

ATTACHMENT 2 TO THE NEONICOTINOID FINAL BEE RISK ASSESSMENTS

Residue Bridging Analysis of Foliar and Soil Agricultural Uses of Neonicotinoids

Associated Chemicals

- Clothianidin (PC code 044309)
- Dinotefuran (PC code 044312)
- Imidacloprid (PC code 129099)
- Thiamethoxam (PC code 060109)

January 2020

**U.S. Environmental Protection Agency
Office of Pesticide Programs
Environmental Fate and Effects Division
Washington, DC**

Table of Contents

1	EXECUTIVE SUMMARY	5
2	INTRODUCTION	9
2.1	Purpose and Scope.....	10
2.2	Organization of this Document.....	10
3	FACTORS INFLUENCING NEONICOTINOID RESIDUES IN POLLEN AND NECTAR	10
3.1	Conceptual Overview.....	10
3.2	Considerations of Crop Biology and Physiology.....	12
3.2.1	Changes in Biomass.....	12
3.2.2	Floral Biology and Attractiveness.....	13
3.2.3	Other Conditions Effecting Residues in Pollen and Nectar.....	13
3.2.4	Evolutionary Relationships and Crop Groups	14
4	DATA AND METHODS	15
4.1	Data Sources and Review.....	15
4.2	Residue Data Coverage	15
4.3	Scope and Limitation of Study Designs	17
4.4	Data Manipulation and Interpretation	18
4.4.1	Residues of Concern.....	18
4.4.2	Level of Detection and Level of Quantitation	18
4.5	Analytical Approach	18
4.5.1	Addressing the Influence of Application Method	20
4.5.2	Addressing Application Timing Relative to Bloom	20
4.5.3	Addressing the Influence of Application Rate.....	21
4.5.4	Accounting for Differences in Days After Last Application	22
4.5.5	Estimating Residue Decline Curves for Use in Tier II Risk Characterization	24
5	EXTRAPOLATION OF NEONICOTINOID RESIDUES AMONG PLANT MATRICES.....	30
5.1	Linear Regression Method	31
5.2	Ratio Method	32
5.3	Choosing the Surrogate Matrix Extrapolation Factor	32
5.4	Anther Residues as a Surrogate for Pollen	32
5.4.1	Linear Regression Method (Pollen vs. Anther)	33
5.4.2	Ratio Method (Pollen/Anther)	35

5.4.3	Choice of Anther-to-Pollen Extrapolation Factor.....	36
5.5	Flower Residues as a Surrogate for Nectar.....	36
5.5.1	Linear Regression Method (Nectar vs. Flower, Foliar Spray).....	37
5.5.2	Ratio Method (Nectar/Flower, Foliar Spray).....	40
5.5.3	Choice of Flower-to-Nectar Extrapolation Factor (Foliar Spray).....	41
5.5.4	Linear Regression Method (Nectar vs. Flower, Soil Application).....	42
5.5.5	Ratio Method (Nectar/Flower, Soil Application)	44
5.5.6	Choice of Flower-to-Nectar Extrapolation Factor (Soil Application)	45
5.6	Flower Residues as a Surrogate for Pollen.....	46
5.6.1	Linear Regression Method (Pollen vs. Flower, Foliar Spray).....	46
5.6.2	Ratio Method (Pollen/Flower, Foliar Spray)	48
5.6.3	Choice of Flower-to-Pollen Extrapolation Factor (Foliar Spray)	50
5.6.4	Linear Regression Method (Pollen vs. Flower, Soil Application).....	50
5.6.5	Ratio Method (Pollen/Flower, Soil Application)	52
5.6.6	Choice of Flower-to-Pollen Extrapolation Factor (Soil Application)	54
6	CROP GROUP SPECIFIC ANALYSIS AND BRIDGING RECOMMENDATIONS.....	55
6.1	Orchard crops.....	55
6.1.1	Crops of Concern for Bees	55
6.1.2	Foliar Applications.....	55
6.1.3	Soil Applications	80
6.2	Berries and Small Fruits	101
6.2.1	Crops of Concern for Bees	101
6.2.2	Foliar Applications.....	102
6.2.3	Soil Applications	123
6.3	Cotton	131
6.3.1	Crops of Concern for Bees	131
6.3.2	Foliar Applications.....	131
6.3.3	Soil Applications	156
6.4	Root and Tuber Crops	156
6.4.1	Crops of Concern for Bees	156
6.4.2	Considerations of Crop Biology/Physiology.....	156
6.4.3	Foliar Applications.....	157
6.4.4	Soil Applications	159
6.5	Legumes	162
6.5.1	Crops of Concern for Bees	162

6.5.2	Foliar Applications.....	162
6.5.3	Soil Applications	165
6.6	Fruiting Vegetables	166
6.6.1	Crops of Concern for Bees	166
6.6.2	Foliar Applications.....	166
6.6.3	Soil Applications	171
6.7	Cucurbits	178
6.7.1	Crops of concern for pollinators	178
6.7.2	Foliar Applications.....	179
6.7.3	Soil Applications	197
6.8	Other Crops Groups (with no residue data).....	215
7	SUMMARY AND CONCLUSIONS.....	216
8	REFERENCES	219
APPENDIX A. PLANT LIFE HISTORY CHARACTERISTICS		220
APPENDIX B. KINETIC ANALYSIS OF NEONICOTINOID RESIDUES COTTON FLORAL NECTAR, EXTRAFLORAL NECTAR AND POLLEN.....		223

1 EXECUTIVE SUMMARY

In conjunction with the Registration Review of the nitroguanidine-substituted neonicotinoid insecticides (*i.e.*, imidacloprid, clothianidin, thiamethoxam, dinotefuran), the U.S. Environmental Protection Agency (USEPA) required the technical registrants of these pesticides to submit field residue data in order to quantify concentrations of these compounds in bee-relevant matrices. Specifically, data on residues of these pesticides in pollen and nectar were required, since these matrices are the primary food sources for honey bees (*Apis mellifera*) and other non-*Apis* bees. These registrants also submitted residue data for other matrices that could potentially be used as surrogates for pollen and nectar (*e.g.*, anthers, flowers, leaves). Since each neonicotinoid insecticide is registered for many crops with different application rates and application methods, the number of unique chemical-crop-application scenarios is large. As a result, it was not considered feasible to generate pollen and nectar residue data for every possible chemical-crop-application scenario with the neonicotinoids in a timely fashion. Instead, a strategic approach was taken for requiring residue data which encompassed the majority of registered crop groups for at least one of the neonicotinoids. Furthermore, in order to assess the relationship among residues in pollen and nectar generated from different neonicotinoids, certain crops or crop groups (*e.g.*, cucurbits, cotton) were represented by all four pesticides. The goal of this strategy was to generate sufficient residue data in order to evaluate the reliability of residue extrapolation (bridging) among chemicals and crops where data were lacking.

This attachment summarizes the available residue data and associated analyses that are being used to support the bridging of residue data among neonicotinoids, crops, and plant matrices for assessing oral exposure of bees. Furthermore, this attachment directly supports the final bee risk assessments for imidacloprid, clothianidin, thiamethoxam and dinotefuran as part of USEPA's Registration Review of these pesticides. Included in this document are analyses of bee-relevant residue data for foliar and soil applications of neonicotinoids to agricultural crops. The analysis of residue data for applications to non-agricultural crops (ornamentals) and seed treatments are summarized in Attachment 3 and Attachment 4, respectively.

Approximately 80 residue studies were considered in this 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 different regulatory authorities involved in the generation of these data.

While many different factors may collectively influence neonicotinoid residues in pollen and nectar, all factors could not be reliably quantified for the purpose of this residue bridging analysis. Therefore, this analysis focuses on a subset of factors that are thought to influence residues in pollen and nectar which could be quantified and evaluated with the submitted data. The influence of the following factors on residues was evaluated in this assessment:

- Chemical;
- Crop;
- Plant matrix (pollen, nectar, flower);
- Season of application;
- Application site;

- Application method; and
- Application timing.

The overall methodology underlying this 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 this Attachment, the following general conclusions can be made among the neonicotinoids:

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 for the neonicotinoid risk assessment, residues from foliar application be considered separately from those associated with soil application.

2. Influence of Application Rate. The results from this 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 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 “site” in this analysis incorporates multiple factors that could influence residues including weather, soil characteristics, hydrology, agronomic practices and crop variety. These findings support the consideration of the number of sites upon which a given risk finding is based as one 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 1-1**.

Table 1-1. 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 are shown in **Table 1-2**. In general, bridging among chemicals and crops is recommended within a crop group. Residue bridging is not recommended between 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 1-2. 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.

2 INTRODUCTION

The nitroguanidine-substituted neonicotinoid insecticides (*i.e.*, imidacloprid, clothianidin, thiamethoxam, dinotefuran; referred to in this document as “neonicotinoids”) are currently registered for use on multiple crops in the United States. The neonicotinoids are currently undergoing Registration Review by the Office of Pesticide Programs (OPP) within the U.S. Environmental Protection Agency (USEPA)¹. Under the Registration Review program, all available information pertaining to the use, benefits and risks associated with a pesticide are evaluated every 15 years to ensure that registered uses meet the applicable statutory standards.² Environmental risks are evaluated by OPP for multiple taxa including birds, mammals, fish, aquatic invertebrates, plants and bees. The current analysis is relevant to assessing exposure and risks to bees.

Guidance for quantifying pesticide risks to bees was published by the USEPA in 2014 (USEPA/PMRA/CDPR, 2014)³. Assessing the potential risks to bees from consuming pesticide residues in pollen and nectar is an integral portion of this guidance. For assessing risks to bees resulting from oral exposure, a tiered process is followed in which methods of increasing complexity and environmental realism are introduced at each successive tier. The first tier (tier 1) begins with the use of “default” (high-end) estimates of exposure combined with measures of effect on individual bees in laboratory-based studies, using the honey bee (*Apis mellifera*) as a surrogate. Importantly, these default estimates of exposure (*i.e.*, concentrations in pollen and nectar) can be refined using data derived from field studies that quantify the magnitude of pesticide residues in pollen and nectar of bee-attractive crops. Information from bee-relevant field residue studies can also be used to inform risks at higher assessment tiers, where effects on entire honey bee colonies are evaluated under semi-field (Tier 2) and full-field (Tier 3) conditions. The analysis described below focuses on residues that may be used for refined Tier 1 and Tier 2 assessments.

As part of the Registration Review process for the neonicotinoid insecticides, numerous field residue studies were required of the registrants and submitted to USEPA for consideration in risk assessment. Several additional field residue studies were required by the California Department of Pesticide Regulation (CDPR) which focused exclusively on California crops and study sites. Since each neonicotinoid insecticide is registered for many crops, application rates and application methods, the number of unique chemical-crop-application scenarios is large. It was therefore not considered feasible to generate pollen and nectar residue data for every possible chemical-crop-application scenario with the neonicotinoids. Instead, a strategic approach was taken for requiring residue data which encompassed all major crop groups for at least one of the neonicotinoids. Furthermore, to assess the relationship among residues in pollen and nectar generated from different neonicotinoids, certain crops or crop groups were represented by all four pesticides (*e.g.*, cucurbits, cotton). This strategic approach for requesting bee-relevant residue data for the neonicotinoids was taken in order to quantify the extent to which residue data could be extrapolated among chemicals, crops, sites and plant matrices for assessing risks to bees.

¹ <https://www.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides>

² Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. §136 et seq. (1996)

³ <https://www.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance>

2.1 Purpose and Scope

The primary purpose of this document is to provide the scientific justification for extrapolating (bridging) residue data across neonicotinoids, crops, sites and plant matrices for use in assessing risks to bees. In addition, the technical basis of new methods used to model dissipation of pesticide residues over time are also summarized.

This analysis, hereafter termed the “residue bridging strategy,” focuses on registered uses involving foliar spray and soil applications of imidacloprid, clothianidin, thiamethoxam and dinotefuran to agricultural crops in the U.S. For registered uses involving seed treatment, a separate analysis was conducted and summarized in the seed treatment bridging document (**Attachment 4**). Similarly, a separate analysis was conducted to support the bridging of pollen and nectar residues associated with registered non-agricultural uses of the neonicotinoids (e.g., ornamental, turf, trunk injection) due in part to the diversity and widely differing characteristics of these uses (**Attachment 3**).

2.2 Organization of this Document

Section 3 of this document provides a conceptual overview of important factors that may affect residues of the neonicotinoids in pollen and nectar of plants. Section 4 describes the key residue bridging questions being addressed and the methods used to address these bridging questions. The analysis supporting the relationship of neonicotinoid residues among different plant matrices (e.g., pollen, nectar, flowers, anthers, leaves) is described in Section 5. Section 6 contains the results of the bridging analysis for each crop group (and application method) along with their key assumptions and uncertainties. Finally, the overall conclusions and recommendations of the neonicotinoid residue bridging effort are summarized in Section 7.

3 FACTORS INFLUENCING NEONICOTINOID RESIDUES IN POLLEN AND NECTAR

3.1 Conceptual Overview

Like all pesticides, residues of neonicotinoids in pollen and nectar can result from their deposition directly onto plant pollen and nectaries (e.g., for foliar sprays applied during bloom). Importantly, however, residues of neonicotinoids in pollen and nectar also occur from their systemic uptake across plant roots, stems and leaves. The systemic transport of neonicotinoids in plants is generally considered xylem mediated, whereby translocation within the plant follows the transpiration stream (i.e., translocation from the roots/stem upward to the leaves and floral tissues in addition to apoplastic movement within the leaves; Sur and Stork, 2003; Bonmatin et al., 2015). This translocation mechanism for neonicotinoids is also consistent with model predictions of pesticide movement based on chemical properties such as Kow and pKa (e.g., Briggs et al. 1983; Trapp et al. 2004).

As a result of their systemic transport within plants, many factors that affect evapotranspiration in plants are expected to influence residues of neonicotinoids in plant tissues (e.g., temperature, relative humidity, precipitation, soil moisture, soil texture; **Figure 3-1**). In addition to the rate and number of applications, the timing of pesticide application is also expected to affect residue concentrations, due in part to pesticide dissipation which may occur between application and bloom. The pesticide application method (e.g., soil vs. foliar spray) may influence residue concentrations in pollen and nectar. For example, with foliar spray applications, the applied pesticide is immediately available for uptake across

the leaves and stem after application while with soil applications, the pesticide must first penetrate the soil and reach the roots before uptake can occur. The time required for this uptake to occur depends in part on the proximity of the roots to the area of pesticide application and factors affecting pesticide leaching to the root zone (soil texture, moisture content, etc.). Given the persistence of the neonicotinoids in soil, it is reasonable to expect that pesticide uptake would continue over an extended period of time as the pesticide in the soil leaches from the application site into the root zone. Differences in the physicochemical characteristics among the neonicotinoids (e.g., degradation rates, sorption/desorption coefficients, hydrophobicity) also could affect residue concentrations in pollen and nectar via differential uptake, translocation and persistence in soil and plant matrices. Finally, biological and physiological characteristics of crops that relate to the timing of pollen and nectar formation, the connectivity of these structures to the plant vasculature, and growth rate and plant development may be particularly important in influencing neonicotinoid concentrations in pollen and nectar.

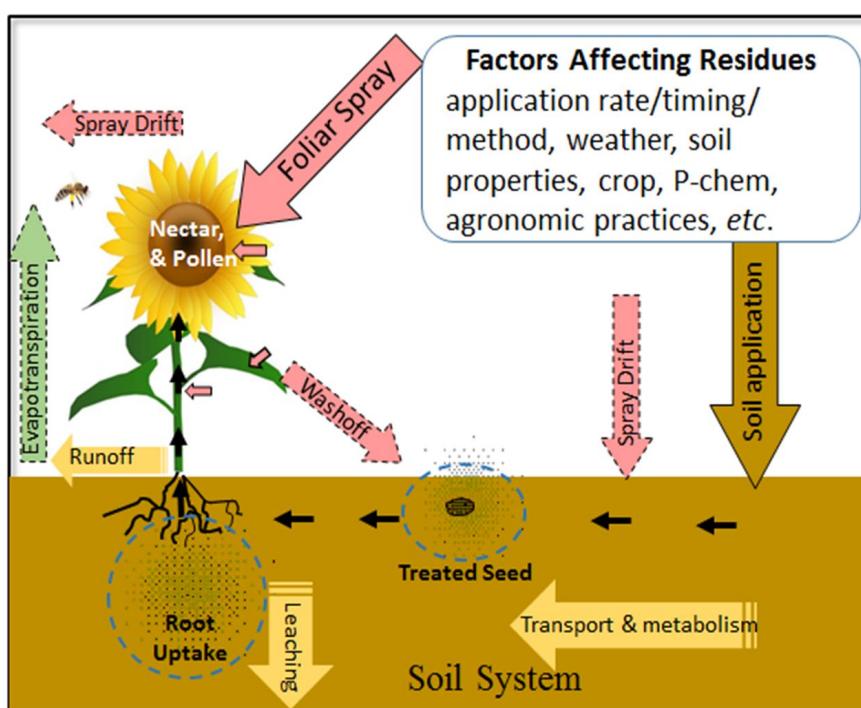


Figure 3-1. Conceptual Diagram of Major Factors Affecting the Expression of Pesticide Residues in Pollen and Nectar

Among the many factors potentially affecting pesticide residues in pollen and nectar, Gierer *et al.* (2019) suggested that crop type, pesticide characteristics, application method and environmental conditions were most important. Currently, the available mechanistic models of pesticide uptake and distribution in plants are either limited in their scope for quantitatively addressing the aforementioned factors or are highly plant-, site- and chemical-specific (USEPA, 2012). Therefore, the bridging strategy described herein is largely empirical (*i.e.*, based on measured residue concentrations in pollen and nectar), which is comparable to other exposure methods (*e.g.*, T-REX) employed by the Environmental Fate and Effects Division- (EFED) of OPP. Previous analyses with a subset of neonicotinoid residue data have indicated that relatively large differences in residue concentrations in pollen and nectar can be associated with factors such as crop, year of application, site, application method and timing of application (Sappington *et al.*, 2018).

3.2 Considerations of Crop Biology and Physiology

Given the diverse array of crops and crop groups upon which uses of neonicotinoids are registered, a conceptual summary of the biological and physiological attributes that may influence residues in pollen and nectar is presented here. Specifically, the neonicotinoids are registered for use on a diverse variety of plant physiologies, including different: life histories (annual vs. perennial), growth habits (*e.g.*, tree, shrub, vine, herb), levels of dormancy (*e.g.*, deciduous vs. evergreen), and frequencies of flowering (*e.g.*, single vs. successional). Given the systemic nature of these compounds, it is possible that differences in plant physiologies may influence the fate of these compounds in plants. Details of these factors are discussed in the subsequent **Sections 3.2.1-3.2.4**. Finally, **Table A-1 in Appendix A** summarizes the different life history traits that may influence residue concentrations in bee-relevant matrices (*e.g.*, nectar and pollen) for a selection of species across the crop groups registered for the neonicotinoids.

3.2.1 Changes in Biomass

The concentration of systemic compounds in various plant tissues and exudates may vary due to changes in biomass after application (*e.g.*, defoliation, rapid growth phases). The significance of these changes in biomass are considered in three primary situations:

1. **Rapid Change in Biomass Prior to Bloom:** This is most easily characterized with the life history of annual and perennial herbs (*e.g.*, cucurbits, fruiting vegetables, root and tubers). A seed or an asexual propagule (*e.g.*, seed potato) is planted then develops significant biomass over the course of some months prior to first bloom. As the potential application approaches the bloom period, the relative change in biomass is less compared to earlier growth stages and therefore, would likely have less of an influence on residue concentrations compared to applications made near planting.
2. **Rapid Change in Biomass After Bloom:** Post-bloom applications and applications made prior to leaf drop may result in significant reduction of concentrations in the remaining plant tissues/exudates due to the loss of chemical through dropped leaves. This phenomenon could be important for plants that bloom immediately post-dormancy (*e.g.*, almonds, cherries) as compared to crops that experience leaf out prior to bloom (*e.g.*, apples, pears). Pre-bloom applications on dormant trees may result in lower concentrations for those that bloom prior to leaf out compared to those that bloom after leaf out because of the increased mobility from sap flow and evapotranspiration from leaves.
3. **Limited Change in Biomass:** The perennial nature of woody crops (shrubs, trees and perennial vines) allows for potential sequestration and seasonal holdover of chemicals within the plant. For evergreen and slow growing taxa, there may be less significant biomass changes prior to bloom and these species often have a short post-winter growth period prior to bloom (*e.g.*, grapevines, cranberry, cherry). Herbaceous crops are planted yearly (or more frequently) and should not have significant residue holdover across crop cycles (exception may be with some crops like potato where the previous season's tubers are used for seed material). In addition, there is typically a much longer period of plant growth prior to bloom for herbaceous crops.

3.2.2 Floral Biology and Attractiveness

The duration and frequency of flowering can influence the magnitude and persistence of pesticide residues in bee relevant matrices. Longer flowering windows provide greater opportunity for a foraging bee to encounter residues. The timing of the initiation and duration of crop bloom differs not only across crops, but also is influenced by weather, water availability, crop varieties and soil nutrients. It is challenging to address all potential bloom conditions for a given crop; however, several general processes are considered.

3.2.2.1 Single flowering event (<1 month)

Examples of a crop with a flowering cycle (determinant) can be found in cherry, almond, apple, blueberry, corn, soybean, and citrus. Each crop variety will go through its bloom cycle usually within a single month. In many cases (*e.g.*, blueberry, apple) the farm or orchard may contain multiple varieties that have overlapping bloom cycles such that the field or orchard has individuals that are in bloom for a longer duration (>1 month) than the bloom cycle of an individual variety. These successional blooming varieties may result in different residue concentrations in floral matrices if the pesticides are applied to all varieties in the field at the same time (*e.g.*, all trees treated prior to the first variety that blooms). It may also extend the potential window of floral visitation and chemical exposure if each variety is individually prescribed treatment prior to bloom.

3.2.2.2 Successional flowering events (> 1 month)

Some crops produce flowers over a long duration (few to several weeks) through successional blooming and indeterminant growth (*e.g.*, tomato, peppers, potato, cotton, cucurbits). These crops tend to have significant vegetative growth throughout the blooming period as compared to plants which have a short bloom period (few to several days), therefore biomass of individuals at first bloom for a successional blooming crop may be considerably less than the biomass at mid- or late season bloom.

3.2.3 Other Conditions Effecting Residues in Pollen and Nectar

While the aforementioned biological traits are considered the primary factors related to concentrations in plant tissues and floral products, the following biological traits may also influence the magnitude and duration of residues in bee relevant matrices. These attributes include:

1. **Timing of nectar secretion.** Some crops secrete nectar differently over course of the day or flowering stage. For instance, many cucurbits produce nectar early in the day within newly opened flowers, and as the flower matures through fertilization of the ovules, nectar production slows. Although nectar production may fluctuate over a day or days, pollen would be available for the duration of the bloom period.
2. **Mechanisms of nectar secretion.** The mechanisms for nectar excretion and the connection of the nectary tissues to plant vasculature may play a role in residue concentrations. Some plants have vascular tissues directly embedded within the nectary tissue which may facilitate the transport of systemic chemicals directly to the nectary where others that lack these vascular intrusions would likely have concentrations related to the active transport of sugars through the non-vascular tissues.

3. **Root Structure.** Root structure and soil interaction likely play a significant role for soil applications. A plant that has a shallow (superficial) root profile in the soil will have more interaction with the top layer of soil (e.g., cucurbits, corn). These shallow root systems are most efficient at capturing nutrients and water from these top layers where residues would be highest. This is in contrast to more deeply rooted taxa (e.g., apples, grapes) which drawl on water at deeper depths and further away from highest concentrations in soil.
4. **Solute transport.** The efficiency or functional traits tied to water conservation and water/sugar transport in xylem and phloem may also play a role in the amount of chemical that is taken into the plant and how it is distributed throughout plant tissues.
5. **Pollen Development.** During the development of pollen, the mass of cells that eventually develop into pollen grains is fully saturated with water and solutes within the anther sac. It is unknown if the measured concentrations in pollen are a result of the deposition of chemicals onto the surface of the maturing pollen grains during the desiccation phase of development or if the chemicals are within the living cells of pollen. However, functionally this may play little role in the potential exposure to organisms consuming pollen, but it may affect the concentrations in pollen in different ways (i.e., dissolved chemical within the anther sac is likely going to result in much higher measured values due to the increasing concentrations during desiccation).

3.2.4 Evolutionary Relationships and Crop Groups

For evaluating the potential exposure of bees to neonicotinoids in pollen and nectar, EFED followed previously established crop groupings used for assessing dietary residues for human health risk assessment and associated tolerances for commodities (40 CFR Part 180, subpart B⁴). The crop groupings are often comprised of crops with similar evolutionary histories in that they are all within the same plant family (e.g., cucurbits = *Cucurbitaceae*, citrus = *Rutaceae*). However, there are exceptions. The fruiting vegetables are mainly comprised of crops from the genus *Solanum* (eggplant, tomato, peppers) of *Solanaceae* but the group also includes okra and roselle which are more closely related to cotton (*Malvaceae*). Another example is that the Root and Tuber group has potato (genus *Solanum*), a close relative of tomato and eggplant but also includes the sweet potato (*Convolvulaceae*), yam (*Dioscoreaceae*), and Jerusalem artichoke (*Asteraceae*); these similarly produce below ground commodities but are not closely related to each other. The Pome Fruits (apple/pear) and Stone Fruits (cherry/apricot/peach) are both comprised of the family *Rosaceae*, however, so do the groups representing berries (e.g., strawberry, black berry etc.).

It is uncertain to what degree the evolutionary relationships may influence the patterns of residues in pollen and nectar; however, a wide diversity of crops representing evolutionarily diverse lineages, various plant growth forms, life history, floral biology and attractiveness were tested as part of the studies discussed herein. It is assumed that these data represent (i.e., serve as reasonable surrogates for) untested crops (e.g., tropical fruits), as well as ornamental species not represented in the available empirical dataset. Justification for inclusion and the breadth of assumed representativeness (surrogacy) is discussed in each section below.

⁴ https://www.ecfr.gov/cgi-bin/text-idx?SID=46e0f15c31b8f5b1c0a348eac9f380e5&mc=true&node=se40.24.180_141&rgn=div8

4 DATA AND METHODS

4.1 Data Sources and Review

Approximately 80 bee-relevant residue studies were considered for inclusion in this residue bridging analysis for registered use of neonicotinoids as foliar or soil applications to agricultural crops. The primary source of these data were registrant-submitted studies that were required as part of Registration Review. These studies were generally conducted from 2009 onward. Typically, these studies included 3-5 sampling events during a growing season, although many had fewer sampling events. In a few cases, older registrant-submitted studies were included when they met the objectives of this analysis. Although considered, residue data from studies published in the open literature were not included in this analysis because such studies did not meet the criteria for including in the analysis. These criteria include:

1. Availability of raw data;
2. Documentation of the amount, frequency, timing and method(s) of pesticide application;
3. Documentation of the crop, site, and agronomic characteristics;
4. Description of the sample collection, handling and processing procedures;
5. Use of hand-collected matrices (not bee or hive-collected matrices);
6. Description of analytical methods, including quality assurance procedures; and,
7. Suitability of detection limits and quality assurance measures.

For each residue study which met these criteria, a Data Evaluation Record (DER) was produced which summarizes the study results and its overall classification for use in risk assessment. These study classifications include: "acceptable," "supplemental," and "unacceptable." Studies classified as acceptable are considered scientifically sound and meet the study scope and performance objectives defined in the applicable study protocol. Studies classified as supplemental are also considered scientifically sound but contain one or more deficiencies that limit their utility in quantitative risk assessment. For example, a supplemental study might not have included the maximum application rate as registered on the product label. Such studies might also have had some trials deemed as unacceptable (e.g., inadvertent pesticide application) but others deemed acceptable. In this case, results from the unacceptable trial(s) were excluded from the analysis. Unacceptable studies are not considered scientifically sound and were not included in the risk assessment.

Detailed summaries of the neonicotinoid residue studies used in this analysis are provided according to crop group in **Section 6**. A cursory summary of the residue data emphasizing the bridging needs is provided below.

4.2 Residue Data Coverage

A summary of bee-relevant residue data considered in the bridging analysis for foliar applications of the neonicotinoids is provided in **Table 4-1**. **Table 4-2** provides the same information for soil applications. It is evident from **Table 4-1** and **Table 4-2** that some crop groups are represented by multiple chemicals and crops (e.g., stone fruits, cucurbits) while other crops (e.g., root & tubers, tree nuts) are represented by just one or two neonicotinoids or none at all (e.g., tropical fruits). As discussed in **Section 2**, it was not practical nor feasible to require residue data for every neonicotinoid and registered crop group. Furthermore, formal guidance has yet to be developed to determine which (and how many) crops should be submitted for risk assessment purposes. Therefore, a strategic approach was taken for

requiring residue data in which some crop groups were heavily represented (to enable evaluation of cross-chemical and cross-crop extrapolations) while other crop groups were represented by fewer chemicals and crops.

Table 4-1. Availability of Bee-Relevant (Pollen and Nectar) Residue Data Resulting from Foliar Spray Applications of Neonicotinoids Among Crops and Crop Groups

Crop Group (#)	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
(1) Root & Tubers	NA	Potato (pre)	NA	NA
(6) Legumes	Soybean (pre)	NA	Soybean (pre)	NR
(8) Fruiting Veg.	Tomato (pre) ¹	NR	Tomato (pre)	Tomato (pre)
(9) Cucurbits	NR (watermelon) ⁴	Pumpkin (pre)	Pumpkin, Cucumber (pre)	Pumpkin, Cucumber (pre)
(10) Citrus Fruits	Orange (pre)	NA	Orange (pre)	NR
(11) Pome Fruits		Apple (post)	Apple (pre)	NR
(12) Stone Fruits	Cherry , (post)	Peach (post)	Cherry, Peach , Plum (post)	Cherry, Peach (post)
(13) Berries / Small Fruits	NA	Grape (pre & post)	Strawberry Blueberry, Cranberry (pre)	Blueberry, Cranberry (pre)
(14) Tree Nuts	NA	Almond (post)	NA	NR
(15) Cereal Grains	NR	NR	NR ¹	NR ²
(20) Oil Seed	Cotton (pre)	Cotton (pre)	Cotton (pre)	Cotton (pre)
(24) Tropical Fruits	NA	NA	NA	NR
Other ³	NA	NA	NA	NA

Crops shown in **bold** indicate the potential for cross-chemical comparisons based on crop, application timing and application method. Yellow highlighted cells indicate uses where residue bridging is needed; Grey shaded cells indicate use is not registered.

NA = data not available; NR = not registered; pre = pre-bloom application; post = post bloom application

¹ registered for barley only (not bee attractive)

² registered for rice only (not bee attractive)

³ includes other bee-attractive crops not assigned a crop group, such as peanut, globe artichoke, etc.

⁴ not registered in the US, but study was conducted in Brazil for registration purposes

Table 4-2. Availability of Bee-Relevant (Pollen and Nectar) Residue Data Resulting from Soil Applications of Neonicotinoids Among Crops and Crop Groups

Crop Group (#)	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
(1) Root & Tubers	NA	Potato (pre)	NA	Potato (pre)
(6) Legumes	NA	NA	NA	NR
(8) Fruiting Veg.	Tomato (pre)	NR	Tomato (pre)	Tomato (pre)
(9) Cucurbits	Melon , Watermelon (pre)	Melon, Pumpkin, Cucumber, Squash (pre)	Melon, Pumpkin, Cucumber, Squash (pre)	Melon, Pumpkin, Cucumber, Squash (pre)
(10) Citrus Fruits	Orange (post)	Orange, lemon (pre & post)	Orange, lemon (pre)	NR
(11) Pome Fruits	NA	NA	NR	NR
(12) Stone Fruits	NA	NA	NR	NA

Crop Group (#)	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
(13) Berries / Small Fruits	Strawberry (pre) Blueberry (post)	Grape (pre)	Strawberry (pre)	NA
(14) Tree Nuts	NR	NA	NR	NR
(15) Cereal Grains	NR	NR ¹	NR	NR
(20) Oil Seed	Cotton (pre)	NR	NR	NR
(24) Tropical Fruits	NA	NA	NR	NR
Other ²	NA	NA	NA	NA

Crops shown in **bold** indicate the potential for cross-chemical comparisons based on crop, application timing and application method. Yellow highlighted cells indicate uses where residue bridging is needed; Grey shaded cells indicate use is not registered.

NA = data not available; NR = not registered; pre = pre-bloom application; post = post bloom application

¹ experimental use permit registered for corn

² includes other bee-attractive crops not assigned a crop group, such as peanut, globe artichoke, etc.

4.3 Scope and Limitation of Study Designs

The design of the residue studies varied both within and among the neonicotinoids and crop groups, in part because they were conducted over different years and for different regulatory authorities which emphasized different regulatory objectives. For example, residue studies required by the USEPA generally included measurements of residues sampled over 3 to 5 time points during early-, mid- and late-bloom (*i.e.*, high temporal coverage) with residue trials distributed across three sites. Those studies required by the California Department of Pesticide Regulation (CDPR) typically involved greater spatial resolution (trials conducted at 9 sites in California) but had much less temporal resolution (samples taken once or twice during bloom).

Generally, a residue trial represented measurements taken during a single growing season at a particular study site. For example, if a study measured residues at three locations (sites) over a single growing season, then it was considered to have three distinct residue trials. If a study measured residues at three sites each over two growing seasons, then that study was considered to have six distinct trials (one for each location/season).

Variability in the timing of residue measurement relative to pesticide application is also a confounding factor both within and among study trials. This variation results not only from different study designs, but also from factors beyond the control of the study investigators (*e.g.*, differential effects of climate on the timing of bloom). Therefore, comparisons of residue measurements across trials may not only reflect chemical, site or crop-specific factors, but also differences in the time elapsed from pesticide application to residue measurement.

Although many in number, the residue studies originate from trials conducted at different times and locations throughout the United States. In all cases, comparisons of residues across chemicals originate from studies conducted at different locations and times. Except for a few studies where multiple crops were tested in the same study, comparisons among crops also incorporate potential influences of different locations and seasons.

In addition to temporal and spatial differences in study design, the matrices used for residue measurement also differed in many cases. Some of these differences were unavoidable (*e.g.*, when the crop does not produce nectar) while others reflected differences in study design or efficiency in sample collection (*e.g.*, hand collected vs. bee collected nectar).

4.4 Data Manipulation and Interpretation

4.4.1 Residues of Concern

In accordance with their respective bee risk assessments, residues of each neonicotinoid are expressed in terms of the stressor (residues) of concern as follows.

- **Clothianidin and Dinotefuran:** Residues are expressed as the parent chemical only (*i.e.*, no degradates of toxicological concern for bees).
- **Thiamethoxam:** Since thiamethoxam degrades to form clothianidin, residues are summed (using molar equivalents) to represent total thiamethoxam and clothianidin exposure and expressed as clothianidin-equivalents (c.e.). In this approach, thiamethoxam residues data are converted to clothianidin equivalents by multiplying the thiamethoxam values by 0.856, which is the ratio of the molecular weights of clothianidin to thiamethoxam (249.7 g/mol / 291.7 g/mol, respectively).
- **Imidacloprid:** In addition to parent imidacloprid (MW=255.7 g/mol), two degradates are of toxicological concern include imidacloprid olefin (MW=253.6 g/mol), 5-hydroxy imidacloprid (MW= 271.7 g/mol). Given the similarity in molecular weights of parent imidacloprid to these degradates (within 5%) and their occurrence at low concentrations relative to parent imidacloprid (typically < 10% of parent), residues for total imidacloprid are determined by summing concentrations of parent imidacloprid, imidacloprid olefin and 5-hydroxy imidacloprid.

4.4.2 Level of Detection and Level of Quantitation

In order to support statistical analysis of the residue data, assumptions were made for the treatment of residue values which were below the level of detection (LOD) and between the LOD and the level of quantification (LOQ) as follows.

- **Concentrations < LOD:** residues were assumed to be $\frac{1}{2}$ the LOD
- **Concentrations > LOD but < LOQ:** residue values were assumed to be $\frac{1}{2}$ the LOQ

For calculating total residues with one or more component residues below the LOD or LOQ, total residues were calculated by summing the assumed concentrations ($\frac{1}{2}$ the LOD or LOQ) for one or more components. In all cases, information was retained to identify when assumed concentrations for residues < LOD or <LOQ had a substantial influence on the statistical analysis and data interpretation.

4.5 Analytical Approach

This analysis examined the extent to which neonicotinoid residues in plants depend on the following factors:

1. Chemical;
2. Crop;
3. Application method (soil vs. foliar);
4. Application rate;
5. Application timing (within a growing season);
6. Season of application;

7. Site of application, and
8. Plant matrix (pollen, nectar, flower, leaf).

The general approach taken was to control for as many of these factors as possible prior to evaluating the influence of a given variable on the residue concentrations. An overview of the general process is shown in **Figure 4-1**. The first step involved segregating data according to the two application methods (foliar spray, soil) and the timing of application relative to bloom (pre-bloom, post bloom) since these factors had a large and obvious impact on residue concentrations. The next step involved normalizing the residue data within each of these groups to a common application rate when comparisons involved applications made at different rates. Next, the impact of time (days after last application) on residue concentrations was addressed either by normalizing to a common day after application or stratifying the residue data into different groups according to common time periods after application. For each of these processed data sets, the following questions were addressed in terms of their impact on residue concentrations.

1. How much does chemical matter?
2. How much does crop matter within a crop group?
3. How much does site matter?
4. How much does growing season matter?
5. How much does the matrix matter?

Appropriate statistical comparisons were conducted when sufficient data were available, including parametric or nonparametric methods of hypothesis testing and/or linear regression. Since addressing these questions involved further parsing of the data to remove confounding variables, sample sizes were often insufficient to permit meaningful statistical comparisons. In these cases, a semi-quantitative approach was taken which included comparisons of the overlap in 95% confidence intervals around the mean values or evaluation of cumulative frequency distributions. Details of the methods used to support the bridging analysis are summarized in the following sections.

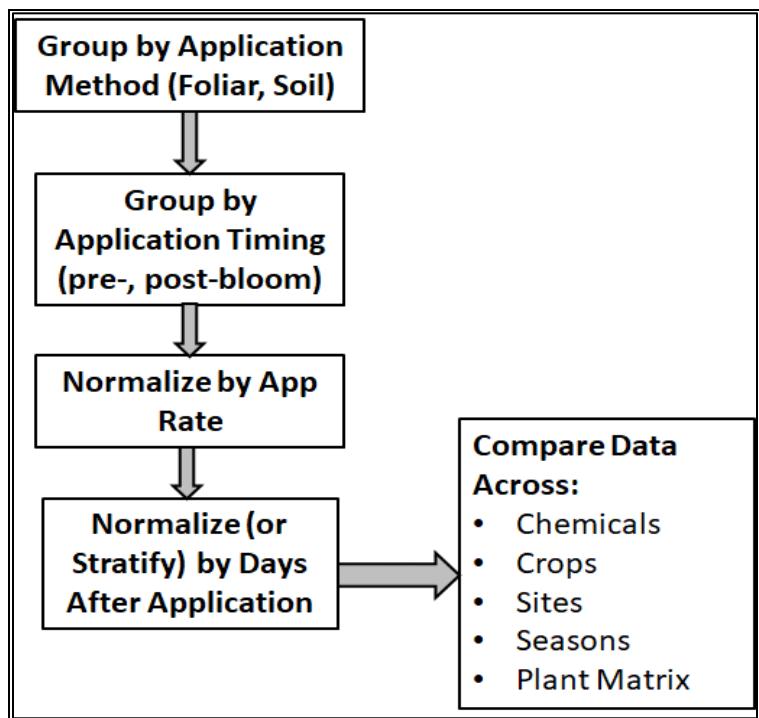


Figure 4-1. General process followed for analyzing bee-relevant residue data

4.5.1 Addressing the Influence of Application Method

Cursory review of the residue data indicated that residue profiles in pollen and nectar differed substantially according to application method (foliar vs. soil applications). Therefore, the residue bridging analysis was conducted within each application methods. In some cases, residue studies employed a combination of application methods (*e.g.*, soil + foliar, seed treatment + foliar). The soil + foliar applications only occurred for selected studies with imidacloprid. Since the amount of pesticide resulting from the soil versus foliar applications could not be reliably determined, these residue studies were excluded from further analysis. For studies that used seed treatment + foliar applications, the resulting contribution of seed treatment is expected to be negligible compared to pre-bloom foliar applications (which were orders of magnitude greater than seed treatment residues), these studies were assumed to have residue profiles consistent with foliar spray applications only and were considered in the analysis of foliar spray residue data.

4.5.2 Addressing Application Timing Relative to Bloom

The neonicotinoid residue studies reflect differences in the timing of application and subsequent sampling of pollen and nectar relative to the bloom period (*i.e.*, some data reflected pre- / at bloom applications while others reflected post-bloom applications). Pre-bloom (and at bloom) residue data reflect applications are those made prior to (or during) the bloom period with residues measured in the same growing season. Post-bloom residue data reflect applications made after bloom with residue measured in the subsequent growing season (the following year). Given the large impact of these different designs had on the residue profiles, residue data comparisons were made within each of these designs rather than among the designs. Clearly, this distinction is only relevant to perennial crops and not annuals.

4.5.3 Addressing the Influence of Application Rate

In regulatory risk assessments used to support pesticide registrations, residue concentrations in plant tissues are widely assumed to scale in proportion to application rate under similar environmental conditions (USEPA 2004, USEPA 2014, EFSA 2013). This assumption was evaluated and further supported by pollen and nectar residue studies which included different application rates (e.g., MRIDs 49881002 and 49950101). Therefore, when comparisons were made within or among residue trials of differing application rates, it was assumed that residues scaled proportional to application rate and residue data were normalized to a common rate (e.g., 0.1 lb a.i./A).

One complication to this assumption occurs when residues are measured following multiple applications to crops, since dissipation of residues (movement + degradation) can occur between the applications. In situations where the dissipation rate is such that a large proportion of pesticide dissipates between applications, residues would be expected to scale more closely to the single rate rather than the cumulative rate. Conversely, when dissipation rate is such that only a small portion of pesticide dissipates between applications, residues would be expected to scale more closely to the cumulative application rate rather than the single application rate. In addition to dissipation rate, the application interval is also relevant to residue concentrations.

Typical application intervals for the neonicotinoid applications range from 5-14 days and typical dissipation rate constants range from 0.02 to 0.35/d (half-lives from 2-30 d) based on single compartment, first order (SFO) kinetics. In order to evaluate the influence of multiple application rates on predicted residues of neonicotinoids in plant tissues, residues were modeled assuming SFO kinetics and application intervals common to the neonicotinoid field residue studies (**Table 4-3**). For half-lives of 3.5 days or shorter, the assumption that residues reflect the last application rate seems reasonable except possibly at the shortest application intervals (e.g., < 5 days). For the longer half-lives (> 10 days), about 40% or more of the pesticide is expected to remain after the first application with intervals from 5-14 days.

Table 4-3. Effect of DT₅₀ on the Percentage of Pesticide Residues Remaining Following Typical Application Intervals Among the Neonicotinoid Residue Studies

DT ₅₀ (d)	k (1/d)	% remaining @ 5 d ⁽¹⁾	% remaining @ 10 d ⁽¹⁾	% remaining @ 14 d ⁽¹⁾
30	0.02	89%	79%	72%
10	0.07	71%	50%	38%
6.9	0.1	61%	37%	25%
3.5	0.2	37%	14%	6%
2.0	0.35	18%	3%	1%

⁽¹⁾ assumes single compartment, first order kinetics. DT₅₀ = dissipation half-life; k = SFO dissipation rate constant

Unfortunately, the dissipation rate constants could not be quantified for a significant portion of the residue studies (e.g., when less than 3 sampling events are quantified or when results of kinetic modeling indicate high uncertainty in estimates of dissipation rate constants). Therefore, normalizing residue values to both the total and the last single application rate was performed in order to evaluate whether normalizing to the total or single application rate was most appropriate.

For orchard crops, foliar studies included either one or two applications. Many of the post-bloom studies involved samples collected months after the last application. Since both applications happened within a

much shorter window (*i.e.*, 1-2 weeks of each other), residues were normalized to the total seasonal rate. For foliar, pre-bloom application data from a study that compared residues from one and two applications, residues were similar when normalized to either 1 or 2 applications (overlapping confidence intervals); however, mean residues were consistently higher for trials with 2 applications. Residues for pre-bloom foliar applications were normalized to the total seasonal rate because: 1) there was no substantial difference between normalizing to 1 or 2 applications; 2) the approach is consistent with what was used for the foliar-post bloom data; and, 3) the dinotefuran data included two applications with unequal rates.

4.5.4 Accounting for Differences in Days After Last Application

Within each of the pre-bloom and post-bloom residue study designs, the amount of time between pesticide application and the initial measurement of pesticide residues varied substantially among trials within and among residue studies. Therefore, it would be expected that differences in the timing of residue measurement would potentially confound the influence the magnitude of residue concentrations among different trials.

