence considered in characterizing colony-level risk to honey bees from imidacloprid applications to attractive root and tubers (sweet potato¹) and herbs/spices

| Line of evidence | Foliar applications (Weakest Evidence of Risk) | Soil Applications (Weakest Evidence of Risk) |
|--|---|--|
| Imidacloprid specific residue data | NA | NA |
| Residue data for other chemicals | Bridged from herbaceous crops: cucurbits, fruiting vegetable, legume and oilseed | |
| Basis for risk call | Risk indicated for cucurbit, fruiting vegetable and oilseed crops | |
| Crop attractiveness ⁽²⁾ | Attractive for specific crops: sweet potato, herbs and spices (nectar and pollen) | |
| Managed pollinators ⁽²⁾ | No or no data | |
| Ecological incidents | None | |
| Spatial extent of risk (acres treated) | 113,000 acres of sweet potato planted ⁽²⁾ , but imidacloprid usage data specific to this crop is not available | |

⁽¹⁾ Other attractive root and tubers without indication that they are harvested prior to bloom include Jerusalem artichoke, edible burdock, dasheen and horseradish

⁽²⁾ Based on USDA 2017

Table 6-36. Lines of evidence considered in characterizing colony-level risk to honey bees from imidacloprid foliar and soil applications to attractive fruiting vegetables (chilis, peppers, okra, roselle)

| Line of evidence | Chilis and Peppers (Foliar & Soil) (Strongest Evidence of Risk) | Okra and Roselle (Foliar & Soil) (Moderate Evidence of Risk) |
|--|--|--|
| Imidacloprid specific residue data | Tomato (soil) | Tomato (soil) |
| Residue data for other chemicals | Chili, tomato (thiamethoxam), tomato, bell pepper (dinotefuran) | Residue data also bridged from herbaceous crops (cucurbits, fruiting vegetable, legume and oilseed) |
| Crop attractiveness ⁽¹⁾ | Attractive for pollen only | Attractive for pollen and nectar |
| Basis for risk call | Residue data for tomato, chili, pepper (all pollen-only producers) indicating potential colony-level risk | Residue data from cucurbits, cotton and pollen only fruiting vegetables indicating potential colony-level risk |
| Managed pollinators ⁽¹⁾ | No or no data | |
| Ecological incidents | 1 bee kill incident (with certainty of either possible or probable) has been reported in association with imidacloprid applications to tomato. | |
| Spatial extent of risk (acres treated) | US acreage ⁽¹⁾ : 71,200 (chilis & peppers); 2400 (okra), but imidacloprid usage data specific to these crops is not available | |

⁽¹⁾ Based on USDA 2017

6.2.10.1. Attractive root and tuber crops

The root and tuber crop group includes, among other members, potatoes, carrots, radish, sugar beets, and various hybrids. For foliar applications, single maximum application rate ranges from 0.04 – 0.05 lb a.i./A, with three or four applications allowed per season. Soil applications are registered with single applications of 0.18 lbs a.i./A (sugar beet in California only) and a maximum annual application rate of 0.31 lb a.i./A for potatoes and 0.38 lb a.i./A for other crops. Seed treatment application rates vary from 0.030 – 0.293 lbs a.i./A calculated from a.i. per seed and seeding rate. Current label language does not contain pollinator restrictive language to any member of this crop group for applications made relative to the bloom period.

Generally speaking, members of the root and tuber crop group are harvested before bloom while also producing pollen and nectar that are noted to be attractive to honey bees. Except when these crops are used for seed production (small percentage of the total acreage for a given use pattern), the exposure to honey bees is expected to be minimal as the crop would be harvested prior to when bees would likely be foraging. Potatoes are noted to require bee pollination but only for breeding programs and are considered attractive to bumble bees but not honey bees. This crop group also contains sweet potatoes which produce both nectar and pollen and is considered attractive to honey bees, bumble bees and solitary bees (USDA, 2017).

Those few crops that are honey bee attractive and not harvested before bloom, including sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish, and turmeric, do not have crop specific residue data available. Risk is therefore estimated from residue data from other herbaceous crops used as a surrogate for these attractive root and tubers. Based on previous risk conclusions for oilseed, cucurbit vegetable, fruiting vegetable, and legume crops, the potential exists for colony-level effects to honey bees from applications to attractive root and tuber crops. However, given the lack of crop-specific data for attractive root and tubers and the extent of extrapolation involved, the strength of evidence supporting this risk finding is considered “weakest.”

6.2.10.2. Attractive fruiting vegetable crops

The fruiting vegetables crop group includes, among other members, eggplant, pepper (bell peppers, chili peppers, and sweet peppers), tomatoes and various hybrids thereof. For foliar applications, the single maximum application rate is 0.08 lbs a.i./A, with three applications allowed per season. Soil applications are registered with a maximum single and annual application rate of 0.5 lbs a.i./A for pepper and okra and 0.38 lbs a.i./A for other crops. Combined foliar and soil applications are allowed with a maximum seasonal application rate of 0.5 lbs a.i./A. According to USDA (2017), members of the fruiting vegetable crop group are largely unattractive to honey bees except for okra and roselle which produce pollen and nectar as well as chilies and peppers which produce only pollen. The acreage for okra (2,400 acres) is less than the combined acreage for bell peppers and chilies (71,200 acres).

Risks from Pollen-Only Producers:

For foliar applications to fruiting vegetables, residue data are available for tomato (pollen only) while residue data for soil applications are available for tomato and bell pepper (pollen only). For chilis and peppers, the available pollen residue data for tomatoes and bell peppers are used as a surrogate because they are in the same crop group (*i.e.*, fruiting vegetables) and same family (*i.e.*, Solanaceae) and both produce pollen only. It is noted that residue data are available for another species in the Solanaceae family (potato); however, these data are not used as a surrogate for attractive fruiting vegetables because of concern that differences in plant physiology and structure (*i.e.*, potatoes produce tubers whereas chilis and peppers do not) may lead to differences in concentrations of neonicotinoids in pollen among the two groups.

For foliar applications to chilis and peppers, nectar equivalent concentrations were derived as described previously from the pollen residue data for tomatoes (Figure 6-22). Data indicates that the colony-level NOAEC and LOAEC are exceed for approximately 10 days following the last application. Beyond 10 days after the last application, neither of these endpoints are exceeded based on existing data. However, the maximum mean nectar-equivalent concentration (*i.e.*, pollen conc./20) exceeds the imidacloprid colony-level NOAEC by **130X** and the LOAEC by more than **60X**. In considering the high magnitude of these exceedances for a crop within the same crop group, the strength of evidence is considered “strongest” in supporting the colony-level risk determination for foliar applications of imidacloprid to chilis and peppers.

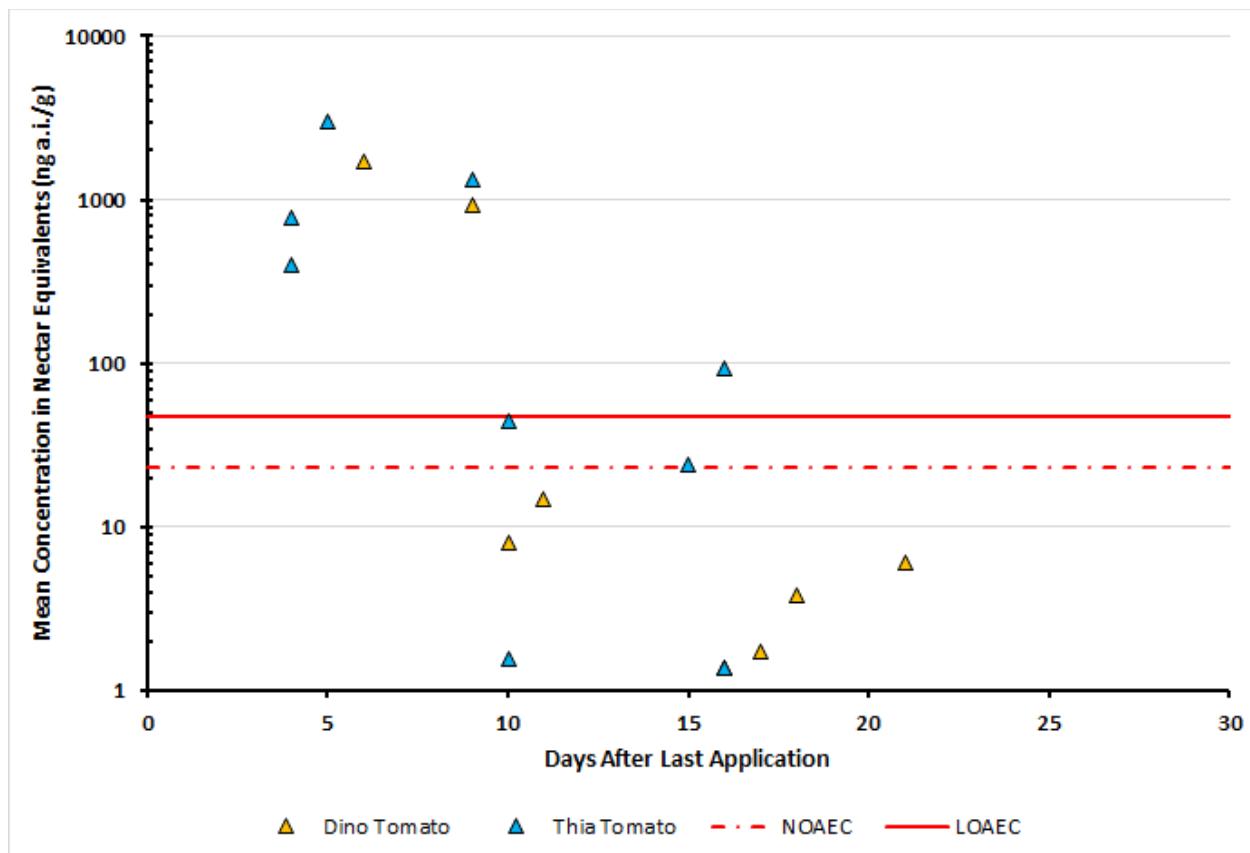


Figure 6-22. Nectar equivalent residues for pollen-only producing fruiting vegetables normalized to the maximum single foliar application rate of imidacloprid (0.08 lb a.i./A)

For soil applications to attractive fruiting vegetables, residue data are available for bell pepper (dinotefuran), chili pepper (thiamethoxam) and tomato (imidacloprid, thiamethoxam, clothianidin; **Figure 6-23**). The imidacloprid colony-level NOAEC is exceeded by nectar-equivalent residues in tomato for all three chemicals and chili pepper for thiamethoxam by up to a factor of **25X**. Notably, residues of the neonicotinoids in tomato and pepper pollen were among the highest residues measured among all the crops with residue data (often in the ppm range). The duration after application that residue exceed the colony-level NOAEC exceeds 70 days and the exceedances pertain to multiple sites. The colony-level LOAEC is exceeded only for dinotefuran tomato residues. In considering these findings, the strength of evidence supporting the potential colony-level risk associated with soil applications to chilis and peppers is considered “strongest.”