When analysis of residue data involved trials with different timing of residue measurements relative to pesticide application, two approaches were taken to minimize the confounding effect of these differences depending on the available data. When sufficient data were available to derive reliable estimates of residue decline kinetics for residue trials, a kinetic-based approach was taken whereby residue values were adjusted to reflect a common “day after last application” (DALA) prior to comparisons being made. In this way, the effect of “time” on residue values could be reduced with comparisons of residue values made at a common DALA. This adjustment to a common DALA required using the dissipation rate constant (k) estimated from each residue trial, the initial measured residue value and an assumption of single, first order kinetics. Details of the kinetic based approach used to adjust for differences in DALA are provided in **Section 4.5.4.1** below.

When reliable estimates of residue decline kinetics could not be made, or when the effect of DALA on residue values was not clearly indicated (*e.g.*, for many post bloom applications, and soil applications), a qualitative approach was taken whereby residue data were evaluated within common ranges of DALA, and/or data were simply evaluated graphically with DALA on the x-axis.

4.5.4.1 Kinetic Approach for Adjusting Residues to a Common DALA

Pre-Screening Trial-Specific Residue Data

Prior to estimating the dissipation rate constant “k” for a given trial, residue data were subject to a pre-screening step to filter out data sets for which reliable estimates of “k” would not be possible. In order to be considered for analysis of dissipation rate constants, trial-specific data sets had to meet the following criteria:

- Residue measurements must be available at 3 or more sampling events;
- Residues must be above the limits of quantitation (LOQ) at 2 or more sampling events; and,
- Generally, 3 or more replicates must have been made per sampling event, although in some cases 2 replicates could still be used (*e.g.*, when samples were lost or when insufficient sample was available).

Estimation of Dissipation Rate Constant (k)

Model Choice. The SFO model was chosen for estimation of “k” as described in NAFTA (2012) and Bohaty *et al.* (2015). Although other ‘higher order’ models are among those recommended for kinetic modeling of pesticides (e.g., double first order in parallel model; DFOP), these were not chosen because most of the trial-specific data sets for pollen and nectar contained 3 to 4 sampling events over the bloom period. Fitting a 4-parameter model such as DFOP and the Indeterminate Order Rate Equation (IORE) model to a data set with less than 5 measurements is considered of questionable utility based on common statistical practices. Furthermore, application of multi-compartment modeling substantially complicates the modeling of residues with marginal benefit in model accuracy in the context of this analysis.

Estimation Procedure. Estimation of dissipation rate constants using the SFO model followed NAFTA recommendations (NAFTA 2012) and USEPA/OPP/EFED standard operating procedures (Bohaty *et al.* 2015). Specifically, “k” was estimated using nonlinear regression of the raw (replicate) data without transformation via the Computer Assisted Kinetic Evaluation (CAKE) program (version 3.3)⁵ which follows the NAFTA guidance and is approved for use in EFED. In addition to the estimate of “k”, other parameters were also calculated including:

- 95% confidence limits around the mean “k”;
- Correlation coefficient (r^2);
- P-value of the regression; and,
- Initial concentration and 95% confidence limits at time zero (C_0)

Post-Screening of Dissipation Rate Constant (k)

Prior to using the trial-specific estimates of “k” to adjust residue concentrations to a common DALA, the “k” estimates were screened for reliability. The following criteria were used to identify values of “k” that were not considered reliable:

- p-value of regression > 0.1;
- values of $r^2 < 0.2$: and,
- lower 95% confidence limit of “k” < 0.

These criteria were chosen so as not to exclude potentially useful trials from further consideration in the bridging analysis, given the limitations in the residue data (relatively few sampling events over time) and the relatively large variability inherent in the data (e.g., it was not uncommon for replicate values of residues to vary by 5X; Sappington *et al.*, 2018). Given this level of variability in the field residue data, an r^2 of 0.2 was selected for screening the model fits because it corresponds to approximately 50% of the variance being explained by the model. In all cases, the plot of the data and model fit was examined individually to qualitatively evaluate model fit and consistency with the residue decline trends. In addition to statistical characteristics of model fit and “k” estimates, the general trend in residue decline data from each trial was described as follows:

⁵ <https://www.tessella.com/showcase/computer-assisted-kinetic-evaluation>

- “Stable” = residues were relatively “flat” over time;
- “Non-monotonic” = residues increased and decreased over time with no apparent consistent trend;
- “Decreasing” = monotonic decrease over time; and,
- “Unknown” = data were insufficient to categorize into any of the three previous residue decline trends (e.g., due to lack of data and/or high variability).

Quality Assurance (QA). Most of the residue data were obtained in electronic (spreadsheet) form as part of the study submissions. During the generation of the DER for these studies, residue data were spot checked against the data reported in the study report by the EPA contractor. Some residue data were entered by hand or importing from other sources (e.g., pdf documents). Transcription of these were also spot checked with the original data to with the study report for quality assurance purposes. Since the kinetic analysis of residue data required entry of data into a separate program (done via copy and paste), a final QA of residue data involved comparing output from the CAKE program to output obtained from an EFED spreadsheet model called the “Degradation Kinetics Calculator”⁶ which was used prior to discovering the CAKE program. This enabled identification of transcription and other errors associated with data manipulation conducted for kinetic modeling. With very few exceptions such as those involving cases of extremely poor model fit, the Degradation Kinetics Calculator and the CAKE program returned the same estimate of “k.” for the same data set. The CAKE program was ultimately chosen for estimating “k” because it provides estimates of statistical confidence in “k” and the overall model fit.

Calculating C_t to Reflect a Common Day After Last Application (DALA)

For the trials with values of “k” deemed reliable, the concentration corresponding to a common DALA (C_t) was estimated by adjusting the initial concentration ($C_{initial(SFO)}$) (i.e., the concentration estimating by the SFO model at the beginning of the residue trial) according to the following equation:

$$C_t = C_{initial(SFO)} e^{(-kt)}$$

where,

C_t = concentration estimated at common DALA (ppb);

$C_{initial(SFO)}$ = concentration estimate at the initial time of residue measurement (ppb);

k = dissipation rate constant (d^{-1}); and,

t = # days between the day of measurement of $C_{initial}$ and that used for C_t .

The value of the common DALA used to estimate C_t varied according to the characteristics of the trials being considered for comparisons. Generally, the DALA was chosen such that the values of C_t would be estimated within the range of days associated with the residue data among all comparable trials so as to limit extrapolation of C_t beyond measured values.

4.5.5 Estimating Residue Decline Curves for Use in Tier II Risk Characterization

In addition to supporting the scientific basis for extrapolating residue data used in the neonicotinoid bee risk assessments, this section summarizes a new methodology used to estimate residue decline curves in

⁶ Degradation Kinetics Evaluator available at: <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-calculate-representative-half-life-values#current>.

of neonicotinoid residues in pollen and nectar for characterizing risks at Tier II. The preliminary bee risk assessments of imidacloprid, clothianidin and thiamethoxam published by the USEPA relied on an empirical approach for applying pollen and nectar residue data in estimating risk to honey bees at the colony level (USEPA 2016, 2017). Specifically, measured concentrations of the neonicotinoids in pollen and nectar were compared directly to the applicable No Observed Adverse Effect Concentration (NOAEC) and Lowest Observed Adverse Effect Concentration (LOAEC) derived from Tier 2 colony feeding studies (CFS). In order to account for expected variability in residue data resulting from numerous factors previously discussed, the preliminary bee risk assessments emphasized comparisons made to maximum residue values reported among all data derived for a given chemical/crop/application method/sample matrix. This empirical approach contains several limitations for estimating risks to bees, including:

1. It does not incorporate uncertainty associated with residue data sets of differing robustness in terms of their ability to capture temporal and spatial variability in pollen and nectar residues (*i.e.*, sparse vs. robust residue data sets). Consequently, the level of protection provided by the maximum observed value is expected to vary as a function of the robustness of the different residue data sets. In other words, maximum observed residue values from data sets with extensive spatial and temporal representation would likely afford a greater level of protection compared to sparse data sets).
2. It does not provide a quantitative estimate of how long pollen and nectar residues would likely exceed levels of concern; and,
3. It may discourage the generation of additional data by registrants since initially, comparisons are made to overall maximum value (*i.e.*, additional data would not lower the overall maximum value, only increase it).

Therefore, to address these primary limitations in the previous empirically-based risk characterization approach, the relationship between residue concentrations in pollen and nectar and the elapsed time after pesticide application (henceforth termed the “residue decline curve”) was quantitatively estimated using a probabilistic approach when feasible. Unlike the methods described in the previous sections which focused on estimating residue decline curves within a particular trial, this probabilistic approach attempts to describe the residue decline curve that is expected to exist among many hypothetical trials for a specified chemical and crop group (*e.g.*, foliar applications of clothianidin to cucurbits).

Importantly, the probabilistic approach could only be applied to residue data for certain crop groups associated with foliar spray applications (*e.g.*, cotton, berries/small fruits). For residue data associated with soil applications, the kinetic analysis revealed inconsistent residue decline curves among the trials (*i.e.*, declining, stable, increasing residues over time). This inconsistency might have resulted from prolonged uptake of neonicotinoids by plants following soil applications during the residue trials. Therefore, the previous empirical approach was used for risk characterization at Tier II. For foliar application to orchard crops, a regression approach was applied across multiple crops and trials since reliable estimates of residue decline kinetics could not be generated for a sufficient number of trials.

The following sections describe the probabilistic and regression approaches used to estimate residue decline curves that were considered for characterizing risk of neonicotinoids to honey bees in the final bee risk assessments.

4.5.5.1 Probabilistic Approach

The probabilistic approach relies on estimating the mean and variance of initial (peak) concentrations in pollen and nectar and their associated dissipation rate constants (k) based on the applicable residue trials (**Figure 4-2, Panels A & B**). These distributions are assumed to be lognormally distributed, with bounds defined by the observed maxima and minima of the distributions. Then, the expected residue for each day of a 60-d simulation was calculated by randomly drawing an initial concentration and a k value from each of the distributions assuming first order, single compartment kinetics. This was repeated 1000 times for each day of the analysis using Microsoft Excel Crystal Ball[®] module, V 11.1.2.3. The 60-d residue decline curve was then estimated based on a specified percentile of concentrations simulated for each day (**Figure 4-2, Panel C**). The statistical attributes of these residue decline curves (e.g., 50th, 70th, 90th percentiles representing 1000 randomly simulated fields) are then compared to colony-level endpoints from the colony feeding studies for characterizing risk.

Using this probabilistic approach, the underlying variability in the observed residue data can be directly incorporated into the risk assessment. This approach is analogous to the approach used by the European Food Safety Authority (EFSA) in their bee risk assessment process (EFSA 2013) and is conceptually consistent with the method used by OPP for assessing risk to birds and mammals from residues on arthropods (USEPA 2012). Importantly, this approach could be used for characterizing risk in a subset of crop groups involving foliar spray applications due to limitations in the underlying data and the lack of consistent residue decline curves associated with soil applications.

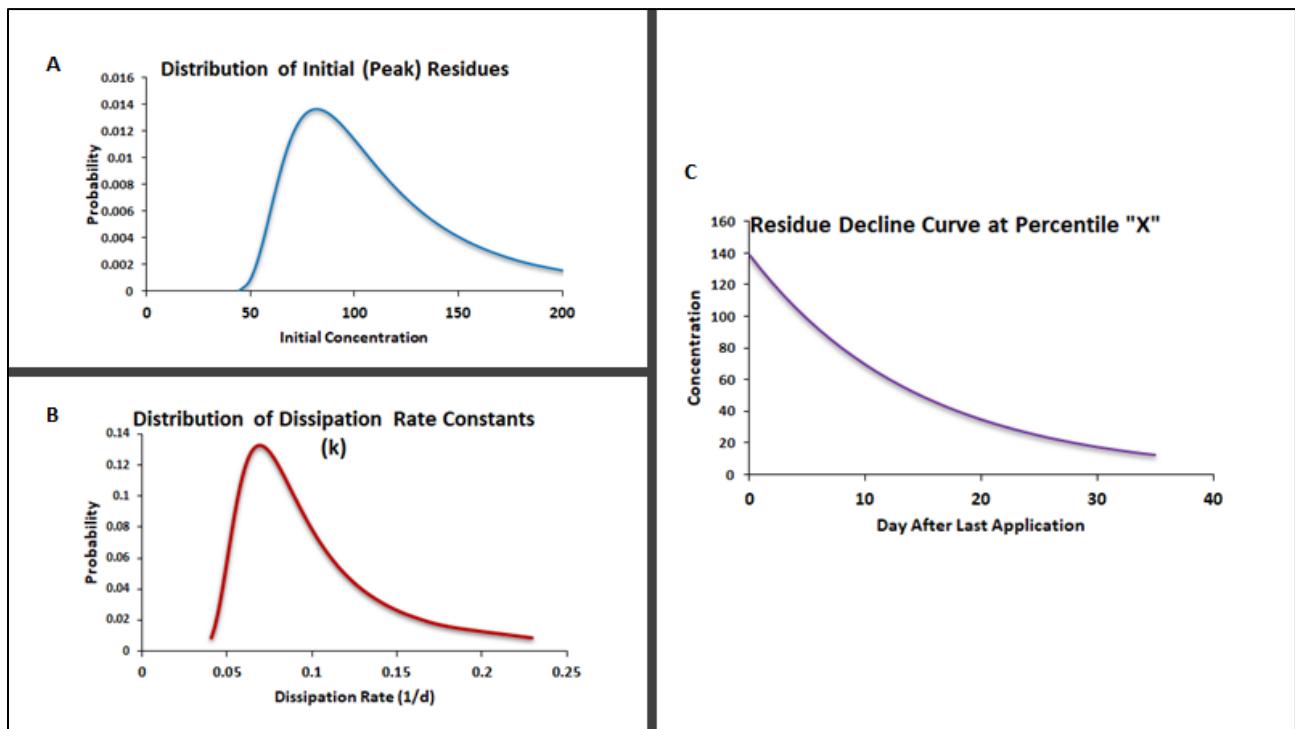


Figure 4-2. Conceptual approach for applying bee-relevant residue data in risk assessment. Variability of peak residues (A) and 1st order dissipation rates (B) are combined through Monte Carlo sampling to estimate residue decline curves associated with a specified percentile (C).

Simulation Scenarios

A simulation scenario is defined by the chemical, crop (or crop group), application method, application timing (e.g., pre-bloom, at bloom, post-bloom), and plant matrix (e.g., pollen, nectar, extrafloral nectar). Should the bridging analysis indicate residue data may be combined among crops and/or neonicotinoids, then a scenario may be defined for one or more neonicotinoids and crops. Within each simulation “scenario”, all residue concentrations are normalized to a standard application rate (e.g., 0.1 lb a.i./A) based on either the last application rate (single application) or the cumulative amount applied in the study (more appropriate for multiple applications with short application intervals). Based on these simulated residue-decline curves, one or more percentiles can be selected for risk characterization (as illustrated for foliar application of imidacloprid to cotton, **Figure 4-3**).

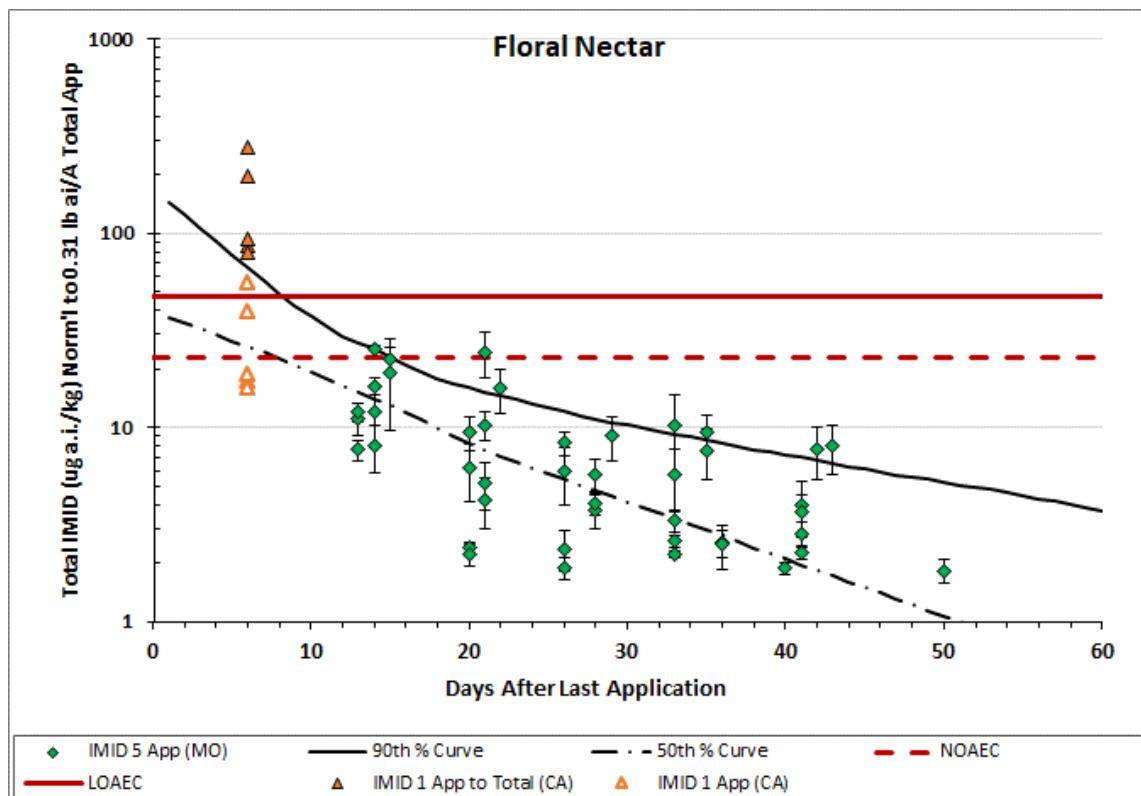


Figure 4-3. Daily mean concentration (+/- 95% CL) of total imidacloprid in cotton floral nectar (adjusted to the maximum seasonal foliar rate of 0.31 lb a.i./A) following seed + 5 foliar applications in 3 MO trials (MRID 49511702) and 1 foliar application in 5 CA

Model Inputs

Input parameters to this simulation include SFO dissipation rate constant (k , 1/d) and the initial concentration ($C_{initial}$) (mean, variance, distribution shape, bounds). For each simulation scenario, a rate constant and initial concentration value is randomly drawn from their respective distribution. This initial concentration is defined as the expected concentration at the beginning of the bloom period.

Estimating the Dissipation Rate Constant (k). All residue dissipation rates constants (k) are estimated and screened for reliability as described previously in **Section 4.5.4** using a single first order (SFO) model.

The distribution of “k” was defined as follows:

- i. **Distribution Shape.** If a sufficient number of dissipation rates are available within a comparable residue scenario⁷, they will be used to identify the most appropriate distribution shape (fit). Only those data sets with greater than 15 “k” values are applicable for fitting a distribution, based on the specifications of the Crystal Ball® software. Trials were run to determine the best fit of data sets that met this criterion. Generally, a log normal distribution was selected, although some distributions were best fit to other distribution types (e.g., Gamma, etc.). However, the overall prediction of “k” values was minimally impacted by the different distribution types and log normal was generally ranked in the top 3 of fits for the available data sets. Therefore, the log normal distribution is used to represent “k” values in the Monte Carlo analysis for all data sets.
- ii. **Distribution Parameters.** For each comparable residue scenario, the appropriate estimate of the central tendency of “k” values within a (mean) and variance (coefficient of variation) is calculated.
- iii. **Distribution Bounds.** One issue with using an unbounded statistical distribution such as normal or lognormal for Monte Carlo modeling is defining the bounds on the distribution shape. This is necessary to prevent scientifically unsupported values from being randomly selected. For each comparable residue scenario, the maximum and minimum dissipation rate was used to set the distribution bounds.

Defining the Distribution of Initial Concentrations ($C_{initial}$). Each $C_{initial}$ is first adjusted to reflect the same DALA prior to its use for Monte Carlo simulation using the trial-specific value of “k” as described in **Section 4.5.4**.

- i. **Distribution Shape.** If a sufficient number of $C_{initial}$ values are available within a comparable residue scenario, it can be used to identify the most appropriate distribution shape. However, similar to the “k” value data set, few data sets had adequate sample numbers to fit the data using Crystal Ball. Similar to determinations of the most appropriate “k” distributions, a sensitivity analysis was performed with a subset of data and the log normal distribution was found to be adequate for a distribution fit. Therefore, the log normal distribution was used to describe the distribution shape for $C_{initial}$ in the Monte Carlo analysis.
- ii. **Distribution Parameters.** Similar to the dissipation rate constant analysis, for each comparable residue scenario, the appropriate estimate of the central tendency of the $C_{initial}$ values within a (mean) and variance (coefficient of variation) is calculated.
- iii. **Distribution Bounds.** The same methodology described above for the dissipation constant was used to determine the bounds on the $C_{initial}$ parameters.

⁷ The definition of a “comparable category” of dissipation rates is currently being evaluated. It may or may not be specific to chemical, crop, matrix, application method.

Correlation of $C_{initial}$ Among Matrices. It is expected that chemical residues measured in one bee-relevant plant matrix (*e.g.*, pollen) will have some degree of correlation to another matrix (*e.g.*, nectar). Potential correlations among residues in different plant matrices were tested for all residue trials where data permit (*i.e.*, regressions of concentrations measured on the same day within a trial among plant matrices). The extent of correlations varies widely from no correlation to significant correlations, in part because of abiotic and biotic factors but are also due to artifacts from study design (*e.g.*, limited data). Using the bounds of these inter-tissue correlation coefficients, a sensitivity analysis of the impact on output of the Monte Carlo results was performed. The correlation did not significantly affect the targeted percentiles of the residue decline curves (*e.g.*, 90th percentile and lower). Therefore, independent distributions were assumed for simplicity sake.

Nectar Equivalence. For matrices other than oilseed crops, Monte Carlo distribution curves were generated in terms of nectar equivalents. Nectar equivalents are equal to nectar residue predictions plus pollen residues divided by 20., as described in **Attachment 1**. For oilseed crops, Monte Carlo distribution curves are generated for nectar, extrafloral nectar and pollen separately.

4.5.5.2 Regression Approach

Due to limitations that prevented reliable estimates of residue decline kinetics from individual trials associated with the orchard crops (*e.g.*, citrus, pome, stone fruits), a regression approach was used to estimate an overall residue decline curve reflecting data combined chemicals, trials, and crops. This approach has the conceptual advantage of using a much larger data set for estimating the residue decline curve compared to trial-specific estimation of “k”. An example of the regression approach applied to foliar applications of neonicotinoids to orchard crops is shown in **Figure 4-4**.

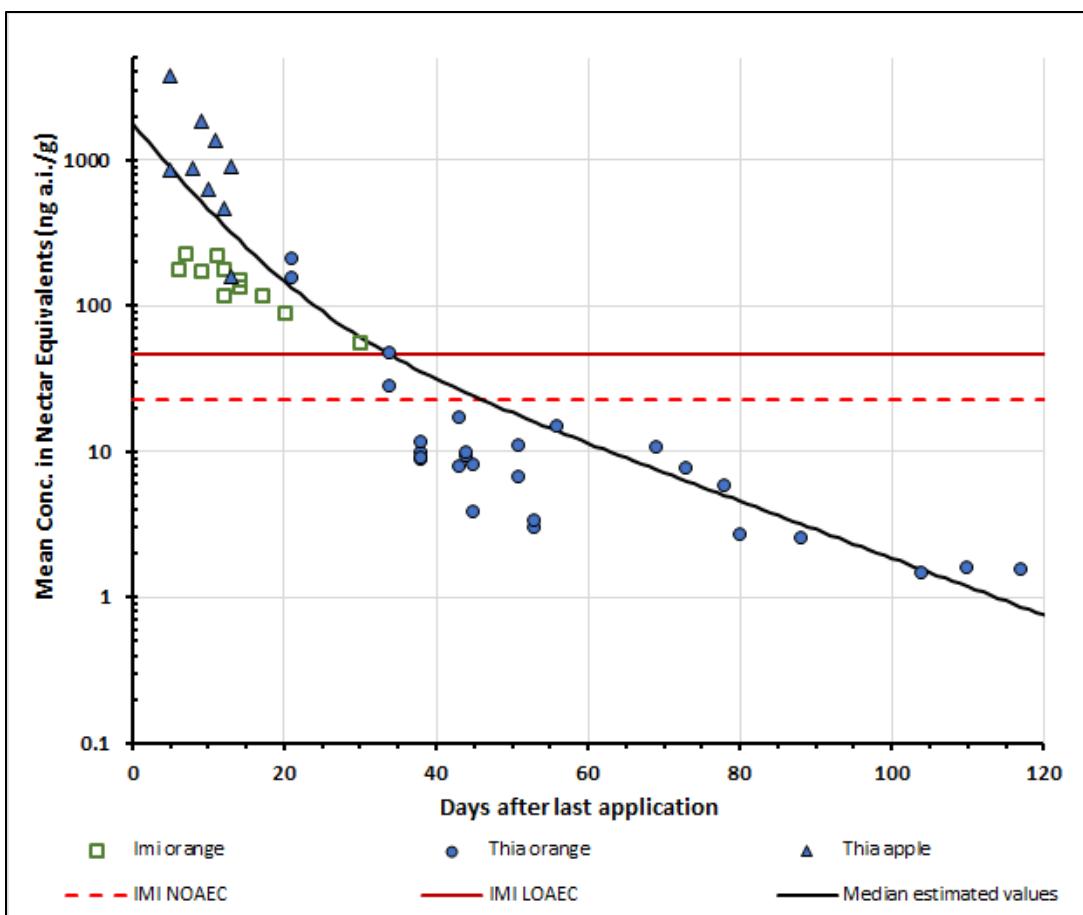


Figure 4-4. Mean-measured neonicotinoid residues (expressed as nectar equivalents) in orchard crops (normalized to 0.5 lb a.i./A) from pre-bloom, foliar applications relative to the imidacloprid colony level NOAEC and LOAEC

5 EXTRAPOLATION OF NEONICOTINOID RESIDUES AMONG PLANT MATRICES

Occasionally, field experiments examining the magnitude of residues in floral matrices have difficulty obtaining a sufficient quantity of nectar and pollen for reliable analysis. In such cases, the registrants have sometimes collected alternate floral matrices, such as anthers or whole flowers, and analyzed the residues therein. This section evaluates how these alternate matrices may be used as surrogates for pollen and nectar by evaluating those situations where data are available for both the relevant matrix and its potential surrogate matrix.

Two methods were used to evaluate the relationship between neonicotinoid concentrations in different plant matrices: linear regression and concentration ratios. The target matrices included pollen and nectar while the surrogate matrices included anthers (for pollen) and flowers (for pollen or nectar). Leaf data was not considered as a surrogate for nectar and pollen residues given the more proximal relationship assumed between two reproductive structures (*e.g.* flowers as a surrogate for nectar) than is assumed for vegetative and reproductive plant tissues. In addition, exploratory analyses with individual residue study trials indicate generally poor relationships between neonicotinoid residue in leaves vs. nectar and/or pollen. However, given the wide availability of leaf data from magnitude of

residue studies (used to develop tolerances), it may be beneficial to investigate this relationship more comprehensively in the future.

Details pertaining to these two methods are described **in Section 5.1 and 5.2**, respectively. With each approach, the residue data evaluated correspond to the residues of concern defined in the respective risk assessments for imidacloprid, clothianidin, thiamethoxam and dinotefuran as follows:

- Imidacloprid (sum of imidacloprid, 5-hydroxy imidacloprid and imidacloprid olefin)
- Clothianidin (clothianidin only)
- Thiamethoxam (sum of thiamethoxam and clothianidin)
- Dinotefuran (dinotefuran only).

5.1 Linear Regression Method

With this method, linear regressions are drawn between the neonicotinoid concentrations in the matrix of interest (*e.g.*, pollen or nectar) and in its potential surrogate (*e.g.*, flower, anther). The slope of these regression relationships reflects the best fit relationship between concentrations in the two plant matrices. Confidence limits around the slope estimates provide information on the uncertainty in this relationship and statistical similarity among slopes from different residue trials. Slopes close to or less than 1 suggest that on average, the alternate matrix (*e.g.*, concentrations in anthers plotted on the x-axis) provides a reasonably protective estimate of concentrations in the desired floral matrix (*e.g.*, pollen plotted on the y-axis). Slopes substantially greater than 1 suggest that on average the alternate matrix provides an under estimate of concentrations in the desired matrix and that an adjustment factor may be needed to be applied to adequately represent residues in pollen or nectar.

Linear regressions were run in Microsoft Excel™ comparing each study's residues in the surrogate and target matrices that were collected in a pairwise fashion (*i.e.*, samples collected within 1 day of each other at a given site). Typically, each residue study contained multiple trials reflecting different locations. Due to the small number of pairwise samples within a given trial, results were combined among trials with in a study for regression analysis. When trials involved different application rates within a study, these were analyzed separately. Datasets with less than 3 pairwise anther and pollen sample means were not included in the regression analysis. In addition to the slope estimate, other parameters were also calculated including:

- 95% confidence limits around the slope;
- X-intercept and associated 95% confidence limits;
- Correlation coefficient (r^2); and
- p-value of the regression

The regressions were then screened for reliability. The following criteria were used to identify regressions that were not considered reliable:

- p-value of regression > 0.1
- r^2 values < 0.25

These reliability criteria were intentionally set to be relatively inclusive given the high degree of variability that has been shown to exist in neonicotinoid field residue data within a study (Sappington *et*

al., 2018) and relatively small data set sizes. The average, median and 90th percentile of study-specific slopes were considered for characterizing the potential use of the surrogate matrix. Given the variability and the relatively small sample sizes associated with the residue data within each residue study, linear regression was also performed on the combined data set of pairwise residue data among studies.

5.2 Ratio Method

In the second method, ratios of concentrations in the target vs. surrogate matrix are derived between individual pairwise samples (*i.e.*, samples taken within 1 day of each other). Within each study, descriptive statistics (mean, median, percentiles) are estimated for these ratios to provide a sense of the central tendency and variance in the target-to-surrogate matrix relationship. These ratios have a similar interpretation as indicated for the slopes previously. As with the regression method, the average, median and 90th percentiles of the average ratios from each study were considered for characterizing the potential use of the surrogate matrix. Given the variability and the relatively small sample sizes associated with the residue data within each residue study, target-to-surrogate tissue ratios of the pairwise data were combined among the available residue studies and descriptive statistics were calculated.

5.3 Choosing the Surrogate Matrix Extrapolation Factor

Two types of surrogate matrix extrapolation factors were derived: 1) 50th percentile extrapolation factor to be used quantitatively in risk assessments based on the median slope or ratio, and 2) a 90th percentile extrapolation factor to be used qualitatively for characterizing the impact of variability in the extrapolation factors on risk conclusions. In choosing which method (regression or ratio) and data set type (study-specific or combined) upon which to derive the 50th and 90th percentiles, the following factors were considered.

- # of regressions that met reliability criteria relative to the number of studies available
- similarity among slopes from study-specific regressions which met reliability criteria
- reliability of the regression from the combined studies
- similarity among mean tissue concentration ratios among residue studies
- evenness in the sample sizes among studies in the combined data set
- influence of potential outliers on 50th and 90th percentile estimates.

In general, preference was given to the ratio method over the regression method for deriving the tissue extrapolation factors when few reliable regressions could be conducted on the study-specific data. Furthermore, preference was generally given to use of the combined residue data set when information from the study-specific data suggested the regression slopes or tissue ratios were relatively similar among studies.

5.4 Anther Residues as a Surrogate for Pollen

The anther is the portion of the stamen where the pollen is produced and may be easier to collect and process compared to pollen alone. Six studies contained anther and pollen residue samples which were sampled concurrently following soil or foliar applications (**Table 5-1**). Most of these studies have small sample sizes and represent individual sampling time points with residues in anthers and pollen collected within 1 day of each other. For each comparable sampling event, mean residues in anther and pollen

(typically from 3 replicate samples each) were compared in pairwise fashion. As all but one of these studies used soil applications, this evaluation focused on the analysis of data from soil applications only.

Table 5-1. Available Residue Studies Containing Concurrent Samples of Pollen and Anthers

Chemical	Crop	Application Method	n	MRID
Clothianidin	Cucurbits (squash & pumpkin)	Soil	8*	49705901
Clothianidin	Potato	Soil	4	49705902
Clothianidin	Potato	Foliar	4	49705902
Imidacloprid	Strawberry	Soil	3	49090502
Dinotefuran	Cantaloupe	Soil	3	50145701
Dinotefuran	Bell Pepper	Soil	4	50145702

*contains a potential outlier

5.4.1 Linear Regression Method (Pollen vs. Anther)

Table 5-2 provides the regression estimates for each of these study pairings of anther and pollen data while **Figure 5-1 (Panels A-C)** provides plots of the three data sets that met the minimum criteria described above for the regression relationship (strawberry-imidacloprid, cucurbits-clothianidin, bell pepper-dinotefuran). The cucurbits (clothianidin) and strawberry (imidacloprid) regression relationships suggest that anther residues are similar to those in pollen (i.e., slopes = 0.84 and 1.2, respectively, with 95% C.L. that include or overlap with 1.0) and have good fits with the residue data ($r^2 > 0.98$ with the removal of a single cucurbit data point). In contrast, the bell pepper (dinotefuran) pollen vs. anther regressions suggest that pollen residues can be approximately 2X higher than anther residues (i.e., slope = 2.1; 95% C.L. = 1.0-3.2). However, the regression relationship for bell pepper is influenced largely by the highest value (143 ng a.i./g-anthers, 261 ng a.i./g-pollen), while the three lower sample means in this study are more suggestive that anther residues would indeed be representative or protective of pollen residues (lower slope). The 95% C.L. also overlap among the three regression relationships, suggesting that they may not be significantly different. Given the small sample sizes with the imidacloprid and dinotefuran data sets, the regressions are sensitive to single high values which contribute disproportionately to the mean squared error. Individual regression relationships for the potato data (slope of 2.5) narrowly fails to meet the minimum criteria for the p-value of 0.1 while that for cantaloupe also fails the p-value significance criterion.

Table 5-2. Statistical Results of Linear Equation Regressions for Pairwise Pollen-Anther Comparisons of Soil Applications of Neonicotinoids

Chemical	Crop	N	Slope (95% C.L.)	R ²	P-value
Clothianidin	Cucurbits	7*	0.84 (0.71-0.96)	0.98	<0.01
Imidacloprid	Strawberry	3	1.2 (-0.59-2.6)	0.99	0.075
Dinotefuran	Bell Pepper	4	2.1 (1.0-3.2)	0.97	0.014
Individual regressions that failed the screening criteria					
Clothianidin	Potato	4	2.5 (-1.3-6.3)	0.80	0.11
Dinotefuran	Cantaloupe	3	0.97 (-11.2-13.2)	0.50	0.50
Average of Trial Slopes**		1.4			
Median of Trial Slopes**		1.2			
90 th Percentile of Trial Slopes**		1.9			

Chemical	Crop	N	Slope (95% C.L.)	R ²	P-value
Combined Regression					
All A.I.s	All Crops	22	1.1 (0.88-1.3)	0.85	<0.01

Bolded italicized values indicate where minimum criteria were not met.

*Outlier removed from dataset

** Excluding regressions that did not meet the minimum criteria

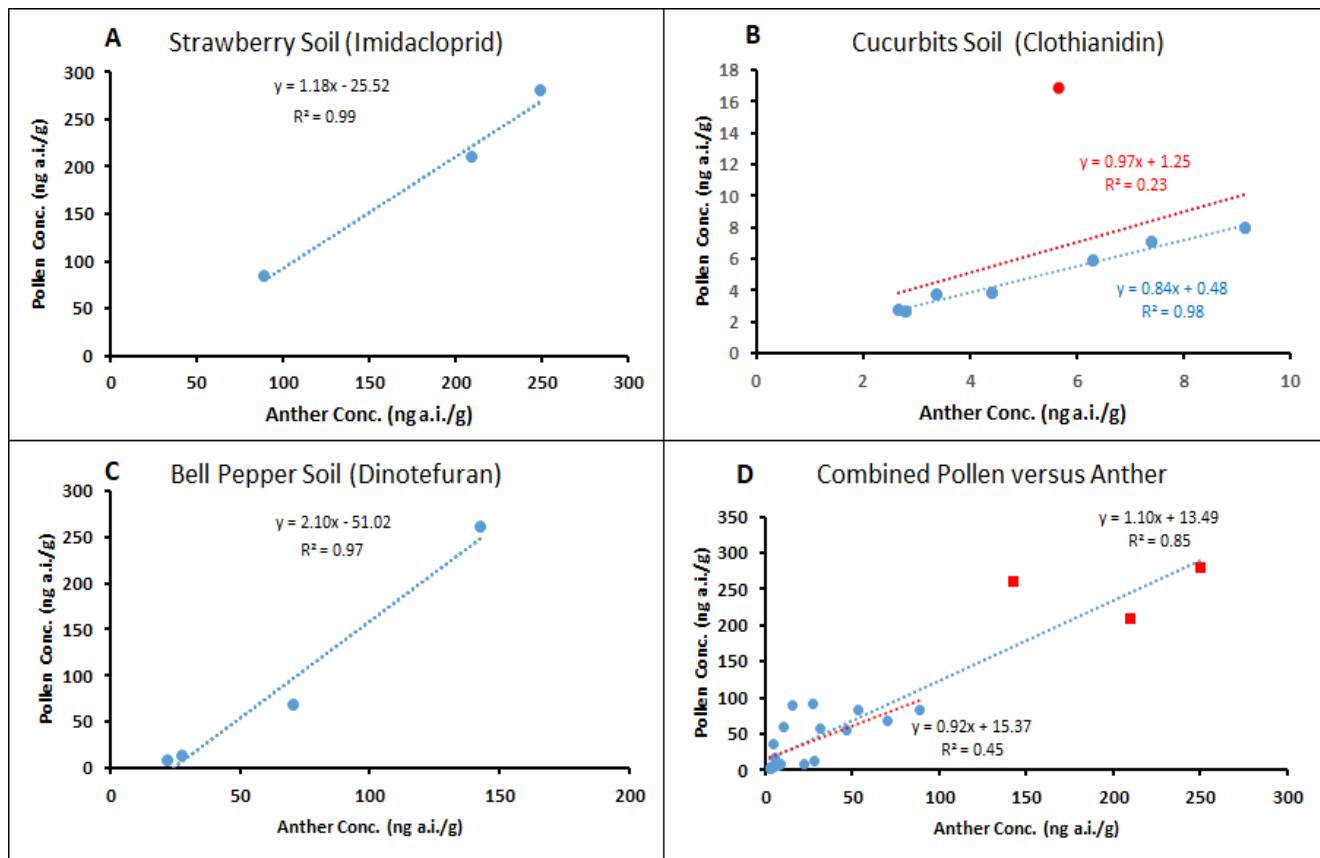


Figure 5-1. Linear Regressions for Mean Concentrations Measured in Anthers and Pollen that Meet Validity Criteria Following Soil Applications of Imidacloprid (A), Clothianidin (B), Dinotefuran (C), or All Data Combined (D). The red dot represents a potential outlier in the cucurbit data (B), the removal of which dramatically increases the regression fit (lower equation). Combining the data from all five soil studies (D), the regression model estimates a slope of 1.1 (upper equation), which is minimally impacted with removal higher values (red boxes, red regression line).

Combining all the data from all 5 soil trials (regardless of the outcome of the individual trial regression relationships), the linear regression model estimates a slope of 1.1 (95% CL=0.88-1.3) suggesting that on average, anther and pollen residues are roughly equivalent (**Figure 5-1D**). It is noted that there are a small cluster of high values (red squares); that could overly impact the regression estimate. However, removal of these values (**Figure 5-1D**, red line) was not found to impact the slope estimate (slope decreases from 1.1 to 0.92), although the fit of the model decreases the R² to only 0.45. The overall regression slope of 1.1 compares favorably to the mean (1.4) and median (1.2) of the three individual regression slopes which passed the screening criteria.

Under conservative assumptions, the 90th percentile of the slope equations indicates that multiplying anther residues by ~2X would yield highly protective approximations of pollen residues. Combining the data in this manner assumes that chemical and crop do not influence the relationship between anther and pollen residues.

5.4.2 Ratio Method (Pollen/Anther)

Under the ratio method analysis, the ratios of mean pollen to anther residues are evaluated across the pairwise data for each study (**Table 5-3**). As with the linear regression analysis above, this method indicated higher concentrations of the neonicotinoids in pollen relative to anthers for potatoes (5.6X on average), though the dinotefuran bell pepper data suggests that anther residues would be representative of pollen exposures on average, in contrast to the linear regression analysis above. Treating each study equally, the median of the 5 average ratios among the trials is 1.0; this suggests that anther and pollen residues are roughly equivalent on average. Notably, average and median pollen-to-anther ratios among the crops and neonicotinoids are relatively similar (within 2X) except for potato.

Table 5-3. Descriptive Statistics of Pollen-to-Anther Ratios for Each Soil-Application Study

Chemical	Crop (treatment)	N	Average Ratio	CV	Min Ratio	Max Ratio	50 th %	90 th %
Clothianidin	Cucurbits	7*	0.95	0.08	0.86	1.08	0.94	1.06
Clothianidin	Potato	4	5.63	0.33	3.42	7.96	5.57	7.28
Imidacloprid	Strawberry	3	1.02	0.09	0.93	1.12	1.00	1.10
Dinotefuran	Canteloupe	3	1.53	0.21	1.20	1.84	1.56	1.78
Dinotefuran	Bell Pepper	4	0.91	0.73	0.36	1.82	0.72	1.56
Mean of Average Ratios		2.0						
50 th Percentile of Average Ratios		1.0						
90 th Percentile of Average Ratios		4.0						

*Apparent outlier removed from analysis

Consideration was also given to combining all the ratio data into a single analysis. Using the combined data set, the median pollen to anther ratio is 1.0, again suggesting that anther and pollen residues are equivalent on average (**Table 5-4**). Under conservative assumptions, the 90th percentile of ratio method for the combined dataset indicates that multiplying anther residues by ~5X would yield highly protective (*i.e.*, upper bound) approximations of pollen residues.

Table 5-4. Descriptive Statistics of Pollen-to-Anther Ratios for the Combined Soil Application Data Set

Statistic	Value
Overall N	22
Average	2.9
Coefficient of Variation	69%
Minimum	0.36
Maximum	8.0
50 th Percentile	1.1
90 th Percentile	5.2

5.4.3 Choice of Anther-to-Pollen Extrapolation Factor

Examining the overall dataset finds that with the possible exception of soil applications to potatoes, neonicotinoid residues in anthers can be considered a reasonable surrogate for residues in pollen, on average. The median slopes from the regression method (0.92-1.2) and the median ratio from the ratio method (1.1) also indicate that residue concentrations in anthers are a reasonable surrogate for residue concentrations in pollen. Given the few number of reliable regressions available for the pollen:anther data set (3), preference is given to the ratio method for deriving the anther-to-pollen extrapolation factors. Results are similar with the analysis of pollen-to-anther ratios within individual studies and combined across studies (**Table 5-3** and **Table 5-4**). However, overall preference is given to the combined ratio data set due to the low number of pairwise anther:pollen samples within each study (n=4-7) and similarity in mean ratios among studies with the exception of potato.

Although insufficient data are available to evaluate residue comparisons in anthers and pollen following foliar applications, the foliar potato data (regression slope of 3.9, average ratio of 6.1) are higher, but relatively similar to the soil potato data (regression slope of 2.5, average ratio of 5.6) suggesting that application method may not have so large an influence on comparisons of anther and pollen residue data in this crop.

Therefore, in the neonicotinoid risk assessments, anther data from either soil or foliar applications are recommended to be used quantitatively with a **1X** factor as a surrogate for pollen where pollen data are lacking (**Table 5-4**, 50th percentile). Additionally, for risk characterization purposes, it is recommended that a **5X** factor be applied to anther data in order to qualitatively evaluate how variability in the pollen-to-anther ratios affects the risk conclusions (**Table 5-4**, 90th percentile).

5.5 Flower Residues as a Surrogate for Nectar

Fifteen residue trials are available with data containing concurrent flower and either nectar and/or pollen samples following foliar (or seed+foliar) applications with either imidacloprid or thiamethoxam (**Table 5-5**). Similarly, 15 residue trials available with data containing concurrent flower and either nectar and/or pollen samples following soil applications (**Table 5-6**). Sample sizes ranged from 5 to 43 pairwise sample means per study for nectar and 1 to 43 pairwise sample means for pollen. Flower and pollen/nectar samples were collected concurrently (or at most one day apart) from the same field.