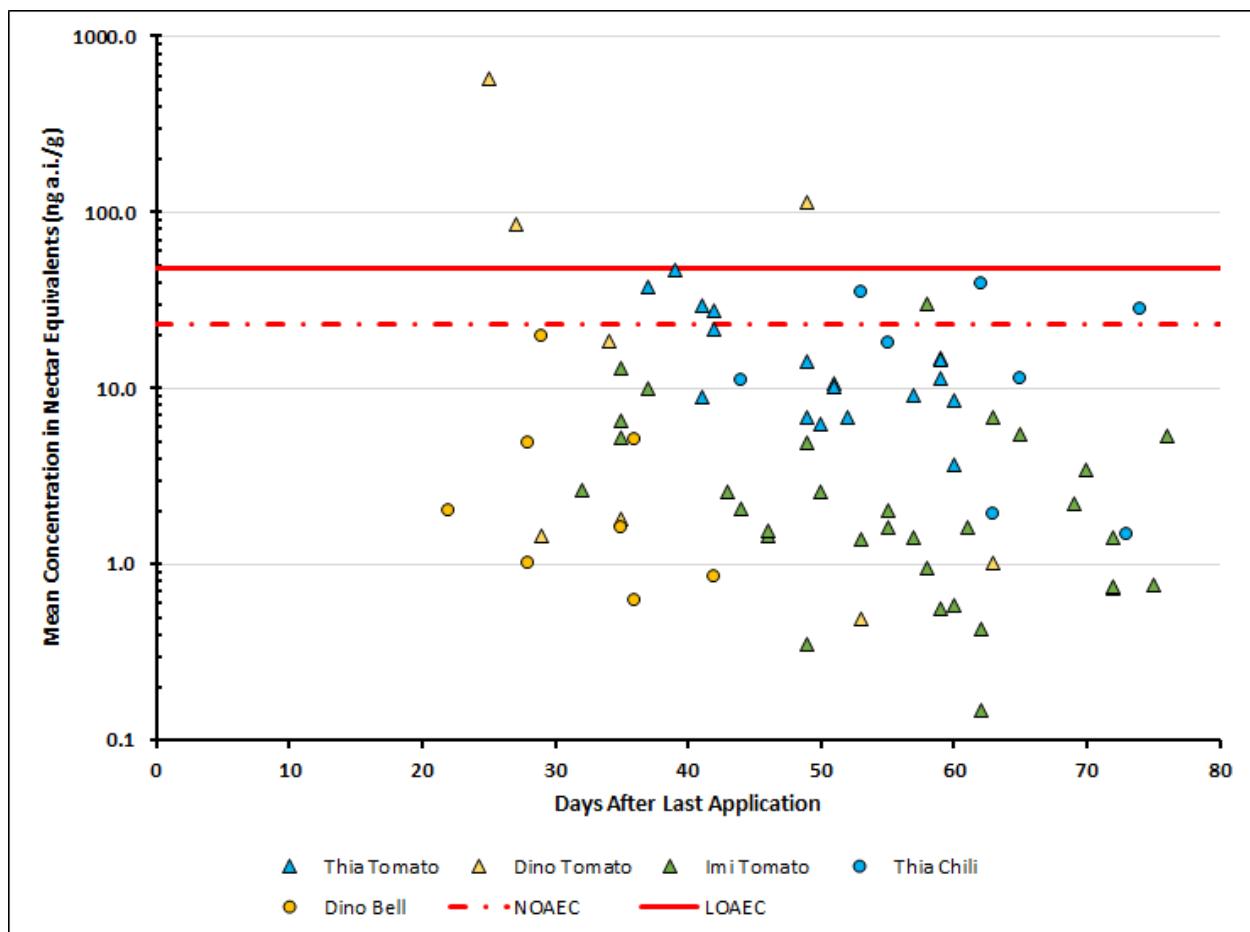


Figure 6-23. Nectar equivalent residues for pollen-only producing fruiting vegetables normalized to the maximum single soil application rate of imidacloprid (0.5 lb a.i./A)

Risks from Nectar and Pollen Producers:

Potential risks associated with the foliar and soil application of imidacloprid to honey bee attractive fruiting vegetables that produce pollen and nectar (okra, roselle) consider two lines of evidence: (1) pollen residue data for tomato and bell pepper, and (2) residue data for other herbaceous crops (cotton, cucurbits). For okra and roselle, the available pollen residue data for tomatoes and bell peppers are relevant because they are all in the same crop group. As discussed above for pollen-only producing fruit and vegetables, residues in pollen for tomato and chili peppers exceed imidacloprid colony-level endpoints, suggesting risk concerns based on pollen alone for both foliar and soil treatments. There is uncertainty in relying only on the tomato and bell pepper pollen data because they are pollen only producers whereas okra and roselle produce both pollen and nectar. Also, both of these species are in a different family (*i.e.*, *Malvaceae*). Therefore, available risk conclusions for foliar and soil applications to cotton, which is also in the *Malvaceae* family (and which only produces honey bee-attractive nectar), are also being considered in drawing risk conclusions for okra and roselle. Since application rates for cotton and fruiting vegetables are similar, the potential for colony-level risk identified for cotton also extends to okra and roselle. In extrapolating the honey bee risk conclusions from cotton nectar exposures to okra flowers, only floral nectar was considered (*i.e.* neither cotton pollen, which was not honey bee attractive

or cotton extrafloral nectar, which okra does not produce were considered). The potential for colony-level risks is also identified for soil applications of imidacloprid to cucurbits, another herbaceous crop that is considered applicable to okra and roselle. When considering all lines of evidence and uncertainty in the aforementioned extrapolations of residue data within and across crop groups, the strength of evidence associated with foliar and soil applications of imidacloprid to okra and roselle is considered “moderate.”

6.2.10.3. Herbs and spices

Imidacloprid is registered for both foliar and soil applications to herbs and spices. Many members of herbs and spices are attractive to honey bees (*e.g.*, mint), although overall acreage is small relative to other crops. There is no restriction on the timing of imidacloprid application to herbs and spices relative to the bloom period and currently no SLUA information is available to characterize the usage of these crops. No studies on the magnitude of residues of any neonicotinoid in bee-relevant matrices of herbs and spices are available. Conclusions from all other herbaceous crops, including oilseed, cucurbit vegetables, legume crops, and, fruiting vegetables are used as a surrogate for herbs and spices. As stated previously in **Sections 6.2.5, 6.2.6, 6.2.10.2, and 6.2.10**, conclusions of risk are present for both foliar and soil applications to all other herbaceous crops therefore, the potential exists for colony-level effects to honey bees. However, the spatial scale is considered small relative to most agricultural crops. Furthermore, there is uncertainty in extrapolating residue information across crop groups. Therefore, considering these factors, the strength of evidence supporting the finding of a potential colony-level risk from applications to herbs and spices is considered “weakest.”

6.2.11. Crops not in a designated crop group

6.2.11.1. Foliar and Soil Applications

There are several uses of imidacloprid that are not associated with a crop group including coffee, artichokes, peanut, hops, and tobacco. In two of these cases, artichokes and tobacco, the crops are harvested before bloom so exposure to bees is expected to be minimal.

Table 6-37 shows the available SLUA data for these non-crop group associated use patterns along with available information on attractiveness.

Table 6-37. SLUA data imidacloprid and use patterns registered for additional foliar and soil use patterns (2004-2013) with no available residue data

| Crop Group Name | Use pattern | Lbs. Applied/yr. | % Acreage Treated (average) | % Acreage Treated (max) | Honey Bee Attractive? (Pollen or nectar) (Y/N) | Harvested Before Bloom? (Y/N) |
|-----------------|-------------|------------------|-----------------------------|-------------------------|--|-------------------------------|
| No Group | Artichokes | <500 | 15 | 60 | Y | Y |
| No Group | Sugarcane | <500 | <2.5 | <2.5 | N | -- |
| No Group | Tobacco | 10,000 | 25 | 40 | Y (pollen) | Y |

Generally speaking, all non-crop group members are registered for both foliar and soil applications. Restrictions for both types of applications during the pre-bloom and bloom period are present for coffee. Based on the residue bridging analysis (**Attachment 2**), residue data from orchard crops were used as a surrogate for coffee. Based on this analysis, the potential exists for colony-level effects to honey bees from post-bloom foliar and soil applications, although the strength of evidence is considered “weak” due to the complete lack of residue data. There are no restrictions relative to the bloom period for applications on artichokes, peanuts, hops, and tobacco, although as previously indicated artichoke and tobacco are harvested before the bloom period. Both hops and peanuts are considered honey bee attractive, but only for pollen. Based on the residue bridging analysis, residue data from pollen only fruiting vegetable crops were used as a surrogate for hops and peanuts. Based on this analysis, the potential exists for colony-level effects to honey bees. When considering the fact that foliar and soil applications are permitted with no restrictions relative to the bloom period, the timing of the application for use patterns would be important to consider (*i.e.* greater potential of risk if applications made pre or during bloom relative to post-bloom).

6.2.11.2. Seed treatment

The only crop not in a defined group and registered for seed treatment with imidacloprid is peanuts. **Attachment 4** also provides recommendations for residues for a Tier II assessment of seed treatments. **Table 6-38** includes the crop-specific recommended value. Seed treatments of imidacloprid on peanuts result in an exposure value that exceeds the imidacloprid CFS NOAEC. However, the strength of evidence is weak as the estimated residue is between the NOAEC and LOAEC (47 ng a.i./g) from the imidacloprid CFS, leading to uncertainty as to whether effects to the colony may occur.

Table 6-38. Tier II assessment for imidacloprid seed treatment of peanuts

| Crop | Tier II concentration (nectar equivalents) | Above IMI CFS NOAEC (23)? | Risk conclusion |
|---------|---|------------------------------|-----------------|
| Peanuts | 28 | Yes | Risk |

6.2.12. Non-Agricultural Crops

The non-agricultural crop group encompasses a wide variety of uses: ornamentals, forestry and residential turf. The risk characterization of these individual groups of plants is presented in the below.

6.2.12.1. Ornamental Uses

Imidacloprid is registered for applications to a diverse group of ornamental species using a variety of methods including foliar spray, broadcast granular, soil drench, and trunk injection in nurseries (grassy areas, field nurseries or containerized ornamentals), commercial properties and residential properties. For foliar and liquid soil applications, the maximum single and seasonal application rate is 0.4 lb ai/A with one application per year (4.6 g/m plant height) or 0.2 lb ai/A with two applications per year. For

broadcast granular applications, the maximum single and seasonal application rate is 0.4 lb ai/A with subsequent irrigation within 24 hours.

Usage data for forestry and ornamentals is limited. The USDA National Agricultural Statistics Service conducts surveys and prepares reports about chemical usage. According to a 2009 report on total usage of nursery and floriculture in the United States, there were 5,100 pounds of imidacloprid, used at an average application rate of 0.11 lb ai/A.

A summary of the lines of evidence considered in the characterization of risk to honey bees from foliar, soil, and trunk injection applications of imidacloprid to ornamentals is shown below in **Table 6-39**. For foliar applications to ornamentals, no imidacloprid-specific residue data were available. However, thiamethoxam residue data were available and considered suitable for bridging to imidacloprid. The thiamethoxam data (expressed as clothianidin equivalent concentrations and adjusted to the maximum imidacloprid application rate) indicate that residues in floral nectar exceed the colony level NOAEC for more than 23 days after the last application by a magnitude of up to **38X** the NOAEC. Residues in nectar from all three plant species assessed contained residues in nectar that exceed the imidacloprid colony-level LOAEC. Although there is uncertainty in extrapolating residues from the thiamethoxam study to those of imidacloprid, the finding of colony-level risk from pre-bloom or during bloom foliar applications is consistent with that observed from agricultural uses of imidacloprid. Furthermore, thiamethoxam residues are an order of magnitude greater than the NOAEC, which likely outweighs uncertainty associated with bridging residues across chemicals. Furthermore, there are multiple bee incidents associated with foliar applications of imidacloprid to ornamentals. Considering these factors, the strength of evidence associated with the potential for colony-level risk from foliar applications of imidacloprid to ornamentals is considered “strongest.”

For soil applications of imidacloprid, strong evidence of risk is indicated, based on floral nectar residues measured of imidacloprid in two species of bee-attractive ornamentals that exceed the colony-level NOAEC by a maximum of **37X** and by more than 600 days after application (**Table 6-39**). These findings are also supported by a supplemental study that demonstrates exceedance of the colony level NOAEC and LOAEC by three species of ornamentals by up to 540 days. Notably, some imidacloprid labels restrict applications to ornamentals during bloom or until after petal drop, which would reduce exposure considerably relative to conditions associated with these studies. Furthermore, there are multiple bee incidents associated with soil applications of imidacloprid to ornamentals. The strength of evidence is considered “strongest” based on the magnitude and duration of exceedance of the imidacloprid colony-level endpoints in addition to the occurrence of bee incidents involving soil applications of imidacloprid to ornamentals.

For trunk injection applications of imidacloprid, moderate evidence of risk indicates a potential for colony-level risk to honey bees foraging on treated fields. Specifically, there is only one supplemental imidacloprid residue study to estimate the risk from trunk injection applications; the utility of the study is low due to the limited temporal spacing of the sampling. The second sample was taken on day 10 and resulted in a maximum residue **2.3X** above the colony-level NOAEC. The third sample was taken 341 days later, and residues were barely detected; therefore, the duration for which the residues were above the NOAEC is unknown. The evidence of risk is supported by an additional registrant submitted

study measuring residues in cherry trees after a trunk injection application of dinotefuran. The bridged data show residues above the colony level NOAEC for 243 days after the last application by up to 52X the imidacloprid colony-level NOAEC. The strength of evidence is “moderate” because evidence of risk is demonstrated by a single time point within an imidacloprid study and extrapolated from the dinotefuran study based on limited data.

Multiple ecological incidents have been associated with imidacloprid applications to ornamental plants that span soil, foliar and injection methods (**Table 5-18**). These incidents were associated with follow-up investigations and/or residue data confirming the presence of imidacloprid in plant or bee matrices. Of these, two were classified as misuses of the product while the remaining incidents (approximately 6) were classified as registered or unknown incidents. Both honey bees and bumble bees were among the bee species affected.

One important attribute to consider when interpreting risks associated with ornamentals is the extent to which bees are likely to forage exclusively on treated plants. Aside from the attractiveness of the ornamental, the extent to which treated ornamentals comprise the dominant food source for a given colony is likely to be highly variable. For example, in residential settings, the spatial and temporal scale associated with treated ornamental plants is likely to be highly fragmented. Thus, it is highly unlikely that ornamental plants will be treated at the same time across the foraging range of honey bees. The highly opportunistic nature of honey bee foraging further complicates interpretation of residues from ornamental plants for risk assessment.

Table 6-39. Lines of evidence in characterizing colony-level risk to honey bees from foliar and soil applications of imidacloprid to ornamentals

| Line of evidence | | Foliar Applications (Strongest Evidence of Risk) | | Soil Applications (Strongest Evidence of Risk) | | Trunk Injection (Moderate Evidence of Risk) | |
|---|---|--|---------------|--|---------------|---|-------------|
| Imidacloprid-specific residue data (Quantitative) | | No data | | Holly, Sweet Pepperbush | | No data | |
| Residue data for other chemicals | | Stargazer Lily (T) Mock Orange (T) Lilac (T) | | Lilac (T) Hedge Cotoneaster (T) Crabapple (T) Stargazer Lily (T) Holly, Pepperbush (D) | | Cherry (D) | |
| Measured data for IMI | Exceedance attribute | NOAEC | LOAEC | NOAEC | LOAEC | NOAEC | LOAEC |
| | Frequency: Number daily mean residue values > NOAEC & LOAEC | No data | No data | 9/10 | 9/10 | No data | No data |
| | Duration: Number of days > NOAEC & LOAEC | No data | No data | 619 | 619 | No data | No data |
| | Magnitude: Ratio of max to NOAEC & LOAEC ⁽¹⁾ (% of diet required to reach NOAEC & LOAEC) | No data | No data | 37X (3.7%) | 18X (5.6%) | No data | No data |
| Measured data for other Neonicotinoids | Frequency: Number daily mean residue values > NOAEC & LOAEC | 18/21 | 16/21 | 9/33 | 8/33 | 9/9 | 8/9 |
| | Duration: Number of days > NOAEC & LOAEC | 21 | 21 | 23 | 23 | 243 | 243 |
| | Magnitude: Ratio of max to NOAEC & LOAEC (% of diet required to reach NOAEC & LOAEC) | 38X (2.6%) | 19X (5.4%) | 12X (8%) | 6X (17%) | 52X (2%) | 25X (4%) |
| Crop attractiveness ⁽¹⁾ | Attractive or highly attractive | | | | | | |
| Managed pollinators ⁽¹⁾ | No | | | | | | |
| Incidents | Multiple incidents associated with soil, foliar and injection applications of imidacloprid have been reported with ornamental plants, mostly involving flowering trees. Imidacloprid was confirmed in plant or bee matrices in most of these incidents. | | | | | | |
| Spatial extent of risk (acres treated) | No usage information available | | | | | | |
| Additional Considerations | Supplemental data indicates high residues (100 to 1000 ug ai/kg) of imidacloprid are detected in nectar of Rhododendron, Shadbush & Cornelius Cherry following soil drench application adjusted to the maximum rate of 4.6 g a.i./m plant height (MRID 47303402, 47303403, 47303404, 47303405, 47303406, 47303407, 47303412). Supplemental data for trunk injection also indicates exceedance of the imidacloprid colony-level endpoints. | | | | | | |

⁽¹⁾Based on USDA 2017

Foliar Applications to Ornamentals

Registrant submitted studies are not available to estimate the residues in ornamentals after foliar applications of imidacloprid. Therefore, thiamethoxam ornamental data (MRID 50425903) is used to assess risk in accordance with the non-agricultural residue bridging analysis (**Attachment 3**). The thiamethoxam data (expressed as clothianidin equivalents and normalized to the maximum application rate of 0.4 lb a.i./A for imidacloprid) are summarized in **Figure 6-24**. Based on the normalized thiamethoxam data, residues in ornamentals are greater than the imidacloprid colony level NOAEC up to at least 21 days and by a factor of up to **38X**. A high frequency of exceeding the NOAEC and LOAEC is also indicated. Residues in nectar from all three plant species assessed contained residues in nectar that exceed the imidacloprid colony-level LOAEC. Notably, some imidacloprid labels restrict applications to ornamentals during bloom or until after petal drop, which would reduce exposure considerably relative to conditions associated with the thiamethoxam study.

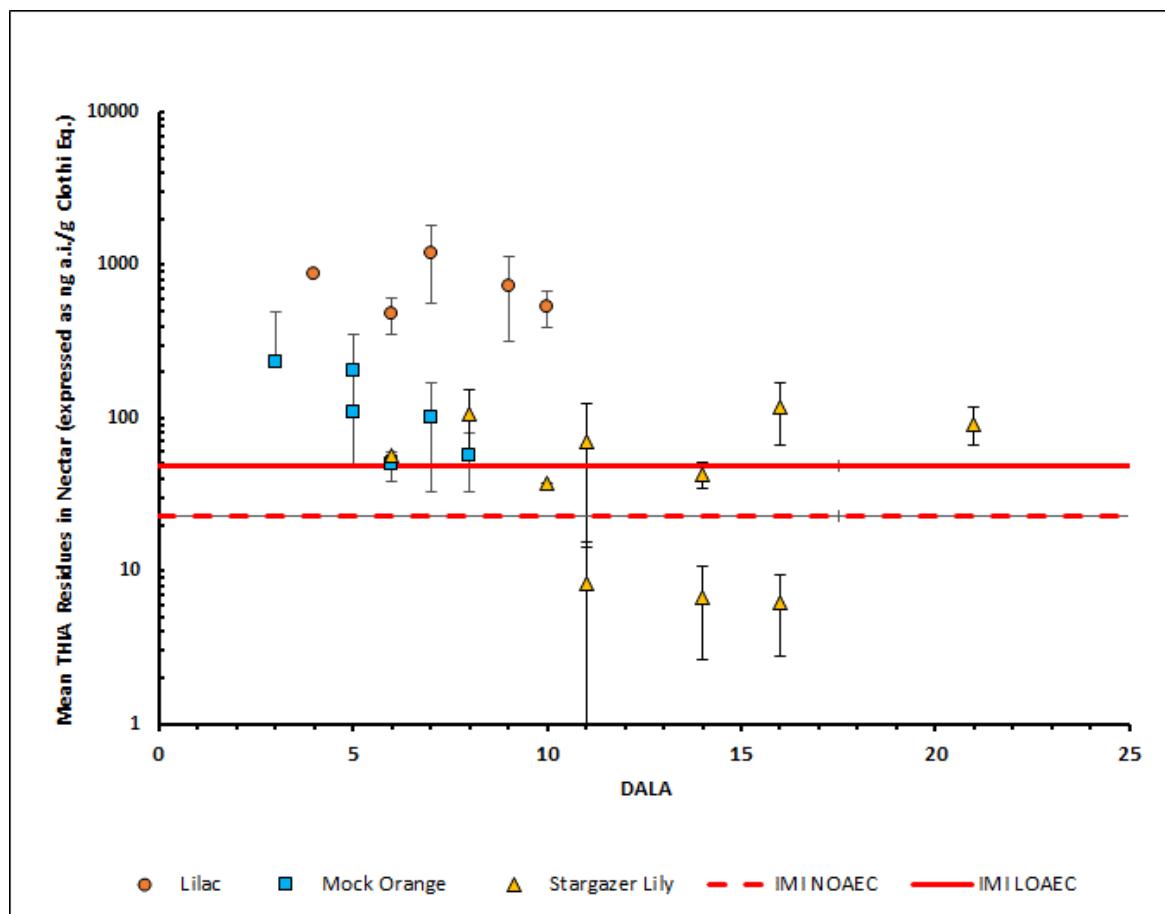


Figure 6-24. Mean residue concentrations in nectar, expressed as Clothi equivalents, following foliar application of thiamethoxam to ornamental plants (MRID 50425903). Data are normalized to the maximum imidacloprid application rate of 0.4 lb ai/A.

Soil Drench Applications to Ornamentals

An open literature study by Mach et al. (2017; MRID 51037901) reported residues of total imidacloprid in nectar and leaves of a broadleaf evergreen tree (foster holly) and a deciduous shrub (sweet pepperbush; **Figure 6-25**). Both plants produce flowers that are attractive to honey bees. Raw data was obtained for this study and it is classified as acceptable for quantitative use in risk assessment. In the study, plants were treated with Merit 2F at a rate of 1.06 g/ 0.305 m of plant height (3.48 g/m height), representing 73.6% of the maximum labeled rate, via simulated soil injection. Applications were made late post-bloom (autumn), pre-bloom (spring), or early post-bloom (summer) to evaluate the impact of application timing on residues. Residue measurements were taken over the course of a 2-year sampling window to evaluate the persistence of imidacloprid in plant tissues. Nectar was extracted from flowers. Due to variable bloom times, each nectar harvest required several days to collect sufficient material for analysis. As a result, pollen samples were taken on different days compared to nectar, preventing combining to a nectar equivalent concentration. Therefore, only residues in nectar are summarized from this study.

When normalized to the slightly higher maximum application rate of 4.6 g/m plant height, concentrations in nectar following autumn or spring applications ranged from 51 to 845 µg a.i./kg, depending on the plant or application timing. Concentrations in nectar following summer applications were lower (12-78 ng a.i./g). Measured residues exceed the colony level NOAEC for imidacloprid for spring (pre-bloom) and summer (early post-bloom) applications. This suggests that residues in woody species from soil applications are sufficiently elevated to pose risks to honey bees foraging on them, even the following season.

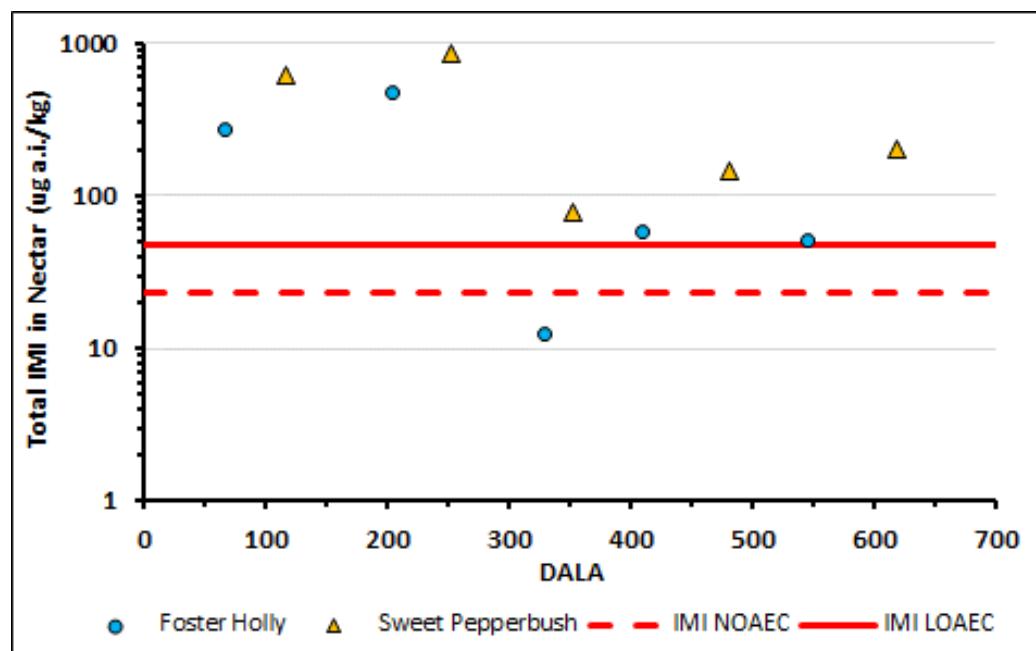


Figure 6-25. Mean residue of total imidacloprid in nectar following soil application to two ornamental shrubs (Mach et al. 2017). Data are normalized to the maximum application rate of 4.6 g a.i./m.