Table 5-5. Available Residue Studies Containing Concurrent Samples of Whole Flowers and Nectar and/or Pollen Following Foliar Applications

Chemical	Crop	Application Method	Matrices Measured	n	MRID
Imidacloprid	Cotton	Seed+Foliar	F, N, P	FN-43; FP-43	49511702
Imidacloprid	Citrus	Foliar	F, N, P	FN-22; FP-21	49521301
Imidacloprid	Cherry	Foliar	F, N, P	FN-13; FP-13	49535601
Imidacloprid	Watermelon	Foliar (3 apps.)	F, N, P	FN-3; FP-3	50357101
Thiamethoxam	Lilac	Foliar	F, N, P	FN-4; FP-2	50425903
Thiamethoxam	Mock Orange	Foliar	F, N, P	FN-5; FP-7	50425903
Thiamethoxam	Stargazer Lily	Foliar	F, N, P	FN-10; FP-9	50425903
Thiamethoxam	Apple	Foliar	F, N, P	FN-9; FP-9	50265504
Thiamethoxam	Blueberry	Foliar (1 apps.)	F, N, P	FN-9*; FP-9	50425901

Chemical	Crop	Application Method	Matrices Measured	n	MRID
Thiamethoxam	Blueberry	Foliar (3 apps.)	F, N, P	FN-9; FP-9	50425901
Thiamethoxam	Cranberry	Foliar	F, N, P	FN-9; FP-9	49804102
Thiamethoxam	Cucumber	Foliar	F, N, P	FN-9; FP-9	49804105
Thiamethoxam	Soybean	Foliar	F, N	FN-5*	49804104
Thiamethoxam	Tomato	Foliar	F, P	FP-6	49804101
Thiamethoxam	Strawberry	Foliar	F, N, P	FN-8; FP-7	50265502

F=Flower, N=Nectar, P=Pollen;

FN and FP = # of pairwise combinations of flower/nectar and flower/pollen

*Contains a potential outlier

Table 5-6. Available Residue Studies Containing Concurrent Samples of Whole Flowers and Nectar and/or Pollen Following Soil Applications

Chemical	Crop	Application Method	Measured Matrices	n	MRID
Thiamethoxam	Strawberry	Soil (high)	F, N, P	FN-8; FP-8	50266001
Thiamethoxam	Strawberry	Soil (low)	F, N, P	FN-8; FP-8	50266001
Thiamethoxam	Squash	Soil	F, N, P	FN-9; FP-9	50265501
Thiamethoxam	Pumpkin	Soil (high)	F, N, P	FN-15; FP-15	50265501
Thiamethoxam	Pumpkin	Soil (low)	F, N, P	FN-12; FP-12	50265501
Thiamethoxam	Musk Melon	Soil	F, N, P	FN-15; FP-15	50265501
Thiamethoxam	Tomato	Soil (Low)	F, P	FP-9	50265507
Thiamethoxam	Tomato	Soil (high)	F, P	FP-9	50265507
Thiamethoxam	Pepper	Soil	F, N, P	FN-5; FP-5	49804103
Thiamethoxam	Lilac	Soil	F, N, P	FN-3; FP-3	50425903
Thiamethoxam	Sargent Crabapple	Soil	F, P	FP-7	50425903
Thiamethoxam	Stargazer Lily	Soil	F, N, P	FN-9; FP-9	50425903
Thiamethoxam	Hedge Cotoneaster	Soil	F, N	FN-9	50425903
Imidacloprid	Strawberry	Soil	F, P	FP-3	49090502
Imidacloprid	Watermelon	Soil	F,N,P	FN-3; FP-1	50357101

F=Flower, N=Nectar, P=Pollen; FN and FP = # of pairwise combinations of flower/nectar and flower/pollen

5.5.1 Linear Regression Method (Nectar vs. Flower, Foliar Spray)

Linear regressions were performed and evaluated for reliability in the same manner as described previously in **Section 5.1**. A total of 14 regressions could be conducted on individual trials containing paired measurements of flower and nectar residues after foliar spray applications (**Table 5-7**). Of these, only 6 regression relationships passed the screening criteria for reliability, 3 with imidacloprid (cotton, citrus, cherry) and 3 with thiamethoxam (apple, blueberry, cucumber). Plots of these regressions are shown in **Figure 5-2**.

Regression slopes and fits varied widely among the 6 trials with regressions that passed the screening criteria. Specifically, the slope of nectar:flower regressions ranged from 0.014 to 4.2 and values of r^2 ranged from 0.30-0.84. The mean and median of the regression slopes are 0.87 and 0.15 respectively,

reflecting the skewness in the distribution of slopes (the slope of 4.2 from the blueberry flower:nectar regression was much higher than the other crops). Since different crops were involved among the two neonicotinoids represented, it is not possible to evaluate the effect of chemical on the nectar:flower regressions without the potentially confounding influence of crop. Within each chemical, the lack of overlapping 95% confidence limits of slopes among crops suggests that the crop may influence the relationship between residues in nectar vs. flowers (**Table 5-7**). It is also worth noting that the overall robustness of the data sets supporting these regressions varies widely (**Figure 5-2**). The most robust data sets are represented by foliar applications of imidacloprid to citrus and cotton (Panels A & B). The remaining data sets are comparatively sparse (Panels C-F) and regression slopes are sensitive to single data points of maximum measured residues (Panels E & F). Even when these maximum residue values are removed from the data sets, regression relationships do not improve (red lines in Panels E & F). Therefore, the utility of these trial-specific regressions appears limited for broadly representing the relationship between nectar and flower residues, at least for these two neonicotinoids.

Table 5-7. Statistical Results of Linear Equation Regressions for Pairwise Nectar-Flower Comparisons of Foliar Applications of Neonicotinoids

Chemical	Crop (treatment)	N	Slope (95% C.L)	R ²	P-value		
Imidacloprid	Cotton	43	0.64 (0.43-0.85)	0.49	<0.01		
Imidacloprid	Citrus	22	0.15 (0.12-0.18)	0.84	<0.01		
Imidacloprid	Cherry	13	0.014 (-0.0001-0.03)	0.30	0.05		
Thiamethoxam	Apple	9	0.16 (0.10-0.22)	0.83	<0.01		
Thiamethoxam	Blueberry (3x)	9	4.2 (-0.71-7.7)	0.54	0.03		
Thiamethoxam	Cucumber	9	0.034 (-0.004-0.07)	0.40	0.07		
Individual regressions that failed the screening criteria							
Imidacloprid	Watermelon	3	0.24 (-0.94-1.4)	0.87	0.23		
Thiamethoxam	Blueberry (1x)	9	0.021 (-0.35-0.39)	0.003	0.90		
Thiamethoxam	Cranberry	9	0.39 (-0.96-1.75)	0.06	0.51		
Thiamethoxam	Soybean	5	0.004 (-0.01-0.02)	0.32	0.33		
Thiamethoxam	Lilac	4	-0.0012 (-0.06-0.06)	0.003	0.94		
Thiamethoxam	Mock Orange	5	0.13 (-0.31-0.56)	0.22	0.43		
Thiamethoxam	Stargazer Lily	10	0.12 (-0.06-0.30)	0.24	0.16		
Thiamethoxam	Strawberry	8	0.087 (-0.14-0.31)	0.13	0.38		
Average of Trial Slopes*		0.87					
Median of Trial Slopes*		0.15					
90 th Percentile of Trial Slopes*		2.4					
Combined regression							
All AI	All Crops	155	0.084 (0.03-0.14)	0.055	0.003		

*Excluding regressions that did not meet the minimum criteria

Bolded italicized values indicate where minimum regression criteria were not met.

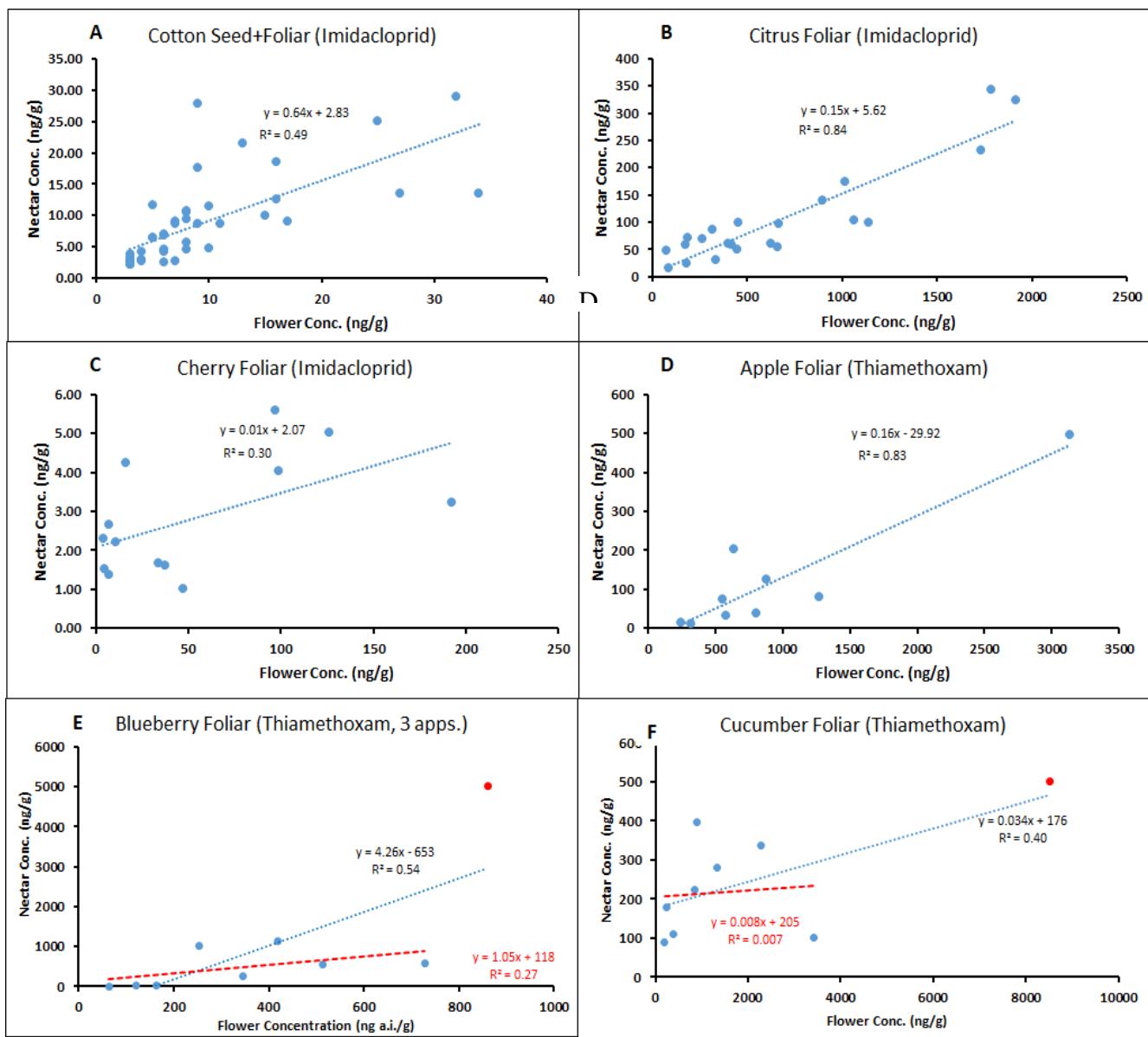


Figure 5-2. Linear Regressions for Mean Measured flower and nectar concentrations that met validity criteria following foliar applications of imidacloprid (A-C) or thiamethoxam (D-F). Red dots represents potential outliers in the blueberry and cucumber data (E-F), the removal of which decreases the regression slope, but also decreases the regression fits (red dashed lines, lower equations).

When the residue data are combined among all 14 trials (Figure 5-3), the regression of nectar:flower has a poor overall fit ($r^2 = 0.055$) although it is statistically significant ($p=0.003$). Based on the results from the trial-specific regressions, it is likely that the poor fit reflects the effect of crop and other confounding factors on the relationship between flower and nectar residues.

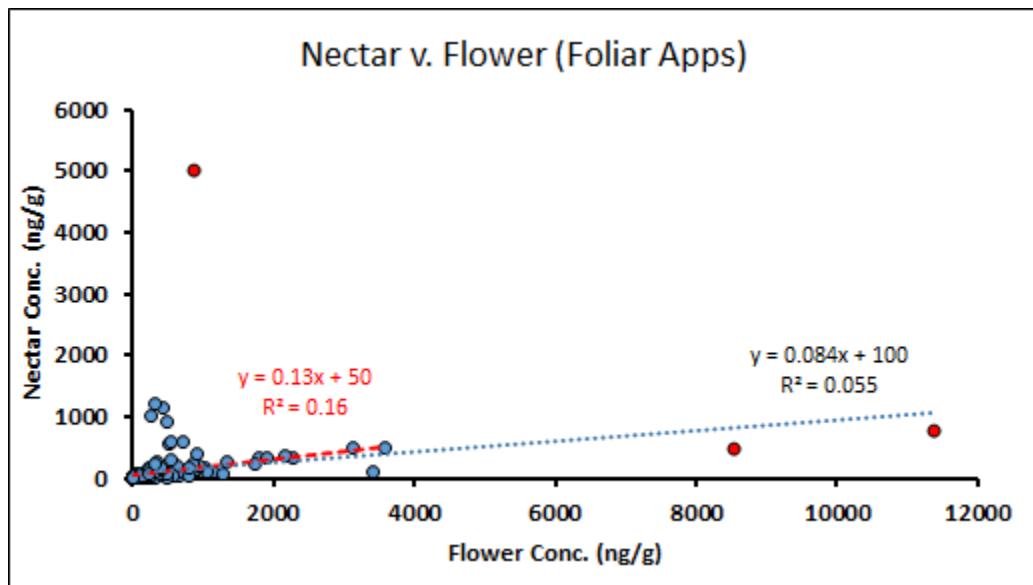


Figure 5-3. Linear Regression of Mean Measured Flower and Nectar Concentrations of Combined Data from all 13 available Foliar Studies. The regression slope of 0.084 is minimally impacted with removal of the the potential outliers represented by the red dotss (red regression line).

5.5.2 Ratio Method (Nectar/Flower, Foliar Spray)

Under the ratio method analysis, the ratios of mean nectar to flower concentrations are evaluated across the pairwise data for each residue trial with foliar applications (Table 5-8). As with the linear regression analysis above, this method indicated floral exposures are protective of nectar residues with the vast majority of studies having average ratios well below 1 and only one study with average ratio overs 1 (foliar applied thiamethoxam to blueberries with multiple applications and a maximum ratio of 1.8). Treating each study equally, the median of the average ratios among the 14 trials indicates that nectar concentrations are approximately 0.3x flower concentrations for foliar applications. As an upper bound estimate, using whole flowers as a direct surrogate for nectar would provide a conservative estimate (i.e., by about 3.3X).

Table 5-8. Descriptive Statistics of Nectar-to-Flower Ratios for Each Foliar-Application Study

Chemical	Crop/Group	N	Average Ratio	CV	Min Ratio	Max Ratio	50 th %	90 th %
Imidacloprid	Cotton	43	1.01	51%	0.39	3.10	0.91	1.34
Imidacloprid	Citrus	22	0.19	67%	0.08	0.66	0.15	0.32
Imidacloprid	Cherry	13	0.17	101%	0.02	0.55	0.06	0.36
Imidacloprid	Watermelon	3	0.27	5%	0.26	0.29	0.27	0.28
Thiamethoxam	Apple	9	0.11	81%	0.03	0.32	0.06	0.19
Thiamethoxam	Blueberry (1x)	9	0.49	112%	0.03	1.55	0.19	1.14
Thiamethoxam	Blueberry (3x)	9	1.77	114%	0.1	5.84	0.82	4.42
Thiamethoxam	Cranberry	9	0.95	121%	0.19	3.69	0.51	2.22
Thiamethoxam	Cucumber	9	0.29	76%	0.03	0.73	0.27	0.51
Thiamethoxam	Soybean	5	0.07	80%	0.01	0.13	0.08	0.12
Thiamethoxam	Strawberry	8	0.42	38%	0.21	0.72	0.38	0.60
Thiamethoxam	Lilac	4	0.11	52%	0.04	1.05	0.14	0.79

Chemical	Crop/Group	N	Average Ratio	CV	Min Ratio	Max Ratio	50 th %	90 th %
Thiamethoxam	Mock Orange	5	0.27	52%	0.16	0.44	0.18	0.43
Thiamethoxam	Stargazer Lily	10	0.18	84%	0.03	0.47	0.16	0.42
Mean of Average Ratios			0.45					
50 th Percentile of Average Ratio			0.27					
90 th Percentile of Average Ratios			0.99					

Consideration was also given to combining all the nectar:flower ratio data. Using this approach, the median nectar-to-flower ratio is approximately 0.3x (**Table 5-9**). Under conservative assumptions, the 90th percentile of ratio method for the combined dataset indicates that multiplying flower residues by ~1.2X would yield highly protective approximations of nectar residues.

Table 5-9. Descriptive Statistics of Nectar/Flower Ratios from the Combined Foliar Application Data Set

Statistic	Value
Number of Sample Means	158
Average	0.58
Standard Deviation	0.77
Minimum	0.008
Maximum	5.8
50 th Percentile	0.32
90 th Percentile	1.2

5.5.3 Choice of Flower-to-Nectar Extrapolation Factor (Foliar Spray)

The majority of linear regressions of trial-specific nectar vs. flower concentrations resulting from foliar applications of imidacloprid and thiamethoxam failed the screening criteria for fit and statistical significance of the slope. Of the 6 trial-specific regressions that passed these criteria, all but one suggested that on average, the concentrations of imidacloprid or thiamethoxam in flowers exceed those in nectar (*i.e.*, slopes less than 1). Additionally, differences in the slopes of these regression suggest that crop type influences the relationship between concentrations in flowers vs. nectar. However, except for two data sets (imidacloprid cherry and cotton), the robustness of these regressions is questionable, either due to issues with fit or the influence of outlying data points. Furthermore, linear regression of the combined nectar and flower residues from all trials also indicates poor fit. Therefore, the regression approach is of questionable utility for generating a ‘default’ extrapolation factor from concentrations in flowers to those in nectar that may be broadly applicable across crops and neonicotinoids.

The ratio method is used instead to support default extrapolations of flower concentrations to nectar concentrations based on associated probabilities of occurrence (50th and 90th percentile). The 50th and 90th percentiles of the average nectar:flower ratios among the 14 trials are 0.27 and 0.99, respectively. This calculation assumes equal weight to average nectar:flower ratios from each trial, which would be appropriate if crop type influences the relationships. However, even if ratios were combined from all 14 data sets, the 50th and 90th percentiles are similar (0.32 and 1.2, respectively). Therefore, in the neonicotinoid risk assessments, flower residue data associated with foliar application are recommended to be used quantitatively with a **0.3X** factor as a surrogate for nectar (50th percentile, **Table 5-8** and **Table 5-9**). Additionally, for risk characterization purposes, it is recommended that a **1X** factor be

applied to flower residues in order to qualitatively evaluate how variability in the nectar-to-flower ratios affects the risk conclusions (90th percentile, **Table 5-8** and **Table 5-9**).

5.5.4 Linear Regression Method (Nectar vs. Flower, Soil Application)

Residue data relating flower and nectar concentrations of neonicotinoids were analyzed separately for soil applications due to the potential influence of application method on this relationship. Such differences in the flower:nectar relationship could, in theory, occur due to the different mechanisms by which neonicotinoids can accumulate in these plant tissues (e.g., translocation via foliar contact with sprays vs. uptake from roots after soil application). Furthermore, foliar spray applications made during bloom could result in greater concentrations in plant tissues compared to soil applications due to the combined effect of direct deposition onto flowers/nectaries and translocation to these tissues.

Linear regressions were performed and evaluated for reliability in the same manner as described in **Section 5.1**. **Table 5-10** provides the regression estimates for each of the study pairings of flower and nectar data following soil applications while **Figure 5-4** provides plots of those data that met the minimum criteria described previously for the regression analysis. Of the 11 trial-specific regressions that were conducted, 6 satisfied the screening criteria for reliability described previously (5 with thiamethoxam and 1 with imidacloprid). Since different crops were represented among each of the 6 trials, it is not possible to evaluate the effect of chemical on the nectar:flower regressions without the potentially confounding influence of crop.

With the exception of muskmelon (imidacloprid), the slopes of these regressions are less than 1, which indicates that residues in flowers are greater (protective) than those in nectar, on average (**Table 5-10**). The imidacloprid data are highly uncertain due to the low number of data points (n=3). Slopes for the flower:nectar relationship for thiamethoxam range from 0.16 to 0.56., and the 95% confidence intervals generally overlap among the different crops represented. The average, 50th and 90th percentile of these 6 trial-specific slopes are 0.45, 0.34 and 0.84, respectively.

When all the flower-nectar pairwise data are combined (**Figure 5-4F**), the regression slope (0.22) is similar as the median slope of the trial-specific slopes (0.34). Variability in the residue data combined from all trials results in a relatively poor fit ($R^2 = 0.31$). Combining the data in this manner assumes that crop does not influence the relationship between flower and nectar residues.

Table 5-10. Statistical Results of Linear Equation Regressions for Pairwise Nectar-Flower Comparisons for Soil Applications of Neonicotinoids

Chemical	Crop (treatment)	N	Slope (95% C.L)	R ²	P-value
Thiamethoxam	Hedge Cotoneaster	9	0.17 (0.11-0.23)	0.858	<0.01
Thiamethoxam	Strawberry (low)	8	0.27 (0.21-0.33)	0.95	<0.01
Thiamethoxam	Squash	9	0.16 (0.13-0.19)	0.95	<0.01
Imidacloprid	Watermelon	3	1.1 (-0.005-2.2)	0.99	0.05
Thiamethoxam	Pumpkin (low)	12	0.41 (0.18-0.63)	0.62	<0.01
Thiamethoxam	Musk Melon	15	0.56 (0.31-0.81)	0.65	<0.01
Individual regressions that failed the screening criteria					
Thiamethoxam	Stargazer Lily	9	-0.013 (-0.30-0.28)	0.0015	0.92

Chemical	Crop (treatment)	N	Slope (95% C.L)	R ²	P-value
Thiamethoxam	Strawberry (high)	8	0.09 (-0.06-0.24)	0.27	0.189
Thiamethoxam	Pumpkin (high)	15	0.076 (-0.06-0.22)	0.095	0.263
Thiamethoxam	Lilac	3	1.2 (-13.0-15.4)	0.54	0.48
Thiamethoxam	Pepper	5	0.56 (-2.1-3.2)	0.13	0.54
Average of Study Slopes*			0.45		
50 th Percentile of Study Slopes*			0.34		
90 th Percentile of Study Slopes*			0.84		
Combined regression					
All AI	All Studies/Crops	96	0.22 (0.16-0.29)	0.31	<0.01

*Excluding regressions that did not meet the minimum criteria

Bolded italicized values indicate where minimum criteria were not met.

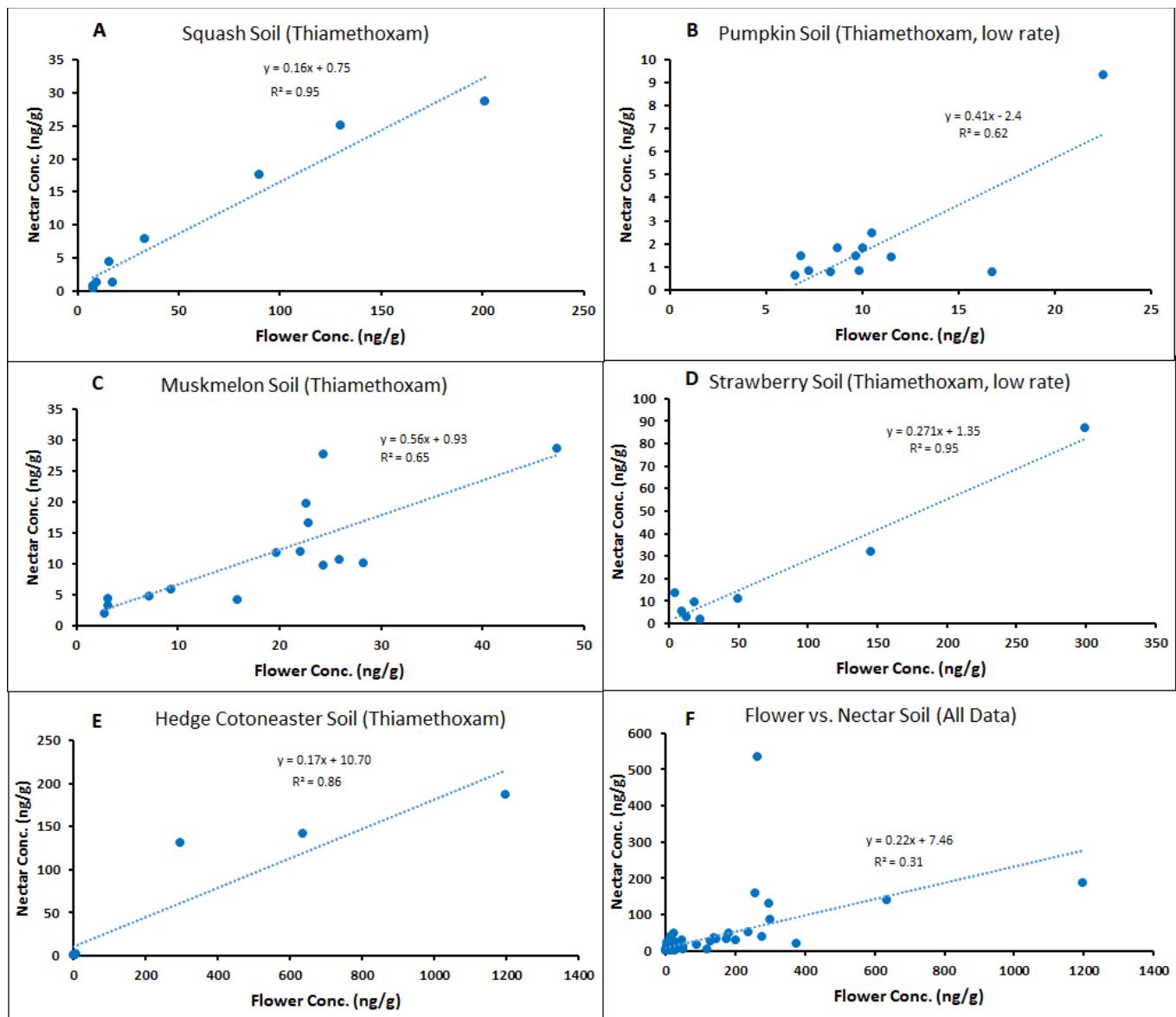


Figure 5-4. Linear Regressions of Mean Measured Flower and Nectar Concentrations That Met Validity Criteria following Soil Applications of Thiamethoxam (Panels A-E) and All Data Combined, Including Imidacloprid (Panel F).

5.5.5 Ratio Method (Nectar/Flower, Soil Application)

Under the ratio method, the ratios of mean nectar-to-flower concentrations are evaluated across the pairwise data for each residue trial with soil applications (Table 5-11). As with the linear regression analysis above, this method indicated floral exposures are protective of nectar residues all but one of the residue trials having average nectar:flower concentration ratios well below 1. Treating each study equally, the median of the study-specific average ratios suggest that nectar concentrations are typically approximately 0.4X flower concentrations following soil applications. As a conservative upper bound, the 90th percentile of the average ratios is approximately 1.0.

Table 5-11. Descriptive Statistics of Ratio Method Results (Nectar:Flower) for Each Soil Application Study

Chemical	Crop	N	Average Ratio	CV	Min Ratio	Max Ratio	50 th %	90 th %
Thiamethoxam	Strawberry (high rate)	8	1.13	134%	0.09	4.26	0.19	2.74
Thiamethoxam	Strawberry (low rate)	8	0.64	151%	0.07	2.97	0.26	1.29
Thiamethoxam	Squash	9	0.16	48%	0.06	0.28	0.14	0.25
Thiamethoxam	Pumpkin (high rate)	15	0.26	63%	0.09	0.54	0.26	0.51
Thiamethoxam	Pumpkin (low rate)	12	0.16	61%	0.05	0.41	0.14	0.23
Thiamethoxam	Musk Melon	15	0.69	46%	0.26	1.42	0.63	1.11
Thiamethoxam	Pepper	5	0.63	125%	0.05	2.01	0.35	1.4
Thiamethoxam	Stargazer Lily	9	0.99	110%	0.03	3.21	0.56	2.64
Thiamethoxam	Hedge Cotoneaster	9	0.35	77%	0.08	0.91	0.3	0.68
Thiamethoxam	Lilac	3	0.37	60%	0.22	0.62	0.27	0.55
Imidacloprid	Watermelon	3	0.17	56%	0.08	0.27	0.16	0.25
Mean of Average Ratios			0.50					
50 th Percentile of Average Ratio			0.37					
90 th Percentile of Average Ratios			0.99					

Consideration was also given to combining all the nectar:flower ratio data for analysis. Using this approach, the median nectar to flower ratio is also 0.3X (**Table 5-12**). Under conservative assumptions, the 90th percentile of ratio method for the combined dataset indicates that using flower residues as a direct one-to-one surrogate would yield very highly protective approximations of nectar residues.

Table 5-12. Descriptive Statistics of Nectar/Flower Ratios from the Combined Soil Application Data Set

Statistic	Value
Number of Sample Means	96
Average	0.51
Standard Deviation	0.70
Minimum	0.028
Maximum	4.26
50 th Percentile	0.27
90 th Percentile	0.99

5.5.6 Choice of Flower-to-Nectar Extrapolation Factor (Soil Application)

About half of the 11 linear regressions of trial-specific nectar vs. flower concentrations resulting from soil applications of imidacloprid and thiamethoxam failed the screening criteria for fit and statistical significance of the slope. Of the 6 trial-specific regressions that passed these criteria, all but one suggested that on average, the concentrations of imidacloprid or thiamethoxam in flowers exceed those in nectar (*i.e.*, slopes less than 1). Based on the median of the 6 trial-specific nectar:flower regression slopes, residues of thiamethoxam and imidacloprid in nectar are about 0.3X those in flowers. When all pairwise nectar:flower data are combined among all 11 trials, a slope of 0.22 is indicated, which is similar to the medial slope from the trial-specific regressions.

Results from the ratio method are similar to those from the regression methods. Specifically, the 50th and 90th percentiles of the average nectar:flower ratios among the 11 trials are 0.37 and 0.99, respectively. This calculation assumes equal weight to average nectar:flower ratios from each trial. The 50th and 90th percentiles are similar when nectar:flower ratios are combined among all trials (0.27 and 0.99 respectively).

Therefore, in the neonicotinoid risk assessments, flower residue data are recommended to be used quantitatively with a **0.3X** factor (50th percentile) as a surrogate for nectar concentrations associated with soil applications). Additionally, for risk characterization purposes, it is recommended that a **1X** factor (90th percentile) be applied to flower residues from soil applications in order to qualitatively evaluate how variability in the nectar-to-flower ratios affects the risk conclusions. These recommendations reflect to the regression and ratio methods of analysis.

5.6 Flower Residues as a Surrogate for Pollen

5.6.1 Linear Regression Method (Pollen vs. Flower, Foliar Spray)

Linear regressions were performed and evaluated for reliability in the same manner as described previously in **Section 5.1**. **Table 5-13** provides the regression estimates for each of the study pairings of flower and pollen data following foliar applications, while **Figure 5-5** provides plots of those data that met the minimum criteria described previously for the regression analysis. Of the 12 trial-specific regressions that were conducted, only 4 satisfied the screening criteria for reliability described previously (2 with imidacloprid and 2 with thiamethoxam). For 3 of the trials, slopes of the pollen:flower regressions range from 1.6 to 2.2 with overlapping 95% confidence limits and r^2 values ranging from 0.54-0.69. With the 4th trial (thiamethoxam, cucumber), a slope of 0.36 is indicated with 95% confidence limits that do not overlap with those of the other 3 trials. The r^2 from the cucumber trial is 0.99, indicating a good fit with the observed data, although it is likely influenced by a single high residue value in this trial. Because different crops were represented among each of the 4 trials, it is not possible to evaluate the effect of chemical on the pollen:flower regressions without the potentially confounding influence of crop. The average, 50th and 90th percentiles of the slopes from these 4 trials are 1.6, 1.8 and 2.2, respectively; however, with only 4 slope values as a basis for analysis, these percentile estimates are considered uncertain and are of questionable reliability.

When all the flower-pollen pairwise data are combined (**Figure 5-5E**), the regression slope is only 0.66, but a poor fit with the data is indicated with an r^2 of only 0.16. Combining the data in this manner assumes that chemical and crop do not influence the relationship between flower and pollen residues. This assumption may not be appropriate given the wide range in regression slopes from trials which failed the reliability criteria varied widely from -0.25 to 5.3.

Given the wide variation in regression slopes among all the trials and the fact that only 4 of the 12 trials resulted in reasonable regression fits to the observed data, making general inferences among crops and neonicotinoids using the pollen:flower regressions from foliar spray applications is considered uncertain and of questionable reliability.

Table 5-13. Statistical Results of Linear Equation Regressions for Pairwise Pollen-Flower Comparisons for Foliar Applications of Neonicotinoids

Chemical	Crop (treatment)	N	Slope (95% C.L.)	R ²	P-value
Imidacloprid	Citrus	22	2.1 (1.1-2.9)	0.54	<0.01
Imidacloprid	Cherry	13	2.2 (1.1-3.3)	0.64	<0.01
Thiamethoxam	Cranberry	9	1.6 (0.64-2.5)	0.69	<0.01
Thiamethoxam	Cucumber	9	0.36 (0.32-0.39)	0.99	<0.01
Individual regressions that failed the screening criteria					
Imidacloprid	Cotton	43	0.33 (0.13-0.53)	0.22	<0.01
Thiamethoxam	Apple	9	0.15 (-0.28-0.57)	0.086	0.44
Thiamethoxam	Blueberry (1x)	9	-0.25 (-0.77-0.26)	0.16	0.28
Thiamethoxam	Blueberry (3x)	9	0.36 (-0.52-1.3)	0.12	0.37
Thiamethoxam	Tomato	6	5.3 (-3.3-14)	0.42	0.16
Thiamethoxam	Mock Orange	7	-0.05 (-0.71-0.61)	0.0076	0.85
Thiamethoxam	Stargazer Lily	9	-0.03 (-0.01-0.35)	0.16	0.28
Thiamethoxam	Strawberry	7	1.0 (-11-13)	0.0089	0.84
Average of Trial Slopes*			1.6		
Median of Trial Slopes*			1.8		
90 th Percentile of Trial Slopes*			2.2		
Combined regression					
All AI	All Crops	153	0.66 (0.41-0.91)	0.16	<0.01

¹ As there were fewer than 3 pairwise mean pollen and flower samples, regression estimates were not made.

*Excluding regressions that did not meet the minimum criteria

Bolded italicized values indicate where minimum criteria were not met.

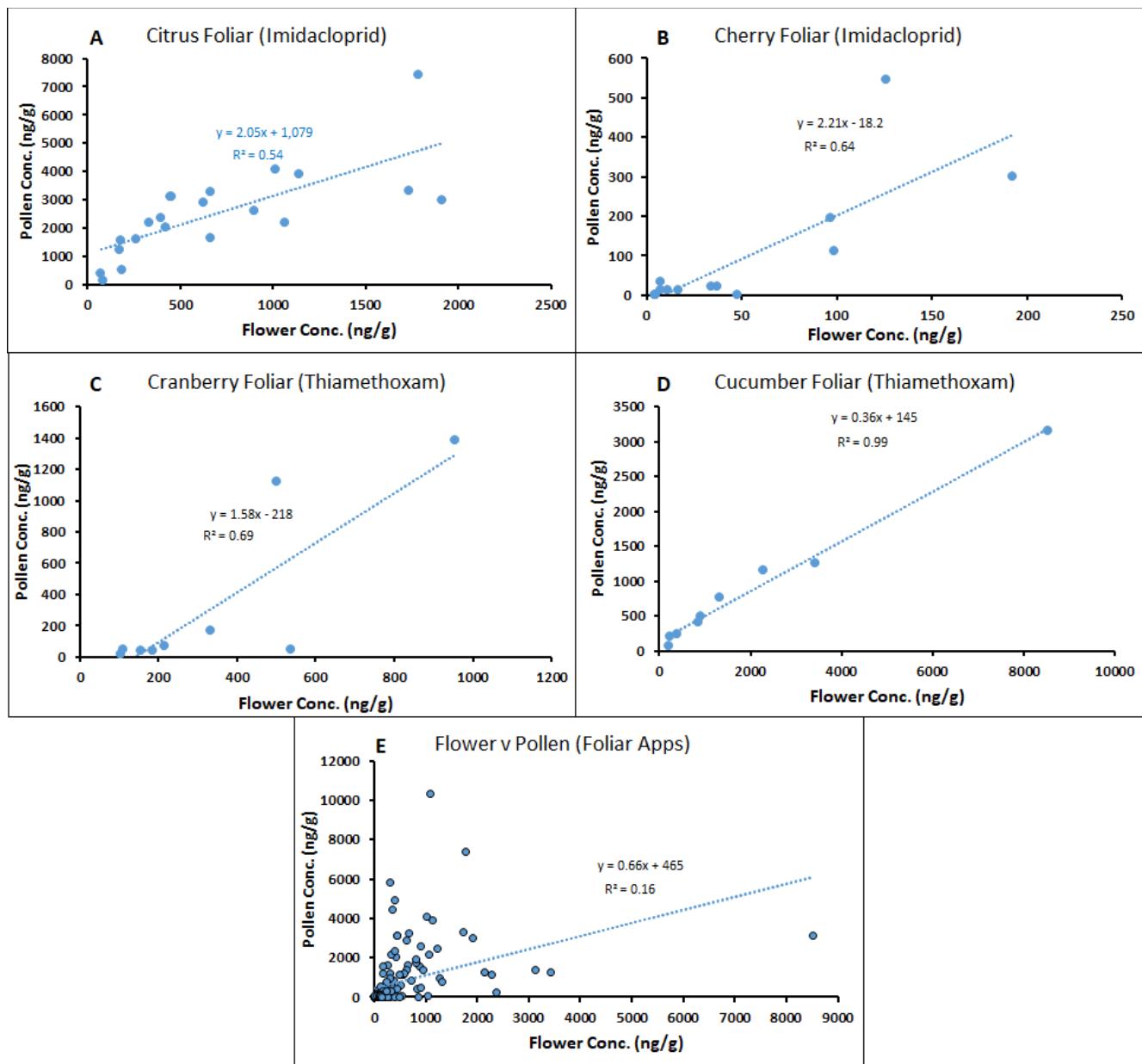


Table 5-14. Descriptive Statistics of Pollen-to-Flower Ratios for Each Foliar Application Study

Chemical	Crop	Application Method	N	Average Ratio	CV	Min Ratio	Max Ratio	50th %	90th %
Imidacloprid	Cotton	Seed+Foliar	43	0.50	158%	0.06	4.8	0.24	1.2
Imidacloprid	Citrus	Foliar	21	4.5	46%	1.6	8.7	4.6	6.8
Imidacloprid	Cherry	Foliar	13	1.5	96%	0.02	4.7	1.1	3.9
Thiamethoxam	Apple	Foliar	9	1.8	56%	0.44	3.7	2.0	2.5
Thiamethoxam	Blueberry	1x Foliar	9	1.4	89%	0.01	3.5	1.2	3.1
Thiamethoxam	Blueberry	3x Foliar	9	0.84	76%	0.01	1.9	1.0	1.4
Thiamethoxam	Cranberry	Foliar	9	0.63	115%	0.08	2.2	0.32	1.6
Thiamethoxam	Cucumber	Foliar	9	0.52	30%	0.37	0.86	0.51	0.68
Thiamethoxam	Lilac	Foliar	2	0.34	100%	0.1	0.58	0.34	0.53
Thiamethoxam	Mock Orange	Foliar	7	0.31	134%	0.01	0.92	0.07	0.9
Thiamethoxam	Stargazer Lily	Foliar	9	0.06	102%	0.002	0.19	0.04	0.16
Thiamethoxam	Strawberry	Foliar	8	6.1	109%	1.3	19	3.1	15
Thiamethoxam	Tomato	Foliar	6	4.4	116%	0.72	12	1.6	11
Mean of Average Ratios				1.8					
50 th Percentile of Average Ratios				0.84					
90 th Percentile of Average Ratios				4.5					

When pollen-to-flower ratios are combined among all the trials into a single data set, the median pollen-to-flower ratio resulting from foliar applications is approximately 0.6X (**Table 5-15**). Using pollen-to-flower ratios derived from the combined data set inherently assumes that ratio probabilities are independent of neonicotinoid and crop. Under conservative assumptions, the 90th percentile of the pollen-to-flower ratios is approximately 5X. Despite the uneven representation of the different trials in the combined data set (*i.e.*, n=43 for cotton vs. n=2 for lilac), the median and 90th percentiles of the trial-specific average ratios (0.84 and 4.5, respectively) are similar to those derived from combined data set (0.63 and 4.7, respectively).

Table 5-15. Descriptive Statistics of Pollen/Flower Ratios from the Combined Foliar Application Data Set

Statistic	Value
Number of Sample Means	153
Average	1.7
Standard Deviation	2.6
Minimum	0.002
Maximum	19
50 th Percentile	0.63
90 th Percentile	4.7

5.6.3 Choice of Flower-to-Pollen Extrapolation Factor (Foliar Spray)

Examining the overall dataset indicates that, in contrast to the flower and nectar relationships following foliar applications, the ratio and slopes of flower and pollen pairwise data are much more variable and residues in flowers are not consistently protective of pollen residues. The regression approach does not seem satisfactory for estimating an overall flower-to-pollen extrapolation factor among crops and neonicotinoids for foliar applications, given that 8/12 trials did not produce regressions of reliable utility and of those that did, wide variability is seen among slopes (6X).

As a result, development a flower-to-pollen extrapolation factor for foliar applications is based on the ratio method. Among the two approaches summarized for the ratio method, preference is given to ratios derived from the individual trial data sets for two reasons. First, the mean pollen-to-flower ratios are highly variable among trials (0.06 to 6.1) which suggests that crop and/or chemical may influence the relationship between residues in flowers and pollen (**Table 5-14**). Second, the representation of the individual trials in the combined data set is highly uneven ($n= 2-43$), which inherently assigns greater weight to two trials with much larger sample sizes (imidacloprid cotton and citrus). Therefore, in the neonicotinoid risk assessments, flower residue data associated with foliar application are recommended to be used quantitatively with a **0.8X** factor as a surrogate for pollen where pollen data are lacking with foliar applications (**Table 5-14**, median ratio). Additionally, for risk characterization purposes, it is recommended that a **5X** factor be applied to flower data in order to qualitatively evaluate how variability in the pollen-to-flower ratios affects the risk conclusions.

5.6.4 Linear Regression Method (Pollen vs. Flower, Soil Application)

Linear regressions were performed and evaluated for reliability in the same manner as described in **Section 5.1**. **Table 5-16** provides the regression estimates for each of the study pairings of flower and pollen data following soil applications, while **Figure 5-6** provides plots of those data that met the minimum criteria described previously for the regression analysis.

Of the 12 trial-specific regressions that were conducted, only 5 trials (imidacloprid strawberry, and thiamethoxam tomato, pepper, squash and Seargent crabapple satisfied the criteria) produced regressions that met the screening criteria for reliability described previously. Slopes for these 5 trials varied widely (by a factor of 10) from 0.07 (thiamethoxam squash) to 0.71 (imidacloprid strawberry) with r^2 values ranging from 0.72-0.99. These slopes indicate on average, concentrations of imidacloprid or thiamethoxam in pollen are below those in flower, by up to a factor of 1.4X to 14X. With the exception of squash and Seargent crabapple, these regression slopes have overlapping 95% confidence limits suggesting that they may not be statistically different from each another. Because different crops were represented among each of the 5 trials, it is not possible to evaluate the effect of chemical on the pollen:flower regressions without the potentially confounding influence of crop. The average, 50th and 90th percentiles of the slopes from these 5 trials are 0.45, 0.56 and 0.65, respectively.

When all the flower-pollen pairwise data are combined **Figure 5-6F**, the regression slope is 0.33 (about midway between the slopes from the 5 individual trials), but the regression fit is very poor with an r^2 of only 0.05. Combining the data in this manner assumes that chemical and crop do not influence the relationship between flower and pollen residues. This assumption may not be appropriate given the wide range in regression slopes from trials which failed the reliability criteria varied widely from -1.7-1.3.

Given the wide variation in regression slopes among all the trials and the fact that only 5 of the 12 trials resulted in reasonable regression fits to the observed data, making general inferences among crops and neonicotinoids using the pollen:flower regressions from soil applications is considered uncertain and of questionable reliability.