Multiple registrant-submitted studies were submitted regarding soil drench applications of imidacloprid to three ornamental species (rhododendron, shadbush, and Cornelius cherry; MRID 47303402, 47303403, 47303404, 47303405, 47303406, 47303407, 47303412). These studies, however, are classified as supplemental due to the limitations in their study design and supporting documentation of quality control procedures. Although not considered sufficiently robust for quantitative use in risk assessment, residue data from these studies do suggest relatively high residues of total imidacloprid in nectar can result from soil drench applications for more than 1 year after application (

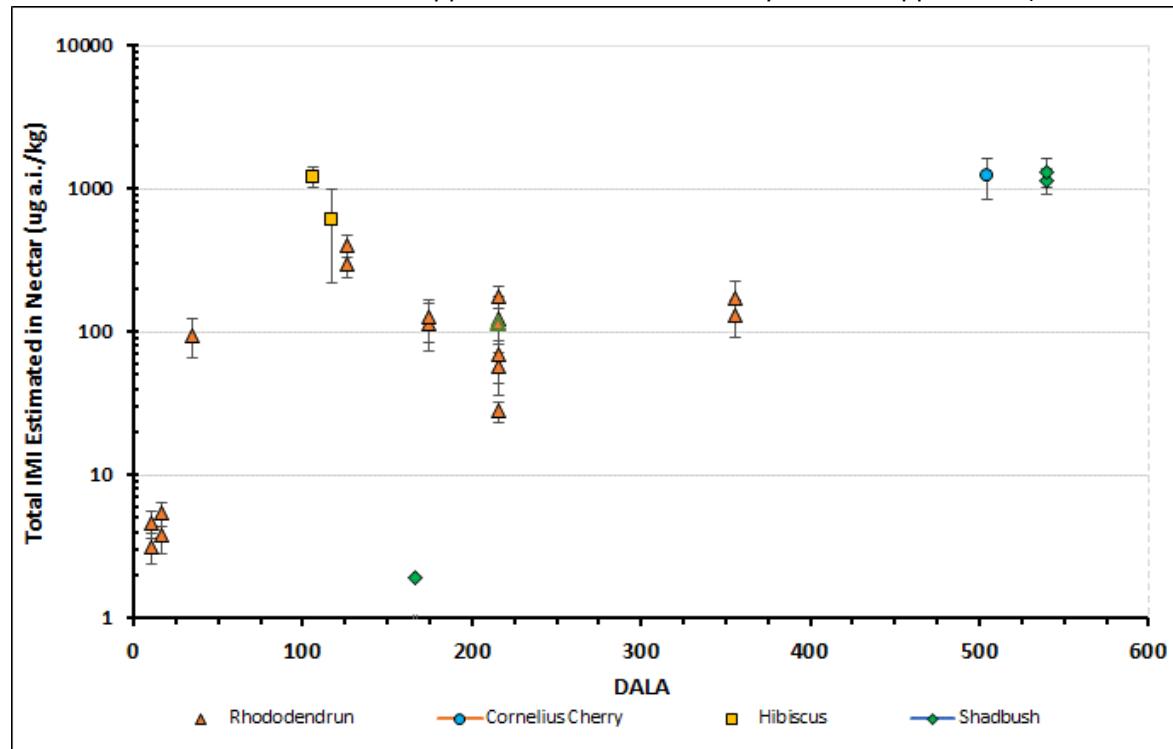


Figure 6-26). The highest residues were observed for hibiscus, Cornelius cherry and shadbush with concentrations approximating 1,000 ug a.i./kg nectar. Additional registrant-submitted data (also supplemental) were submitted for soil drench applications to the horse chestnut, lime tree, and apple tree (MRID 47303408, 47303410, 47303411). However, insufficient information was available to normalize residue concentrations to maximum labeled application rates.

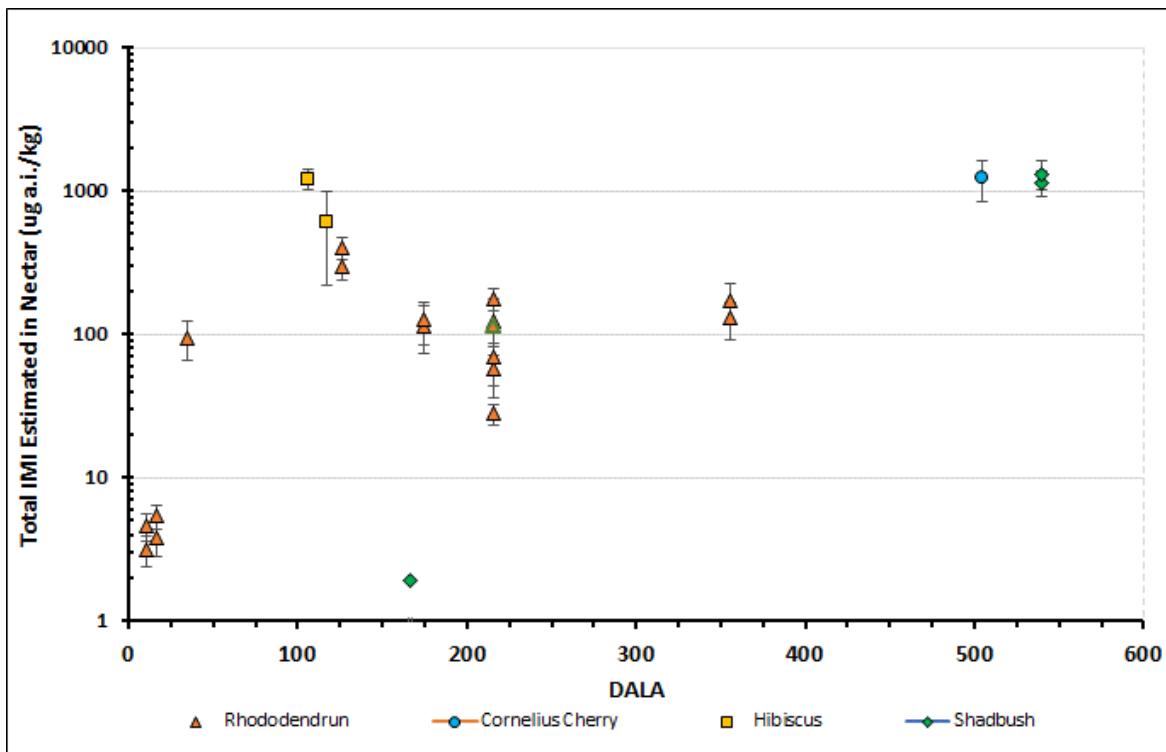


Figure 6-26. Mean residue concentrations (95% C.L.) in nectar of three ornamental plants following soil drench application of imidacloprid. Data are from multiple supplemental studies and are normalized to a maximum rate of 4.6 g/m plant height.

Ornamental residue data from soil application that are considered suitable for quantitative use in risk assessment are available for thiamethoxam (MRID 47303407). Based on the residue bridging analysis presented in **Attachment 3**, the thiamethoxam ornamental data are used to strengthen the weight of evidence in the risk characterization for soil applications of imidacloprid to ornamentals. Specifically, nectar residues (expressed as clothianidin equivalents) in ornamentals are greater than the colony level NOAEC up to at least 23 days for imidacloprid when normalized to the maximum application rate of 0.4 lb ai/A (**Figure 6-27**). The highest residues were for lilac and hedge cotoneaster which approached 30X the NOAEC, while residues in mock orange and stargazer lily are more variable but generally below the colony-level NOAEC for imidacloprid. These data suggest that residues from soil applications to ornamentals are sufficient to pose a colony-level risk to honey bees.

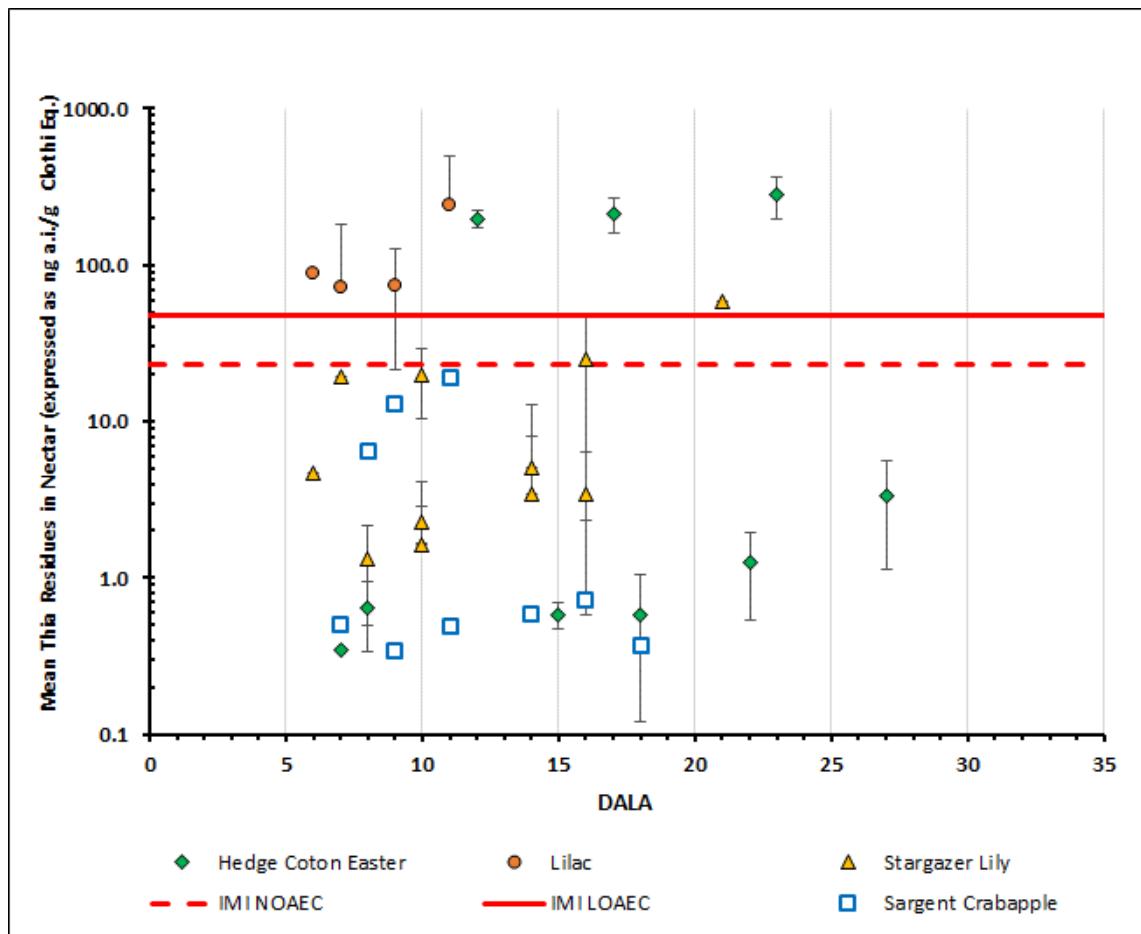


Figure 6-27. Mean residue concentrations in nectar, expressed as Clothi equivalents, following soil drench application of thiamethoxam to ornamental plants (MRID 50425903). Data are normalized to the maximum imidacloprid application rate of 0.4 lb ai/A.

Trunk Injection Applications to Ornamentals

Registrant submitted data are available for trunk injection applications to horse chestnut (47303409; 47303414), however this study is considered supplemental and is used qualitatively only. **Figure 6-28** presents the mean measured residues estimated in nectar of horse chestnut following an application of imidacloprid via trunk injection normalized to a maximum rate of 0.09 g/cm trunk diameter in May. As with the soil drench imidacloprid studies, residue data were available for flower only; therefore, nectar was estimated by multiplying flower residues by a factor of 0.3 (**Attachment 2**). Due to the paucity of data available from this study, it is difficult to make firm conclusions regarding the concentrations of imidacloprid estimated in nectar of horse chestnut following trunk injection.

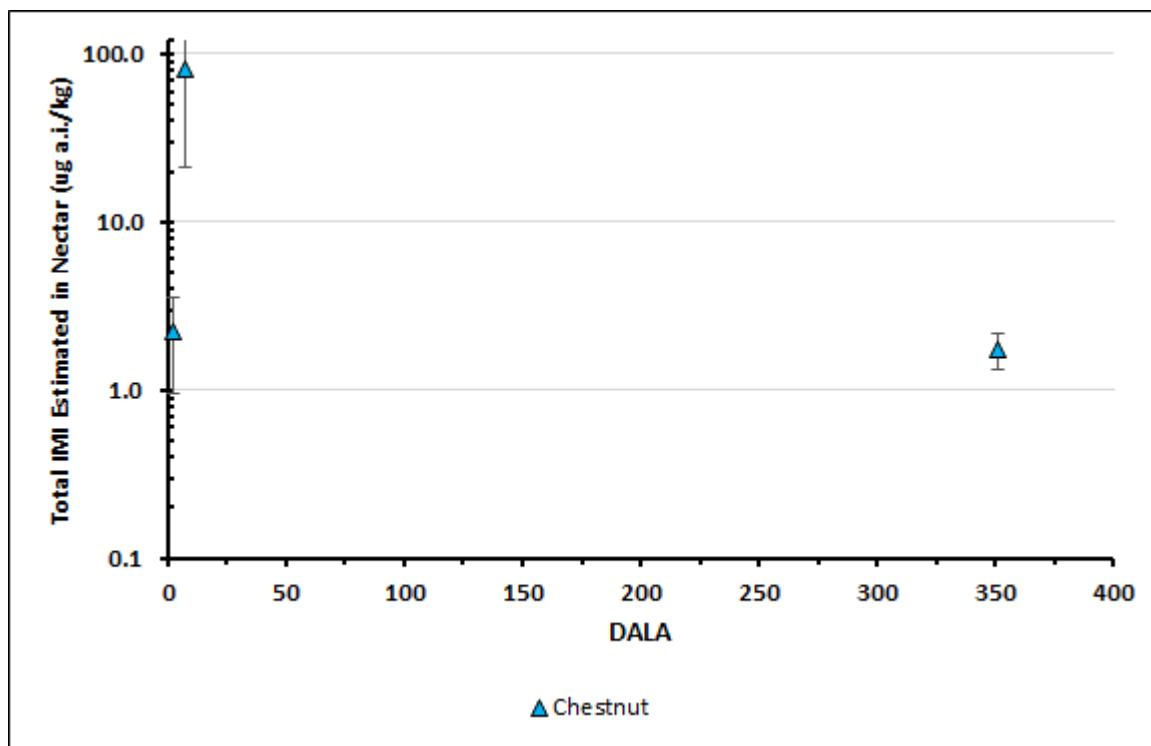


Figure 6-28. Mean residue concentrations, expressed in terms of nectar equivalents following trunk injection of total imidacloprid to horse chestnut trees normalized to max app rate of 0.09 g/cm trunk diameter.

Additional tree injection data is available for dinotefuran (Figure 6-29) which are considered acceptable for quantitative use in risk assessment. Based on the residue bridging analysis presented in Attachment 3, the dinotefuran data are used to strengthen the weight of evidence in the risk characterization for trunk injection applications of imidacloprid to ornamentals. These data show an additional line of evidence for risk of imidacloprid trunk injections. Similar to the imidacloprid data, the sampling dates limit the utility of the residue data. It is unknown how long the residues persist above the NOAEC and whether or not they continue to increase after the last sampling event. However, the data do show that residues from trunk injection may pose a colony-level risk to honeybees after explanation, extending to 243 days after the application.

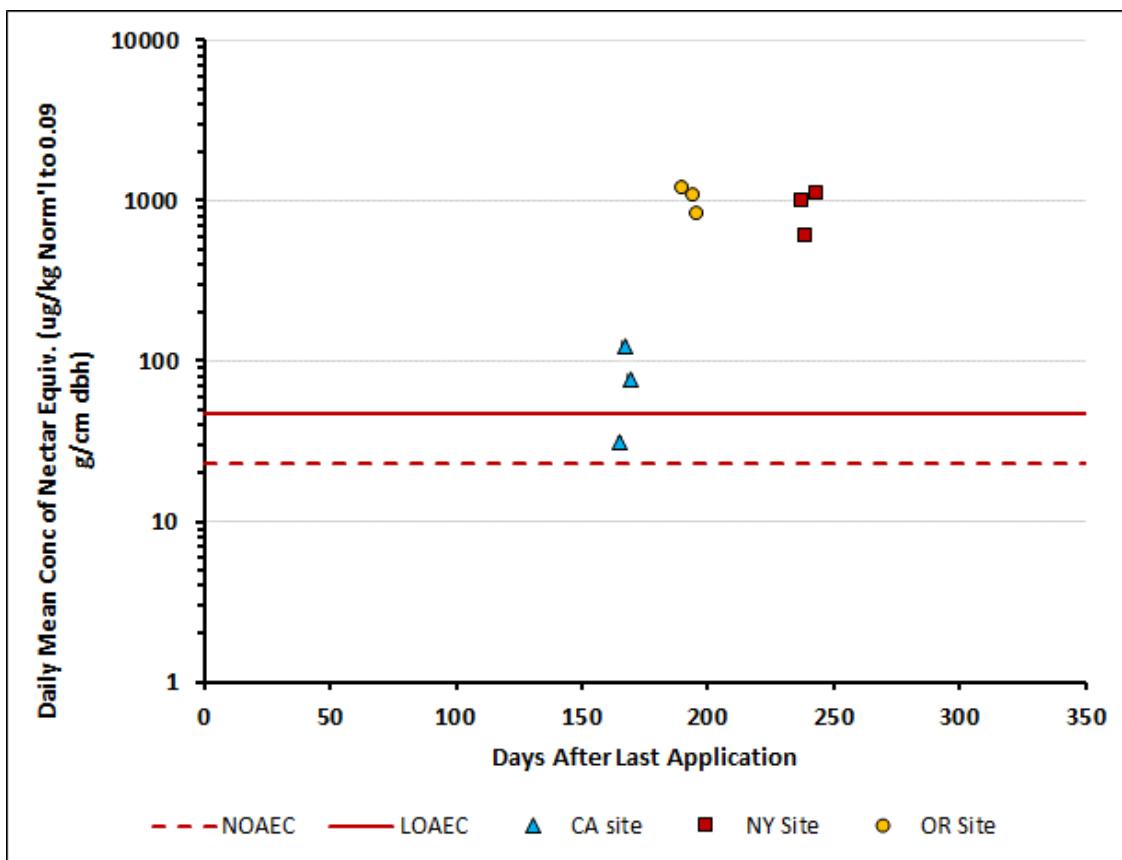


Figure 6-29. Mean residue concentrations expressed in terms of nectar equivalents following trunk injection dinotefuran to the cherry tree normalized to the max app rate of 0.09 g/cm trunk diameter

6.2.12.2. *Forestry Uses*

Imidacloprid is also registered for applications to a diverse group of forestry species using a variety of methods including foliar spray, broadcast granular, soil drench and trunk injection in wooded areas, nurseries, or tree plantations. For liquid foliar applications, the maximum single application rate is 0.1 lb ai/A with 5 applications, resulting in a maximum seasonal application rate of 0.5 lb ai/A. For soil applications, the maximum single and seasonal application rate is 0.5 lb ai/A with subsequent irrigation within 24 hours. Trunk injection applications for both ornamentals and forestry have a maximum single and seasonal application rate of 0.9 g/10 cm.

No registrant studies or open literature studies were available to estimate the bee-relevant residues for imidacloprid or other neonicotinoids following application to trees in a forest setting. Therefore, woody ornamentals are used as a surrogate for trees registered for forestry uses.

The maximum seasonal application rate for forestry for foliar and soil applications (0.5 lbs ai/A) is higher than the maximum seasonal application rate for ornamentals (0.4 lb ai/A). Therefore, the potential for colony-level risk associated with woody ornamentals (*e.g.*, Mach et al., 2017; MRID 51037901) is considered applicable to honey-bee attractive forest species.

6.2.12.3. Turf Uses

Imidacloprid is registered for applications to commercial and residential turfgrass using a variety of methods including foliar spray and broadcast granular applications. Maximum single and seasonal application rate is 0.5 lb ai/A with subsequent irrigation within 24 hours and/or mechanical incorporation to move the chemical into the root zone (**Appendix A of USEPA 2017**). Usage information is not available for residential or commercial turf uses of imidacloprid.

Although turfgrass itself is not attractive to honey bees and other non-*Apis* bees, flowering weeds such as clover and dandelions are commonly distributed among turfgrass and are considered attractive to bees. For commercial turfgrass production (e.g., sod farms), agronomic practices including mowing and broadleaf weed control greatly limit the presence of blooming weeds to the point of complete eradication. Therefore, oral exposure of bees through applications of imidacloprid to commercial turfgrass is not considered a likely exposure route of concern. For residential turfgrass applications, the presence of flowering weeds which are attractive to bees cannot be reasonably precluded, since weed control practices vary widely among homeowners and commercial lawncare practices. Therefore, a reasonable potential exists for exposure of bees to imidacloprid applications to residential turfgrass.

Registrant-submitted residue data on imidacloprid in blooming weeds associated with turfgrass application were not available for assessing oral risks to bees. However, one open literature study was available which quantified residues of imidacloprid (and clothianidin) in white clover following application to turfgrass (Larson *et al.* 2015 Larson et al. (2015; MRID 51026401). In their study, Larson *et al.* (2015) quantified residues of imidacloprid in nectar of white clover following a single application of 0.4 lb ai/A (MERIT® 75 WSP) liquid formulation. Separate trials were conducted in June and August 2013 (4 replicates per trial) in which applications were made during bloom of clover in the turfgrass. Residues of imidacloprid (parent only) were measured in nectar 1 day after application and again 21 days later in newly blooming clover after mowing (**Table 6-40**). This study is classified for qualitative use in risk assessment due to limitations with the raw data provided for independent analysis³⁰.

Results from Larson el al (2015) indicate relatively high levels of imidacloprid residues occur in clover nectar 1 day after receiving direct foliar spray application (**Table 6-40**). Mean residues in 2 trials ranged from approximately 5,500 to 6,600 µg/kg, which exceeds the colony level NOAEC and LOAEC for imidacloprid by **100X**. However, 21 days later, mean residues of imidacloprid in nectar of newly bloomed clover after mowing were much lower (8-26 µg/kg). Since residues were not measured in between these times, the duration of exceedance of the NOAEC and LOAEC is not known with precision. Notably, concentrations of clothianidin, applied at the same application rate as imidacloprid, are within 2X of imidacloprid during both sampling times. This finding suggests that the uptake and translocation of imidacloprid and clothianidin in white clover are comparable, which is consistent with their similar physicochemical and fate properties.

As an indication of the potential hazard of the clover nectar to bees, these authors conducted a subsequent bioassay by feeding this same nectar to the Insidious Flower Bug, *Orius insidiosus*. Honey

³⁰ Although raw data on residue measurements provided by the study author confirm the reported residue values, data provided on analytical QA/QC were incomplete.

bees were not used in the bioassay due to insufficient nectar volume. Results from their bioassay indicate a significantly increase in % mortality of *O. insidiosus* (> 90%) after 24 hours feeding on nectar which was collected 1-d after direct application. Mortality in controls was 20% after 24 hours. However, when *O. insidiosus* was fed nectar collected 21 days after application on newly blooming clover, mortality was not significantly different from controls (20-30%). These results from the residue measurements suggest that imidacloprid residues in nectar of blooming weeds measured immediately following foliar turfgrass application greatly exceed levels associated with individual and colony level effects in honey bees. Acute toxicity was also noted on an insect species when fed this same nectar. However, the duration of exceedance of the colony level NOAEC is not known with precision, but it appears to approximate 21 days or less when clover is mowed. Therefore, there is uncertainty when comparing these results to those of the colony level feeding study which involved a 6-week exposure. No ecological incidents involving impacts to bees from applications of imidacloprid to turf have been reported. In considering these lines of evidence and associated uncertainties, “moderate” strength of evidence supports the conclusion that applications of imidacloprid to residential turf (in the presence of blooming weeds) present a potential colony-level risk to honey bees.

Table 6-40. Summary of imidacloprid and clothianidin residues in white clover nectar following foliar applications to turfgrass

| Species | App Method | App rate | Application Timing | Measurement DALA | Conc. in Nectar ($\mu\text{g ai/kg}$) ⁽¹⁾ | Conc. in Pollen ($\mu\text{g ai/kg}$) | Reference (Classification) |
|--|------------|----------------------------|--------------------|--|--|---|--|
| IMIDACLOPRID | | | | | | | |
| <i>Kentucky Blue Grass & Tall Fescue with 30% White Clover (<i>Trifolium repens</i>)</i> | Foliar | 0.4 lb ai/A (MERIT 75 WSP) | June 3 Aug 15 | 1 1 | 5,493 \pm 1040 6588 \pm 752 | NA | <i>Larson et al. (2015); MRID 51026401 (Qualitative)</i> |
| | | | June 3 Aug 15 | 21 (after mowing) 21 (after mowing) | 8.4 \pm 2.2 26 \pm 10 | NA | |
| CLOTHIANIDIN | | | | | | | |
| <i>Kentucky Blue Grass & Tall Fescue with 30% White Clover (<i>Trifolium repens</i>)</i> | Foliar | 0.4 lb ai/A (ARENA 5 WDG) | June 3 Aug 15 | 1 1 | 2,992 \pm 541 2882 \pm 228 | NA | <i>Larson et al. (2015); MRID 51026401 (Qualitative)</i> |
| | | | June 3 Aug 15 | 21 (after mowing) 21 (after mowing) | 6.2 \pm 2.1 18 \pm 15 | NA | |

⁽¹⁾ mean \pm SE (n=4). Parent imidacloprid only

6.3. Risk Characterization of Non-*Apis* Bees

Consistent with the Agency’s 2014 risk assessment guidance for bees, the preliminary risk assessment of registered agricultural uses of imidacloprid focuses on the honey bee, *A. mellifera*. This *Apis*-centric focus reflects two important considerations: 1) honey bees are widely recognized as the most important

managed pollinator in most regions of the world from both a commercial and ecological perspective;³¹ and 2) standardized test methods for evaluating exposure and effects of chemicals in a regulatory context are much more developed with the honey bee compared to non-*Apis* bees (USEPA *et al.* 2014; USEPA 2012³²), although recent progress has been made on test method development for bumble bees³³. Nonetheless, within North America alone, there are an estimated 4,000 species of bees (Michener 2007) and this number rises to more than 20,000 worldwide (Fischer and Moriarty 2014). 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*), and blue orchard bees (*Osmia lignaria*), and the Japanese horn-faced bee (*O. cornifrons*). Importantly, a growing body of information indicates native bees (in addition to other insect pollinators such as flies, moths, butterflies, beetles, wasps, and ants) play an important role in crop and native plant pollination, besides their overall ecological importance via maintaining biological diversity. Although the current risk assessment process for bees does not include a formal process that is specific to non-*Apis* bees, available data related to the potential exposure of non-*Apis* bees to imidacloprid and subsequent effects are summarized here in relation to the previously described risk assessment for the honey bee.