Table 5-16. Statistical Results of Linear Equation Regressions for Pairwise Pollen-Flower Comparisons for Soil Applications of Neonicotinoids

Chemical	Crop (treatment)	N	Slope (95% C.L)	R ²	P-value
Imidacloprid	Strawberry	3	0.71 (-0.04-1.5)	0.99	0.053
Thiamethoxam	Pepper	5	0.56 (0.02-1.1)	0.79	0.045
Thiamethoxam	Seargent Crabapple	7	0.34 (0.11-0.58)	0.73	0.01
Thiamethoxam	Squash	9	0.07 (0.03-0.11)	0.72	<0.01
Thiamethoxam	Tomato (high rate)	9	0.57 (0.15-0.99)	0.60	0.014
Individual regressions that failed the screening criteria					
Thiamethoxam	Tomato (low rate)	9	0.08 (-0.61-0.77)	0.011	0.79
Thiamethoxam	Pumpkin (high rate)	15	0.08 (-0.10-0.26)	0.069	0.35
Thiamethoxam	Pumpkin (low rate)	12	0.10 (-0.25-0.44)	0.037	0.55
Thiamethoxam	Lilac	3	-0.02 (-0.98-0.93)	0.073	0.82
Thiamethoxam	Musk Melon	15	1.3 (-2.6-5.2)	0.038	0.49
Thiamethoxam	Stargazer Lily	9	0.10 (-0.09-0.29)	0.19	0.24
Thiamethoxam	Strawberry (high rate)	8	-1.7 (-5.2-1.9)	0.18	0.29
Thiamethoxam	Strawberry (low rate)	8	0.10 (-1.0-1.2)	0.007	0.84
Average Slope*			0.45		
Median Slope*			0.56		
90 th Percentile Slope*			0.65		
All AI	All Crops	126	0.33	0.051	<0.01

*Excluding regressions that did not meet the minimum criteria

Bolded italicized values indicate where minimum criteria were not met.

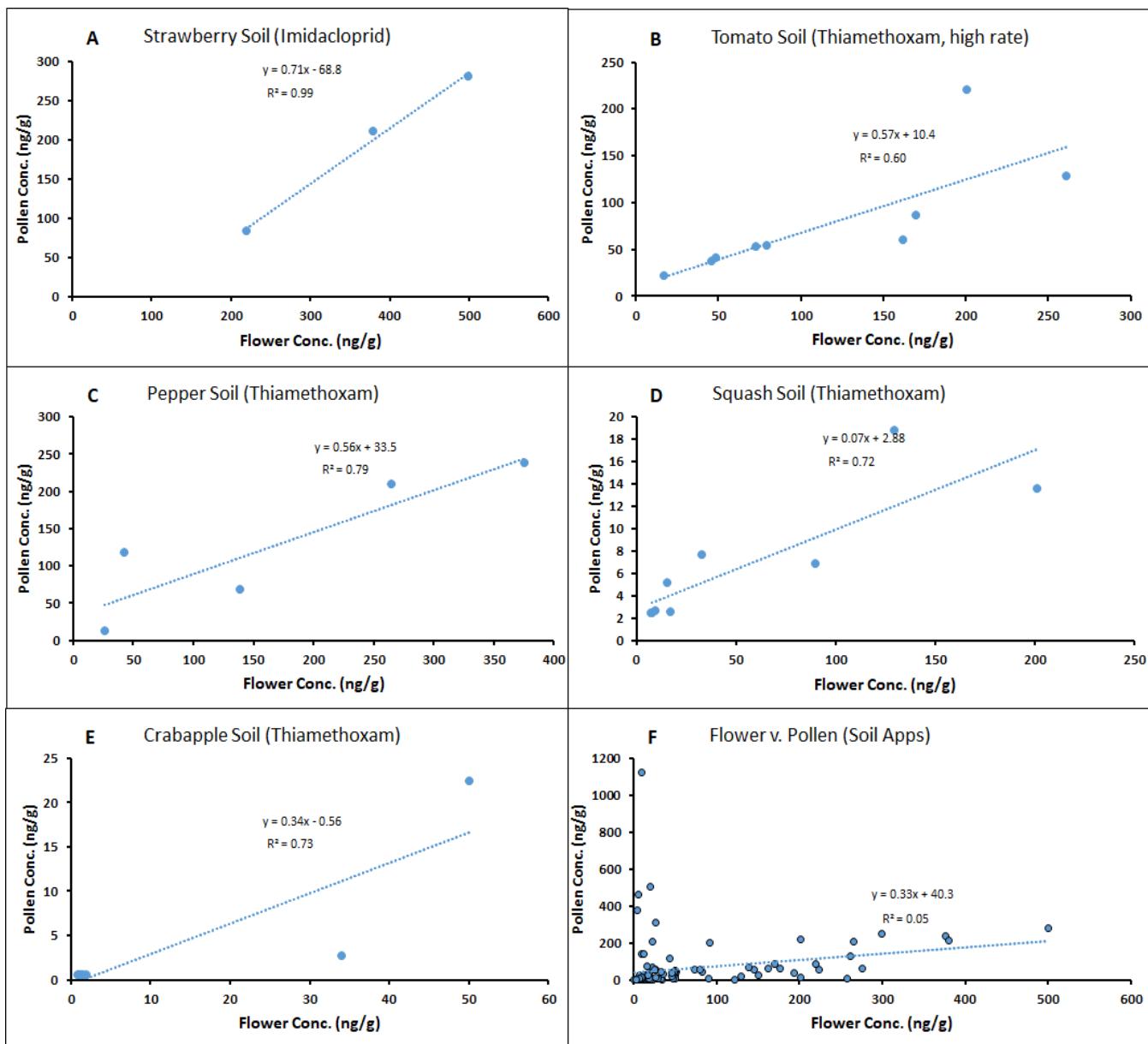


Figure 5-6. Linear Regressions of Mean Measured Flower and Pollen Concentrations That Met Validity Criteria following Soil Applications of Imidacloprid (Panel A), Thiamethoxam (Panels B-E) and All Data Combined, (Panel F).

5.6.5 Ratio Method (Pollen/Flower, Soil Application)

Under the ratio method analysis, the ratios of mean pollen-to -flower residues are evaluated across the pairwise data for each study for soil (**Table 5-17**) applications. Based on the median values of pollen:flower concentration ratios, residues in flowers are protective of those in pollen (average ratios below 1) in 10 of the 14 trials with pairwise data. It is noted that average pollen-to-flower ratios greatly exceed 1 from the thiamethoxam strawberry trials (16 and 31 for the low and high rate trials, respectively). Further review of the underlying residue data indicate that these high pollen-to-flower ratios are driven by exceptionally high values of pollen from one site (California) in these studies. In these cases, residues of thiamethoxam in pollen exceeded those in leaves, which is uncommon with all

of the other residue trials from soil application or the other sites within this study. It is not known why thiamethoxam residues in strawberry pollen from the CA site are so elevated relative to flowers. However, they do not appear to be representative of soil applications of thiamethoxam made to strawberries at other sites, those made to other crops, or of imidacloprid applications made to strawberries. Therefore, the summary statistics for the trial-specific pollen-to-flower ratios were determined with and without inclusion of the CA strawberry residue data for thiamethoxam.

Table 5-17. Descriptive Statistics of Pollen-to-Flower Ratios for Each Soil Application Study

Chemical	Crop	Application Method	N	Average Ratio	CV	Min Ratio	Max Ratio	50 th %	90 th %
Imidacloprid	Strawberry	Soil	3	0.50	21%	0.38	0.56	0.55	0.56
Imidacloprid	Watermelon	Soil	1	1.2	N/A	1.2	1.2	N/A	N/A
Thiamethoxam	Tomato	Soil (high rate)	9	0.75	39%	0.37	1.3	0.71	1.1
Thiamethoxam	Tomato	Soil (low rate)	9	0.66	96%	0.18	2.2	0.44	1.2
Thiamethoxam	Strawberry	Soil (high rate)	8	31	159%	0.22	124	1.9	100
Thiamethoxam	Strawberry	Soil (low rate)	8	16	183%	0.39	84	5.6	36
Thiamethoxam	Pepper	Soil	5	1.0	96%	0.44	2.8	0.63	2.0
Thiamethoxam	Squash	Soil	9	0.21	49%	0.07	0.33	0.23	0.32
Thiamethoxam	Pumpkin	Soil (high rate)	15	0.45	51%	0.07	0.99	0.43	0.68
Thiamethoxam	Pumpkin	Soil (low rate)	12	0.36	57%	0.07	0.79	0.38	0.54
Thiamethoxam	Musk Melon	Soil	15	1.8	177%	0.10	12	0.58	3.9
Thiamethoxam	Lilac	Soil	3	1.1	160%	0.03	3.2	0.15	2.6
Thiamethoxam	Seargent Crabapple	Soil	7	0.34	45%	0.08	0.51	0.35	0.49
Thiamethoxam	Stargazer Lily	Soil	9	0.41	183%	0.004	2.4	0.17	0.7
Statistic			All Data		All Data Except Strawberry CA Site				
Mean of Average Ratios			3.9		1.9				
50 th Percentile of Average Ratios			0.71		0.75				
90 th Percentile of Average Ratios			11.4		1.2				

Based on the trial-specific statistics for pollen-to-flower ratios with the thiamethoxam strawberry CA data included, the mean, median and 90th percentile ratios are 3.9, 0.71 and 11.4, respectively. With omission of the thiamethoxam CA strawberry data (10 values), the mean, median and 90th percentiles are 1.9, 0.75 and 1.2, respectively. Clearly, the biggest impact of the CA thiamethoxam strawberry data on the pollen-to-flower ratios lies with the 90th percentile estimate, reflecting the extreme skewness of the full data set.

When pollen-to-flower ratios are combined among all the trials into a single data set, the median pollen-to-flower ratio resulting from foliar applications are approximately 0.5X (with the thiamethoxam CA strawberry data) and 0.4X (without these data; **Table 5-18**). Using pollen-to-flower ratios derived from the combined data set inherently assumes that ratio probabilities are independent of neonicotinoid and crop. Under conservative assumptions, the 90th percentile of the pollen-to-flower ratios from the

combined data set are approximately 3X and 2X with and without inclusion of the thiamethoxam CA strawberry data. The median pollen-to-flower ratios from the trial-specific averages (~0.71-0.75) are relatively similar to those from the combined data set (~0.45 and 0.43) with and without inclusion of the thiamethoxam CA strawberry data.

Table 5-18. Descriptive Statistics of Pollen/Flower Ratios from the Combined Soil Application Data Set

Statistic	Full Data Set	All Data Except Strawberry CA Site (Thiamethoxam)
Number of Sample Means	113	107
Average	3.9	0.84
Standard Deviation	16	1.7
Minimum	0.004	0.004
Maximum	124	12
Median	0.45	0.43
90 th Percentile	2.7	1.8

5.6.6 Choice of Flower-to-Pollen Extrapolation Factor (Soil Application)

Examining the overall dataset indicates that, in contrast to the flower and nectar relationships following soil applications, the ratio and slopes of flower and pollen pairwise data are much more variable and residues in flowers are not consistently protective of pollen residues. The regression approach does not seem satisfactory for estimating an overall flower-to-pollen extrapolation factor among crops and neonicotinoids from soil applications given that only 8/14 trials did not produce regressions of reliable utility and of those that did, wide variability is seen among slopes (10X).

As a result, preference is given to the ratio method for developing the flower-to-pollen extrapolation factor for soil applications of neonicotinoids. Among the two approaches summarized for the ratio method, preference is given to ratios derived from the combined data set among trials for two reasons. First, with the exception of the thiamethoxam strawberry trials, mean pollen-to-flower ratios are relatively similar among trials with >3 ratios represented (0.21-1.8, with most between 0.21 and 0.75); (Table 5-17). Second, the impact of the exceptionally high pollen-to-flower ratios from the thiamethoxam CA strawberry trial on the summary statistics is not nearly as prevalent in the combined data set when compared to those derived from the individual trials. Therefore, in the neonicotinoid risk assessments, flower residue data associated with soil application are recommended to be used quantitatively with a **0.5X** factor as a surrogate for pollen where pollen data are lacking (Table 5-18, median ratio from the combined ratio data set). Additionally, for risk characterization purposes, it is recommended that the risk assessments apply a **3X** factor to flower data in order to qualitatively evaluate how variability in the pollen-to-flower ratios affects the risk conclusions.

6 CROP GROUP SPECIFIC ANALYSIS AND BRIDGING RECOMMENDATIONS

6.1 Orchard crops

6.1.1 Crops of Concern for Bees

Orchard crops cover several crop groups, including pome fruit (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), the majority of orchard crops are considered attractive to bees. In addition, many orchard crops (*e.g.*, almonds, apples) require managed pollinator services. Therefore, exposure to bees from orchard crops is considered in the neonicotinoid bee assessments for registered uses of these crops.

6.1.2 Foliar Applications

6.1.2.1 Summary of Label Rates/Restrictions

Of all four chemicals, thiamethoxam has the most registered uses for pre-bloom foliar applications to orchard crops, with registrations on all tree crop groups (*i.e.*, pome, stone and tropical fruits; citrus and tree nuts). Clothianidin and imidacloprid are only registered on citrus, with existing pre-bloom application intervals (clothianidin is approximately 3 months and imidacloprid is 10 d). Dinotefuran is registered on peaches and nectarines. Clothianidin, imidacloprid and thiamethoxam are registered for foliar, post-bloom applications to all orchard crop groups. Dinotefuran is only registered for use on peaches and nectarines. The maximum rates for pre-bloom and post-bloom foliar applications of these four chemicals are included in

Table 6-1.

Table 6-1. Maximum foliar application rates (in lb a.i./A) and number of applications for neonicotinoids on orchard crops (based on current labels)

Orchard crop group	Clothianidin	Imidacloprid	Thiamethoxam*	Dinotefuran
Pre-bloom				
Pome fruit	NR	NR	0.074 x 3	NR
Stone fruit	NR	NR	0.075 x 2	0.18 x 1 **
Citrus	NR	0.25 x 2	0.072 x 2	NR
Tree nuts	NR	NR	0.053 x 2	NR
Tropical fruits	NR	NR	0.053 x 3	NR
Post-bloom				
Pome fruit	0.2 x 1	0.25 x 2	0.074 x 3	NR
Stone fruit	0.2 x 1	0.1 x 5	0.075 x 2	0.18 x 1 **
Citrus	0.2 x 1	0.25 x 2	0.072 x 2	NR
Tree nuts	0.1 x 2	0.1 x 3	0.053 x 2	NR
Tropical fruits	0.1 x 2	0.1 x 5	0.053 x 3	NR

NR = not registered

*Clothianidin-equivalent rates

**Includes peach and nectarine, not registered for other stone fruit crops.

6.1.2.2 Available Residue Data

Residue data are available from studies involving pre- and post-bloom foliar applications to different orchard crops. For pre-bloom applications, pollen and nectar residue data are available from three studies that involve applications of imidacloprid or thiamethoxam to oranges and thiamethoxam application to apples (**Table 6-2**). For post-bloom applications, residue data are also available from several studies, including applications of clothianidin to almonds, apples and peaches, imidacloprid application to cherries, dinotefuran applications to cherries and peaches and thiamethoxam applications to cherries, peaches and plums.

Table 6-2. Residue studies for orchard crops treated with foliar applications of neonicotinoids

Crop	Chemical	# sites (Locations)	Application Rate, # of Apps, (interval)	# Seasons	# sampling events (per season)	MRID	Classification
Pre-bloom							
Orange	Imidacloprid	2 (FL)	0.29 lb a.i./A x 2 (8-10 d interval)	2	5-6	49521301	Supplemental**
Orange	Thiamethoxam	3 (FL, CA)	0.074 lb a.i./A* x 1 or 2 (7 d interval)	1	3-6	50425902	Acceptable
Apple	Thiamethoxam	3 (NY, VA, WA)	0.074 lb a.i./A* x 1	1	3	50265504	Acceptable
Post-bloom							
Almonds	Clothianidin	9 (CA)	0.1 lb a.i./A x 1	2	1	50154302	Acceptable
Apple	Clothianidin	3 (ON, OR)	0.1875 lb a.i./A x 1	2	1	50154304	Supplemental***
Cherry	Imidacloprid	4 (NY, OR)	0.5 lb a.i./A x 1	2	2	49535601	Acceptable
Cherry	Dinotefuran	3 (NY, CA, OR)	0.23+0.31 lb a.i./A (6-7 d interval)	1	3	50145706	Acceptable
Cherry	Thiamethoxam	3 (CA)	0.074 lb a.i./A* x 2 (7-8 d interval)	2	1	50096606	Acceptable
Peach	Clothianidin	3 (GA, SC, CA)	0.1 lb a.i./A x 2 (10-16 d interval)	2	1	50154303	Acceptable
Peach	Dinotefuran	3 (NY, CA, OR)	0.09+0.18 lb a.i./A (6-7 d interval)	1	3	50456901	Acceptable
Peach	Thiamethoxam	3 (CA)	0.074 lb a.i./A* x 2 (7 d interval)	2	1	50096606	Acceptable
Plum	Thiamethoxam	4 (CA)	0.074 lb a.i./A* x 2 (7 d interval)	1 or 2	1	50096606	Acceptable

*Clothianidin-equivalent rates

**Quantitative data are only available from 2 sites.

***Two sites are located too close together for this study to represent geographically diverse areas.

In addition to these studies, there are also residue data available from two imidacloprid studies (MRIDs 49662101 and 49819401) involving both soil and foliar applications to orchard crops (apples and stone fruit). Because these studies involve different types of applications, it is unknown how foliar and soil applications contribute to the magnitude of the residues. Therefore, residues from these studies are not considered here for the bridging strategy.

Available residue data for pollen and nectar from the aforementioned pre-bloom foliar applications of neonicotinoids to orchard crops are shown in **Figure 6-1**, and those associated with post-bloom foliar

applications are shown in **Figure 6-2.** . These plots combine residue data (normalized to 0.1 lb a.i./A) from different neonicotinoids, orchard crops, sites and season of application where applicable. Several general observations can be made based on these plots. First, residues in both pollen and nectar associated with pre-bloom foliar applications show distinct declines over time while those associated with post-bloom applications do not. Second, residues in pollen tend to be an order of magnitude greater than those in nectar, from either pre-bloom or post-bloom foliar applications. Finally, and as expected, residues measured shortly after pre-bloom foliar applications are 1-2 orders of magnitude greater than those resulting from post-bloom applications. The following sections describe the bridging needs for the orchard crop residue data and evaluate various factors that influence the variability in neonicotinoid residues in pollen and nectar.

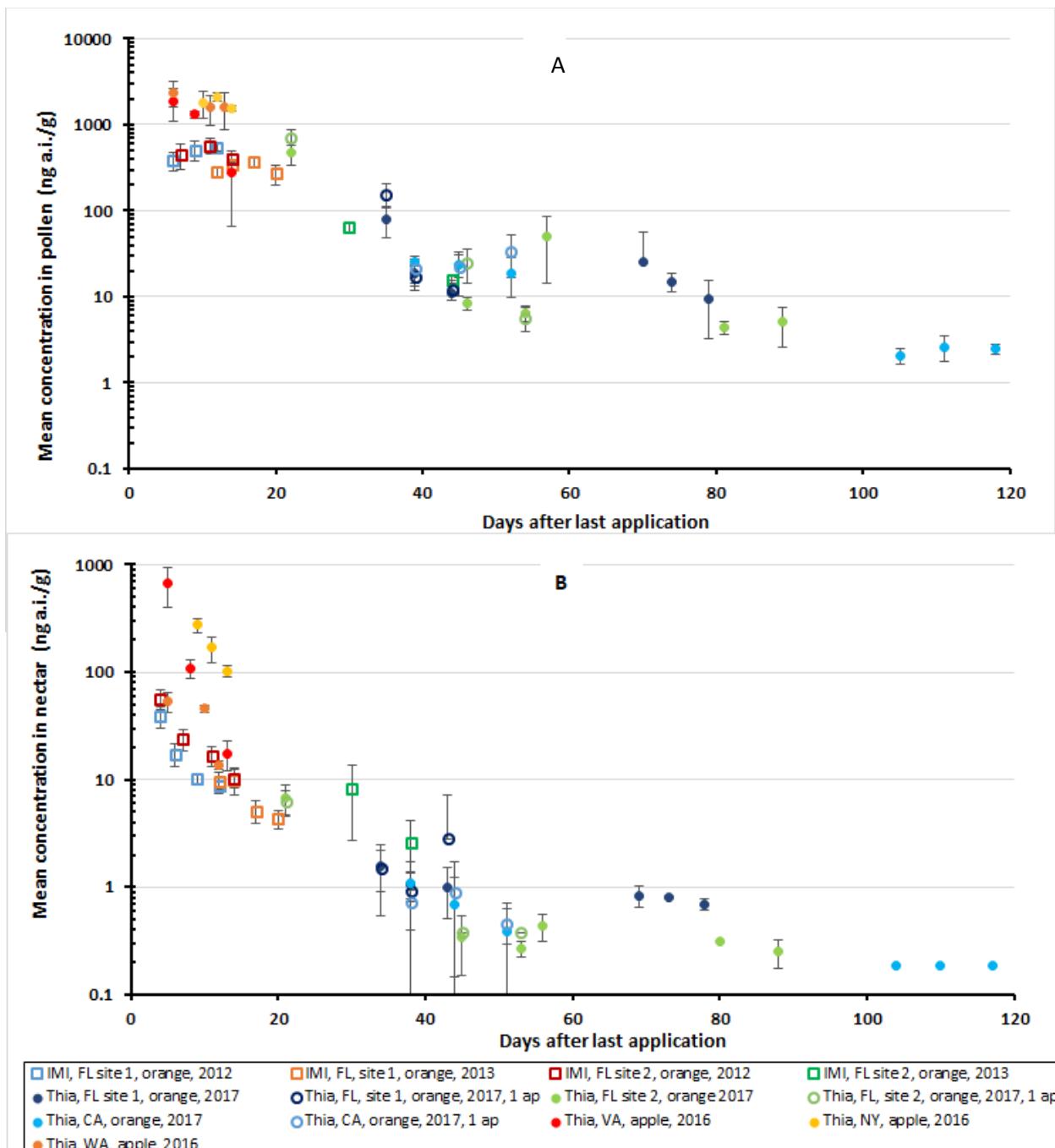


Figure 6-1. Mean concentrations in pollen (A) and nectar (B) following pre-bloom foliar applications to orchard crops. Error bars represent 95% confidence interval. Values normalized to total application rate of 0.1 lb a.i./A. Imi = imidacloprid; Thia = thiamethoxam, Clothi = clothianidin, Dino = dinotefuran. Note that thiamethoxam residues are expressed as clothianidin equivalents.

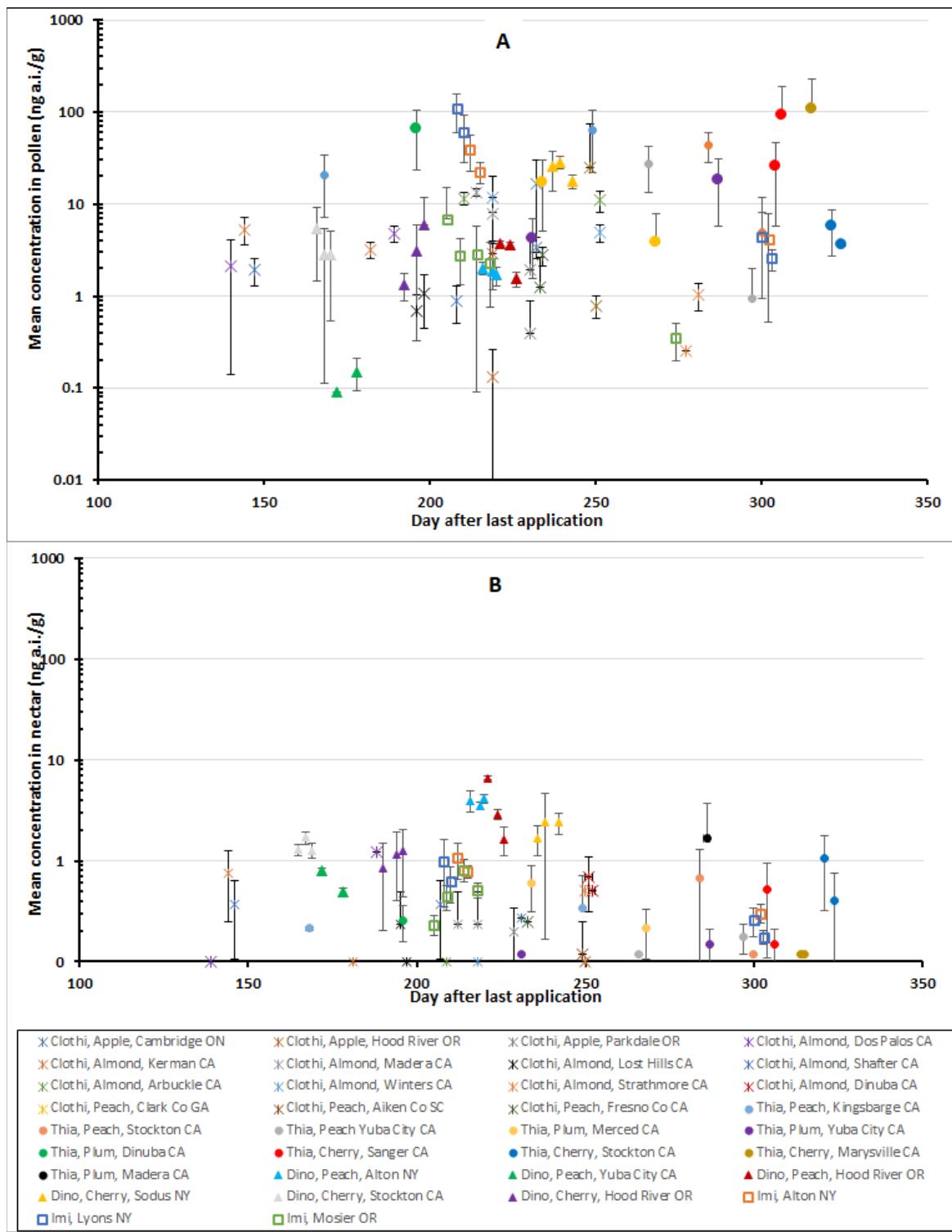


Figure 6-2. Mean concentrations in pollen (A) and nectar (B) following post-bloom foliar applications to orchard crops. Error bars represent 95% confidence interval. Values normalized to total application rate of 0.1 lb a.i./A. Imi = imidacloprid; Thia = thiamethoxam, Clothi = clothianidin, Dino = dinotefuran. Note that thiamethoxam residues are expressed as clothianidin equivalents.

6.1.2.3 Bridging Needs (Gaps)

For pre-bloom, foliar applications, no residue data are available for clothianidin applications to citrus or dinotefuran applications to peaches and nectarines. In addition, no residue data are available for thiamethoxam residues in stone fruit, tropical fruit or tree nuts (**Table 6-3**). For post-bloom applications, residue data are available for 7 different studies where one of the 4 neonicotinoids was applied post-bloom to orchards. Each chemical includes at least one stone fruit crop. Residue data for clothianidin also include data for apples and almonds. **Table 6-3** lists the available studies by crop group and chemical and identifies areas where bridging is needed (*i.e.*, indicated by “*No data*”). The analysis below will consider options for bridging the available data to address these gaps.

Table 6-3. Identification of data gaps for registered foliar applications of neonicotinoids on tree crops

Orchard crop group	Clothianidin	Imidacloprid	Thiamethoxam	Dinotefuran
Pre-bloom				
Pome fruit	NR	NR	Apple (MRID 50265504)	NR
Stone fruit	NR	NR	No data	No data
Citrus	No data	Orange (MRID 49521301)	Orange (MRID 50425902)	NR
Tree nuts	NR	NR	No data	NR
Tropical fruit	NR	NR	No data	NR
Post-bloom				
Pome fruit	Apple (MRID 50154304)	No data	No data	NR
Stone fruit	Peach (MRID 50154303)	Cherry (MRID 49535601)	Cherry, peach, plum (MRID 50096606)	Cherry, peach (MRIDs 50145706, 50456901)
Citrus	No data	No data	No data	NR
Tree nuts	Almond (MRID 50154302)	No data	No data	NR
Tropical fruit	No data	No data	No data	NR

NR = not registered

6.1.2.4 Influence on Residues of Application Rate and Number of Applications

One study is available to evaluate the influence of thiamethoxam application rates on residues in pollen and nectar following foliar applications to an orchard crop. In this study, thiamethoxam was applied (pre-bloom) to oranges in CA and FL at either one or two applications of 0.074 lb a.i./A (clothianidin equivalents; 7-d application interval; MRID 50425902). **Figure 6-3** and **Figure 6-4** depict residues in pollen and nectar (respectively) collected from orange trees treated once or twice with thiamethoxam. For both figures, the graph on the left represents the mean residues from the study not normalized to application rate, while the graph on the right represents residues normalized to the same total application rate (0.1 lb a.i./A). When residues are not normalized, mean residues from the samples involving 2 applications were consistently higher than those from 1 application. Confidence intervals

around the means overlapped for many of the samples. When residues were normalized to the same total application rate, there is no clear pattern to whether residues from 1 or 2 applications are higher. In addition, confidence intervals for the same time points for 1 and 2 applications overlap when residues are normalized. One uncertainty in this approach, is that it does not account for dissipation of residues between the two applications; however, this factor does not appear to influence the results. This analysis suggests that mean residues from a single or two applications are similar, and thus supports the normalization of residues by the last application rate or to the total application rate over the season for reducing the influence of differential application rates on neonicotinoid residues. Therefore, in the subsequent analyses in this section, residues will be normalized to the total application rate. The rational for normalizing includes the following: 1) there is no substantial difference between normalizing to last or total application rate; 2) the thiamethoxam studies had unequal rates for the same trials; and 3) it is consistent with the approach used for post-bloom residue data.

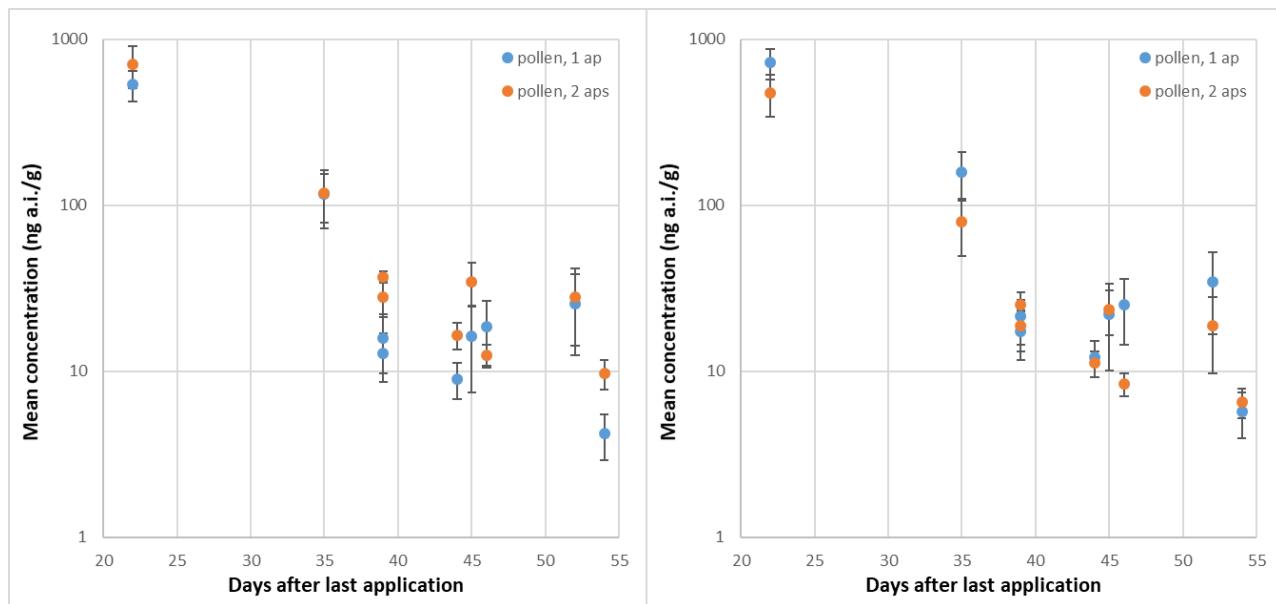


Figure 6-3. Mean residues in pollen following thiamethoxam applications to orange trees (MRID 50425902). Left graph depicts unadjusted residues. Right graph depicts residues normalized to total application rate of 0.1 lb a.i./A

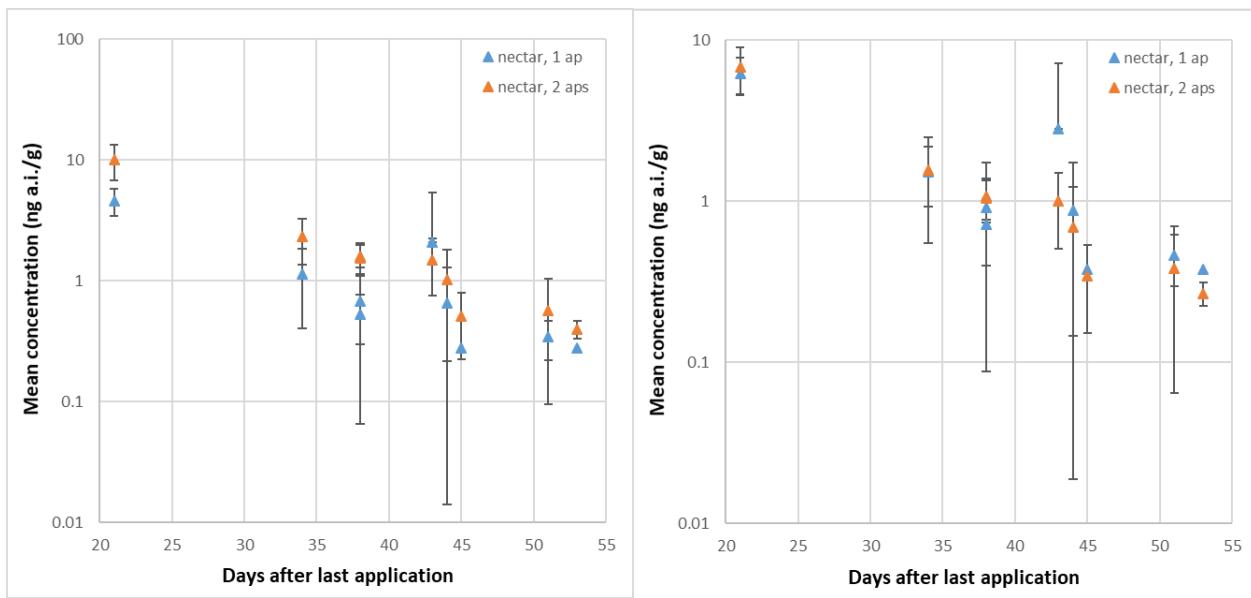


Figure 6-4. Mean residues in nectar following thiamethoxam applications to orange trees (MRID 50425902). Left graph depicts unadjusted residues. Right graph depicts residues normalized to total application rate of 0.1 lb a.i./A

6.1.2.5 Influence of Sampling Day (Time) on Residue Values

Residues from pre-bloom applications made within 20 days of bloom are generally 1-2 orders of magnitude higher than pre-bloom applications made >20 days before bloom. Pre-bloom applications made within 20 days of bloom also yield residues in pollen and nectar that are 1-2 orders of magnitude greater than residues measured from post-bloom applications (which take place >140 days before the next bloom). **Table 6-4** lists the range of mean residue values for pollen and nectar from orchard crops with different time periods between bloom and application. **Figure 6-1** and **Figure 6-2** shown previously depict individual mean values for nectar and pollen.

Table 6-4. Range of mean values for orchard crops treated with neonicotinoids via foliar applications. Ranges broken out by different times between bloom and application date. Concentrations in ng a.i./g, normalized to 0.1 lb a.i./A rate.

Days before bloom when application was made	Concentration in nectar (ng a.i./g)*		Concentration in pollen (ng a.i./g)*	
	Pre-bloom	Post-bloom	Pre-bloom	Post-bloom
1-10	10-671	NA	382-2373	NA
11-20	4-169	NA	272-2119	NA
21-50	<LOD-8	NA	8-719	NA
50-100	<LOD-1	NA	4-50	NA
101-120	<LOD	NA	2-3	NA
140-150	NA	<LOD-1	NA	2-5
150-200	NA	<LOD-1	NA	<LOD-65
201-250	NA	<LOD-7	NA	<LOD -109
251-300	NA	<LOD-2	NA	0.3-44
301-325	NA	<LOD-1	NA	3-108

NA = not applicable; *Where chemical was not detected, LOD = 0.25 ng a.i./g for nectar and 0.5 for pollen

Data from individual trials were analyzed to determine whether dissipation rate constants (k) could be reliably quantified. For all post-bloom applications, residues were generally similar over the course of the sampling period, preventing quantification of dissipation rates. Therefore, dissipation rate constants were only calculated for the studies that involved pre-bloom applications (Table 6-5 and Table 6-6). Reliable k values were calculated from the thiamethoxam apple and imidacloprid orange studies; however, the majority of the k values calculated from the thiamethoxam orange study were not reliable according to criteria described in Section 4.5.4. One major factor that lead to this determination was the sampling period associated with the thiamethoxam orange study. The first sample of the study was collected several weeks after the last application. When samples were collected, they already represented substantial dissipation, with values in the single digit ppb range. In addition, several trials had residues (in nectar) that were below the LOQ. Therefore, k values were not calculated.

When considering just the reliable rate constants (Figure 6-5), k values range from 0.11 to 0.60 d^{-1} (DT_{50} from 1.1 to 6.5 days) and 95% confidence intervals for nectar from the thiamethoxam apple and imidacloprid orange studies overlap. Similarly, for pollen, reliable k values range from 0.06 to 0.48 d^{-1} (DT_{50} from 1.4 to 11 days) and confidence intervals for thiamethoxam in apple, thiamethoxam in orange and imidacloprid in orange all overlap. Although the pool of reliable k values is clearly limited (*i.e.*, 2 chemicals, 2 crops, 1-3 sites/crop), these data suggest that site, chemical and crop do not have an overriding influence the dissipation rate of neonicotinoids in nectar or pollen following pre-bloom, foliar applications to orchard crops. This finding is further supported by visual inspection of Figure 6-1, which illustrates a relatively consistent decline in residue among neonicotinoids, orchard crops and sites.

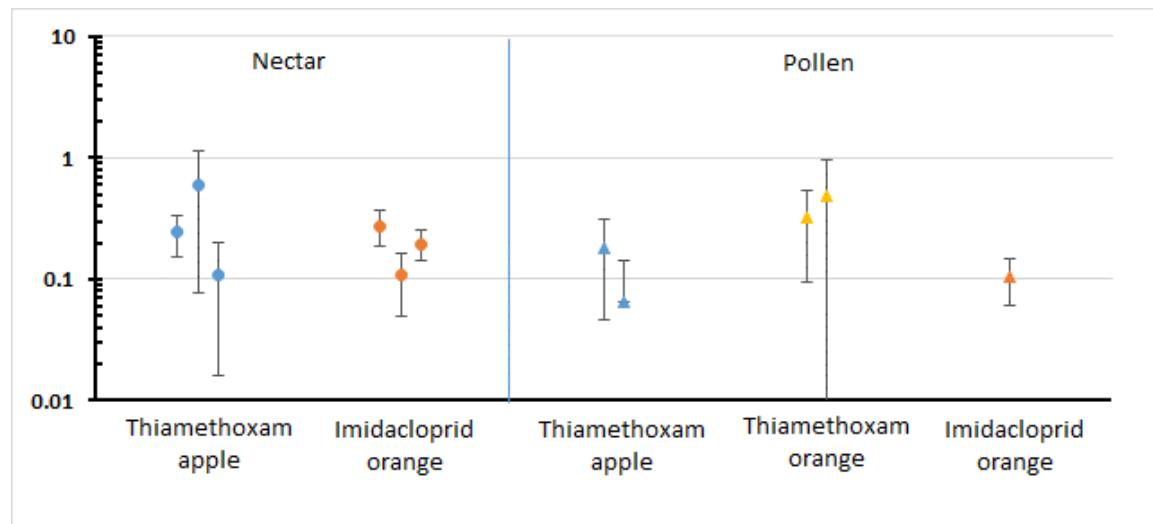


Figure 6-5. Dissipation rate constants (reliable) for pollen and nectar from pre-bloom applications of thiamethoxam and imidacloprid to apples and oranges

Table 6-5. Dissipation rate constants (k) derived for residues in nectar from foliar, pre-bloom applications

Chemical	Crop	Location	k (95% CI)	Half-life (d)	R ²	P	First measurement (DALA)	Reliable k?	Comments
Thiamethoxam	Apple	NY	0.25 (0.15-0.34)	2.8	0.9	2.1E-04	9	Y	
		VA	0.60 (0.072-1.1)	1.1	0.9	1.6E-02	5	Y	
		WA	0.11 (0.016-0.20)	6.3	0.6	1.4E-02	5	Y	
	Orange	FL 1-2	0.022 (-0.0059-0.049)	32.0	0.339	5.3E-02	69	N	First measurement = 1.2 ng a.i./g
		FL 1-3	0.054 (-0.027-0.14)	12.8	0.2667	7.9E-02	34	N	First measurement = 2.3 ng a.i./g
		FL 1-4	0.13 (-0.093-0.36)	5.1	0.1971	8.7E-09	34	N	First measurement = 0.5 ng a.i./g
Imidacloprid	Orange	FL	0.28 (0.19-0.37)	2.5	0.81	2.5E-06	8	Y	
		FL	0.11 (0.050-0.16)	6.5	0.53	4.6E-04	10	Y	
		FL	0.20 (0.17-0.25)	3.5	0.84	4.3E-07	8	Y	

DALA = days after last application

Table 6-6. Dissipation rate constants (k) derived for residues in pollen from foliar, pre-bloom applications

Chemical	Crop	Location	k (95% CI)	Half-life (d)	R ²	P	First measure (DALA)	Reliable k?	Comments
Thiamethoxam	Apple	NY	0.037 (-0.069-0.14)	18.7	0.1	2.2E-01	10	N	
		VA	0.18 (0.047-0.32)	3.8	0.7	7.7E-03	6	Y	
		WA	0.064 (-0.017-0.15)	10.8	0.3	5.3E-02	6	Y	
	Orange	FL 1-2	0.12(-0.13-0.36)	0.1	0.20	8.7E-09	70	N	No trend
		FL 1-3	0.32 (0.096-0.55)	2.2	0.82	1.28E-11	35	Y	
		FL 1-4	0.48 (0.005-0.96)	1.4	0.81	2.63E-11	35	Y	
		FL 2-2	0.09 (-0.053-0.23)	7.7	0.67	8.96E-02	57	N	
		FL 2-3	0.16 (-0.19 -0.51)	4.3	0.94	1.54E-01	22	N	Second sample taken at DALA = 46
		FL 2-4	0.14 (-0.013 -0.30)	4.9	0.97	3.38E-02	22	N	Second sample taken at DALA = 46
		CA 3-2	No K value can be calculated				105	N	Flat
		CA 3-3	0.021 (-0.017-0.059)	32.5	0.21	1.12E-01	39	N	High variability, no clear trend
		CA 3-4	No K value can be calculated				39	N	High variability, no clear trend
	Imidacloprid	FL (005-12)	No K value can be calculated	Stable	0.09	5.0E-01	5	N	Flat
		FL (005-13)	0.0095 (-0.033-0.052)	72.8	0.02	3.2E-01	12	N	Flat
		FL (006-12)	0.007 (-0.043-0.057)	99.4	0.01	3.8E-01	14	N	Flat
		FL (006-13)	0.11 (0.059-0.15)	6.6	0.91	4.9E-04	30	Y	

DALA = days after last application

6.1.2.6 Effect of Application Timing (Pre- and Post-Bloom) on Residue Values

Neonicotinoid residues in nectar and pollen from pre- and post-bloom applications are shown previously in **Figure 6-1** and **Figure 6-2** depict the nectar and pollen (respectively) residue data available for foliar applications. In order to allow equal comparisons, residues are normalized to a total application rate of 0.1 lb a.i./A. This involved dividing measured residues by the total seasonal application rate (**Table 6-1**) and multiplying by 0.1 lb a.i./A. When considering residues resulting from pre-bloom and post-bloom applications, the magnitude of residues in pollen and nectar tend to be substantially lower for post-bloom compared to pre-bloom applications to orchard crops. Pre-bloom applications made closer to bloom (*i.e.*, ≤20 d before bloom) generate residue levels in pollen and nectar that are generally 1-2 orders of magnitude higher than pre-bloom applications occurring >20 d and all post-bloom applications (**Table 6-4**, **Figure 6-1** and **Figure 6-2**). Therefore, the effect of application timing is considered to have a major impact on neonicotinoid residues in bee-relevant matrices of orchard crops.

6.1.2.7 Effect of Year and Site on Residue Values

Only three studies are available with permit evaluation of the impact of year (growing season) and site on residues in pollen and nectar of orchard crops (one with imidacloprid and two with thiamethoxam). In the study involving pre-bloom foliar applications of imidacloprid to orange trees, residues from different sites (collected at similar times) and the same year (2012) were similar in both nectar and pollen (**Figure 6-6** red and blue squares). Residues collected from different years (2012 and 2013) at the same site were only sampled at one similar time point at site 1 (**Figure 6-6**, DALA⁸ 12, orange and blue squares). Nonetheless, mean residues in nectar have overlapping confidence intervals, and those in pollen are within a factor of 2X.

In the thiamethoxam orange study (MRID 50425902), mean residues collected from different sites at similar times between 40-60 days after last application have confidence intervals that generally overlap (**Figure 6-7**). With the thiamethoxam apple study, the number of residue measurements made on the same or similar day after application is limited (MRID 50265504, **Figure 6-8**). Mean residues in nectar from different sites on DALA 5 and 13 differ by an order of magnitude and confidence intervals do not overlap. With pollen, mean residues from different sites on DALA 6 are similar, but those on DALA 14 differ by about 4X with non-overlapping confidence limits. Between DALA 9 and 13, thiamethoxam residues are similar among sites.

In summary, the majority of comparisons suggest that residues are similar between sites and years within the same study as a result of pre-bloom foliar applications to orchard crops. However, there is some evidence that residues measured at different sites can be substantially different (up to an order of magnitude). Such differences may result from multiple factors that can impact the bioavailability and translocation of neonicotinoids (*e.g.*, weather, soil properties). Therefore, based on the limited data available, the impact of site and year on neonicotinoid residues appears to be modest in most cases, but cannot be dismissed as a potentially important factor influencing pollen and nectar residues from pre-bloom applications to orchard crops.

⁸ Here and elsewhere in this report, DALA = days after last application

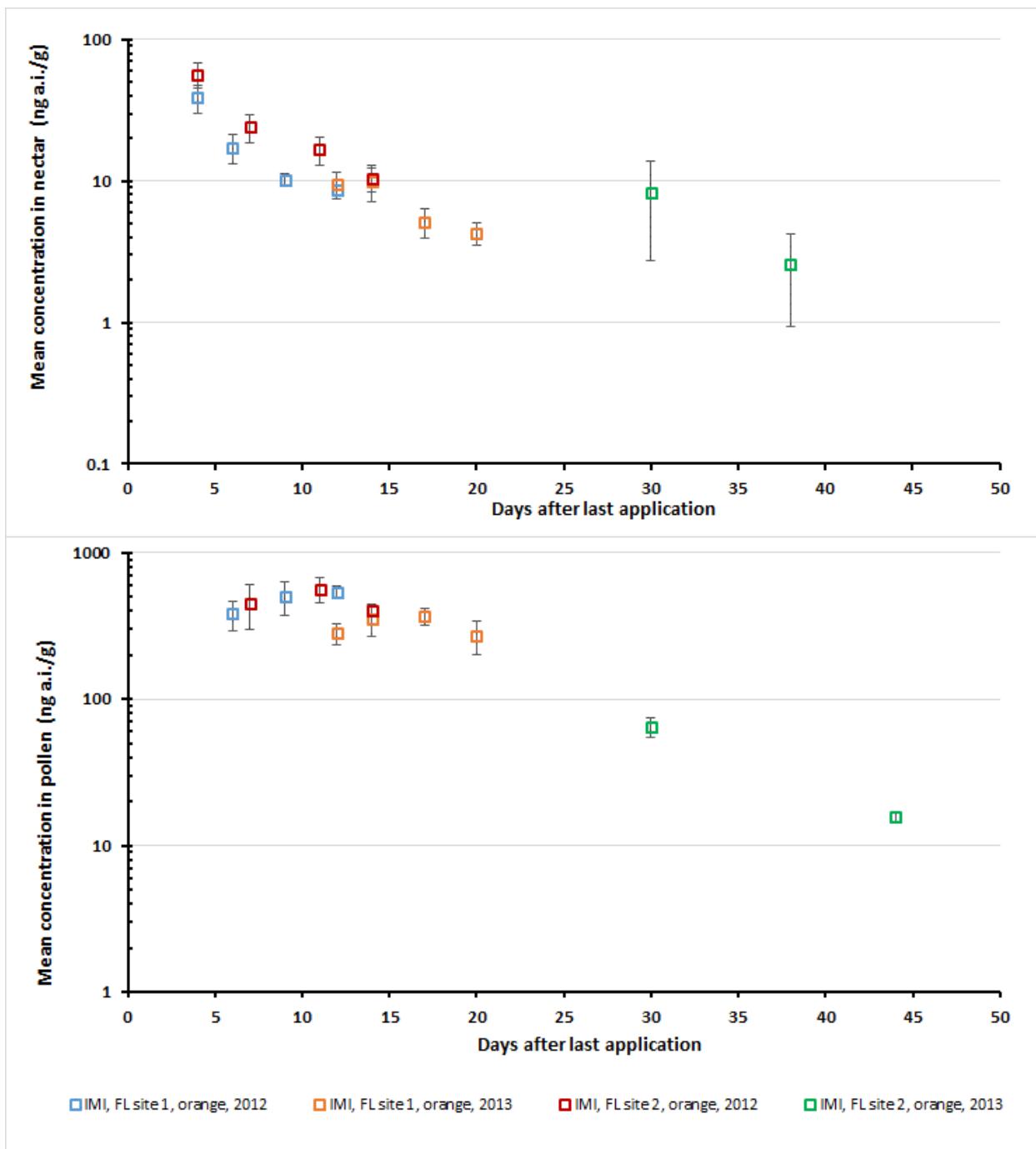


Figure 6-6. Comparison of mean imidacloprid residues (expressed as total imidacloprid) in nectar (top) and pollen (bottom) from pre-bloom applications to orange trees at different sites and years. (MRID 49521301). Error bars = 95% confidence interval.

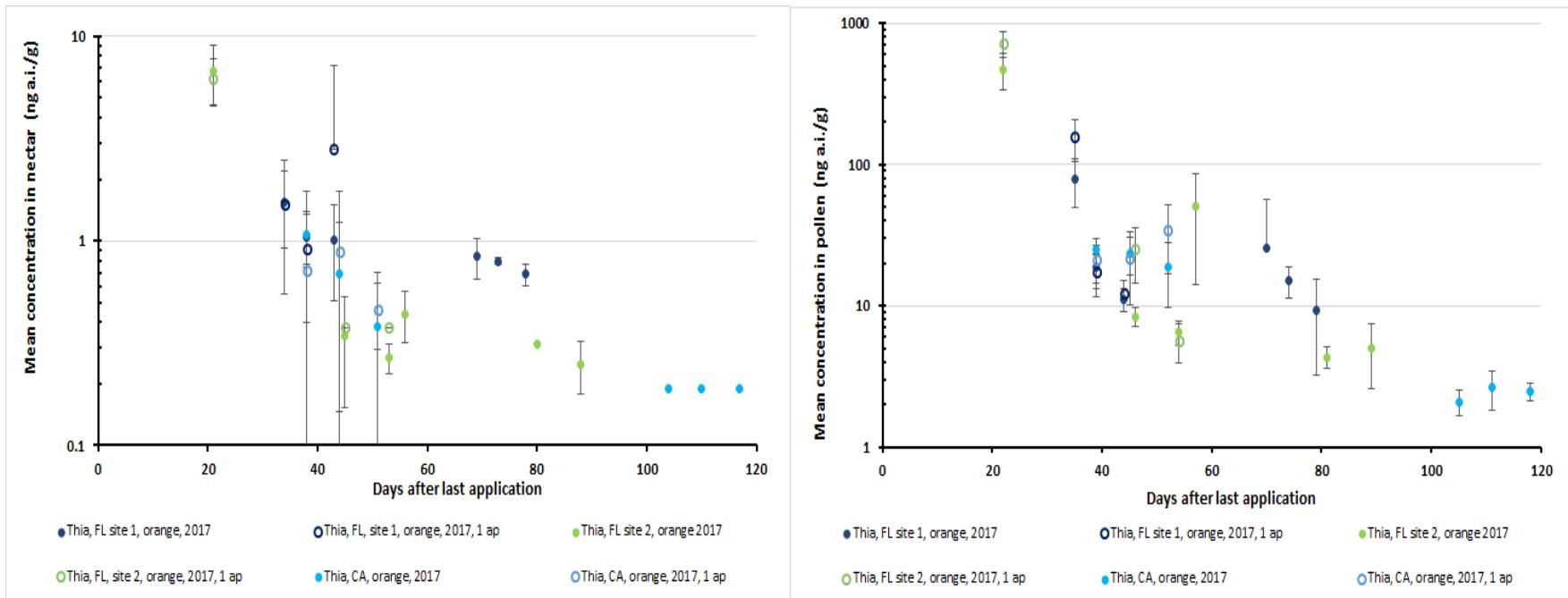


Figure 6-7. Comparison of mean thiamethoxam residues (expressed as clothianidin equivalents) in nectar (left) and pollen (right) from orange blossoms treated pre-bloom at different sites (MRID 50425902). Error bars = 95% confidence interval.

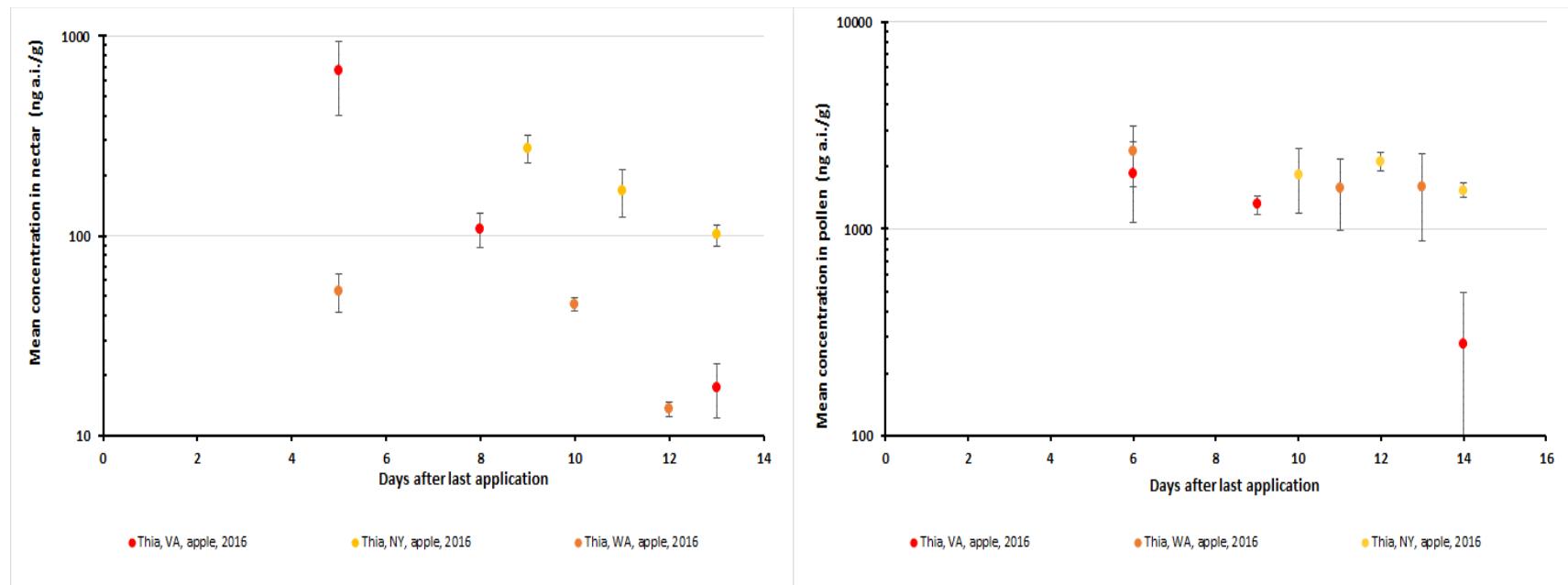


Figure 6-8. Comparison of mean thiamethoxam residues (expressed as clothianidin equivalents) in nectar (left) and pollen (right) from apple blossoms treated pre-bloom (MRID 50425904). Error bars = 95% confidence interval.

For post-bloom, foliar applications, different residue studies are available for all four chemicals with multiple sites represented for the same orchard crop. In these studies, samples of pollen and nectar collected during the bloom season following applications. Residues of imidacloprid in nectar and pollen from a post-bloom application to cherries at three different sites are depicted in **Figure 6-9**. Dinotefuran residues in peach and cherry orchards are depicted in **Figure 6-10**. Mean residues of clothianidin in pollen and nectar from apple, almond and peach trees that received post-bloom foliar applications are shown in **Figure 6-11**. The apple and peach studies included three different sites each. The almond study included 9 different sites. Finally, **Figure 6-12** depicts residues of thiamethoxam in pollen and nectar of peach, plum and cherry trees following post-bloom, foliar applications. There were 3 sites for peach and cherry and 4 for plum.

With imidacloprid, mean residues in cherry nectar and pollen at the two NY sites are similar (with overlapping confidence intervals) but those at 1 site (Mosier, OR) appear lower than the NY sites (**Figure 6-9**). With dinotefuran, mean residues in peach nectar and pollen at two sites collected at similar times (DALA 210-230) are within a factor of 2X to 3X, although confidence limits do not overlap for some sample means (**Figure 6-10, top panels**). Mean residues of dinotefuran in cherry nectar are similar across all 3 sites (within 2X and overlapping confidence intervals) despite large differences in the timing of measurements, while those in pollen differ substantially at the NY site compared to the other two sites (**Figure 6-10, bottom panels**). With clothianidin, residues in apple, almond and peach nectar are all at or below 1 ng a.i./g, and are generally similar with overlapping confidence limits (**Figure 6-11, left panels**). In contrast, residues of clothianidin in apple, almond and peach pollen are substantially greater by an order of magnitude at 1 or 2 sites relative to the others (**Figure 6-11, right panels**). Mean residues of thiamethoxam in nectar from post-bloom applications to peach, plum and cherry are also low in magnitude (< 2 ng a.i./g) with confidence that generally overlap (**Figure 6-12, left panels**). With pollen, mean residues of thiamethoxam in these crops are substantially greater at some sites (> 10X), but high variability in replicate samples results in wide confidence intervals that generally overlap (**Figure 6-12, right panels**).

In summary, the majority of comparisons suggest that neonicotinoid residues are similar between sites and season within the same study (within 2-3X) as a result of post-bloom foliar applications to orchard crops. There is, however, evidence that residues measured at some sites can be substantially different (up to an order of magnitude), which is a similar finding from the previous evaluation of pre-bloom foliar applications. Thus, while the impact of site on neonicotinoid residues appears to be modest in most cases (particularly with nectar), site-specific differences cannot be dismissed as a potentially important factor influencing pollen and nectar residues from pre-bloom applications to orchard crops. This finding supports the need to evaluate residue data from multiple sites for assessing neonicotinoid risks to bees.

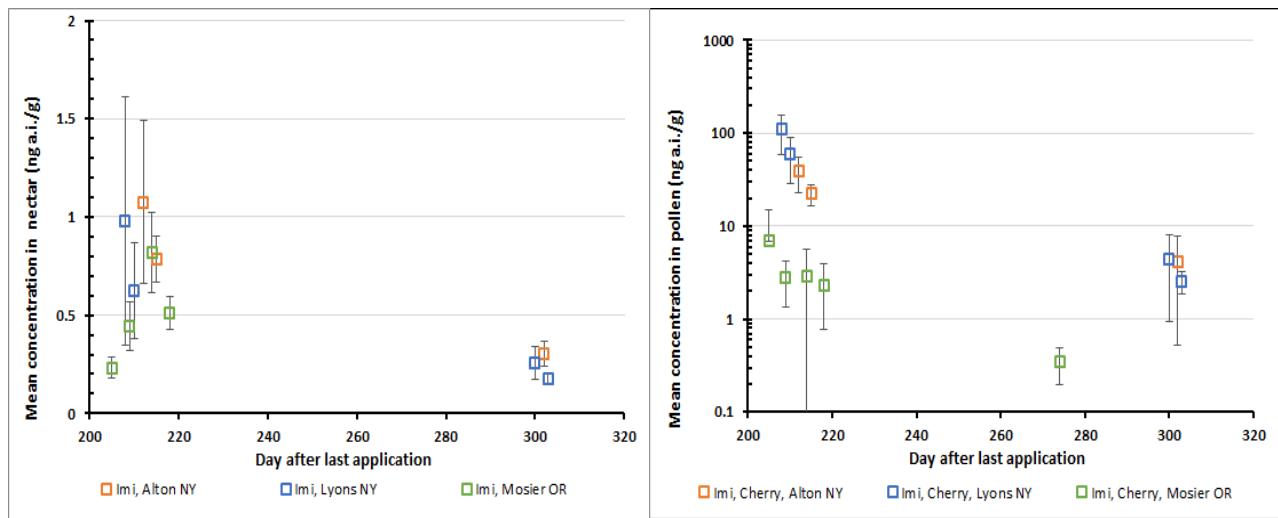


Figure 6-9. Mean imidacloprid residues in nectar (left) and pollen (right) from post-bloom, foliar applications to cherry orchards (MRID 49535601). Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval.

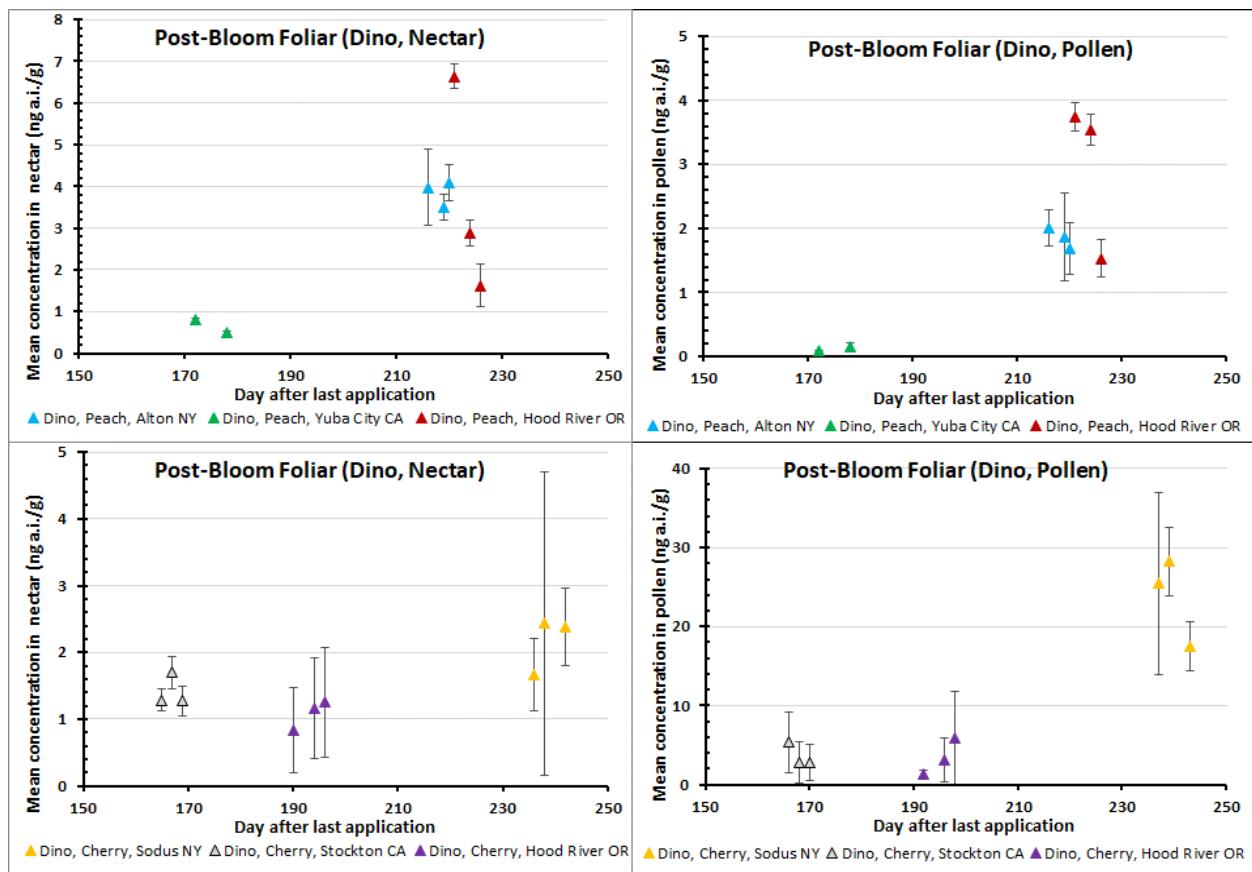


Figure 6-10. Mean dinotefuran residues in nectar (left) and pollen (right) from post-bloom, foliar applications to peach (top MRID 50456901) and cherry (bottom; MRID 50145706) orchards. Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval.

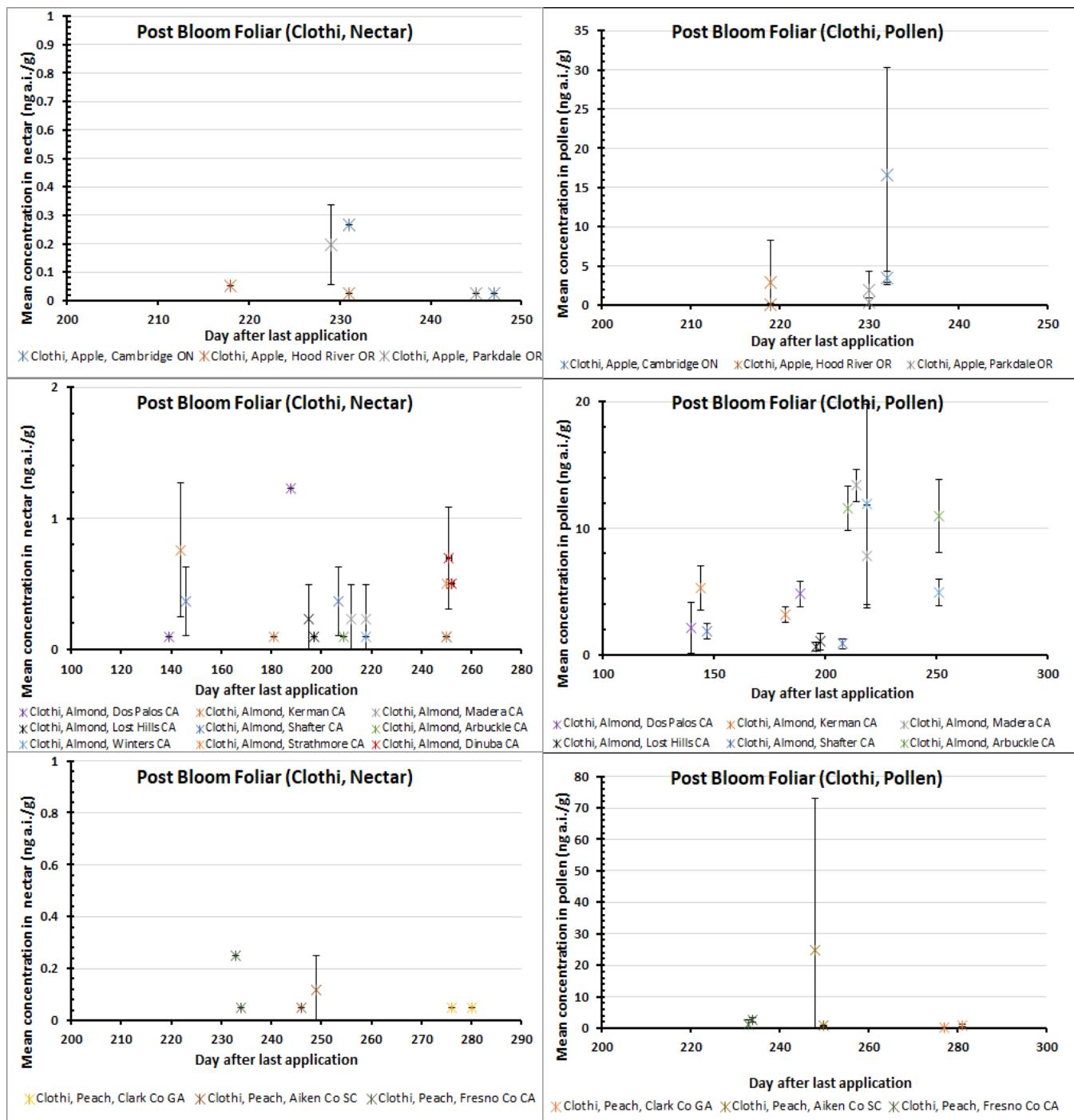


Figure 6-11. Mean clothianidin residues in nectar (left) and pollen (right) from post-bloom, foliar applications to apple (top; MRID 50154304), almond (middle; MRID 50154302) and peach (bottom; MRID 50154303) orchards. Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval.

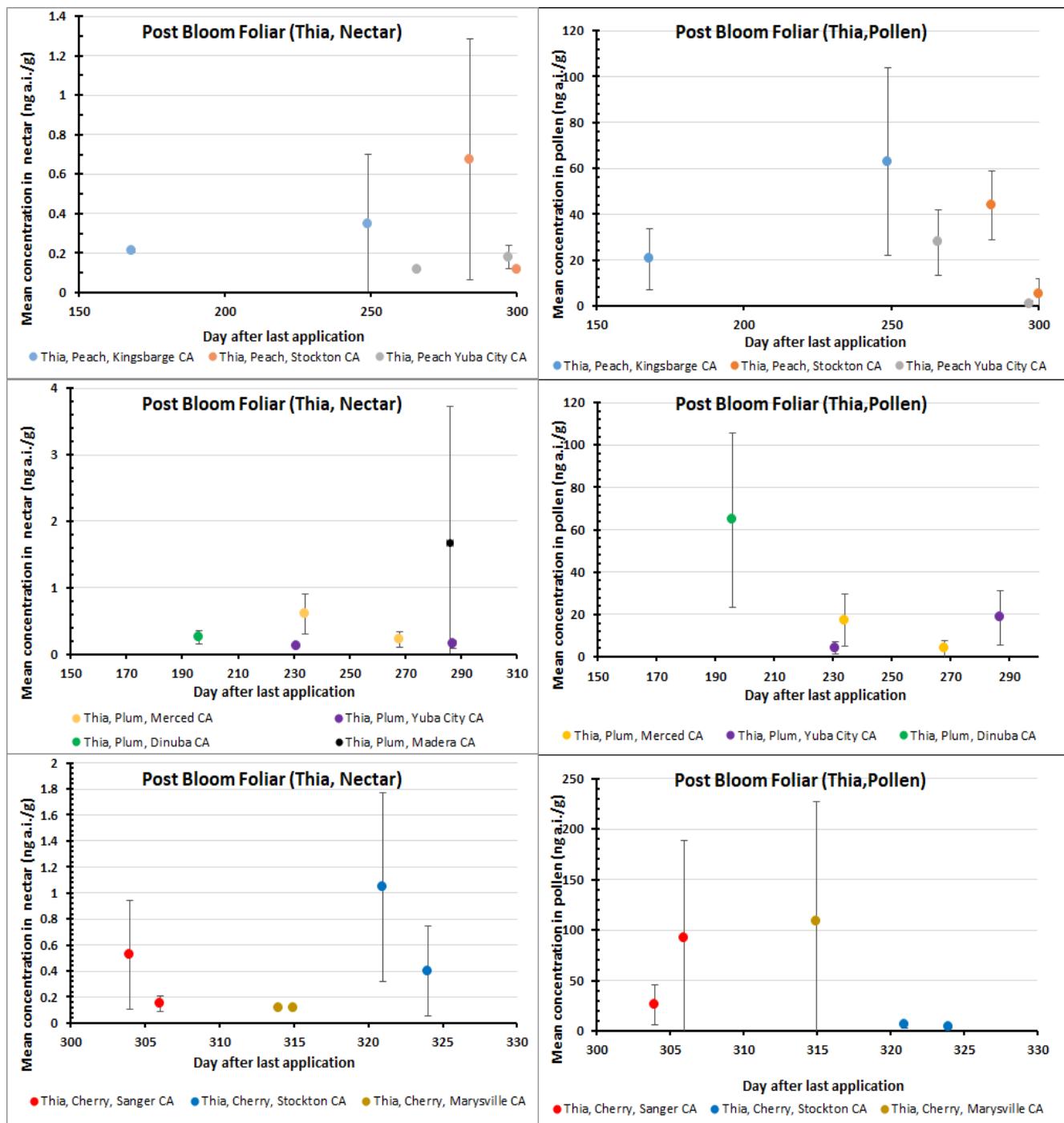


Figure 6-12. Mean thiamethoxam residues (expressed as clothianidin equivalents) in nectar (left) and pollen (right) from post-bloom, foliar applications to peach (top), plum (middle) and cherry (bottom) orchards (MRID 50096606). Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval.

6.1.2.8 Effect of Crop on Residue Values

For pre-bloom applications, thiamethoxam data are available for two different crops (apple and orange). Unfortunately, the timing of when samples were collected for the two different crops did not overlap.

(apple samples were collected between 6-14 days after last application; orange samples were collected between 22-118 days after last application). Furthermore, these data originate from different sites, thus introducing a potential confounding factor in the crop-to-crop comparisons. Despite these limitations, when comparing samples collected at 14 and 22 DALA, residues in nectar and pollen were similar in order of magnitude. In addition, when considering the full apple and orange datasets, they seem to follow similar declining trends (**Figure 6-13**).

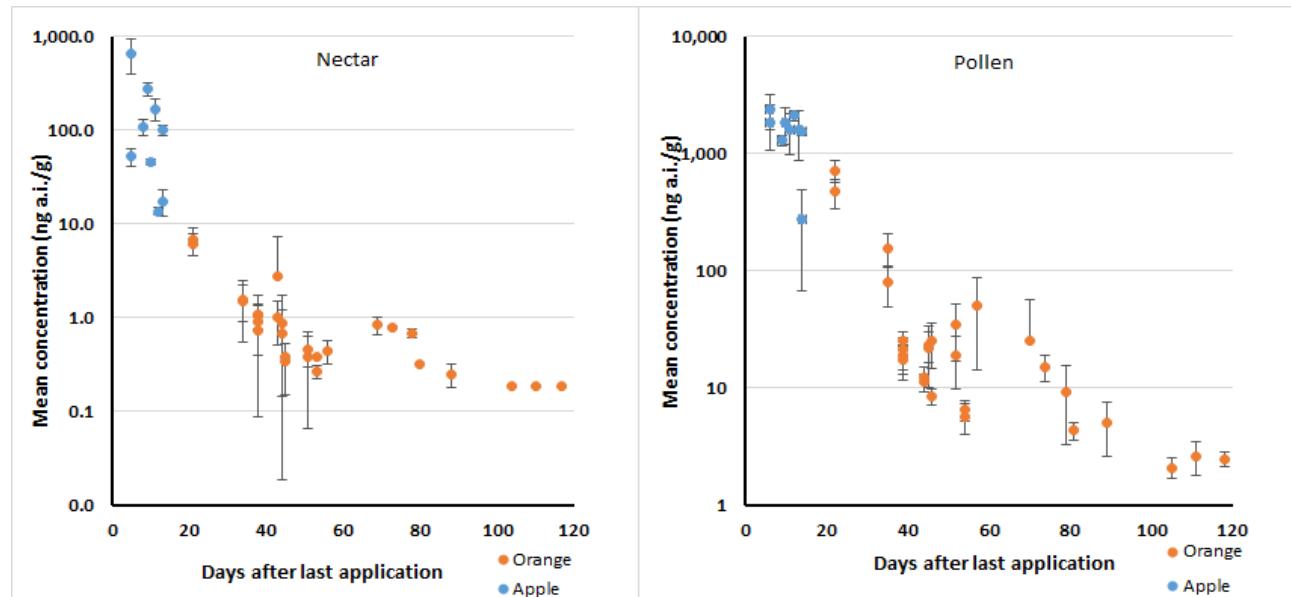


Figure 6-13. Mean thiamethoxam residues (expressed as clothianidin equivalents) in nectar (left) and pollen (right) from pre-bloom, foliar applications to orange and apple orchards. Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval.

For post-bloom applications, **Figure 6-14** depicts residues in clothianidin, thiamethoxam and dinotefuran in nectar (left panels) and pollen (right panels) from various orchard crops, represented by different symbol shapes. Again, since these data originate from different sites among crops, it is not possible to remove differences due to site. When examining the potential effect of crop on residues in nectar, no consistent trend is indicated, and differences in mean residues among sites within a crop are similar in magnitude to those occurring between crops. A similar finding is seen with residues in pollen from orchard crops. Therefore, within the context of variability in residues among sites, this analysis suggests that crop does not have an overriding influence on residues of neonicotinoids in pollen and nectar of orchard crops.

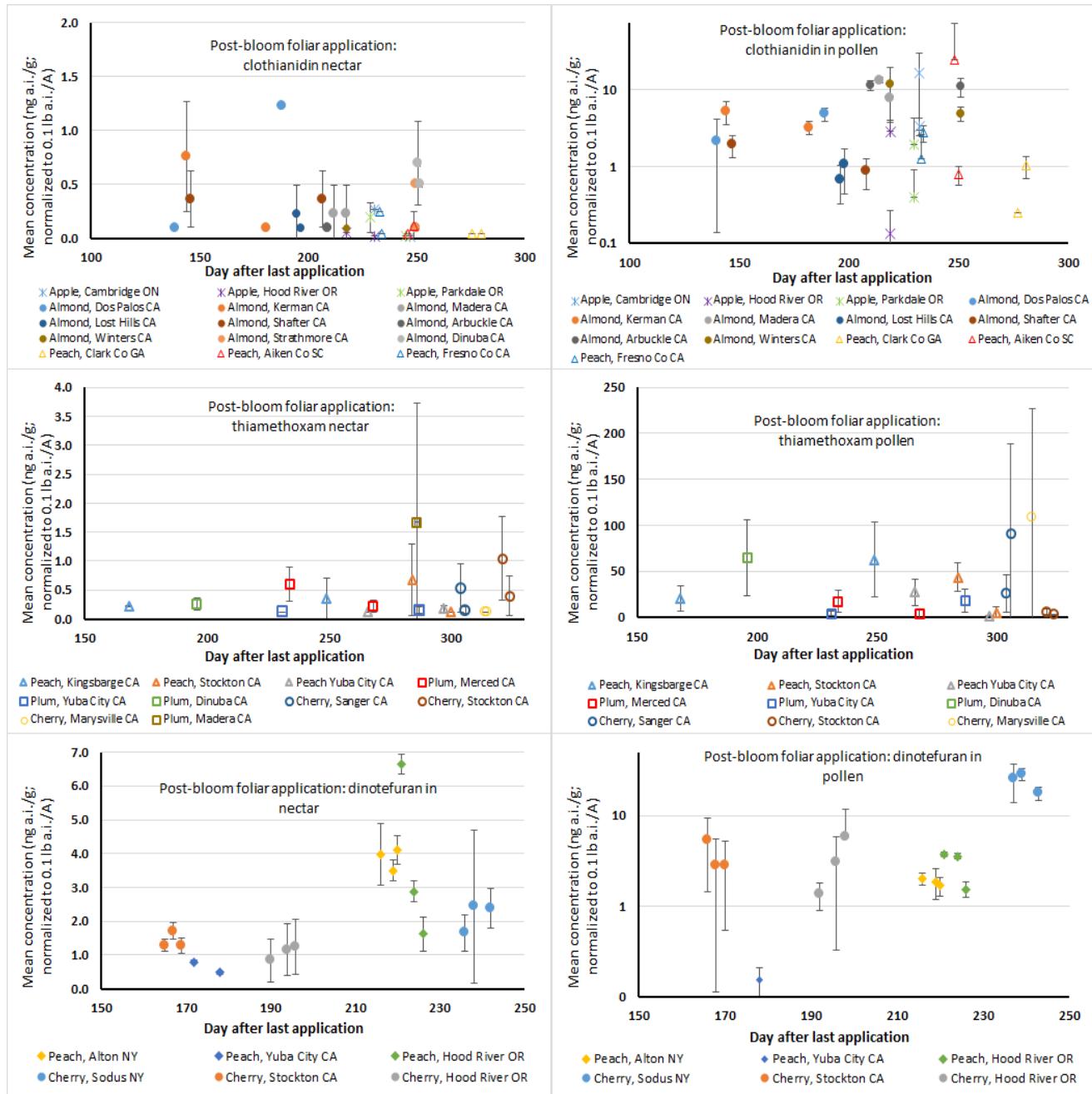


Figure 6-14. Mean neonicotinoid residues in nectar (left) and pollen (right) from post-bloom, foliar applications. Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval.

6.1.2.9 Effect of Chemical on Residue Values

Data are available for different chemicals and the same crop for pre-bloom applications to oranges (imidacloprid and thiamethoxam; **Figure 6-15**), post-bloom applications to peaches (clothianidin, thiamethoxam and dinotefuran) and post-bloom applications to cherries (imidacloprid, thiamethoxam and dinotefuran; **Figure 6-16**).

For the pre-bloom applications, orange residue data samples were collected at different times, which complicates comparisons. Imidacloprid data were collected within days to weeks before bloom, while thiamethoxam samples were collected weeks to months before bloom. **Figure 6-15** depicts the imidacloprid and thiamethoxam residue data in orange pollen and nectar. Samples collected during overlapping time periods (*i.e.*, 20-50 days after last application) are on the same order of magnitude for the two chemicals. Also, when considering the trends of the data, the imidacloprid and thiamethoxam data seem to follow similar trends in declining residues as timing of application relative to bloom increases. This suggests that for pre-bloom applications to oranges, chemical does not influence residue levels.

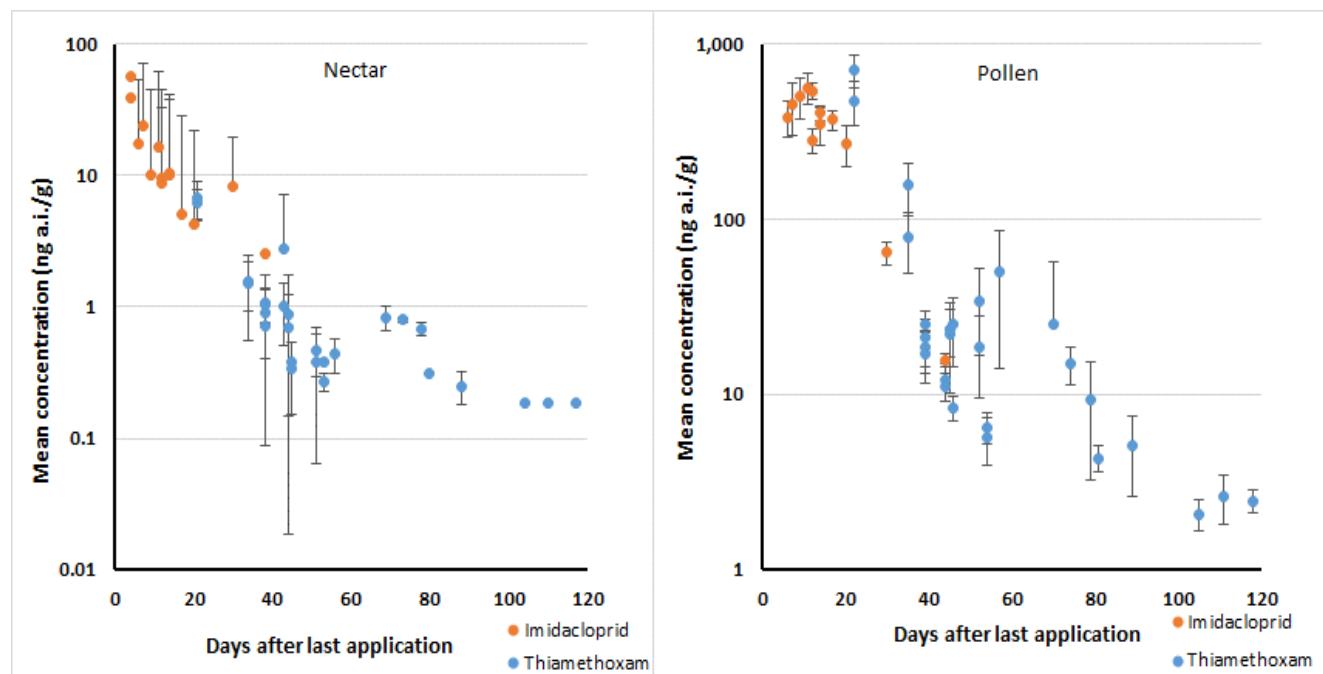


Figure 6-15. Thiamethoxam and imidacloprid residues in nectar (left) and pollen (right) from pre-bloom, foliar applications to oranges. Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval.

For post-bloom applications, residues in peach and cherry nectar are <10 ng a.i./g, with many samples with levels below the LOD (**Figure 6-16**). Residues in pollen are highly variable, ranging <1 to 100 ng a.i./g. These residue data reflect measurements different sites and seasons of application among chemicals. Within a chemical, differences in mean residues between sites or application season are comparable to those observed among chemicals. Therefore, within the context of variability in residues among sites, this analysis suggests that chemical does not have an overriding influence on neonicotinoid residues in pollen and nectar measured after post bloom applications to orchard crops.

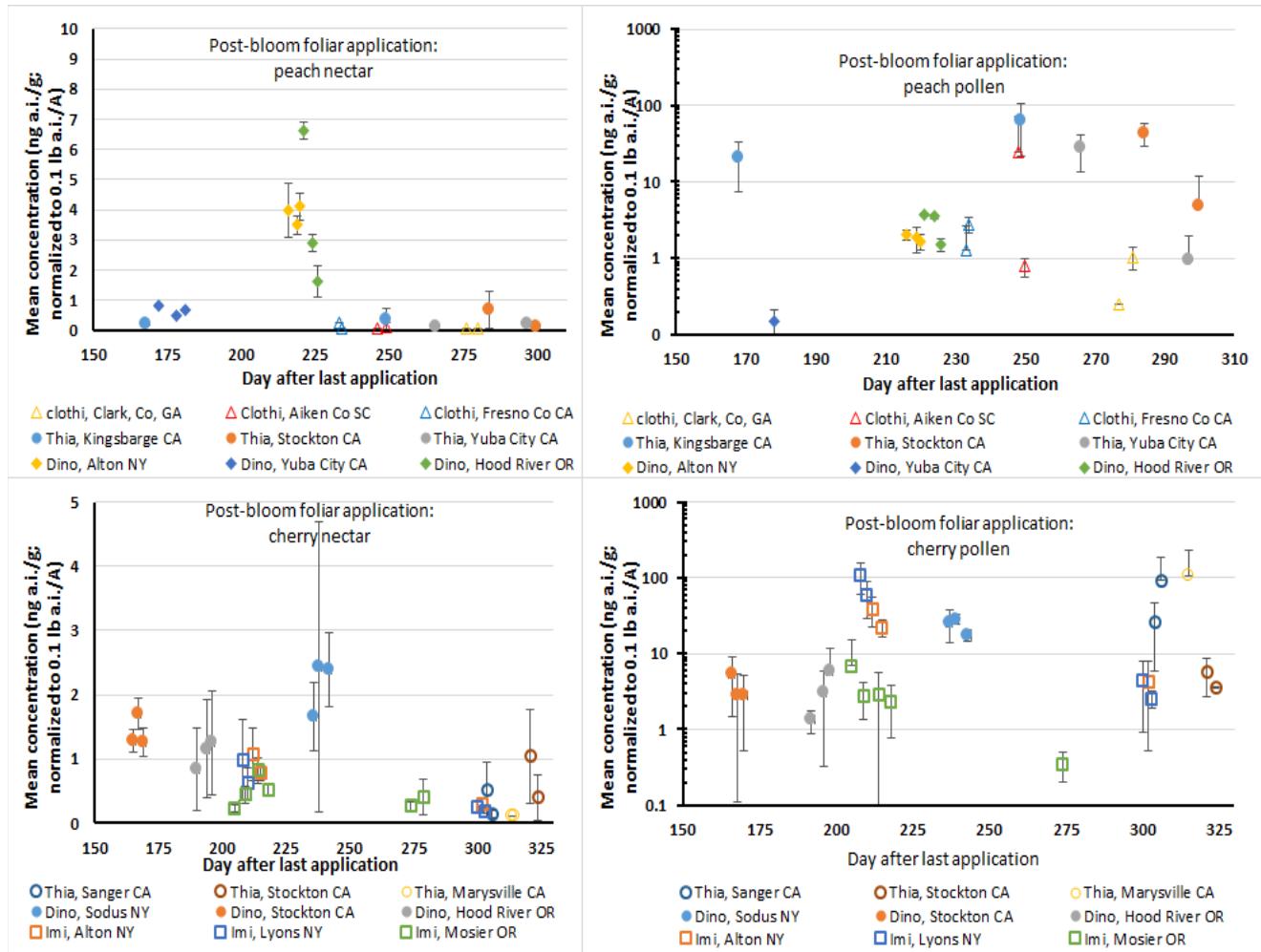


Figure 6-16. Mean neonicotinoid residues in nectar (left) and pollen (right) from post-bloom, foliar applications to peach (top) and cherry (bottom) orchards. Residues normalized to 0.1 lb a.i./A application rate. Error bars represent 95% confidence interval (Imi = imidacloprid; Thia = thiamethoxam, Clothi = clothianidin; Dino = dinotefuran).