6.3.1. Exposure Considerations

Several aspects of the biology and ecology of non-*Apis* bees lead to important differences in the route and extent to which they may be exposed to pesticides compared to honey bees. These aspects have been reviewed previously (EFSA 2012, Fisher and Moriarty 2014) and are summarized here briefly. Specifically, many non-*Apis* bees are smaller in size and thus, would receive a higher dose on a contact exposure basis (*i.e.*, greater surface area to volume ratio) via intercepting droplets of sprayed pesticide. Most non-*Apis* bees are solitary nesting species³⁴ and therefore, loss of a single nesting adult would have a much greater consequence on reproduction (at least for that nest) compared to the loss of a single adult foraging honey bee. Furthermore, the foraging range of non-*Apis* bees tends to be much smaller than that of honey bees. As a consequence, non-*Apis* bees that occupy areas adjacent to treated fields may be exposed to pesticides at a higher proportion of their foraging area compared to honey bees, which can forage over long distances (~7 km) in which they are more likely to encounter untreated forage areas. For ground nesting bees, exposure via direct contact with soil may be a major route of exposure unlike that for the honey bee. Soil and leaf material are known to be used extensively by some non-*Apis* bees for nest construction, which may lead to different types of exposures (*e.g.*, prolonged contact exposure with contaminated residues on treated foliage).

³¹ According to Tautz, J. (2008), approximately 80% of the world's flowing plants are pollinated by insects and 85% of these by honey bees. In all, the list of flowering plants pollinated by honey bees includes 170,000 species.

³² USEPA. 2012. White Paper in Support of the Proposed Risk Assessment Process for Bees. Submitted to the FIFRA Scientific Advisory Panel for Review and Comment September 11 – 14, 2012. Office of Chemical Safety and Pollution Prevention Office of Pesticide Programs Environmental Fate and Effects Division, Environmental Protection Agency, Washington DC; Environmental Assessment Directorate, Pest Management Regulatory Agency, Health Canada, Ottawa, CN; California Department of Pesticide Regulation <http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0543-0004>

³³ Compilation of results of the ICPPR non-*Apis* working group with a special focus on the bumble bee acute oral and contact toxicity ring test 2014 ICPPR Non-*Apis* Working Group. Available at: <http://pub.jki.bund.de/index.php/JKA/article/view/5352>

³⁴ Colonies of the social non-*Apis* bees (*e.g.*, bumble bees and stingless bees) tend to be smaller than honey bees.

To investigate the extent to which exposure estimates for honey bees may serve as a surrogate for non-*Apis* bees, comparisons were made in the daily consumptions rates of pollen and nectar available from the literature as compiled by EFSA (2012). Although there are a number of uncertainties associated with these consumption estimates, the data in **Table 6-41** and **Table 6-42** suggest that proposed food consumption rate for adult honey bee workers (292 mg/bee/day) is similar to that for adult bumble bee (210-402 mg/bee/day) and is greater than that of adult female European mason bee and alfalfa leaf cutting bees (45-193 and 110-165 mg/bee/day, respectively). Food consumption rates estimated for 5-day old honey bee larvae (120 mg/bee/day) are greater than rates for larvae of the other non-*Apis* bees (7.8-83 mg/bee/day). These data suggest that the Tier I exposure assessment conducted for oral ingestion of imidacloprid by adult honey bees would be representative (and generally protective) for adults of these particular non-*Apis* bees. However, it is noted that unlike honey bee larvae which are fed processed pollen and nectar in the form of bee bread, larvae of bumble bees and other non-*Apis* bees consume pollen and nectar directly which may lead to differential exposure relative to *Apis* larvae.

Table 6-41. Comparison of oral exposure to pollen and nectar for adult *Apis* and Non-*Apis* bees¹

| Species | Nectar consumption rate (mg/bee/day)* | Pollen consumption rate (mg/bee/day) | Total food consumption rate (mg/bee/day) |
|---|---------------------------------------|--------------------------------------|--|
| Honey bee worker (<i>A. mellifera</i>) | 292 | 0.04 | 292 |
| Bumble bee (<i>Bombus spp.</i>) | 183-372 | 27-30 | 210-402 |
| European mason bee (<i>Osmia cornuta</i>) | 45-193 | N/A | 45-193 |
| Alfalfa leaf-cutting bee (<i>Megachile rotundata</i>) | 110-165 | N/A | 110-165 |

¹From EFSA (2012); N/A = not applicable

Table 6-42. Comparison of oral exposure to pollen and nectar for larval *Apis* and Non-*Apis* bees¹

| Species | Male/female | Nectar consumption rate (mg/bee/day) * | Pollen consumption rate (mg/bee/day) * | Total food consumption rate (mg/bee/day) |
|---|-------------|--|--|--|
| Honey bee (<i>A. mellifera</i>) | Female | 117 | 2.7 | 120 |
| Bumble bee (<i>Bombus spp.</i>) | unknown | 60 | 22-23 | 82-83 |
| European mason bee (<i>Osmia cornuta</i>) | Female | 1.8 | 16.3 | 18 |
| | Male | 1.1 | 9.5 | 11 |
| Alfalfa leaf-cutting bee (<i>Megachile rotundata</i>) | Female | 6.2 | 3.1 | 9.3 |
| | Male | 5.2 | 2.6 | 7.8 |

¹ From EFSA (2012); * = from stored provisions

As discussed previously, non-*Apis* bees are expected to have contact exposure to pesticides via soil and plant material used for nest construction. For the European mason bee, contact exposure to mud by adult females has been estimated at 200 – 400 mg/bee/day. Similarly, contact exposure of alfalfa leaf cutting bees has been estimated at 173 mg/bee/day. Due to the limitations in available data, the current

risk assessment process for honey bee does not address exposure via soil and foliar contact exposure which are likely more important for some non-*Apis* bees.

Another important aspect to consider regarding the potential exposure of non-*Apis* bees to imidacloprid is the extent to which they are attracted to agricultural crops to which it is registered for use. Based on a recent compilation of crop attractiveness ratings for *Apis* and non-*Apis* bees (USDA 2017), bumble bees are classified as being as (or more) attracted to the crops registered for imidacloprid use as honey bees. For certain crops (*e.g.*, tomatoes, blueberries), bumble bees are commercially managed to provide pollination services (although tomato pollination primarily occurs in greenhouses).

6.3.2. Toxicity Considerations

6.3.2.1. Tier I (Organism) Level

In this section, Tier I (organism level) toxicity data for *Apis* and non-*Apis* bees are compared in order to evaluate the relative sensitivity of *Apis* and non-*Apis* bees to imidacloprid. Details of the studies from which these data were obtained are described earlier in **Section 5.1**. Based on these data, the overall range of acute contact toxicity is summarized below in **Table 6-43** for *Apis* and non-*Apis* bees. While data for non-*Apis* bees are far less abundant compared to *Apis* bees and uncertainties have been noted previously related to the conduct of these studies, the acute contact toxicity of imidacloprid to non-*Apis* bees (0.02 – 0.66 µg a.i./bee) appears to be within the lower bound of that observed with *Apis* bees (0.013 – 0.24 µg a.i./bee), when considering all formulation types and data sources.

Table 6-43. Comparison of imidacloprid acute contact toxicity to *Apis* and non-*Apis* bees

| Species | Source | Formulation | LD ₅₀ Range (µg a.i./bee) | n |
|--|--------------------------------|-------------|--------------------------------------|----|
| Honey bee (<i>A. mellifera</i>) | Registrant submitted | TGAI | 0.043 – 0.10 | 5 |
| Honey bee¹ (<i>A. mellifera</i>) | Open literature | TGAI | 0.013 – 0.23 | 11 |
| Honey bee¹ (<i>A. mellifera</i>) | Registrant and open literature | TEP | 0.03 – 0.24 | 4 |
| Bumble bee (<i>Bombus terrestris</i>) | Open literature | TEP | 0.02 | 1 |
| Japanese orchard bee (<i>Osmia cornifrons</i>) | Open literature | TEP | 0.66 | 1 |
| Stingless bee (<i>Melipona quadrifasciata</i>) | Open literature | TEP | 0.023 | 1 |

¹ includes subspecies *carnica* and *caucasica*.

Value in **bold** indicates the LD₅₀ used in to assess risks to the honey bee. Data sources are described in **Section 5.1**. Non-definitive (>) values are excluded from this table.

The overall range in acute oral toxicity of imidacloprid to *Apis* and non-*Apis* bees is summarized below in **Table 6-44**. For non-*Apis* bees, only two definitive LD₅₀ values were available for *B. terrestris*. While

again the availability of data for non-*Apis* bees is extremely limited, these data also suggest that at an organism level, the acute oral toxicity of imidacloprid to *B. terrestris* is well within the ranges observed for *A. mellifera*. Therefore, at least for the few non-*Apis* bee species for which comparative toxicity data are available, the Tier I assessment conducted for the honey bee appears to be reasonably representative of these currently tested non-*Apis* species.

Table 6-44. Comparison of imidacloprid acute oral toxicity to *Apis* and non-*Apis* bees

| Species | Source | Formulation | LD ₅₀ Range (µg a.i./bee) | n |
|---|--------------------------------|-------------|--------------------------------------|---|
| Honey bee (<i>A. Mellifera</i>) | Registrant submitted | TGAI | 0.0039 – 0.15 | 3 |
| Honey bee¹ (<i>A. Mellifera</i>) | Open literature | TGAI | 0.0037 – 0.54 | 7 |
| Honey bee¹ (<i>A. Mellifera</i>) | Registrant and open literature | TEP | 0.011 – 0.19 | 8 |
| Bumble bee (<i>Bombus terrestris</i>) | Registrant and open literature | TEP | 0.02-0.17 | 2 |

¹ includes subspecies *carnica* and *caucasica*.

Value in **bold** indicates the LD₅₀ used in to assess risks to the honey bee. Data sources are described in **Section 5.1**. Non-definitive (>) values are excluded from this table.

6.3.2.2. Tier II (Colony Level)

Data concerning the effects of imidacloprid on non-*Apis* social bees are available for only the bumble bee (*B. terrestris* or *B. impatiens*); however, these data are relatively plentiful (2 tunnel studies and 8 feeding studies; **Table 5.2**). For various reasons described in **Section 5.2** including lack of raw data to verify statistical endpoints, these data are considered only for qualitative use in this risk assessment. When evaluating the effects of pesticides on bumble bees at the colony level, it is important to consider the differences in biology with respect to honey bees. Specifically, bumble bee colonies do not survive over wintering, rather only queens overwinter and are available for propagation in the following spring. Although the science behind pesticide risk assessment with bumble bees is still evolving,³⁵ a clearly important consideration with respect to maintaining the stability of bumble bee populations is the production and propagation of queens; however, this is true for honey bee colonies as well even though the queen is not alone.

With respect to the tunnel studies in which application of a formulated product to a surrogate crop is evaluated, only data from Gels (2000; MRID 47796308) are considered informative for risk characterization. In this study, Gels (*ibid*) reported statistically significant reductions (60%) in number of workers and brood chambers (72%) of tunneled *B. impatiens* colonies 28-days after spray applications of 0.3 lbs. a.i./A of Merit® 75 WP to turf containing flowering white clover. Interestingly, statistically-significant effects were not observed following application of granular Merit® 0.5 G (0.4 lbs. a.i./A) to turf nor when irrigation immediately followed the aforementioned spray application. However, the

³⁵ <http://pub.jki.bund.de/index.php/JKA/issue/view/1087>

statistical power of this study appears low due to the small sample size such that reductions of up to 70% were not statistically significant for some endpoints. It is also noted that there is uncertainty in the suitability of maintaining bumble bee colonies in tunnels for 28-days. Given these uncertainties, this study suggests that spray applications of 0.3 lbs. a.i./A to turf containing bumble bee-attractive flowering plants may cause deleterious effects on bumble bee worker production.