6.1.2.10 Bridging Recommendations

In summary, the analysis above indicates that the timing of application relative to bloom has a substantial and consistent influence on neonicotinoid residues in pollen and nectar. Specifically, residues that are quantified following applications made weeks before bloom are 1-2 orders of magnitude greater than applications made months prior to bloom and post-bloom applications. Furthermore, residues associated with pre-bloom applications display a consistent declining trend over time while those associated with post-bloom applications do not. Regarding the impact of site and season (year), the majority of comparisons indicated residues are similar among sites and seasons (years). However, there is evidence that site and season can have a substantial impact on residues by approximately 1 order of magnitude in some situations. This analysis indicates that that crop and chemical do not exhibit a consistent or overriding impact on neonicotinoid residues in orchard crops when considering the variability that exists among sites within a chemical.

It is therefore recommended that available orchard data be bridged across crop and chemical for risk assessment purposes. Because of the influence of timing, residue data for pre-bloom and post-bloom applications should be considered separately in the bee risk assessments. Therefore, all pre-bloom applications for apples and oranges for thiamethoxam and imidacloprid are recommended for use in characterizing risk to bees from pre-bloom applications to orchards. Similarly, residues associated with post-bloom applications to orchard crops are recommended for bridging among crops and chemicals where necessary. Residue data should be normalized to the total application rate registered for the specific chemical of interest. Since a weight of evidence approach is used for risk assessment purposes, residues specific to the crop and chemical of interest may be considered separately for characterization purposes.

It should be noted that no pre-bloom residue data are available for stone fruit, tree nuts or tropical fruit. Therefore, it is assumed that residues for apples and oranges are representative of these crops. No post-bloom, foliar application data are available for citrus or tropical fruit. It is assumed that available apple, stone fruit and almond data are representative of these crops.

As discussed previously, residues from post-bloom applications are relatively stable for months after the application. Therefore, dissipation of residues is not modeled for characterization risk from post-bloom applications. For pre-bloom applications, residues collected within weeks of the application clearly are much higher than those collected later. For pre-bloom applications, it is recommended that the characterization include the duration of time when exposure exceeds the CFS NOEC and LOEC. Unlike other crop groups where a Monte Carlo analysis was conducted, an insufficient number of trial-specific rate constants are available for pre-bloom foliar orchard data. As an alternative, the decline kinetics of normalized pollen and nectar residues from all data for orchard crops was modeled using a first order, single compartment model as described earlier in **Section 4.5.4**. Results from this kinetic analysis indicates the following rate constants (and 95% confidence limits) are applicable to neonicotinoid residues resulting from pre-bloom, foliar applications to orchard crops:

- Pollen: $k = 0.078$ (0.035-0.121) d^{-1}
- Nectar: $k = 0.150$ (0.0052-0.295) d^{-1}

The following initial concentration ($C_{initial}$) should be used for each matrix:

- Pollen: 2300 ng a.i./g (normalized to 0.1 lb a.i./A total)
- Nectar: 318 ng a.i./g (normalized to 0.1 lb a.i./A total)

These rate constants are based on the combined residue data for thiamethoxam and imidacloprid studies involving apples and oranges (MRIDs 49521301, 50425902 and 50265504; **Figure 6-17**) and are recommended for use in risk characterization of the neonicotinoid bee risk assessments. Although the model fit for nectar is poor below 1 ng a.i./g, the error associated with this poor fit is not a primary concern from a risk assessment perspective since the onset of colony level effects from the neonicotinoid colony feeding studies exceeds 1 ppb by 1-2 orders of magnitude.

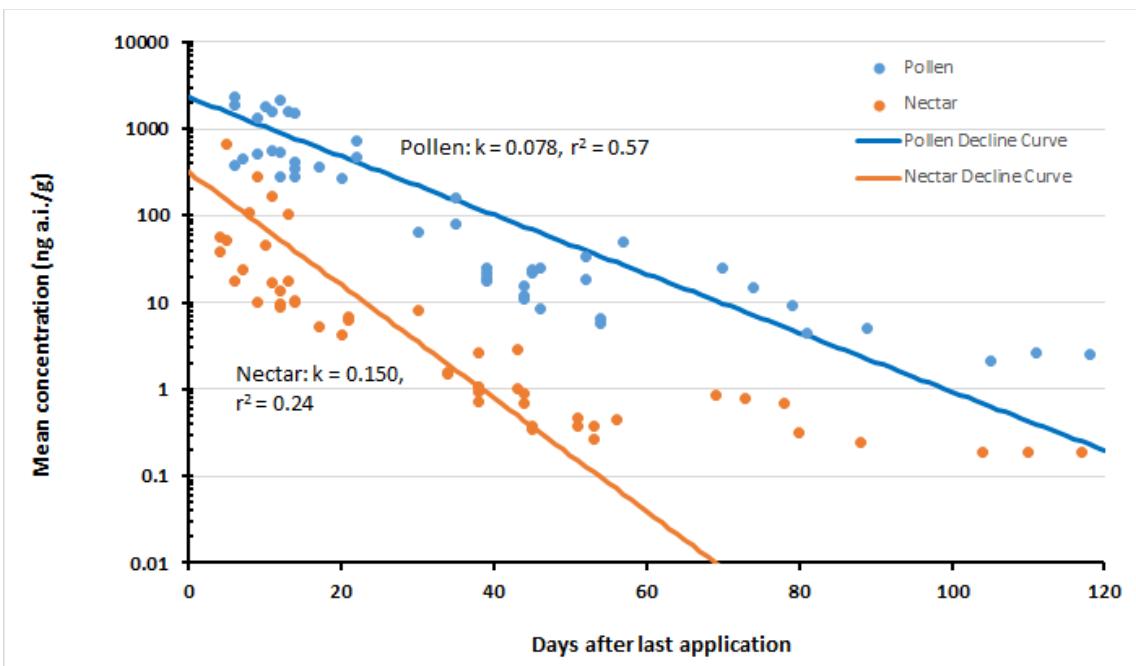


Figure 6-17. Mean residues of neonicotinoids (imidacloprid and thiamethoxam) in pollen and nectar (circles) following pre-bloom foliar applications to apples and oranges. Lines represent residue modeled using first order dissipation rate constants (k) and estimated initial concentrations at day 0.

When the residues in nectar and pollen are combined to provide an estimate of the total nectar equivalence (*i.e.*, nectar + pollen/20; **Attachment 1**), the following nectar equivalent residue and associated decline curve is estimated for risk characterization purposes (**Figure 6-18**).

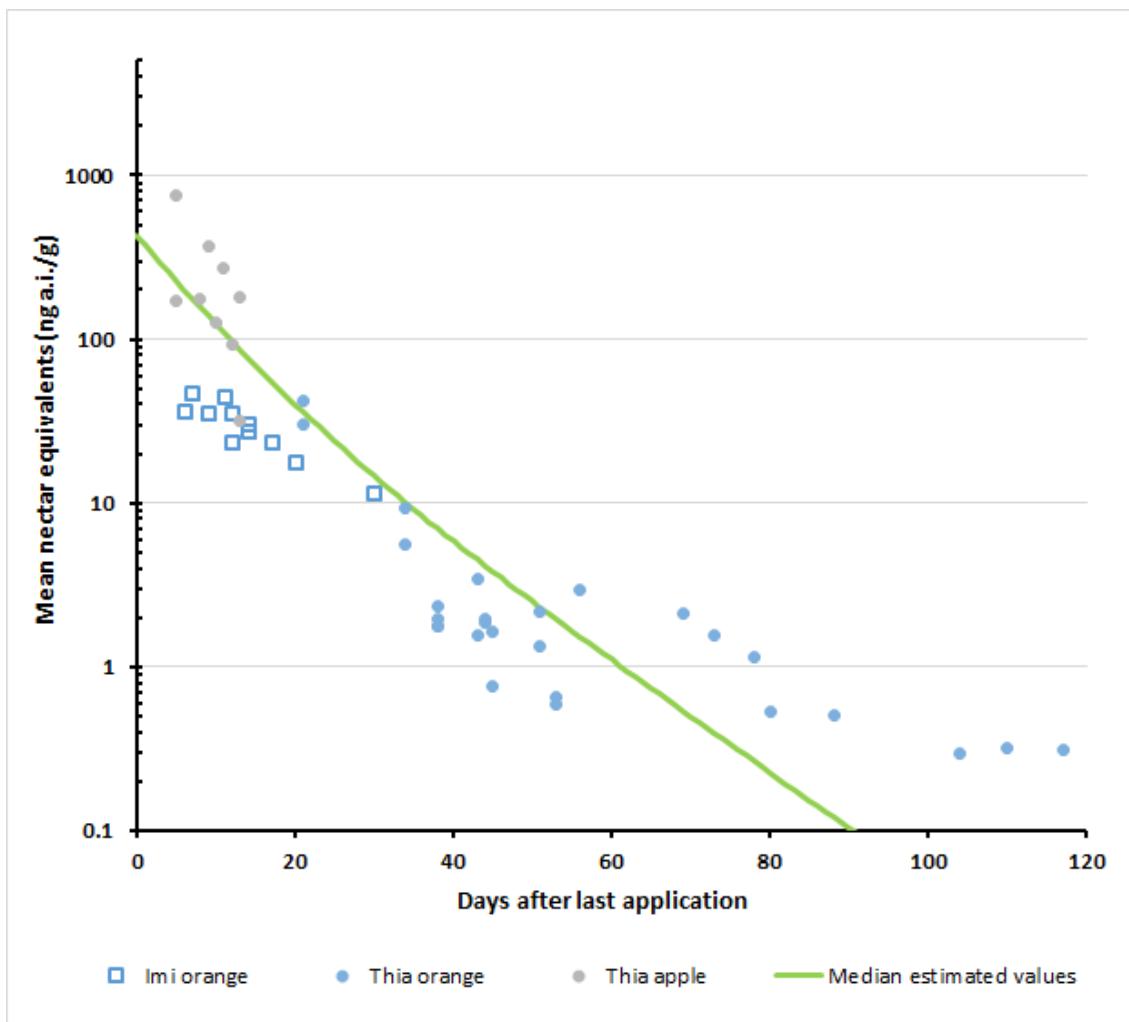


Figure 6-18. Mean residues of neonicotinoids (imidacloprid and thiamethoxam) expressed as nectar equivalence (circles) following pre-bloom foliar applications to apples and oranges. The line represents modeled residue decline using first order dissipation rate constants (k) and estimated initial concentrations for pollen and nectar. Residues are normalized to 0.1 lb a.i./A.

6.1.3 Soil Applications

6.1.3.1 Summary of Label Rates/Restrictions

Table 6-7 summarizes the pre-and post-bloom soil application rates registered for orchard crop groups. For pre-bloom, applications are very limited for clothianidin and imidacloprid, with applications only allowed on citrus. Clothianidin and imidacloprid are allowed as post-bloom soil applications to the majority of the orchard crop groups (the exception is applications of clothianidin to tree nuts). Dinotefuran is only registered as a soil treatment on stone fruit, with applications allowed as pre- or post-bloom. Thiamethoxam is registered as a soil treatment for pre-or post-bloom applications to citrus.

Table 6-7. Soil application rates (in lb a.i./A) and number of applications (x n) for neonicotinoids on orchard crops (based on current labels)

Orchard crop group	Clothianidin	Imidacloprid	Thiamethoxam*	Dinotefuran
Pre-bloom				
Pome fruit	NR	NR	NR	NR
Stone fruit	NR	NR	NR	0.27 lb/A x 1
Citrus	0.2 lb/A x 2	0.5 lb/A x 1	0.15 x 1	NR
Tree nuts	NR	NR	NR	NR
Tropical fruits	NR	NR	NR	NR
Post-bloom				
Pome fruit	0.2 x 1	0.38 x 1	NR	NR
Stone fruit	0.2 x 2	0.38 x 1	NR	0.27 x 1
Citrus	0.2 x 2	0.5 x 1	0.15 x 1	NR
Tree nuts	NR	0.5 x 1	NR	NR
Tropical fruits	0.1 x 2	0.5 x 1	NR	NR

NR = not registered

*Clothianidin-equivalent rates

6.1.3.2 Available Residue Data

Residue data are available from studies involving pre- and post-bloom soil applications to citrus for thiamethoxam, clothianidin and imidacloprid (**Table 6-8**). Mean residues of the neonicotinoids in nectar and pollen from the studies listed in **Table 6-8** are shown in **Figure 6-19** and **Figure 6-20**, respectively. These residue values are normalized to a common application rate of 0.1 lb a.i./A. Note that nectar data were collected in all of the studies listed in **Table 6-8**; however, pollen samples were only collected in some of them. Therefore, differing amounts of data are shown in **Figure 6-19** and **Figure 6-20**. In addition, no residue data were available for imidacloprid in pollen from these studies.

Unlike residues associated with foliar applications to orchard crops, those resulting from soil applications do not display a distinct declining trend with time after application, at least when data are combined across neonicotinoids and crops.

As noted previously, there are also residue data available from two imidacloprid studies (MRIDs 49662101 and 49819401) involving both soil and foliar applications to orchard crops (apples and stone fruit). Because these studies involve different types of applications, it is unknown how foliar and soil applications contribute to the magnitude of the residues. Therefore, residues from these studies are not considered here for the bridging strategy.

Table 6-8. Residue studies for orchard crops treated with foliar applications of neonicotinoids

Crop	Chemical	# sites (Locations)	Application Rate, # of Apps, (interval)	# Seasons	# sampling events per season)	MRID	Classification
Pre-bloom							
Orange	Thiamethoxam	2 (FL)	0.074, 0.110, 0.15, 0.22 or 0.48* lb a.i./A x 1	2	3	49881002/ 50096603	Supplemental
Orange	Thiamethoxam	4 (CA)	0.074, 0.15, 0.22 or 0.48* lb a.i./A x 1	1 or 2	3	49881001/ 50096601	Acceptable
Orange	Thiamethoxam	6 (CA)	0.15* lb a.i./A x 1	2	1	49950101/ 50131102	Acceptable
Lemon	Thiamethoxam	3 (CA)	0.15* lb a.i./A x 1	2	1	49950101/ 50131102	Acceptable
Pre- and Post-bloom							
Orange	Clothianidin	1 (FL)	0.2 lb a.i./A x 1	2	1 or 11	49317901	Supplemental
Orange	Clothianidin	4 (FL)	0.26 lb a.i./A x 1	1 or 2	3	50478201	Supplemental
Lemon	Clothianidin	4 (AZ)	0.1 lb a.i./A x 1	2	3	50478201	Supplemental
Post-bloom							
Orange, tangerine	Imidacloprid	11 (CA)	0.25, 0.51 or 1.0 lb a.i./A x 1	1	1	49090504	Supplemental

*Clothianidin-equivalent rates

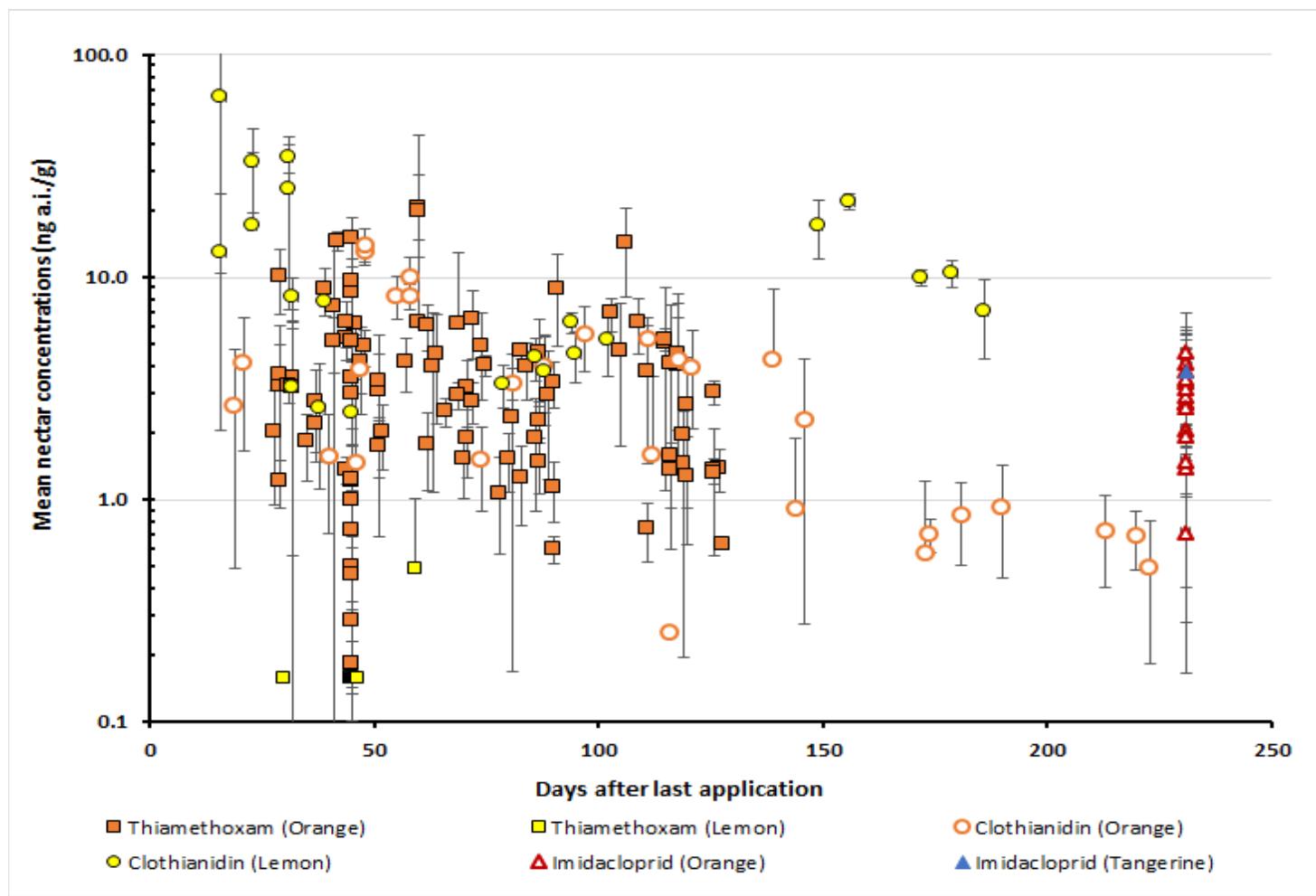


Figure 6-19. Nectar mean residue data available from soil applications of neonicotinoids to citrus. Data are normalized to an application of 0.1 lb a.i./A. Error bars represent 95% confidence intervals.

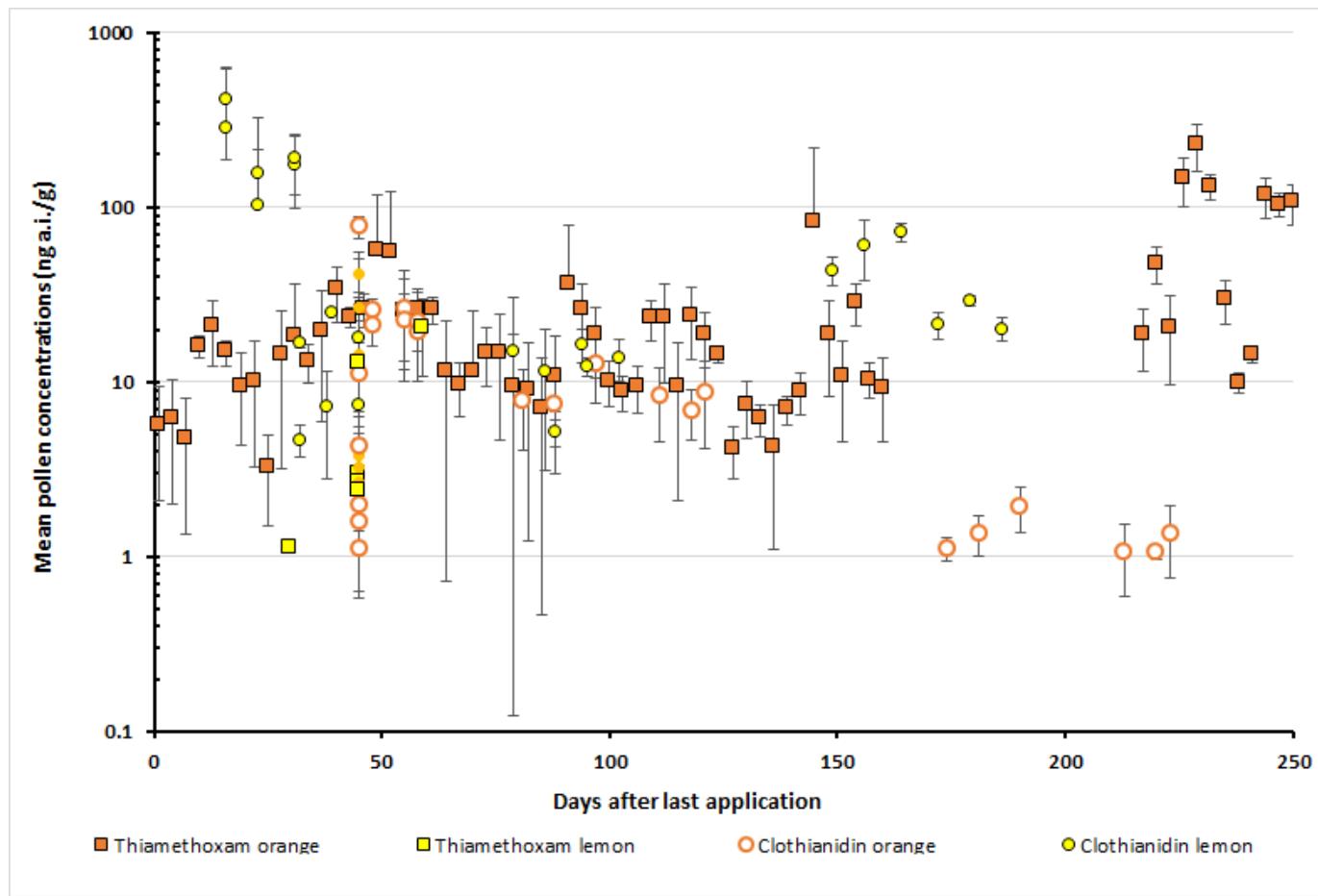


Figure 6-20. Pollen mean residue data available from soil applications of neonicotinoids to citrus. Data are normalized to an application of 0.1 lb a.i./A. Error bars represent 95% confidence intervals.

6.1.3.3 Bridging Needs (Gaps)

For pre-bloom soil applications, no residue data are available for imidacloprid applications to citrus or dinotefuran applications to stone fruit. For post-bloom applications, no residue data are available for those chemicals with applications allowed on pome, stone and tropical fruit. Data are also not available for imidacloprid applications to tree nuts or thiamethoxam applications to citrus. **Table 6-9** identifies the available studies by crop group and chemical and identifies areas where bridging is needed (*i.e.*, indicated by “No data”).

Table 6-9. Identification of data gaps for registered soil applications of neonicotinoids on tree crops

Orchard crop group	Clothianidin	Imidacloprid	Thiamethoxam*	Dinotefuran
Pre-bloom				
Pome fruit	NR	NR	NR	NR
Stone fruit	NR	NR	NR	No data
Citrus	Orange and lemon (49317901 and 50478201)	No data	Orange and lemon (49881002, 49881001 and 49950101)	NR
Tree nuts	NR	NR	NR	NR
Tropical fruits	NR	NR	NR	NR
Post-bloom				
Pome fruit	No data	No data	NR	NR
Stone fruit	No data	No data	NR	No data
Citrus	Orange and lemon (49317901 and 50478201)	Orange, tangerine (49090504)	No data	NR
Tree nuts	NR	No data	NR	NR
Tropical fruits	No data	No data	NR	NR

NR = not registered

6.1.3.4 Influence of Application Rate on Residues

All of the soil residue studies involved a single application (per season); therefore, the influence of number of applications on residue values is not evaluated for soil applications. There are two thiamethoxam studies (MRIDs 49881002 and 49881001) that included multiple trials conducted at the same time using different application rates (ranging from 0.074 – 0.48 lb a.i./A). This allows for consideration of the influence of application rate on residues. Residue values in nectar and pollen (respectively) of orange blossoms collected from the two studies are summarized in **Figure 6-21** and **Figure 6-22**. The left graph in each figure depicts the un-normalized, mean residues from the studies. These graphs show that the residues from trials with lower application rates are lower in value compared to the residues from higher application rates. Un-normalized residues taken at similar time points vary by as much as two orders of magnitude, with the majority (90%) of the data differing by a factor of ≤30 for nectar and ≤55 for pollen. When residues are normalized to the same application rate, they are more similar. For nectar, 90% of the data differ by a factor of ≤9.2, while for pollen, the majority of data differ by a factor of ≤23. This analysis supports the decision to normalize residues to a standard application rate.

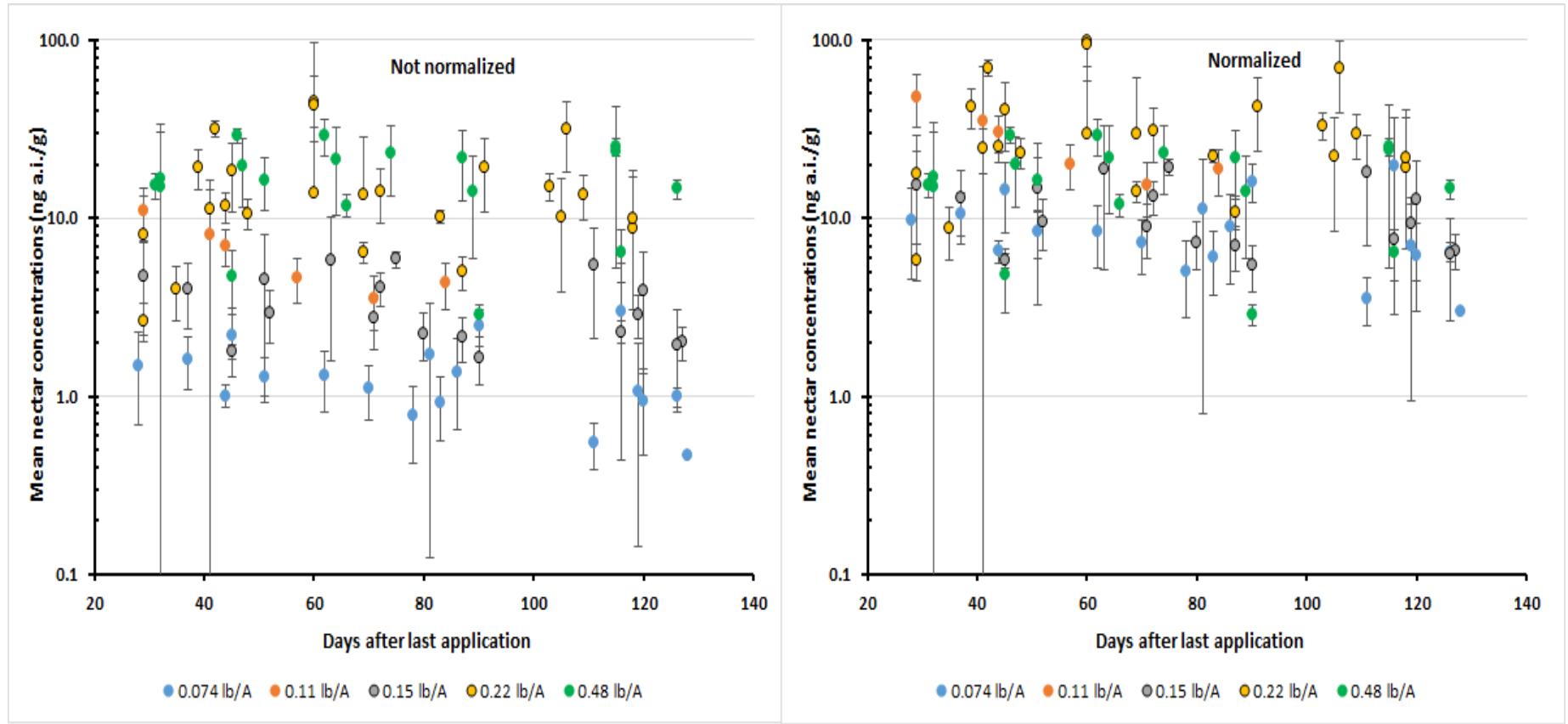


Figure 6-21. Mean residues of thiamethoxam (expressed as clothianidin equivalents) in orange nectar from orange following soil applications at different rates. Left graph represents un-normalized mean residues while the right graph represents mean residues normalized to an application rate of 0.48 lb a.i./A. Error bars represent 95% confidence interval around mean.

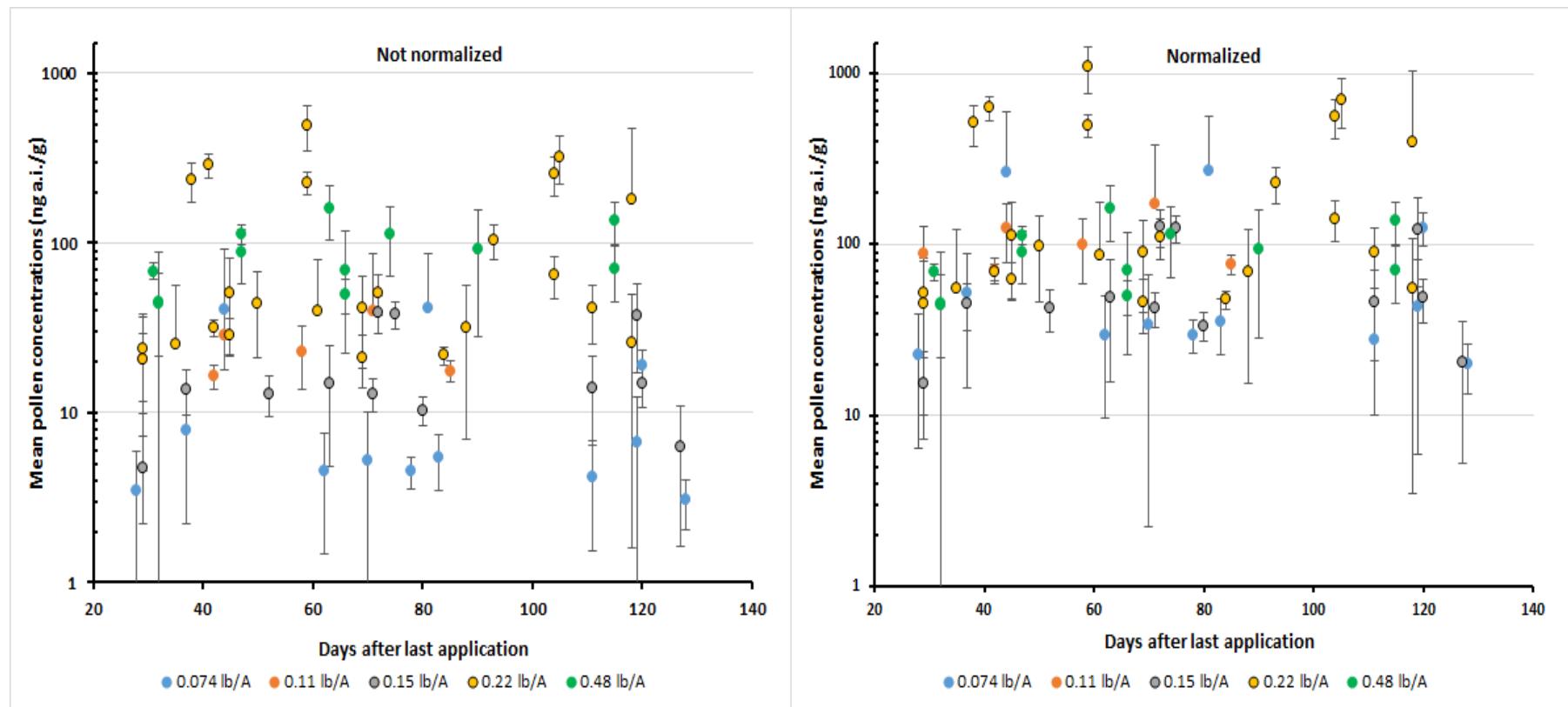


Figure 6-22. Mean residues of thiamethoxam (expressed as clothianidin equivalents) in orange pollen from orange following soil applications at different rates. Left graph represents un-normalized mean residues while the right graph represents mean residues normalized to an application rate of 0.48 lb a.i./A. Error bars represent 95% confidence interval around the mean.

6.1.3.5 Influence of Sampling Day (Time) and Application Timing on Residue Values

Residues in pollen are generally an order of magnitude greater than those in nectar. As depicted in **Figure 6-19**, **Figure 6-20** and **Table 6-10**, available residues representing similar time periods for the same matrix generally vary by an order of magnitude. During the sampling periods of the available studies, the residues do not show a clear decline pattern. As discussed previously for foliar applications, residues decline substantially within 20 days after application. For the available soil application studies, only 3 sets of samples were collected within these time periods which prevents evaluation of the decline of residues within 20 days of a soil application. Samples of pollen and nectar collected within 120 days are on the same order of magnitude as those collected 16 d after bloom. Therefore, the available residue data for soil applications indicate relatively consistent residues for months after application, suggesting that residue levels are stable over time. This may be related to the nature of the application method, whereby pesticide in treated soil continues to become available for uptake in plants weeks or months after application. As a result, a kinetic analysis of individual trials was not conducted for residue data collected from soil applications to orchard crops. No obvious difference in residues from pre-bloom and post-bloom applications is observable in the available data.

Table 6-10. Range of mean values for orchard crops treated with neonicotinoids. Ranges broken out by different times between bloom and application date. Concentrations in ng a.i./g, normalized to 0.1 lb a.i./A rate

Days before bloom when application was made	Concentration in nectar	Concentration in pollen
16	27-85	285-412
19	2.6	NA
21-23	4.1-33	NA
25	NA	103-157
28-30	0.16-10	1.1-19
31-40	1.6-34	4.7-190
41-50	0.16-15	1.1-132
51-60	0.49-21	8.8-227
61-70	1.5-6.1	6.2-34
71-80	1.1-6.5	6.2-36
81-100	0.60-8.9	5.2-56
100-120	0.25-14	5.7-147
121-140	0.63-4.3	4.2-8.7
141-160	0.91-22	44-61
161-180	0.58-10	1.1-72
210-230	0.49-4.6	1.1-1.4

NA = not applicable

6.1.3.6 Effect of Year and Site on Residue Values

In order to evaluate the effect of year and site on neonicotinoid residues following soil applications, data were grouped by chemical and crop and compared. Residues of thiamethoxam in nectar and pollen of lemon are shown in **Figure 6-23**; those for thiamethoxam in oranges are shown in **Figure 6-24**; and those for clothianidin in lemon and oranges are provided in **Figure 6-25** and **Figure 6-26**, respectively. Finally, residues of imidacloprid in orange nectar are shown in **Figure 6-27**. Each of these figures depicts the

mean residue for individual trials and separate years. All residues are normalized to an application rate of 0.1 lb a.i./A.

For thiamethoxam lemon, limited data are available from which to compare sites (mostly one mean value per site; **Figure 6-23**). Mean residues of thiamethoxam (expressed as clothianidin equivalence) in nectar are all below 1 ng a.i./g, at or near the limits of quantitation. Mean residues of thiamethoxam in pollen are notably higher, but within an order of magnitude with overlapping confidence intervals when taken at the same time (~45 days after application).

Mean residues of thiamethoxam in orange nectar among 6 sites in California and 2 sites in Florida from multiple years generally fall between 1 and 10 ng a.i./g, with confidence intervals that typically overlap (**Figure 6-24**). Mean residues in pollen across sites and years are more variable, ranging from about 1-100 ng a.i./g. While many confidence intervals overlap among mean values of thiamethoxam residues in pollen, mean residues at some sites appear distinctly higher or lower (1-2 orders of magnitude) compared to other sites/years at similar time points, with non-overlapping confidence intervals. This suggests that site can occasionally have a substantial impact on thiamethoxam residues in orange pollen. A similar outcome is seen with clothianidin residues in nectar and pollen from lemon and oranges (**Figure 6-25** and **Figure 6-26**, respectively), where by mean residues from most sites and years are commonly within 10X at similar time points, but occasionally exceed 10X for a few sites. Residues of imidacloprid in orange nectar 231 days following soil application are within 10X among sites (**Figure 6-27**).

In summary, the majority of comparisons suggest that residues are similar between sites and years within the same study as a result of soil applications to orchard crops. However, there is some evidence that residues measured at different sites can be substantially different (beyond an order of magnitude). Such differences may result from multiple factors that can impact the bioavailability and translocation of neonicotinoids (*e.g.*, weather, soil properties). Therefore, based on the limited data available, the impact of site and year on neonicotinoid residues appears within 10X in most cases, but cannot be dismissed as a potentially important factor influencing pollen and nectar residues from soil applications to orchard crops.

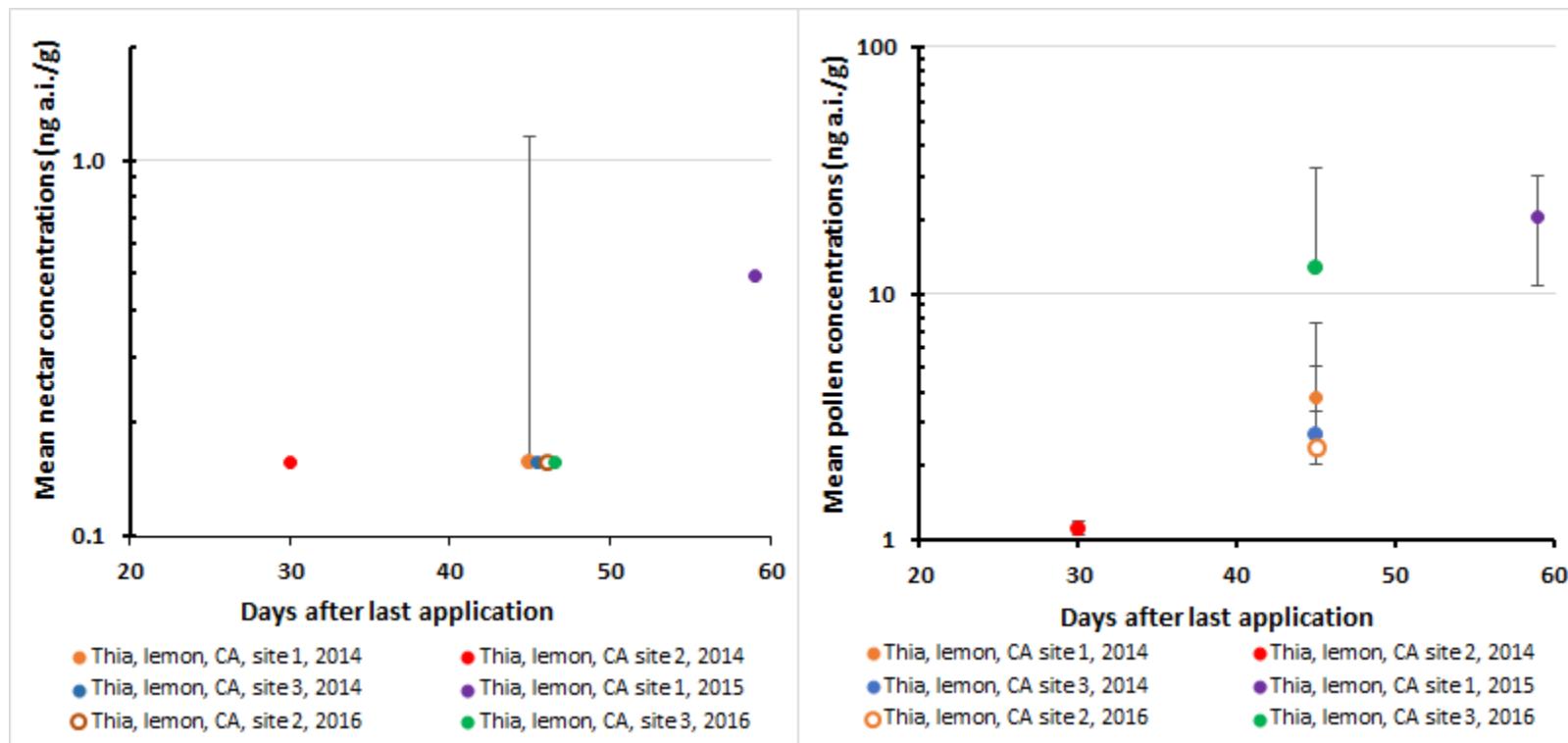


Figure 6-23. Concentrations of thiamethoxam (expressed as clothianidin equivalents) in nectar (left) and pollen (right) from lemon blossoms following soil applications (MRID 50131102). Error bars represent 95% confidence interval around the mean.

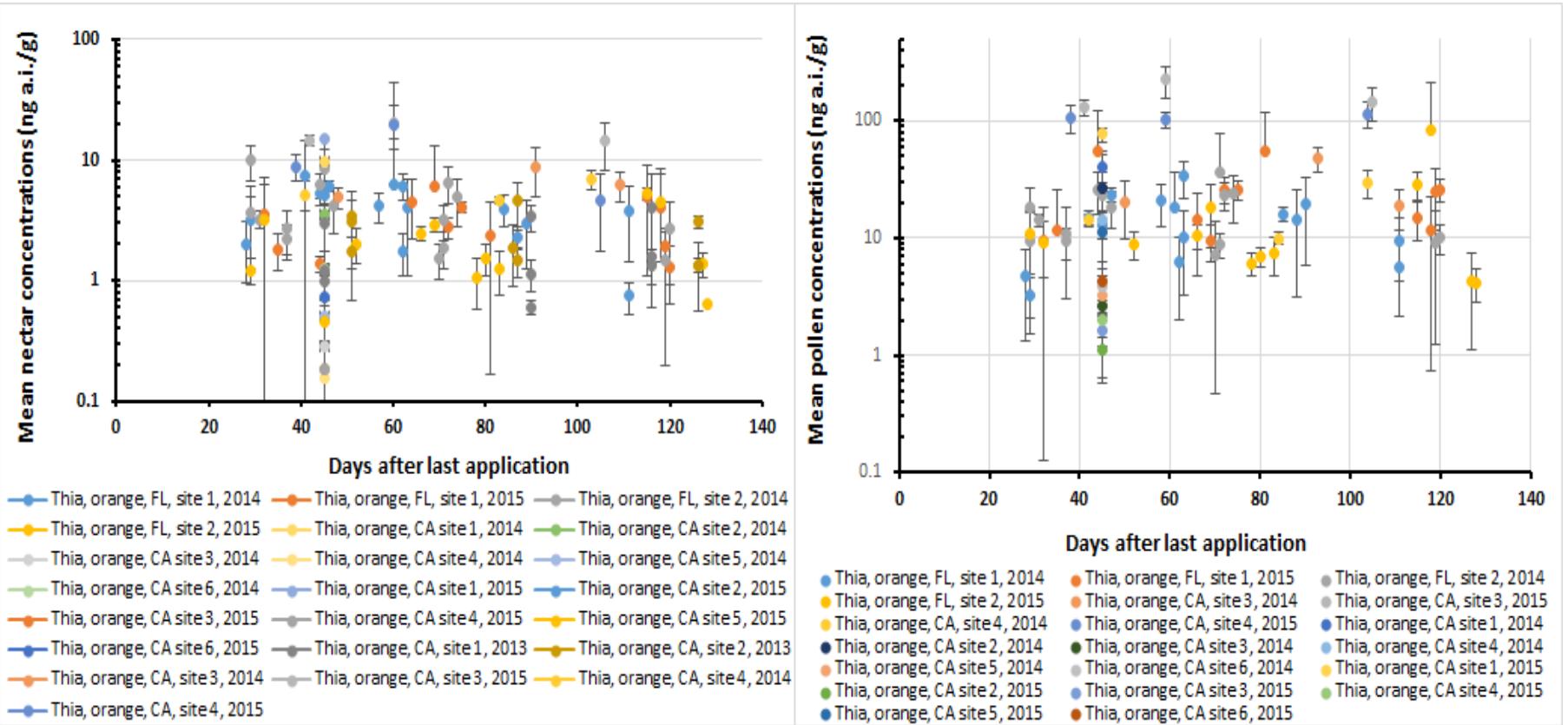


Figure 6-24. Concentrations of thiamethoxam (expressed as clothianidin equivalents) in nectar (left) and pollen (left) from orange blossoms following soil applications. Error bars represent 95% confidence interval around the mean.

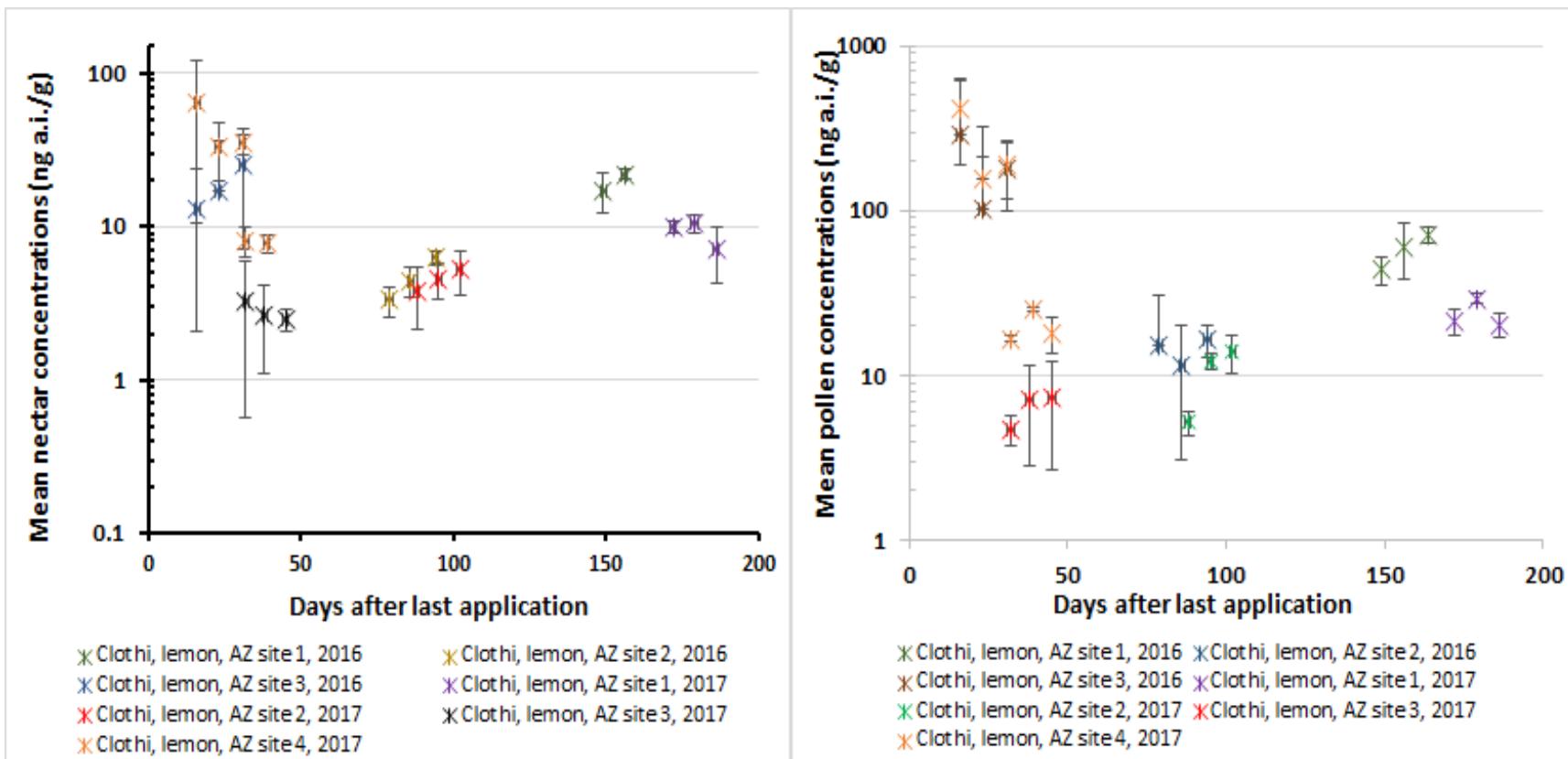


Figure 6-25. Concentrations of clothianidin in nectar (left) and pollen (right) from lemon blossoms following clothianidin soil applications (MRID 50478201). Error bars represent 95% confidence interval around the mean.

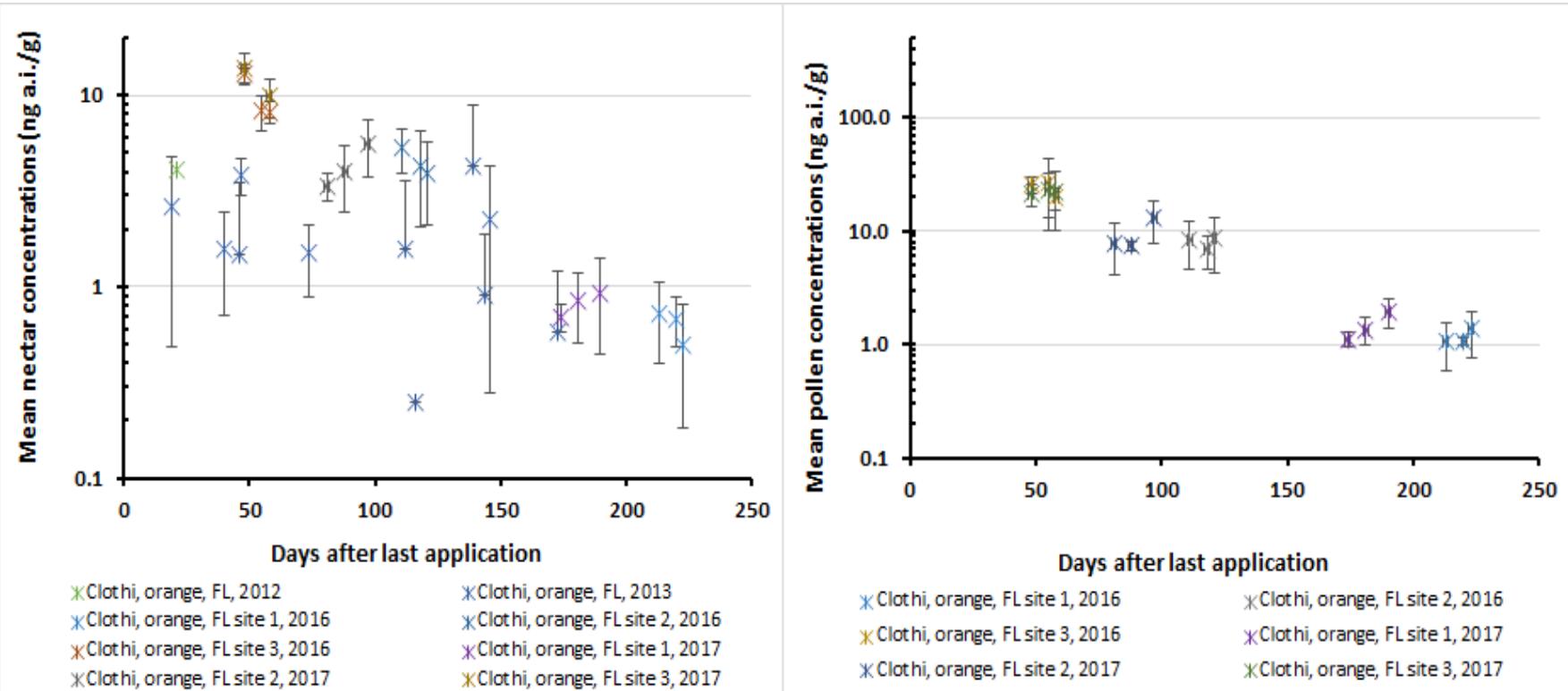


Figure 6-26. Concentrations of clothianidin in nectar (left) and pollen (right) from orange blossoms following soil applications of clothianidin. Error bars represent 95% confidence interval around the mean.

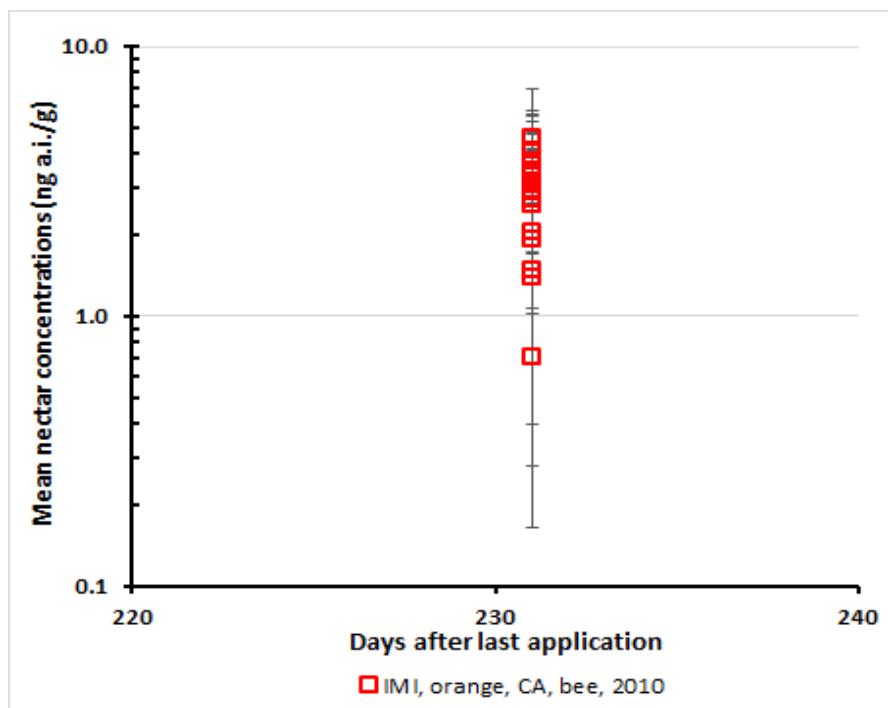


Figure 6-27. Concentration of total imidacloprid in nectar from orange blossoms following soil applications (MRID 49090504). Residues represent multiple sites. Error bars represent 95% confidence interval around the mean.

6.1.3.7 Effect of Crop on Residue Values

Residue data are available for orange and lemon nectar and pollen treated with either thiamethoxam or clothianidin. Keeping chemical constant, residue data for different crops can be compared to evaluate whether crop has an influence on residue levels. One limitation to the available data is that much more data are available for oranges compared to lemons. Given the variability observed in available residues, there is some question about how representative the lemon data are for residues in the field. Furthermore, these data originate from different sites, thus introducing a potential confounding factor in the crop-to-crop comparisons. Despite these limitations, this analysis considers the orange and lemon data that are available. There are also data available for imidacloprid residues for oranges and one time point for tangerines. Given the limited number of sampling periods and sites for tangerines, imidacloprid residues are not considered here.

When considering the thiamethoxam data, there are residue data which allow for the comparison of residues in lemon and orange nectar and pollen (Figure 6-28). Residue data (expressed as clothianidin equivalents) for lemons reflect 3 sites collected at two different years (1 time point per site/year) while those for orange reflect 12 sites with two years per site. Residues were collected for 1 or 3 time points. In nectar, residues collected at 5 of the 6 sites were below the LOD at 30 and 45 d after application. The mean quantified residue at the 6th site was 0.5 ng a.i./g. Since confidence intervals were not available for nectar residues, ranges of available means are compared for lemons and oranges. In orange nectar, mean residues ranged from <LOD to 20.5 ng a.i./g. Residue samples collected at a similar time-period as lemons (*i.e.*, 28-50 d) ranged from <LOD to 15 ng a.i./g. For pollen, residues ranged 1.1-20 ng a.i./g for

lemons and 1.1-227 ng a.i./g for oranges. When comparing the residue data for the two crops, residues for lemons overlap with the low end of the range of orange residues, with values 2 orders of magnitude lower than the high end of the orange nectar. For pollen, residues for lemon and orange overlap, with the lower end of the range of lemon residues one order of magnitude below the high end of the orange residues. When considering the confidence intervals of the pollen data, residues for lemons and oranges overlap at similar time points. As noted above, there are much less residue data available for lemons, and therefore these data may not represent the full range of expected residues. Importantly, since the majority of these data originate from different sites and years among crops, there is a potential influence of site or year on variability observed in residues among these two crops.

There is one location that is common to both orange and lemon with the thiamethoxam study: San Luis Obispo, CA. With nectar, thiamethoxam residues are below the LOD or LOQ for both lemon and orange, thus preventing meaningful comparisons from being made. With pollen, mean residues in lemon and orange measured in 2014 are 3.0 and 14.5 ng a.i./g, respectively. In 2015, mean residues of thiamethoxam in lemon and orange pollen are 20.3 and 2.0 ng a.i./g, respectively, which is the reverse of the trend seen 2014. Thus, there is no consistent impact of crop on residues in orange and lemon measured at this location.

For clothianidin, the available pollen and nectar data are similar in the number of sites and time periods (**Figure 6-29**). Residues of pollen and nectar were collected from four orange sites and four lemon sites at two different years, with multiple sampling periods per site/year. An additional study is available where residues in nectar were collected from orange trees at 1 additional site for two years. When comparing residues in oranges and lemons, their ranges are similar for both nectar and pollen. For nectar, the range is <0.16-21 ng a.i./g for oranges and <0.16-65 ng a.i./g for lemons. For pollen, the range is 1.1-27 ng a.i./g for oranges and 4.7-412 ng a.i./g for lemons. When considering samples taken at similar time points, confidence intervals for lemons and oranges typically overlap for nectar samples. This is also the case for residues in pollen, which have overlapping confidence intervals for similar time points for applications made approximately 120 days before bloom. For post-bloom applications made between 170 and 190 days before bloom, pollen residues in lemon appear to be an order of magnitude higher than those in orange. Since the confidence intervals associated with these values do not overlap, this suggests that there may be difference in post-bloom residues in pollen for these two crops (**Figure 6-29**). However, as discussed previously, it is not possible to separate the potential influence of site-to-site differences on the residue values among crops (*i.e.*, the lemon data are from Arizona while the orange data are from Florida).

When considering the overlap of the residues for nectar for clothianidin and for thiamethoxam, no consistent trend is indicated, and differences in mean residues among sites within a crop are similar in magnitude to those occurring between crops. A similar finding is seen with residues in pollen from orchard crops. Therefore, within the context of variability in residues among sites, this analysis suggests that crop does not have a consistent or overriding influence on residues of neonicotinoids in pollen and nectar following soil applications to orchard crops

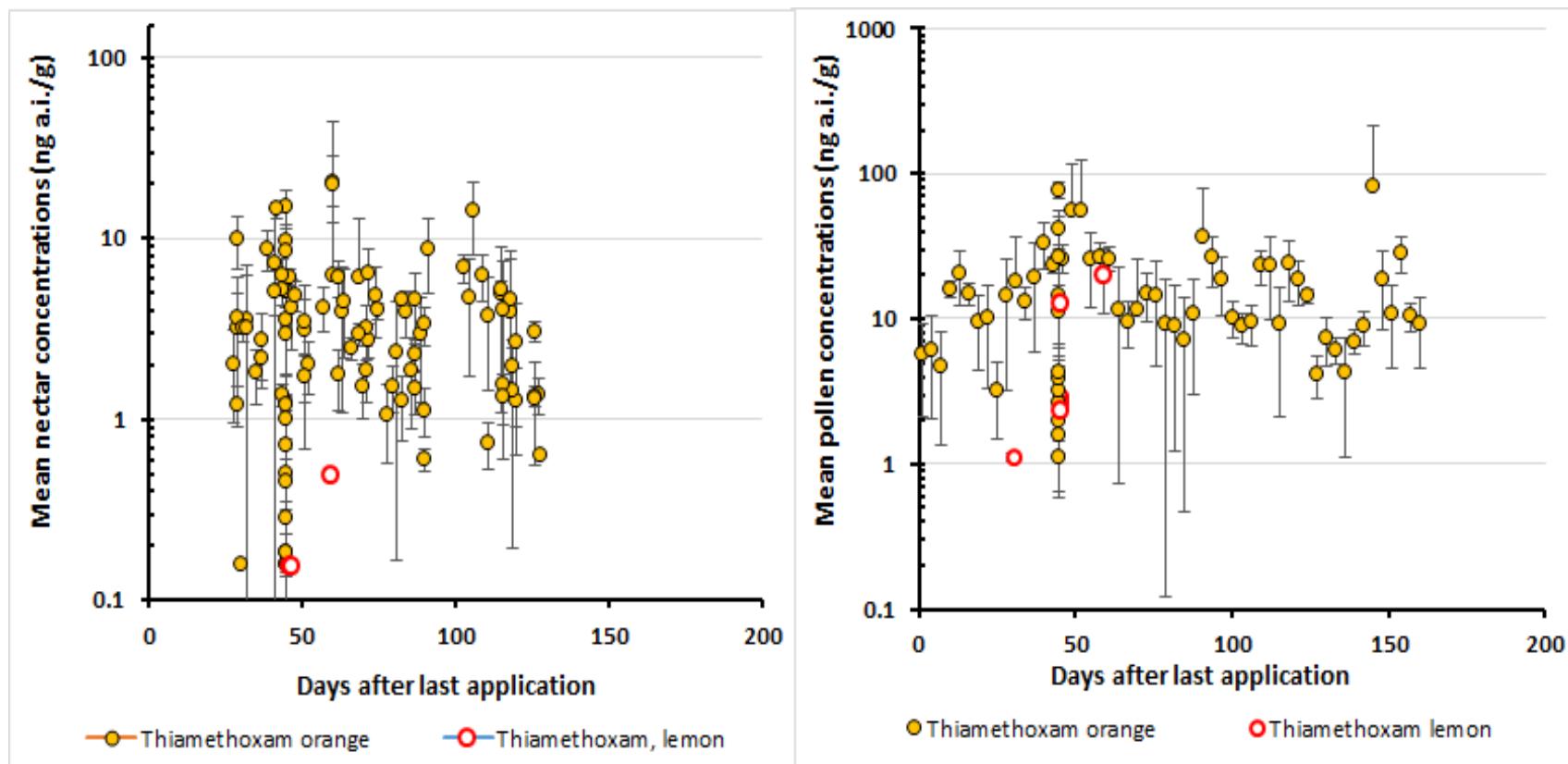


Figure 6-28. Mean residues of thiamethoxam (expressed as clothianidin equivalents) in orange and lemon nectar (left) and pollen (right) following soil applications of thiamethoxam. Residues are normalized to an application rate of 0.1 lb a.i./A. Error bars represent 95% confidence interval around the mean.

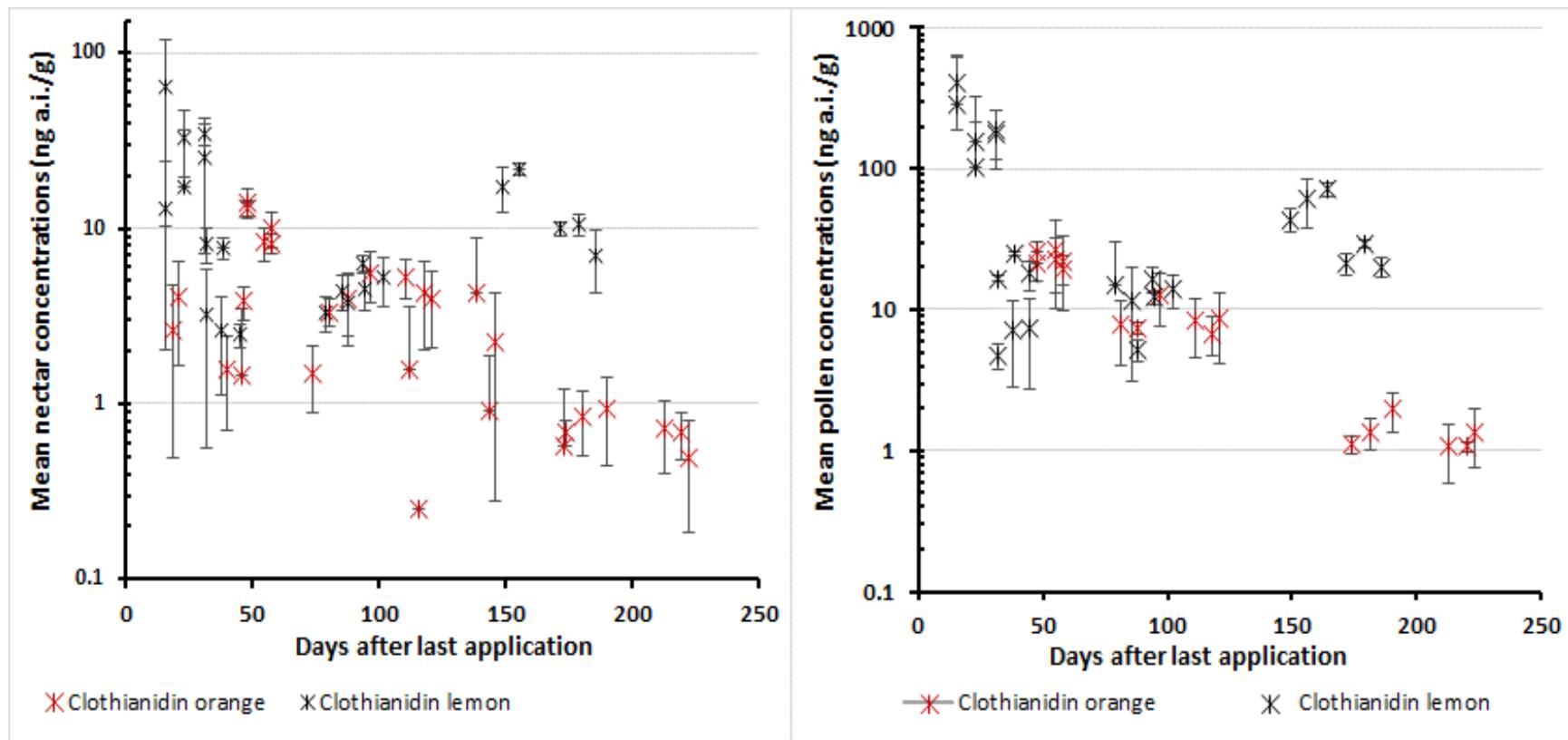


Figure 6-29. Mean residues of clothianidin in orange and lemon nectar (left) and pollen (right) following applications of clothianidin via soil. Residues are normalized to an application rate of 0.1 lb a.i./A. Error bars represent 95% confidence interval around the mean.

6.1.3.8 Effect of Chemical on Residue Values

In order to consider the effect of chemical on residue values in pollen and nectar, residues for different chemicals are compared for the same crop. Residues for clothianidin and thiamethoxam in lemon pollen and nectar are compared (**Figure 6-30**). Residues in orange pollen are available for both clothianidin and thiamethoxam. For orange nectar, residues are available for clothianidin, thiamethoxam and imidacloprid (**Figure 6-31**).

For lemon, nectar residues of thiamethoxam expressed as clothianidin equivalents (range: <LOD-0.5 ng a.i./g) are lower than those in clothianidin (range: 2.5-65 ng a.i./g). Since confidence intervals were not available for lemon nectar, they were not considered in making comparisons. For lemon pollen, residues of thiamethoxam (range: 1.1-13 ng a.i./g) and clothianidin (range: 4.7-412 ng a.i./g) overlap. When considering the confidence intervals of samples collected at similar times relative to application, confidence intervals overlap for clothianidin and thiamethoxam (**Figure 6-30**). As discussed above, the limited number of thiamethoxam sites leads to uncertainty in the representative of these data as residues in thiamethoxam in lemon, in addition to the impact of measurements taken at different sites and years.

For oranges, mean residues in nectar overlap for thiamethoxam expressed as clothianidin equivalents (range: <LOD – 21 ng a.i./g), clothianidin (range: 0.25-14 ng a.i./g) and imidacloprid (range: 0.71-4.6 ng a.i./g; **Figure 6-31**). Pollen residues for thiamethoxam expressed as clothianidin equivalents (range: 1.1-227 ng a.i./g) and clothianidin also overlap (1.1-27 ng a.i./g). When considering the confidence intervals of samples collected at similar times relative to application, confidence intervals overlap for clothianidin and thiamethoxam for both nectar and pollen (**Figure 6-31**).

Within a chemical, differences in mean residues between sites or application season are comparable to those observed between chemicals. Therefore, within the context of variability in residues among sites, this analysis suggests that chemical does not have an overriding influence on neonicotinoid residues in pollen and nectar measured after soil applications to orchard crops.

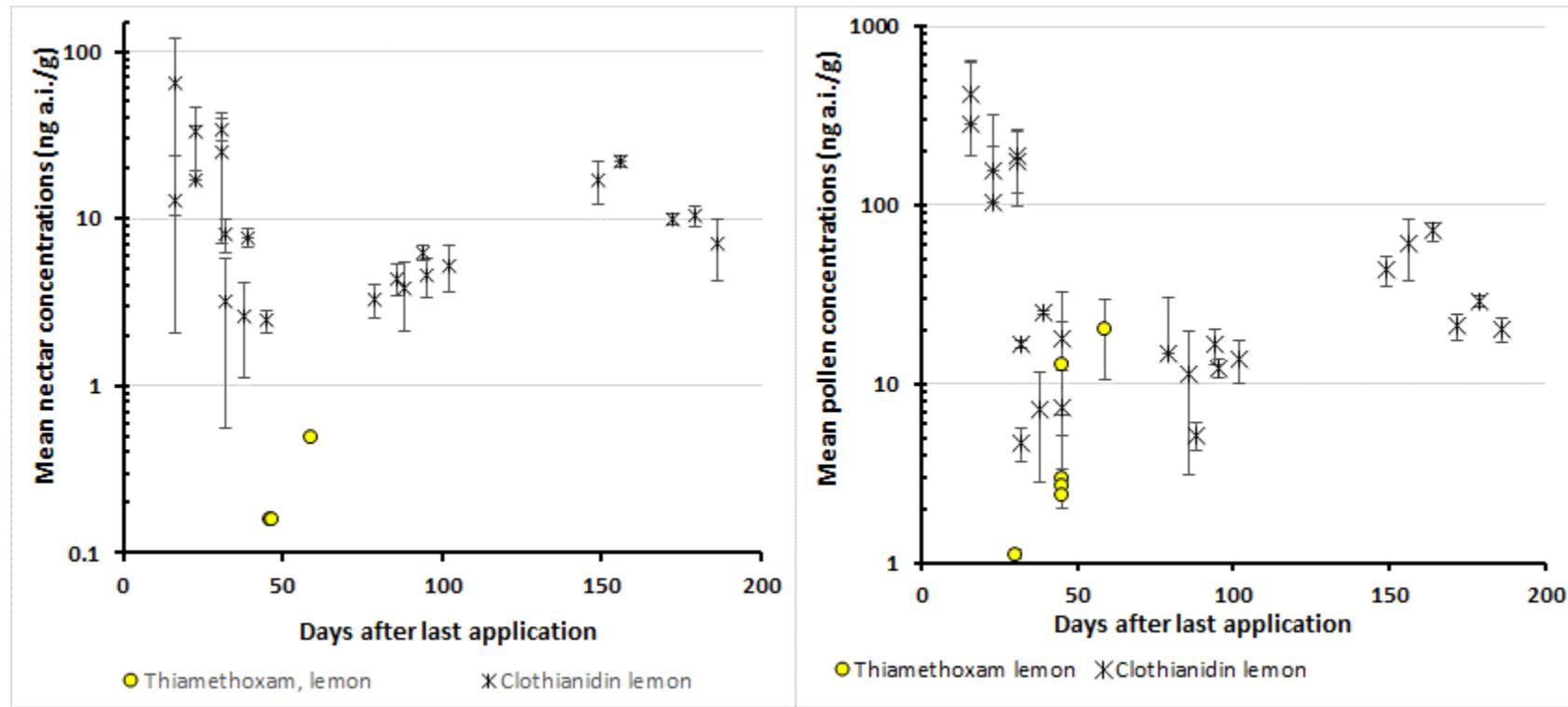


Figure 6-30. Mean residues in lemon nectar (left) and pollen (right) following applications of clothianidin and thiamethoxam (expressed as clothianidin equivalents) via soil. Residues are normalized to an application rate of 0.1 lb a.i./A. Error bars represent 95% confidence interval around the mean.

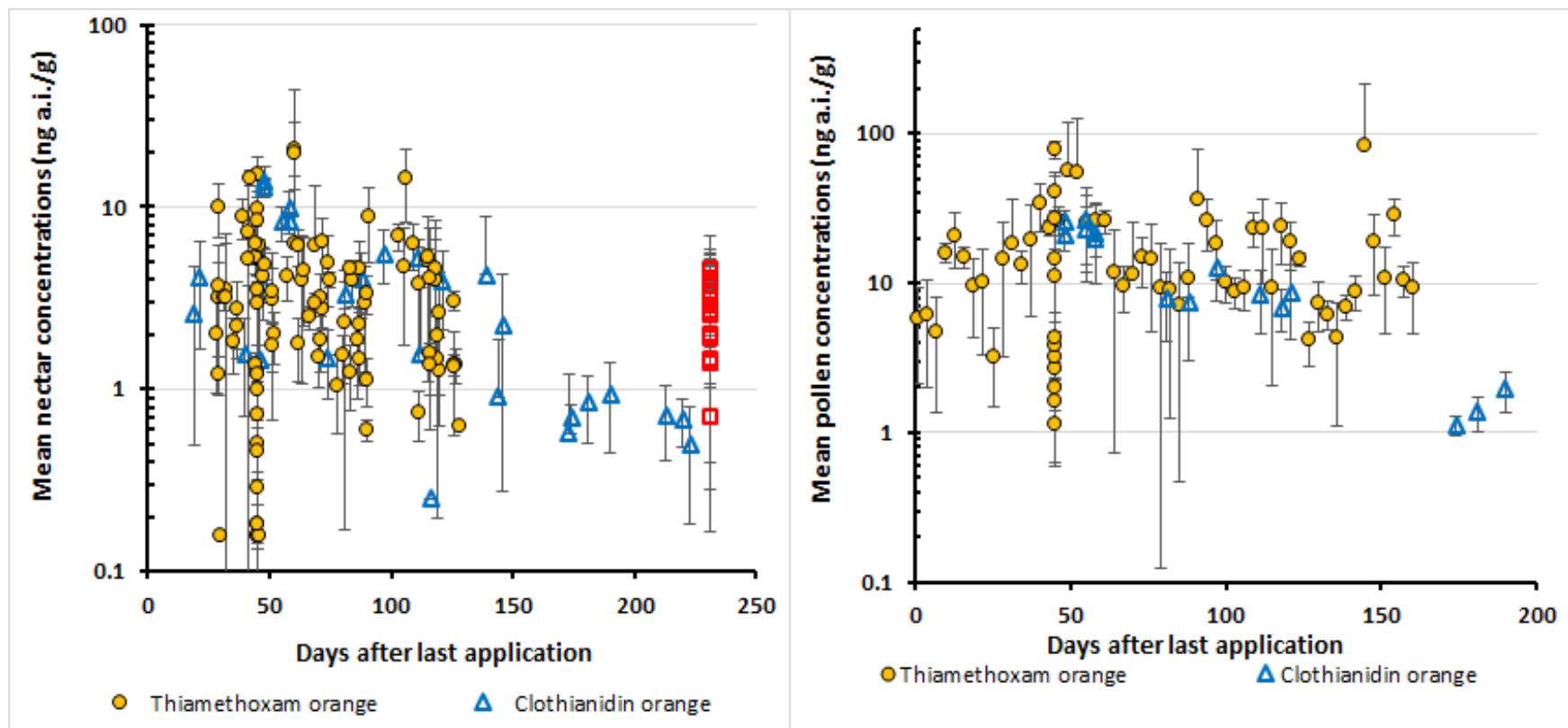


Figure 6-31. Mean residues in orange nectar (left) and pollen (right) following applications of clothianidin and thiamethoxam (expressed as clothianidin equivalents) via soil. Residues are normalized to an application rate of 0.1 lb a.i./A. Error bars represent 95% confidence interval around the mean.

6.1.3.9 Bridging Recommendations

Analysis of the available pollen and nectar residue data indicates that chemical and crop do not have a consistent or overriding influence on neonicotinoid residues following soil application to orchard crops. As observed with foliar applications to orchard crops, the majority of comparisons indicated residues are within an order of magnitude among sites and seasons (years). However, there is evidence that site and season can have a substantial impact on residues by approximately 1-2 orders of magnitude in some situations. Unlike residues in pollen and nectar resulting from foliar applications, those resulting from soil applications do not display a consistent declining trend over time, as residues appear to be relatively consistent (stable) over many months. Therefore, unlike foliar applications, it is not necessary to distinguish between pre-and post-bloom residue data for soil applications.

As discussed previously, orange and lemon residue data are available for clothianidin and thiamethoxam (and some limited data are available for imidacloprid applied to oranges). For soil applications, several data gaps remain (**Table 6-9**), including:

- Applications of dinotefuran to stone fruit;
- Applications of clothianidin to pome, stone and tropical fruits; and,
- Applications of imidacloprid to pome, stone and tropical fruit as well as tree nuts.

Given the lack of influence of chemical and crop on residue data, it is recommended that available data for clothianidin, thiamethoxam and imidacloprid from soil applications be bridged across orchard crops and neonicotinoids the data gaps bulleted above. There are some uncertainties in this approach. First, the only available data are for two citrus crops. It is assumed that these data are representative of residues in species from other tree crop groups. Second, the majority of the residue data are for thiamethoxam and clothianidin, with limited data for imidacloprid (nectar only from one time point). It is assumed that these data can be used for imidacloprid and dinotefuran.

For other crop groups (*e.g.*, berries and small fruits, cucurbits), a Monte Carlo analysis involving residue data and dissipation rate constants was conducted to allow risk assessors to estimate the duration of time when residues pose a risk to bees. Since the available residue data for soil applications do not show appreciable dissipation, rate constants were not quantified. Therefore, it is recommended that the risk assessors use the available data discussed in this section, normalize it to the application rates registered for the chemical specific uses on relevant orchard crop groups, and compare the data (means) to the NOEC and LOEC values from the CFSs.

6.2 Berries and Small Fruits

6.2.1 Crops of Concern for Bees

The berry and small fruit crop group (13-07) contains a diverse group of commodities, including bushberries (*e.g.*, blueberry), caneberries (*e.g.*, raspberry), large shrubs and trees (*e.g.*, elderberry), climbing vines (*e.g.*, grape), and low growing berries (*e.g.*, strawberry). According to the USDA guidance the attractiveness of crops to bees and other bees (USDA 2017), the majority of berry and small fruit crops are considered attractive to bees, with some requiring managed pollination services (*e.g.*,

blueberries). Therefore, exposure to bees from berry and small fruit crops will be considered in the neonicotinoid bee assessments for registered uses of these crops.

6.2.2 Foliar Applications

6.2.2.1 Summary of Label Rates/Restrictions

Imidacloprid is registered for pre- and post-bloom applications on strawberry and grape, though strawberry requires a 10-d pre-bloom interval. Bushberries and caneberries are registered for post-bloom applications only. Clothianidin is registered for post-bloom applications to bushberries and caneberries; applications to grapes are not restricted. Thiamethoxam is registered for all types of berries and small fruits with no restrictions. Similarly, dinotefuran registrations do not restrict application; however, dinotefuran is not currently registered for use on strawberries. The maximum rates for pre- and post-bloom foliar applications of these four chemicals are included in **Table 6-11**.

Table 6-11. Maximum foliar application rates (in lb a.i./A) and number of applications for registered neonicotinoids uses on berry and small fruit crops (based on current labels).

Berry and Small Fruit Crop Group	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
Pre-bloom Applications				
A: caneberries (e.g., raspberry)	NR	NR	0.04 x 2	NR
B: bushberries (e.g., blueberry)	NR	NR	0.053 x 2	NR
C: large shrub/tree (e.g., choke cherry)	NR	NR	NR	NR
D: small fruit vine climbing (e.g., grape)	0.047 x 3	NR	0.047 x 2	0.132 x 2
E: Small fruit vine climbing, except grape (e.g., fuzzy kiwifruit)	NR	NR	0.047 x 2	NR
F: Small fruit vine climbing, except fuzzy fruit (e.g., grape)	0.047 x 3	0.1 x 2	0.48 x 2	0.135 x 2
G: low growing berry (e.g., strawberry)	0.1 x 1	NR	0.053 x 2	0.135 x 2
H: low growing berry, except strawberry (e.g., cranberry, blueberry)	NR	NR	0.053 x 2	0.18 x 2
Post-bloom Applications				
A: caneberries (e.g., raspberry)	0.1 x 3	NR	0.04 x 2	NR
B: bushberries (e.g., blueberry)	0.1 x 5	NR	0.053 x 2	NR
C: large shrub/tree (e.g., choke cherry)	NR	NR	NR	NR
D: small fruit vine climbing (e.g., grape)	0.1 x 1	NR	0.047 x 2	0.132 x 2
E: Small fruit vine climbing, except grape (e.g., fuzzy kiwifruit)	NR	NR	0.047 x 2	NR
F: Small fruit vine climbing, except fuzzy fruit (e.g., grape)	0.047 x 3	0.1 x 2	0.48 x 2	0.135 x 2
G: low growing berry (e.g., strawberry)	0.1 x 1	0.1 x 2	0.053 x 2	0.135 x 2

Berry and Small Fruit Crop Group	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
H: low growing berry, except strawberry (e.g., cranberry, blueberry)	NR	NR	0.053 x 2	0.18 x 2

*Application rates expressed as clothianidin-equivalents.

NR = not registered

6.2.2.2 Available Residue Data

Pollen and nectar data are available for clothianidin, thiamethoxam, and dinotefuran from 6 studies, representing 4 crops within the berry and small fruit crop group (**Table 6-12**). Mean residues of neonicotinoids in nectar and pollen following pre-bloom foliar applications to berry crops are shown in **Figure 6-32** and **Figure 6-33**, respectively. **Figure 6-34** depicts the mean residue pollen data for post-bloom foliar applications to berries. These residue values are normalized to 0.1 lb a.i./A. It is evident that residues in nectar and pollen decline over the course of the 35 days of measurements. The dataset for post-bloom applications is very limited, representing only one chemical, crop and matrix (*i.e.*, clothianidin, grape, pollen). In addition, the sampling window is relatively short and may not accurately capture residue declines that might occur over longer time periods. Furthermore, no data are available to inform year-to-year variability on the same site.

Table 6-12. Residue studies for berry and small fruit crops with foliar applications of clothianidin, thiamethoxam, or dinotefuran.

Crop	Chemical	# of Sites (Location)	Matrix	Appl. Rate, #, Int.	Application Timing	# of Seasons	# of Sampling events	MRID	Classification
Blueberry	Thiamethoxam	3 (CA, WA, CAN- Quebec)	Pollen, Nectar, Flower	0.063 x 1 0.063 x 3 (5-10d)	Pre-bloom	1	3	50425901	Acceptable
	Dinotefuran	3 (NY, OR, WI)	Pollen, Nectar	0.18 x 2 (13d)	Pre-bloom	1	3	50145707	Acceptable
Cranberry	Thiamethoxam	3 (NY, OR, WI)	Pollen, Nectar	0.063 x 3 (5-10d)	Pre-bloom	1	3	49804102	Acceptable
	Dinotefuran	3 (NY, OR, WI)	Pollen, Nectar	0.18 x 2 (14d)	Pre-bloom	1	3	49841002	Acceptable
Grape	Clothianidin	3 (CA, OR, CAN- Ontario)	Pollen	0.1	Pre-bloom and Post-bloom	1	3	50154305	Acceptable
Strawberry	Thiamethoxam	9 (CA)	Pollen, Nectar	0.063 x 3 (10d)	Pre-bloom	1	1	50265502	Acceptable

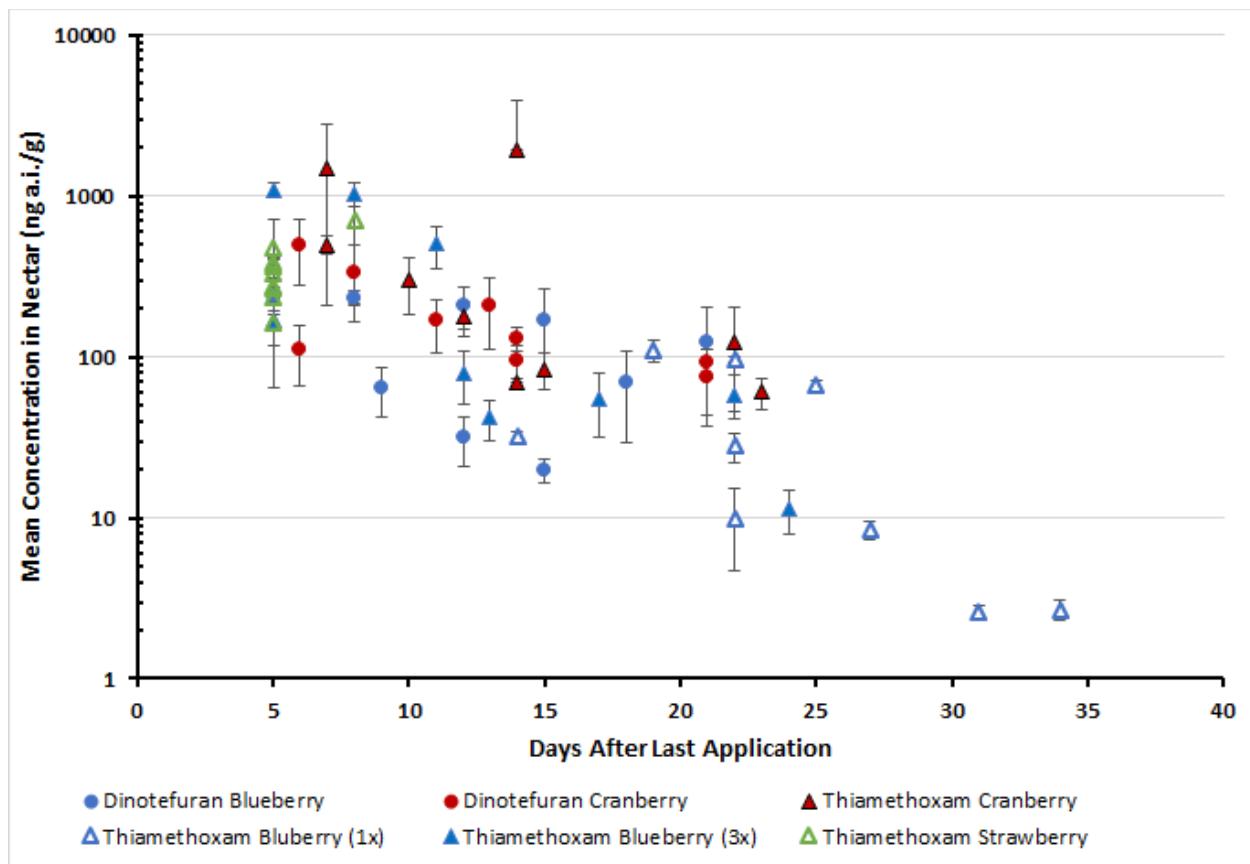


Figure 6-32. Mean residues (and 95% confidence intervals) of thiamethoxam (expressed as clothianidin equivalents) and dinotefuran in nectar of berry crops from pre-bloom foliar applications. Values are normalized 0.1 lb a.i./A based on the last application rate.

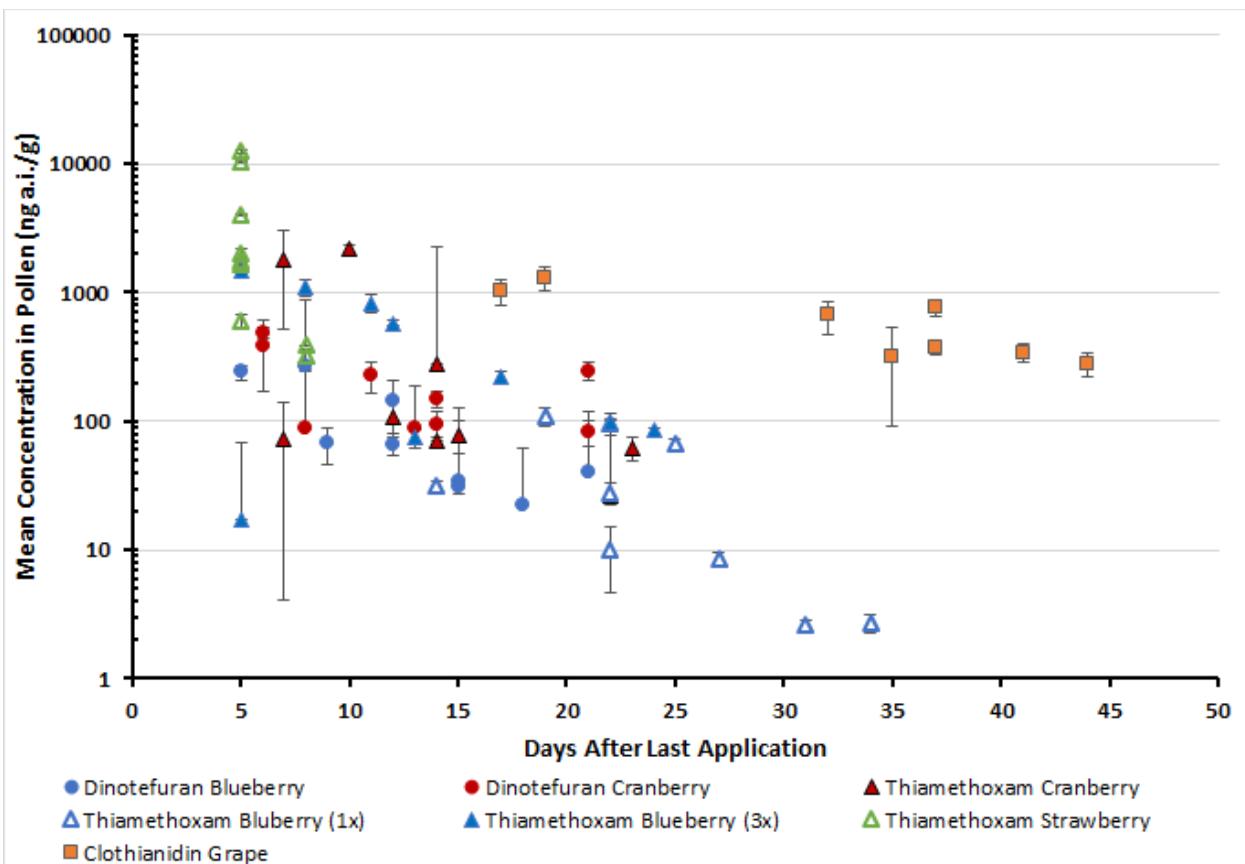


Figure 6-33. Mean residues (and 95% confidence intervals) of clothianidin, thiamethoxam (expressed as clothianidin equivalents), and dinotefuran in pollen of berry crops from pre-bloom foliar applications. Values are normalized 0.1 lb a.i./A based on the last application rate.