Much more data are available on the prolonged oral exposure of bumble bee colonies to imidacloprid and these data suggest a relatively congruent profile of imidacloprid effects at the colony level (Mommaerts 2010, MRID 48151502; Gill 2012, MRID 49719618; Laycock 2012, MRID 49719622; Laycock and Cresswell 2013, MRID 49719621; Bryden 2013, MRID 49719607; Gill and Raine 2014; Whitehorn 2012, MRID 49719634; Feltham 2014, MRID 49719617). Details of these studies are summarized in **Section 5.2** and **Appendix E**. Rather, the levels at which imidacloprid resulted in colony-level effects to bumble bees is summarized relative to the oral (sucrose) NOAEC of 25 µg/L observed with the honey bee (MRID 49510001). Specifically, 6 of the 8 aforementioned studies tested sucrose concentrations fed to *B. terrestris* colonies that included (or spanned) 10 µg/L in sucrose, as indicated in **Figure 6-30**.

Despite differences in the duration of exposure (14 days to 11 weeks), colony sizes and methods used to assess effects on the colonies, 4 of these studies documented major (and statistically significant) effects on *B. terrestris* colonies fed 10 µg/L imidacloprid in sucrose, including (but not limited to) increased worker mortality, decreased numbers of worker bees produced, reductions in foraging efficiency, increased time required to collect pollen, and decreases in the quantity pollen collected. In some cases, worker bee production increased which was presumably as a compensatory response to reduced food provisions. Notably, 2 of these 6 studies (Laycock 2012; Laycock and Cresswell 2013) report 42% reduction in fecundity for microcolonies fed 1 µg/L imidacloprid (TGAI) for 14 days and an EC₅₀ of 1.4 µg/L for brood production after the same duration of exposure. These levels approach the limit of detection of imidacloprid in nectar (0.7 µg/L). Interestingly, when *B. terrestris* colonies were fed uncontaminated sucrose following the 14-day exposure, brood production recovered to the level of the control group. This suggests that the duration of exposure of *B. terrestris* colonies to imidacloprid is critical with respect to expression of colony-level effects and that recovery of colonies is possible given sufficient time off dose.

Two other studies (Whitehorn 2012 and Feltham 2014) fed *B. terrestris* colonies a mixture of low levels of imidacloprid in sucrose and pollen for 14 days in the laboratory followed by 4-6 weeks off dose in the field. At 0.7 µg/L (sucrose) and 6 µg/L (pollen), Whitehorn (2012) report an 85% reduction in queen production and significantly reduced colony weight relative to controls. Feltham (2014) reported reductions of 28% and 31% in collected pollen and foraging efficiency, respectively, following 14 days at the same dose levels in sucrose and pollen. These findings are significant given the widespread occurrence of imidacloprid in nectar above these levels following application to crops, including seed treatment. As noted in the Section 5, however, these studies were not considered suitable for quantitative use in the risk assessment, and therefore additional data (*i.e.* Tier II and Tier III studies with *Bombus*) would benefit the risk characterization for non-*Apis* bees.

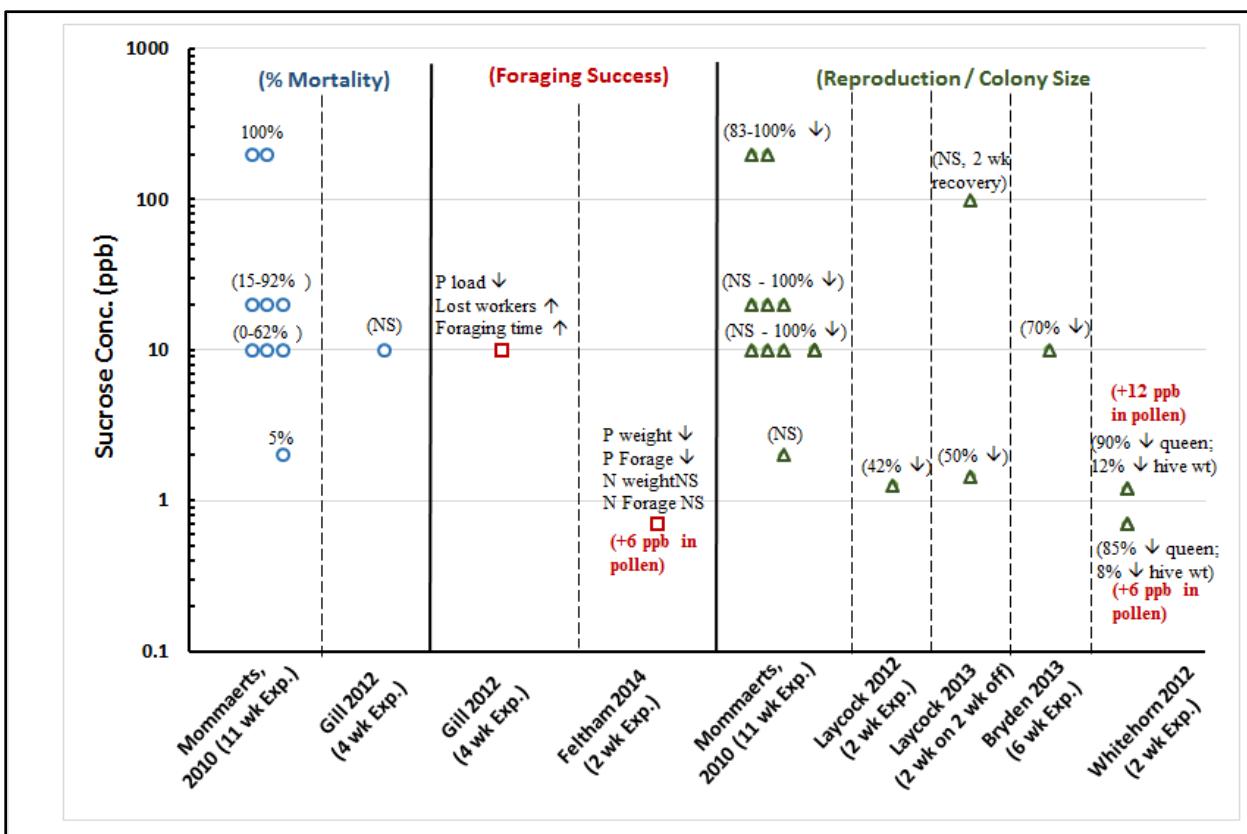


Figure 6-30. Comparison of effect levels from qualitative Tier II feeding studies on *B. terrestris* obtained from the open literature (numbers in parentheses refer to the magnitude of effects and/or additional exposure to pollen)

6.4. Additional Lines of Evidence

Monitoring of residues in agricultural and hives

As described in **Section 4**, there are several studies available in the open literature that investigated the residues of imidacloprid both in agricultural fields with known imidacloprid use, as well as the various hive matrices of colonies in areas across the United States and Europe. The agricultural field studies (Bonmatin 2005 and 2007), which sampled pollen residues from seed-treated corn and sunflower determined that while the frequency of quantifiable residues ranged from between 36 – 58% of the total samples analyzed, the mean concentrations of detectable residues ranged from 0.6 – 3.0 µg/L, which was just above the LOQ of these studies.

In the hive monitoring studies, surveys conducted across the United States and Europe measured residues in various hive matrices for the presence of imidacloprid. In some studies, known areas of diseased colonies were sampled in addition to healthy colonies while for other studies this information was not always present. These studies generally indicated (inclusive of all study areas) that imidacloprid was generally detected in 10% or less of pollen, honey, wax or honey bee samples (highest concentration was reported in trapped pollen at 149 µg/L). In studies where there was a higher

frequency of imidacloprid detections (*e.g.* Chauzat *et al.* 2006 and 2009), the mean residues ranged from below the LOD – 5.7 µg/L, a level 5-fold below the Tier II colony feeding study. In other studies (Bee Research Institutes 2008, and Mullin *et al.* 2010) several hundred samples were tested in each study from various matrices with imidacloprid being detected a maximum of 2.9% across both studies. Stoner and Eitzer (2013) screened over 300 pollen samples and while imidacloprid was detected in 12% of the samples, the mean residues of 5.2 µg/L were similar to those found in the work by Chauzat *et al.* In recent work by Lu (2015), monthly pollen and honey samples were collected across hives in Massachusetts and screened exclusively for neonicotinoid pesticides. While imidacloprid was detected in 57% of the pollen samples and 53% of the honey samples, the mean residues were 0.1 µg/L (equivalent to the LOQ) and 0.58 µg/L, respectively.

An additional point to be made from these studies is that for all studies except Lu (2015) (which screened only for neonicotinoid pesticides) multiple pesticides were found in the same samples, with some samples containing up to 12 pesticides. In the majority of these cases, the *Varroa* mite treatment miticides fluvalinate, coumaphos, and amitraz were detected, in some cases in up to 98% of the assessed samples, depending on the matrix (Mullin *et al.*, 2010). Additionally, fungicides, particularly those of the sterol biosynthesis inhibitor class that include the triazole fungicides were detected with high frequency.

This discussion illustrates, that while imidacloprid has an estimated usage of over 1 million pounds of applied active ingredient on an annual basis in the U.S., monitoring surveys in agricultural fields and hive matrices generally do not detect the chemical with great frequency. In cases where the frequency of detections was 50% or more, the mean residues typically did not exceed 5 µg/L (inclusive of all assessed matrices).

While the suite of reported pollinator incidents originating from agricultural uses with analytical confirmation of residues is small (*i.e.* 6 incidents), a lack of reported incidents does not equate to the absence of honey bees and other pollinators losses due to the registered use patterns of imidacloprid.

7. CONCLUSIONS

Exposure of bees through direct contact by foliar spray of imidacloprid (*i.e.*, interception of spray droplets either on or off the treated field) and oral ingestion (*e.g.*, consumption of contaminated pollen and nectar) represent the primary routes of exposure considered in this assessment. Exposure of bees to imidacloprid via drift of abraded seed coat dust, is also considered a route of concern. Risk are demonstrated by several bee kill incidents reported at the time of corn planting. The Agency is working with different stakeholders to identify best management practices and to promote technology-based solutions that reduce this potential route of exposure.

The Tier I risk assessment using screening-level EECs concludes that all uses (foliar, soil and seed) pose a risk to adult honey bees from both acute and chronic on-field exposures to imidacloprid. Some crops are not attractive to honey bees (including many root and tuber vegetables and fruiting vegetables) and on field risk is assumed to be low. In cases where crops are harvested for food prior to bloom (including

root and tuber vegetables, bulb vegetables, leafy vegetables, brassica leafy vegetables), risk on field is assumed to be low, as the crop is not attractive prior to bloom. Crops that are grown for seed may still pose an on-field risk to bees, although the spatial extent is limited. Screening-level EECs were refined with measured residues in pollen and nectar of representative crops. Based on refined tier I analysis, the legume and cereal grain crop groups were classified as low risk. When refined RQs exceeded LOCs, a higher-tiered assessment was conducted using available residue data as well as Tier II toxicity data (*i.e.*, colony feeding studies).

7.1. Foliar applications

Available residue data from other neonicotinoid compounds (*i.e.* clothianidin, thiamethoxam, and dinotefuran) were used to increase the robustness of the dataset and increase confidence in risk conclusions for imidacloprid. Regardless of chemical, nectar equivalencies (combined nectar plus pollen exposure) exposure estimates derived from the measured residues in pollen and nectar overlap with exposure levels that are associated with the onset of colony-level effects in honey bees for multiple crops and crop groups. However, the strength of evidence supporting these risk conclusions vary (**Table 7-1**).

The strength of evidence is considered “strongest” for pre-bloom, foliar applications of imidacloprid to the following crops/crop groups:

- Citrus, banana/plantain
- Cotton (combined foliar+soil)
- Berries/small fruits
- Attractive fruiting vegetables (chilies, peppers)
- Attractive ornamentals and forest trees

The strength of evidence is considered “moderate” for foliar applications to the following crops/ crop groups:

- Cotton (pre-bloom)
- Turf (residential, pre-bloom)

The strength of evidence is considered “weakest” for foliar applications to the following crops/crop groups:

- Attractive root/tubers
- Citrus, pome, stone, tropical fruit (post-bloom)
- Herbs/spices
- Hops/peanuts

7.2. Soil Applications

Similar to foliar applications, available residue data from other neonicotinoid compounds (*i.e.* clothianidin, thiamethoxam, and dinotefuran) were used to increase the robustness of the dataset and increase confidence in risk conclusions for soil applications of imidacloprid. Regardless of chemical, nectar equivalencies (combined nectar plus pollen exposure) exposure estimates derived from the measured residues in pollen and nectar overlap with exposure levels that are associated with the onset of colony-level effects in honey bees for multiple crops and crop groups. However, the strength of evidence supporting these risk conclusions vary (**Table 7-1**).

The strength of evidence is considered “strongest” for pre-bloom, soil applications to the following crops/crop groups:

- Citrus, banana/plantain
- Berries/small fruit
- Cucurbits
- Attractive fruiting vegetables
- Attractive ornamentals and forest trees

The strength of evidence is considered “moderate” for soil applications to the following crops/crop groups:

- Citrus (post bloom)
- Tree nuts (post-bloom)
- Cotton
- turf (residential)

The strength of evidence is considered “weakest” for soil applications to the following crops/crop groups:

- Attractive root/tubers
- Legumes
- Pome, Stone, Tropical Fruit (post bloom)
- Herbs/spices
- Hops/peanut

7.3. Seed Treatment Applications

Regardless of chemical, the likelihood of exposure similar to the colony-level risks from seed treatment was considered low at the tier II level for oilseed and some legume crops. Refined analyses using a synthesis of residue data (**Attachment 1**) however, suggest a potential for on-field risks from seed treatment uses on beans and peanuts because of a very high application rate. However, the strength of evidence associated with this risk finding is considered weak (**Table 7-1**).

Table 7-1. Summary of on-field risk findings for honey bees (*Apis mellifera*) for the registered use patterns of imidacloprid

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|---------|-------------------------|-----------------------------------|------------------------------------|---|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| 1 | Root/Tuber Vegetables | No | Foliar | NA | NA | NA | NA | LOW RISK ⁴ |
| | | | Soil | | | | | |
| | | | Seed ¹² | | | | | |
| | | Yes ⁵ | Foliar | <i>Cucurbits (C, T, D)</i> <i>Oilseed (C, T, D)</i> | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Soil | | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Seed ¹² | | Yes | Yes | No | LOW RISK |
| 3 | Bulb Vegetables | No | Soil | NA | No | NA | NA | LOW RISK ⁴ |
| | | | Seed ¹² | | No | | | |
| 4 | Leafy Greens Vegetables | No | Foliar | NA | No | NA | NA | LOW RISK ⁴ |
| | | | Soil | | No | | | |
| 5 | Brassica Vegetables | No | Foliar | NA | No | NA | NA | LOW RISK ⁴ |
| | | | Soil | | No | | | |
| | | | Seed ¹² | | No | | | |
| | | Yes | Foliar | Soybean | Yes | No | No | LOW RISK |
| 6 | Legumes | Yes | Soil | No | Yes | NA | Yes | RISK ⁸ (Weakest evidence) |
| | | | Seed (soybean, peas) ¹² | Soybean | Yes | Yes | No | LOW RISK |
| | | | Seed (beans) ¹² | No | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Foliar | NA | NA | NA | NA | LOW RISK ⁴ |
| 8 | Fruiting Vegetables | No | Soil | | | | | |
| | | | Foliar | <i>Tomato (T, D), Chili (T), Pepper (D), Cucurbits (C, T, D)</i> <i>Oilseed (C, T, D), Soybean (I, T)</i> Tomato <i>Tomato (T, D), Chili (T), Pepper (D), Cucurbits (C, T, D)</i> <i>Oilseed (C, T, D), Soybean (I, T)</i> | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | Yes ⁶ | Soil | | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|---------|------------------------|-----------------------------------|---------------------|--|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| 9 | Cucurbit Vegetables | Yes | Soil | Melon, watermelon <i>Pumpkin (C, T, D), cucumber (C, T, D), cantaloupe (C), muskmelon (T), melon (D), squash (C, T, D)</i> | Yes | Yes | Yes | RISK⁸ (Strongest evidence) |
| 10 | Citrus Fruits | No ⁹ | Foliar | NA | NA | NA | NA | LOW RISK⁴ |
| | | | Soil | NA | NA | NA | NA | LOW RISK⁴ |
| | | Yes | Foliar (pre-bloom) | Oranges <i>Apple and Orange (T)</i> | Yes | Yes | Yes | RISK⁸ (Strongest evidence) |
| | | | Foliar (post-bloom) | Almonds (C), Apple (C), Cherry (T, D, I), Peach (C, D, T), and Plum (T) | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| | | | Soil (pre-bloom) | Lemon and Orange (C, T) | Yes | Yes | Yes | RISK⁸ (Strongest evidence) |
| | | | Soil (post-bloom) | Lemon and Orange (C) | Yes | Yes | Yes | RISK⁸ (Moderate evidence) |
| 11 | Pome Fruits | Yes | Foliar (post-bloom) | Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T) | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| | | | Soil (post-bloom) | Apple⁷ <i>Orange and Lemon (C)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| 12 | Stone Fruits | Yes | Foliar (post bloom) | Cherry <i>Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| | | | Soil (post-bloom) | Cherry, peach, apricot, plum⁷ <i>Orange and Lemon (C)</i> | Yes | Yes | Yes | RISK⁸ (Weakest evidence) |
| 13 | Berries / small fruits | Yes | Foliar (pre-bloom) | Blueberry (D, T), Cranberry (T, D), Grape and Strawberry (T) | Yes | Yes | Yes | RISK⁸ (Strongest evidence) |

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|---------|--------------------------------------|-----------------------------------|--------------------------|--|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| | | | Foliar (post-bloom) | Grape (C) | Yes | Yes | No | LOW RISK ⁸ |
| | | | Soil (pre-bloom) | Strawberry (T), Grape (C) | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | | Soil (post-bloom) | Blueberry | Yes | Yes | No | LOW RISK ¹³ |
| 14 | Tree nuts | Yes | Foliar (post-bloom) | Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T) | Yes | Yes | No | LOW RISK ⁸ |
| | | | Soil (post-bloom) | Orange and Lemon (C) | Yes | Yes | Yes | RISK ⁸ (Moderate evidence) |
| 15 | Cereal Grains | Yes | Seed ¹² | Corn | Yes | No | No | LOW RISK |
| | | No | Seed ¹² | NA | NA | NA | NA | LOW RISK ⁴ |
| 19 | Herbs / Spices | Yes | Foliar | Cucurbits (C, T, D) Oilseed (C, T, D) | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Soil | | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| 20 | Oilseed ¹⁰ | Yes | Foliar | Cotton | Yes | Yes | Yes | RISK (Moderate evidence) |
| | | | Soil | Cotton | Yes | Yes | Yes | RISK (Moderate evidence) |
| | | | Soil + Foliar | Cotton ⁷ | Yes | Yes | Yes | RISK (Strongest evidence) |
| | | | Seed ¹² | No | Yes | Yes | No | LOW RISK ⁸ |
| None | Tropical Fruits, coffee, pomegranate | Yes | Foliar (post-bloom) | Almonds (C), Apple (C), Cherry (T, D), Peach (C, D, T), and Plum (T) | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Soil (post-bloom) | Orange and Lemon (C) | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | Banana, plantain | Yes | Foliar, Soil (pre-bloom) | Oranges Apple and Orange (T) | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |

| Group # | Crop Group | Honey Bee Attractive ¹ | Appl. Method | Residue Data Used Quantitatively | Individual Bee (Tier I) Risk | | Honey Bee Colony (Tier II) Risk | Risk Conclusions (Strength of Evidence) ^{2,3} |
|---------|--------------------------|-----------------------------------|-------------------------|--|------------------------------|------------------|---------------------------------|--|
| | | | | | On Field Default | On Field Refined | | |
| | Tobacco, globe artichoke | No | Foliar, Soil | NA | NA | NA | NA | LOW RISK ⁴ |
| | Hops, peanut | Yes | Foliar | Tomato <i>Tomato (T, D), Chili (T), Pepper (D)</i> | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | | | Soil | | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | Peanuts | Yes | Seed ¹² | No | Yes | Yes | Yes | RISK ⁸ (Weakest evidence) |
| | Turf (residential lawn) | Yes | Foliar, Soil | No | Yes | Yes | Yes | RISK ¹¹ (Moderate evidence) |
| | Turf (commercial sod) | No | Foliar, Soil | NA | NA | NA | NA | LOW RISK ¹¹ |
| | Ornamentals | No | Foliar, Soil, Injection | No | NA | NA | NA | LOW RISK ⁴ |
| | | Yes | Foliar | <i>Lilly, mock orange, lilac (T)</i> | NA | NA | Yes | RISK ⁸ (Strongest evidence) |
| | | | Soil | Holly, Pepperbush <i>Lilly, mock orange, lilac (T)</i> | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | | injection | <i>Cherry (D)</i> | NA | NA | Yes | RISK ⁸ (Moderate evidence) |
| | Forestry | No | Foliar, Soil, Injection | NA | NA | NA | NA | LOW RISK ⁴ |
| | | Yes | Foliar | <i>Mock orange, lilac (T)</i> | NA | NA | Yes | RISK ⁸ (Strongest evidence) |
| | | | Soil | Holly, Pepperbush <i>Mock orange, lilac (T)</i> | Yes | Yes | Yes | RISK ⁸ (Strongest evidence) |
| | | | Injection | <i>Cherry (D)</i> | NA | NA | Yes | RISK ⁸ (Moderate evidence) |

NA = not assessed. Residue data for imidacloprid indicated by crops in **bold**; residue data bridged from other neonicotinoids are shown in *italics as follows*: C = Clothianidin; D = Dinotefuran; T = Thiamethoxam).

¹ Based on USDA 2017. *Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen*.

² Green indicates a low potential for risk; red indicates a potential for risk. Strength of evidence refers to the confidence in the risk conclusion based on the available lines of evidence.

³ If crop is not attractive to bees or is harvested prior to bloom (USDA 2017), Tier I RQs are not calculated on the treated field and risk conclusion is “LOW RISK.”

⁴ Agronomic practices indicate root/tubers, globe artichoke, tobacco, bulb, leafy brassica and most fruiting vegetables are harvested prior to bloom, unless grown for seed (USDA 2017). Other members of a crop group are not attractive to bees. These factors limit exposure of bees on the treated field. Exposure may occur on the treated field if crop is grown for seed (*i.e.*, when the crop is allowed to flower). Although imidacloprid may be applied to crops grown for seed, the spatial footprint for these uses is expected to be limited due to low pounds applied/yr and specific geographic areas where crops are grown for seed.

⁵ Exposure is presumed for honey bee-attractive root and tubers (sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish) since available information does not indicate they are harvested prior to bloom (USDA 2017).

⁶ Applies to chilies, peppers, roselle and okra which are considered honey bee attractive (USDA 2017).

⁷ Residue data reflect combined soil + foliar application.

⁸ Due to limited or lack of data for imidacloprid, this risk finding is supported by residue data from other neonicotinoids applied to crops within this crop group using the same application method (but scaled to the imidacloprid application rate). Risk findings for the following crop groups were also supported by residue data from other crop groups. For attractive root/tubers and herbs/spices, risk finding was supported by residue data from other herbaceous crops (cucurbits, cotton, fruiting vegetables, legumes). For tree nuts and tropical fruits, risk finding was supported by residue data from orchard crops. For hops and peanut (soil & foliar, risk conclusions were bridged from pollen only-producing fruiting vegetables. For beans and peanut (seed treatment), risk finding was supported by all available neonicotinoid residue data for seed treatments. For foliar and soil applications to ornamentals, risk finding was also supported by ornamental data for thiamethoxam. Risks from forestry uses were assessed from woody ornamentals.

⁹ During bloom, mandarin orange trees are tented with nets to prevent pollination from bees.

¹⁰ Cotton is registered for all application methods. All other members of the oilseed group including canola and sunflower are registered only for seed treatment use.

¹¹ For uses on residential turf (lawns), a potential for exposure of bees exists for attractive blooming weeds (*e.g.*, clover). Qualitative data suggests that residues of imidacloprid in nectar of clover following turf applications at the maximum label rate can exceed Tier I levels of concern and the Tier II honey bee colony NOAEC for up to two weeks. Uses on commercial sod production are not expected to result in exposure of bees due to management practices which limits the occurrence of weeds.

¹² Risk conclusions for seed treatments are based on the oral route of exposure and drift of abraded seed coat dust is not considered.

¹³ Assumes post bloom applications occur ≥ 200 days prior to bloom during following season.

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