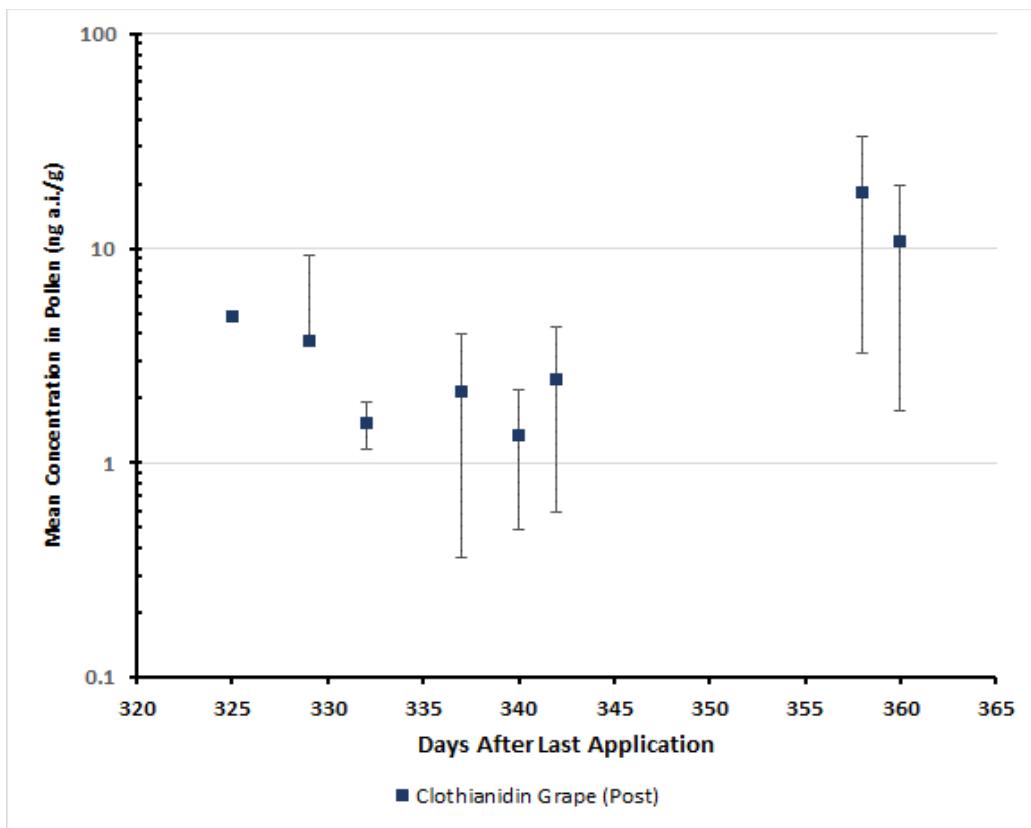


Figure 6-34. Mean residues (and 95% confidence intervals) of clothianidin in pollen of grapes from post-bloom foliar applications of clothianidin. Values are normalized to total application rate of 0.1 lb a.i./A.

6.2.2.3 Bridging needs (gaps)

For pre-bloom foliar applications of the 4 neonicotinoids to berries or small vines, no residue data are available for imidacloprid. In addition, no residues are available for thiamethoxam or dinotefuran applications to small vines (Table 6-13). For post-bloom applications, residue data are only available for clothianidin applications to small vines. Table 6-13 summarizes the available studies by crop group and chemical and identifies areas where bridging is needed (*i.e.*, indicated by “No data”). The analyses below will consider options for bridging the available data to address these gaps.

Table 6-13. Identification of data gaps for registered foliar pre- and post-bloom applications of neonicotinoids on berry and small fruit crops.

Berry and Small Fruit Crop Group	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
Pre-bloom Applications				
A: caneberries (<i>e.g.</i> , raspberry)	NR	NR	No data	NR
B: bushberries (<i>e.g.</i> , blueberry)	NR	NR	Blueberry MRID 50425901 Cranberry MRID 49804102	NR

Berry and Small Fruit Crop Group	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
C: large shrub/tree (e.g., choke cherry)	NR	NR	NR	NR
D: small fruit vine climbing (e.g., grape)	No data	NR	No data	No data
E: Small fruit vine climbing, except grape (e.g., fuzzy kiwifruit)	NR	NR	No data	NR
F: Small fruit vine climbing, except fuzzy fruit (e.g., grape)	No data	Grape MRID 50154305	No data	No data
G: low growing berry (e.g., strawberry)	No data	NR	Strawberry MRID 50265502	No data
H: low growing berry, except strawberry (e.g., cranberry, blueberry)	NR	NR	Blueberry MRID 50425901 Cranberry MRID 49804102	Blueberry MRID 50145707 Cranberry MRID 49841002
Post-bloom Applications				
A: caneberries (e.g., raspberry)	No data	NR	No data	NR
B: bushberries (e.g., blueberry)	No data	NR	No data	NR
C: large shrub/tree (e.g., choke cherry)	NR	NR	NR	NR
D: small fruit vine climbing (e.g., grape)	No data	NR	No data	No data
E: Small fruit vine climbing, except grape (e.g., fuzzy kiwifruit)	NR	NR	No data	NR
F: Small fruit vine climbing, except fuzzy fruit (e.g., grape)	No data	Grape MRID 50154305	No data	No data
G: low growing berry (e.g., strawberry)	No data	NR	No data	No data
H: low growing berry, except strawberry (e.g., cranberry, blueberry)	NR	NR	No data	No data

NR = not registered

6.2.2.4 Influence of Sampling Day (Time) on Residue Values

Pre-bloom applications of neonicotinoids made within 20 days of measurement during bloom also yield residues in pollen and nectar that are 2-3 orders of magnitude greater than residues measured from post-bloom applications (which take place >325 days before the next bloom), noting that post-bloom residues are only available with pollen.

Table 6-14 lists the range of mean residue values for pollen and nectar from berry and small fruit crops with different time periods between bloom and application.

Table 6-14. Range of mean values for berry and small fruit crops treated with neonicotinoids. Ranges broken out by different times between bloom and application date. Concentrations in ng a.i./g, normalized to 0.1 lb a.i./A rate.

Days before bloom when application was made	Concentration in nectar		Concentration in pollen	
	Pre-bloom	Post-bloom	Pre-bloom	Post-bloom
1-10	48-2508	NA	4.9-3534	NA
11-20	11-3735	NA	0.93-1564	NA
21-35	0.46-196	NA	7.4-861	NA
36-70	NA	NA	27-400	NA
90-215	NA	NA	206-256	NA
325-340	NA	NA	NA	0.5-9.5
341-360	NA	NA	NA	1.1-32

NA = not applicable

6.2.2.5 Differences in Dissipation Rate Constants (k)

Given the strong influence of sampling day on neonicotinoid residues in pollen and nectar following pre-bloom applications (**Figure 6-32**, **Figure 6-33** and **Figure 6-34**), the dissipation kinetic parameters (e.g., k and initial concentration) were investigated for their potential in describing the overall behavior residues over time in berry and small vine crops, as described previously in **Section 4.5.5**. The following sections describe the characteristics of the dissipation rate constants (k) and estimated initial concentrations (Day 0) and factors that influence their values.

Effect of Chemical, Crop, Matrix, and Location on k

For pre-bloom foliar applications sufficient data are available to support the derivation and analysis of dissipation rates (k) in pollen, nectar and flowers. Application information for the studies that are suitable for use in the kinetics analysis are presented in **Table 6-15**. The thiamethoxam strawberry study (MRID 50265502) was not included in this analysis because pollen and nectar residues were measured at one time point only.

Table 6-15. Summary of residue studies suitable or use in kinetics analyses.

Crop	Chemical	Appl. Rate, #, Int.	Number of Trials	Initial DALA
Blueberry	Thiamethoxam	0.063 x 1 0.063 x 3 (5-10d)	3 3	14-23 5-14
	Dinotefuran	0.18 x 2 (13d)	3	5-15
Cranberry	Thiamethoxam	0.063 x 3 (5-10d)	3	6-10
	Dinotefuran	0.18 x 2 (14d)	3	6-8
Grape	Clothianidin	0.1	3	32-37

DALA = days after last application

Data from individual trials were analyzed to determine whether dissipation rate constants (k) could be reliably quantified. For post-bloom foliar applications to grape, sampling intervals were too short to reliably model dissipation of residues. For pre-bloom foliar applications, dissipation rate constants were calculated for pollen, nectar, and flower separately (**Table 6-16**, **Table 6-17**, **Table 6-18**, respectively).

Most of the k values calculated based on pollen residues were not reliable due to high variability in residue values across replicates, non-monotonic declines or flat responses (*i.e.*, negligible dissipation). Flat responses may be a function of short sampling intervals (where insufficient time elapsed between samples for appreciable dissipation to occur) or stable residues. Removal of trials with stable residues may introduce some bias into the parameterization of k . A total of 7 reliable k values for pollen which range from 0.083-0.27 d^{-1} (corresponding to DT_{50} values between 2.6-8.4 days). For nectar, 11 k values are considered reliable and range from 0.017-0.26 d^{-1} (corresponding to DT_{50} values between 2.7-41 days). With flowers, 9 reliable k values are available that range from 0.072-0.46 d^{-1} (corresponding to DT_{50} values from 1.5-9.6 days). Among all matrices, all but one DT_{50} value deemed reliable is less than 10 days.

Table 6-16. Summary statistics for first order dissipation rate constants (k) estimated for residues of clothianidin, thiamethoxam (expressed as clothianidin equivalents), and dinotefuran in pollen of berries and small fruits after pre-bloom foliar applications.

Chemical	Crop	Trial	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
Clothianidin	Grape	B-CA-Pre	0.15 (0.15-0.16)	4.5	0.91	<0.001	37	Y	
		C-OR-Pre	0.16 (0.042-0.27)	4.5	0.50	0.018	32	Y	
		B-CA-Post	0.12 (N/A)	5.6	nd	nd	325	N	High variability at mid time point; short sampling interval; long DALA
		C-OR-Post	0.1 (0-0)	6.9	nd	nd	337	N	Short sampling interval; long DALA
Dinotefuran	Blueberry	Hood River, OR	0.063 (-0.050-0.18)	11.0	0.16	0.16	5	N	High variability; flat response
		Penn Yann, NY	0 (-0.19-0.19)	Stable	0.015	0.50	15	N	Non-monotonic; variability in samples at last time point
		Warrens, WI	0.088 (-0.014-0.19)	7.9	0.32	0.073	9	N	Hi variability at first time point; short sampling interval
	Cranberry	Bandon, OR	0.12 (-0.0095-0.25)	5.7	0.45	0.061	6	N	High variability at first and last time points
		Eagle River, WI	0.23 (0.0039-0.46)	3.0	0.38	0.048	8	N	Non-monotonic; potentially stable beyond 10 days.
		Williamstown, NY	0 (-0.078-0.078)	Stable	0.002	0.50	6	N	Non-monotonic; no decline
Thiamethoxam	Blueberry	1 App - QBC	0.083 (0.0042-0.16)	8.4	0.50	0.021	19	Y	
		1 App - WA	0.11 (0.050-0.18)	6.1	0.79	0.002	23	Y	
		3 Apps - QBC	0.10 (0.060-0.14)	7.0	0.84	0.0003	5	Y	
		3 Apps - WA	0.18 (0.093-0.27)	3.9	0.89	0.0009	14	Y	
	Cranberry	Bandon, OR	0.27 (-0.071-0.61)	2.6	0.77	0.052	6	Y	

Chemical	Crop	Trial	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
		Eagle River, WI	0.65 (0.60-0.70)	0.7	0.74	<0.001	9	N	Stable starting day ~ 10, short sampling interval; poor model fit
		Williamstown, NY	0.01 (-0.015-0.034)	70.5	0.12	0.19	7	N	flat response

* based on criteria described in **Section 4.5.5**; DALA = Day after last application

Table 6-17. Summary statistics for first order dissipation rate constants (k) estimated for residues of clothianidin, thiamethoxam (expressed as clothianidin equivalents), and dinotefuran in nectar of berries after pre-bloom foliar applications.

Chemical	Crop	Trial	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
Dinotefuran	Blueberry	Hood River, OR	0.017 (-0.017-0.050)	41.2	0.12	0.19	5	N	
		Penn Yann, NY	0.083 (-0.080-0.25)	8.4	0.10	0.18	15	N	
		Warrens, WI	0.21 (0.11-0.31)	3.3	0.77	0.003	9	Y	
	Cranberry	Bandon, OR	0.016 (-0.049-0.081)	42.4	0.042	0.32	6	N	High variability
		Eagle River, WI	0.21 (0.077-0.36)	3.2	0.64	0.011	8	Y	
		Williamstown, NY	0.15 (0.062-0.23)	4.8	0.78	0.006	6	Y	
Thiamethoxam	Blueberry	1 App - QBC	0.076 (0.038-0.12)	9.1	0.78	0.0011	19	Y	
		3 Apps - CA	0.15 (0.085-0.22)	4.6	0.92	0.0005	5	Y	
		3 Apps - QBC	0.10 (0.030-0.18)	6.7	0.66	0.006	5	Y	
		3 Apps - WA	0.12 (0.026-0.21)	5.9	0.71	0.010	12	Y	
		1 App - CA	0.17 (0.10-0.19)	4.2	0.96	<0.001	14	Y	
		1 App - WA	0.23 (0.15-0.31)	3.0	0.95	0.0002	22	Y	
	Cranberry	Bandon, OR	0.060 (-0.10-0.22)	11.6	0.16	0.21	7	N	High variability
		Eagle River, WI	0.26 (0.085-0.43)	2.7	0.74	0.005	10	Y	
		Williamstown, NY	0.26 (0.15-0.38)	2.7	0.97	0.0005	7	Y	

* based on criteria described in **Section 4.5.5**; DALA = Day after last application

Table 6-18. Summary statistics for first order dissipation rate constants (k) estimated for residues of clothianidin, thiamethoxam (expressed as clothianidin equivalents), and dinotefuran in flowers of berries after pre-bloom foliar applications.

Chemical	Crop	Trial	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*
Thiamethoxam	Blueberry	1 App - CA	0.14 (0.080-0.20)	5.0	0.92	<0.001	14	Y
		1 App - QBc	0.092 (0.021-0.16)	7.5	0.62	0.009	19	Y
		1 App - WA	0.072 (0.022-0.12)	9.6	0.67	0.006	22	Y
		3 Apps - CA	0.076 (0.057-0.095)	9.2	0.95	<0.001	5	Y
		3 Apps - QBc	0.12 (0.064-0.18)	5.6	0.82	0.001	5	Y
		3 Apps - WA	0.073 (0.048-0.097)	9.5	0.90	0.0001	12	Y
	Cranberry	Bandon, OR	0.084 (0.054-0.11)	8.3	0.91	0.0002	6	Y
		Eagle River, WI	0.46 (0.34-0.58)	1.5	0.98	<0.001	8	Y
		Williamstown, NY	0.11 (0.059-0.15)	6.5	0.86	0.0006	6	Y

* based on criteria described in **Section 4.5.5**; DALA = Day after last application

When considering just the rate constants deemed to be reliable for pollen and nectar, the 95% confidence intervals overlap for the vast majority of the trials with no obvious trend among crops or matrices (**Figure 6-35**). This finding suggests that site, chemical, and crop do not contribute an overriding influence the dissipation rates in nectar or pollen for pre-bloom foliar applications.

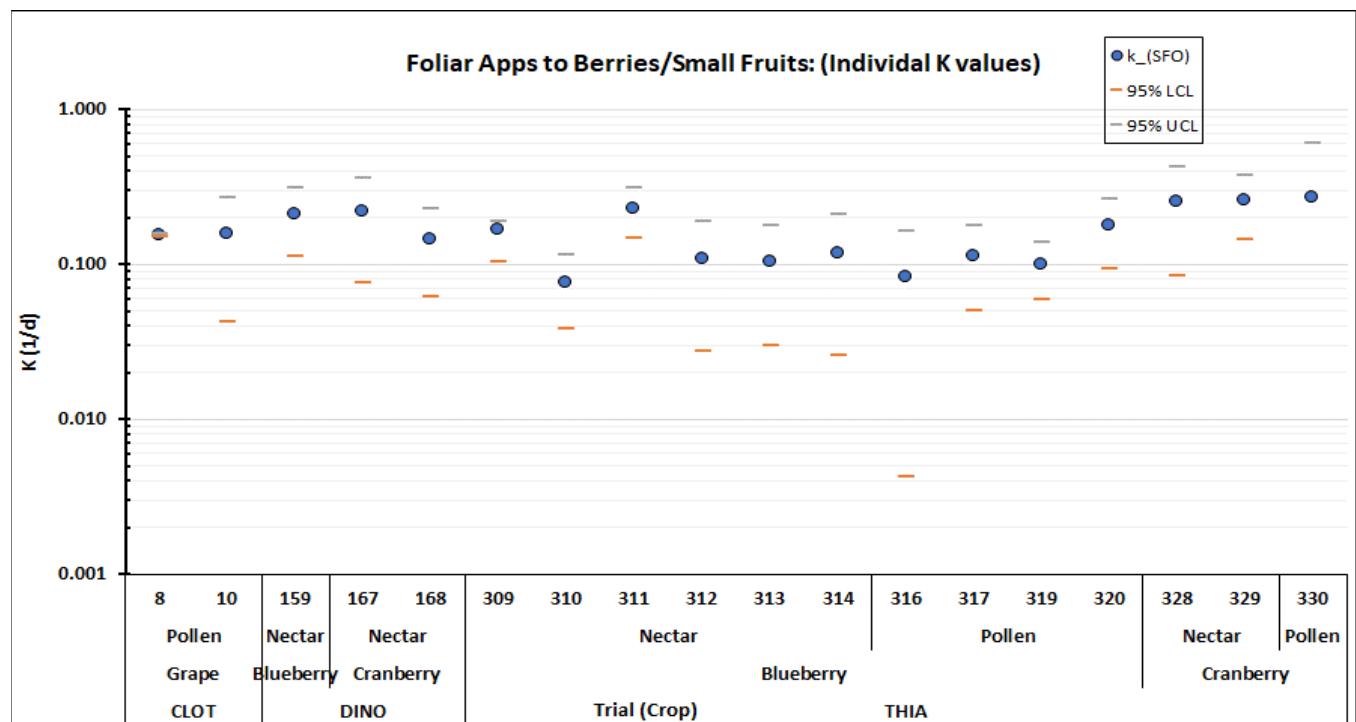


Figure 6-35. Individual k values in nectar and pollen from residue trials of foliar application to berries and small vines. Blue dots represent the k value based on a single first order (SFO) kinetics; orange and grey bars = 95% confidence interval. Numbers designate different trials. THIA = thiamethoxam, DINO = dinotefuran, CLOT = clothianidin.

Summary statistics for the nectar and pollen-specific k-values estimated for neonicotinoid residues in berries are shown in **Table 6-19**. It is noted that mean k-values among chemicals within a matrix and across matrices are similar (0.149-0.191).

Table 6-19. Summary statistics for chemical and matrix-specific k-values associated with pre-bloom foliar applications to berries adn small vines.

Chemical/Matrix	Mean K (1/d)	Standard Deviation	Min K (1/d)	Max K (1/d)	# Trials
Nectar					
Dinotefuran	0.191	0.040	0.145	0.217	3
Thiamethoxam	0.165	0.074	0.076	0.260	8
Nectar Total	0.172	0.066	0.076	0.260	11
Pollen					
Clothianidin	0.155	0.001	0.155	0.156	2
Thiamethoxam	0.149	0.076	0.083	0.269	5
Pollen Total	0.151	0.062	0.083	0.269	7

Chemical/Matrix	Mean K (1/d)	Standard Deviation	Min K (1/d)	Max K (1/d)	# Trials
Combined Nectar and Pollen	0.164	0.063	0.076	0.269	18

Based on these data and analyses, the following parameters in **Table 6-20** are recommended for modeling the dissipation of neonicotinoid residues in nectar and pollen resulting from pre-bloom, foliar applications to berries and small fruits. These parameters are intended for use in the Monte Carlo modeling of residue decline curves as described in **Section 4.5.5**.

Table 6-20. Kinetic parameters recommended for use in the Monte Carlo analysis of neonicotinoid residues in berry and small fruit crops following foliar application

Statistic	Final Combined Foliar Berry Dissipation Rate (k) in d ⁻¹
Mean	0.164
STD	0.063
Min	0.076
Max	0.269
n	18

6.2.2.6 Effect of Chemical, Crop, Matrix, and Site on Residue Values

For those residue trials with reliable estimates of kinetic parameters (k, C_initial), the effect of chemical, crop, matrix and site on residues in pollen and nectar was further evaluated. With these trials, residue values can be adjusted to reflect a common day after last application (DALA) so that the influence of elapsed time on neonicotinoid concentrations can be minimized.

Figure 6-36 shows the range of initial measured values of neonicotinoids in nectar for blueberry and cranberry and pollen for blueberry, cranberry, and grape. These initial measurements were made anywhere from 7 to 22 DALA for nectar and 5-37 DALA for pollen. With nectar, mean residues initially measured in each trial vary by approximately 60X (15 to 891 ng a.i./g) with the highest concentrations generally correlated with the shortest DALA (5-7 days after last application). This suggests an adjustment for time is relevant. In pollen, the difference between initial measured concentrations is roughly a factor of 10 (from 80-969 ng a.i./g), with higher concentrations generally correlated with the shortest sampling interval (5-6 days after last application). However, mean residues initially measured in grape residues are at the upper range of observed concentrations despite having the longest sampling interval (32-37 days after last application).

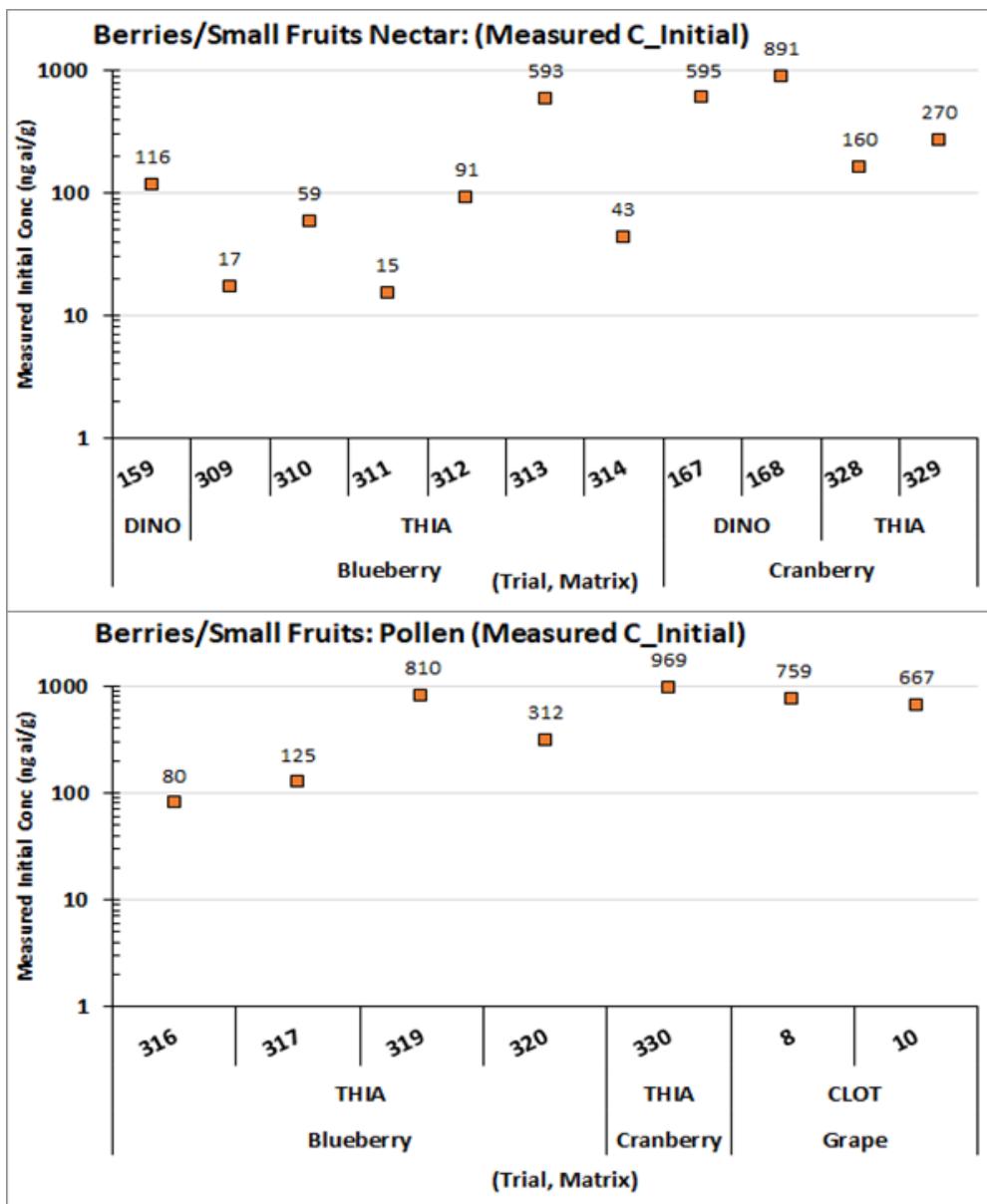


Figure 6-36. Average concentrations initially measured in nectar (top) and pollen (bottom) among trials of berry/small vine crops. Numbers above chemical names designate different trials. DINO = dinotefuran, THIA = thiamethoxam, CLOT = clothianidin. Thiamethoxam expressed as clothianidin equivalents.

Using the k values from the individual trials presented in **Table 6-16** and **Table 6-17** above, the initially measured concentrations ($C_{initial}$) in pollen and nectar from each residue trial with a valid "k" estimate were adjusted to 10 days after last application using the following equation:

$$C_{initial \text{ SFO (Day 10)}} = C_{initial \text{ SFO (Day X)}} e^{(k \times [X-10])}$$

where,

- $C_{initial \text{ SFO (Day 10)}}$ = Concentration adjusted to day 10 using SFO model
- $C_{initial \text{ SFO (Day X)}}$ = Concentration estimated on the initial sampling day (X) using SFO model
- k = Dissipation rate constant (1/d) estimated using SFO model
- X = Day of initial sampling from the residue trial

The adjustment was made to 10 days since this time point fell within the range of measured data for most of the trials except for grape.

Neonicotinoid concentrations in nectar and pollen adjusted to DALA 10 are presented in **Figure 6-37**. For nectar, normalizing each residue value estimated on the initial day of sampling to a common sampling day (day 10) reduces the range in residues from 60X to 15X. For pollen in blueberries and cranberries, normalizing to day 10 reduces the range in residues from 10X to 5X; however, residue values for grape are now 100X greater than those in blueberry and cranberry. This finding is likely due to the large degree of extrapolation required when adjusting residue measurements made initially on days 32-37 to 10 days after last application; therefore, these adjust values are considered highly uncertain. With the exception of grapes, normalizing the initial concentrations measured in the berry residue trials substantially reduces the variation in residues in pollen and nectar. It is also noted that adjusted residues in pollen are up to an order of magnitude greater than those in nectar, which is consistent with results from other crops evaluated in this document.

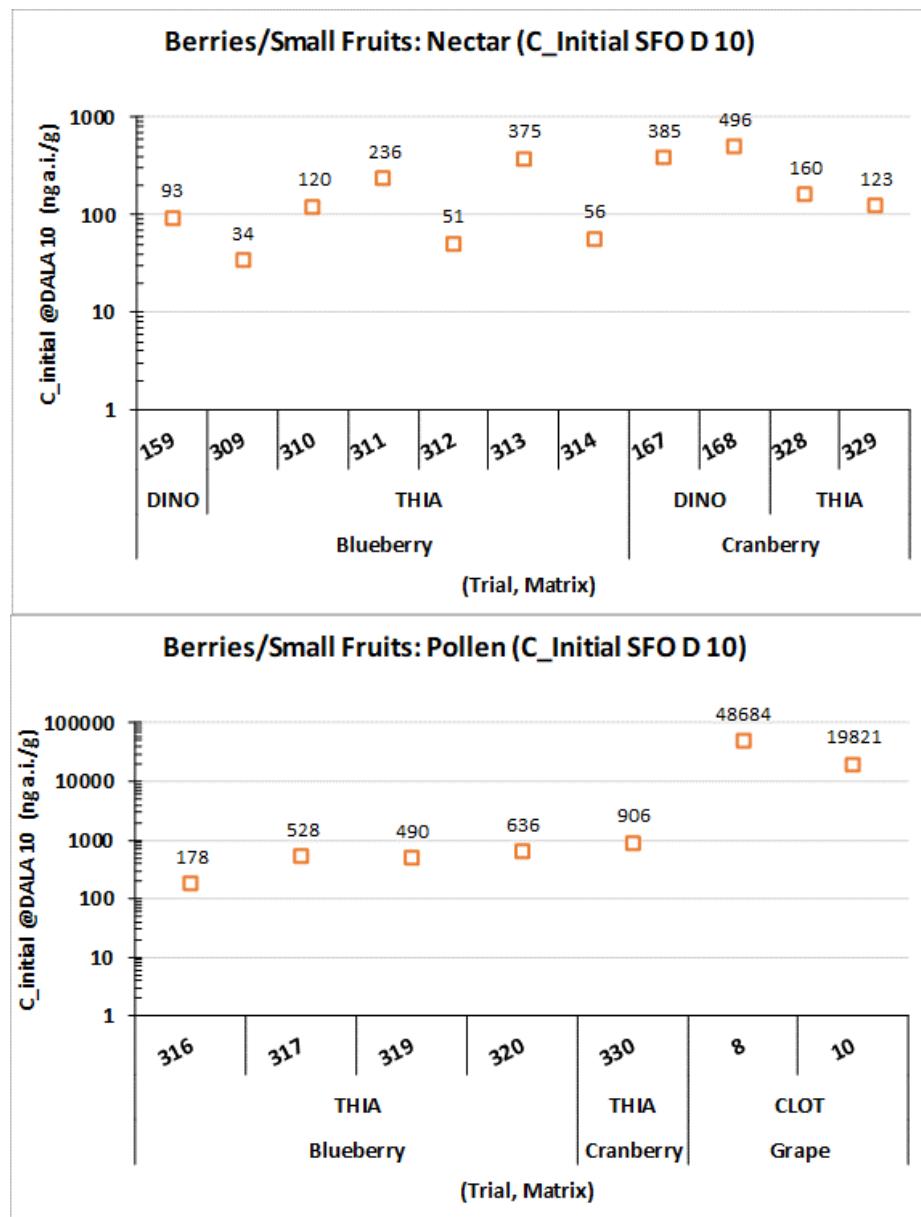


Figure 6-37. Average initial concentration in nectar (top) and pollen (bottom) normalized to a common sampling day (DALA 10) among trials and berry/small vine crops. Orange squares represent the individual trial means normalized to Day 10. DINO = dinotefuran, THIA = thiamethoxam, CLOT = clothianidin. Thiamethoxam expressed as clothianidin equivalents.

Differences in application rates among trials is another potential contributor to observed variability in residue data. To account for this factor, residues adjusted to 10 DALA described previously were further normalized to a rate of 0.1 lb a.i./A based on last application (Figure 6-38). Single application rates in these trials vary from 0.05 to 0.18 lb a.i./A while total application rates vary from 0.05 to 0.36 lb a.i./A. After normalizing to 0.1 lb a.i./A based on the last application rate, concentrations in blueberry nectar still vary by approximately 10X (similar to the range of un-normalized values in Figure 6-37), while residues in cranberry nectar vary by 1.5X (compared to about 3X for un-normalized values). With pollen, normalizing by the last application rate still results in an overall range of 5X for blueberry and cranberry,

while the values for grape remain unchanged (applications to grape were made at the same 0.1 lb a.i./A rate).

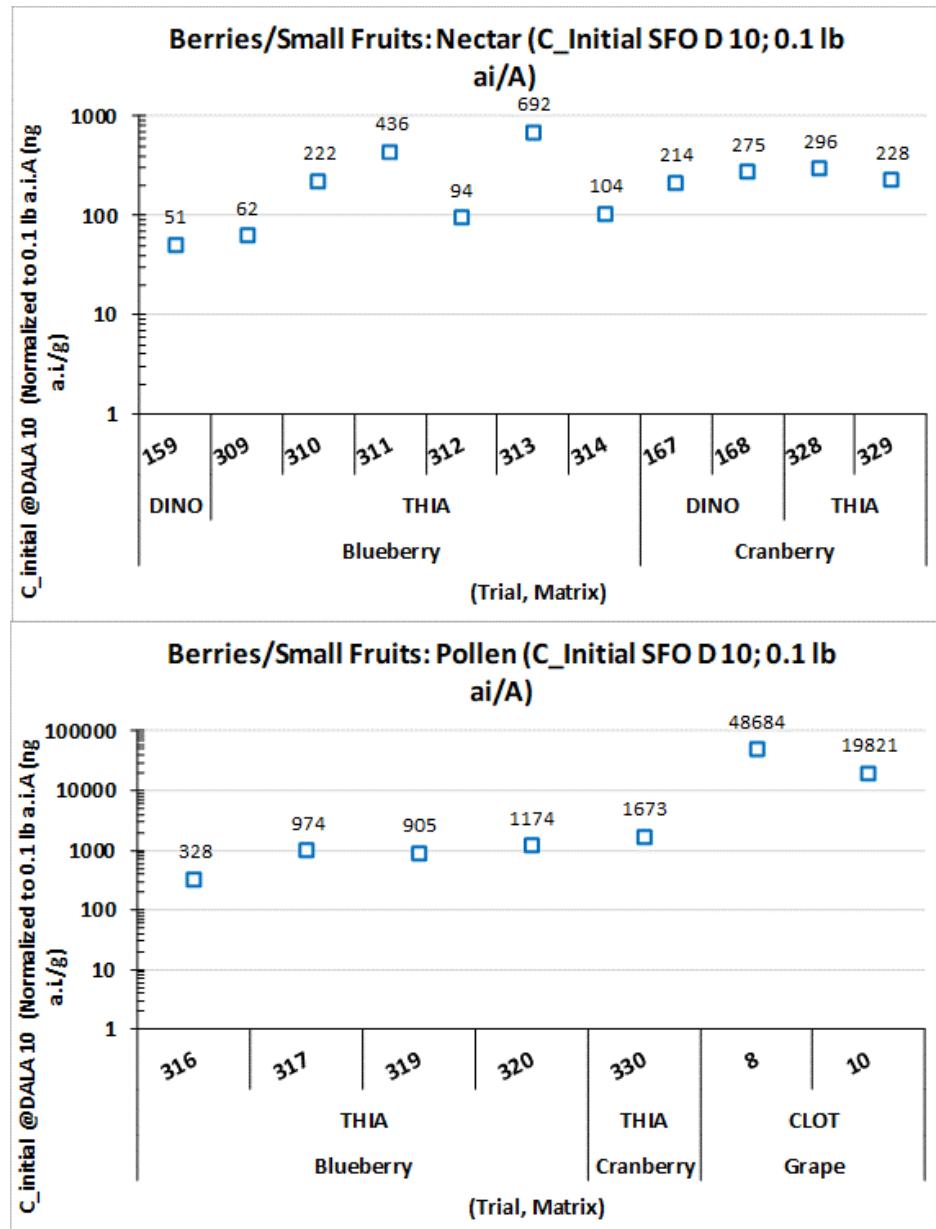


Figure 6-38. Average initial concentration in nectar (top) and pollen (bottom) adjusted to a common sampling day (DALA 10) and normalized to a common last application rate (0.1 lb a.i.) among trials and berry/small vine crops. Blue squares represent the individual trial means normalized to Day 10. DINO = dinotefuran, THIA = thiamethoxam, CLOT = clothianidin. Thiamethoxam expressed as clothianidin equivalents.

Normalizing residue values to total application rate provided similar results as normalizing to the last application rate in the context of reducing variability in the range of residue values for each chemical (**Table 6-21**). Therefore, Monte Carlo analysis of residue dissipation kinetics will be based on normalization of C_{Initial} to the last application rate.

Table 6-21. Summary of initial concentrations (C_initial) of neonicotinoids in nectar and pollen of berry/small vine crops adjusted to 10 DALA and normalized to last or total application rate.

Chemical	Normalized to 0.1 lb a.i./A Based on LAST Application		Normalized to 0.1 lb a.i./A Based on TOTAL Application		# Trials
	Mean C_initial @ DALA10 (ng a.i./g)	STD (Range) of C_initial @ DALA10 (ng a.i./g)	Mean C_initial (@ DALA10)	Range of C_initial (@ DALA10)	
Nectar					
Dinotefuran	180	116 (51-275)	90	26-138	3
Thiamethoxam	267	211 (62-692)	149	31-436	8
Combined (Dino+Thia)	243	188 (51-692)	133	23-436	11
Pollen					
Clothianidin*	34,252	20410 (19820-48680)	34,252	20410 (19820-48680)	2
Thiamethoxam	1011	328-1673	510	302-974	5

Bold values are recommended for use in Monte Carlo modeling of berry/small fruit residue decline curves for the 4 neonicotinoids

* these data are for grape and are considered uncertain due to the large degree of extrapolation required to adjust residue values to 10 DALA.

With respect to the effect of chemical there is little evidence to suggest that chemical exerts a substantial influence on residue values based on comparison of nectar in blueberry and cranberry for dinotefuran and thiamethoxam (**Figure 6-38**). With respect to pollen, large differences in normalized residue values occur with clothianidin, but this reflects a different crop (grape) and these DALA adjusted values are considered uncertain due to the high degree of extrapolation involved (from DALA 32-37 to DALA 10). Therefore, comparisons with the DALA adjusted grape data are considered inconclusive.

Within a chemical and crop, variation in residue values adjusted to a common DALA and application rate appear to reflect site-to-site differences, as the trials were conducted at different sites. Regarding the effect of crop, DALA and rate-normalized residues for cranberry and blueberry nectar vary within the same order of magnitude for thiamethoxam and dinotefuran, suggesting a lack of overriding influence of crop on these residue values (**Figure 6-38**). Unadjusted residues of clothianidin in pollen of grape are high despite being measured more than a month after application. Adjusting these residues to DALA 10 results in even higher residues. Although residues in grape reflect a unique neonicotinoid (clothianidin), dissipation rate constants are similar to the other neonicotinoids. Therefore, it appears that residues in grape pollen may not be reflective of other berries (**Figure 6-33**).

6.2.2.7 Effect of Application Timing (Pre-, Post-Bloom) on Residue Values

Data to evaluate the effect of application timing (*i.e.*, pre- vs. post-bloom applications) are only available in pollen for clothianidin applications to grape (**Figure 6-39**). When considering residues in pollen resulting from pre-bloom and post-bloom applications, the residues are 2-3 orders of magnitude lower for post-bloom compared to pre-bloom. As seen with foliar applications of the neonicotinoids to other crops, the timing of application (pre vs. post bloom) has a major impact on residues.

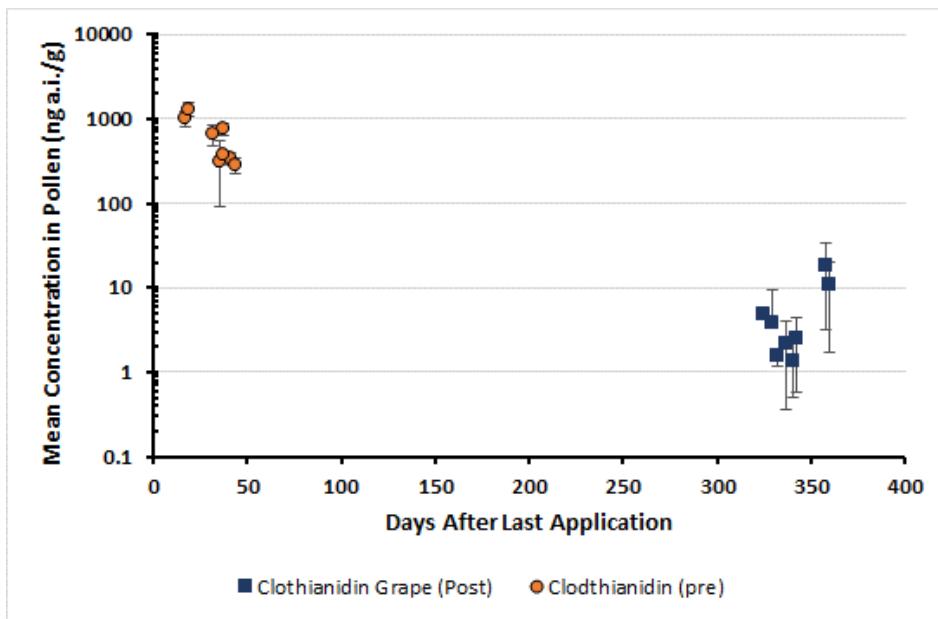


Figure 6-39. Mean concentration of clothianidin in pollen following foliar applications (pre- and post-bloom) to grapes. Orange circles represent individual trial means for pre-bloom applications; blue squares represent individual trial means for post-bloom applications. Lines are the 95% confidence intervals. Values normalized to last application rate of 0.1 lb a.i./A.

6.2.2.8 Bridging Recommendations

In summary, the analyses above suggest that chemical, crop, matrix and site do not have an obvious influence on dissipation rates constants (k) for pollen and nectar from berry and small fruit crops receiving pre-bloom foliar applications. Therefore, it is recommended that dissipation rate constants be bridged across crop, chemical, and matrix. The analysis above indicates that the timing of application relative to bloom has a substantial influence on residues, at least in pollen. Because of this difference, residue data for pre-bloom and post-bloom applications should be kept separate for risk assessment purposes. The dataset for post-bloom applications is very sparse and is of limited utility in bridging.

For pre-bloom foliar applications, the analyses suggest that crop may have an influence on residue concentrations. Blueberry and cranberry concentrations are similar across crop and matrix; however, grape concentrations are substantially higher (2-3 orders of magnitude). It is recommended that the thiamethoxam and dinotefuran blueberry and cranberry data be bridged across all chemicals for evaluating oral exposure from neonicotinoid uses on berries. Residues in pollen are approximately 10X those in nectar and therefore, should be evaluated separated for risk assessment purposes.

For grape, the only data available are for clothianidin. The analyses of dissipation rate constants and blueberry/cranberry residue concentrations suggest that chemical does not have an obvious influence on residues in pollen and nectar. Therefore, it is reasonable to use grape as a surrogate for the other chemicals registered for pre-bloom applications to grape. While residues for the thiamethoxam strawberry study are not suitable for kinetics analysis, the concentrations are generally within the same range as residues in blueberry and cranberry from similar sampling intervals (Table 6-22). This suggests that the bridged pre-bloom foliar application blueberry and cranberry data may be a reasonable surrogate for strawberry.

Table 6-22. Comparison of residues at different time points across studies.

Days after last application	Concentration in Nectar			Concentration in Pollen		
	Strawberry	Blueberry	Cranberry	Strawberry	Blueberry	Cranberry
5-7	95-697	82-799	82-2,508	574-13,858	4.9-1,535	42-2,483
8-10	370-1,200	47-851	165-434	189-534	56-1,012	323-3,534

In addition to evaluating oral risk to bees based on observed (measured) residue values in berry nectar and pollen, the aforementioned kinetic analysis of these residues can be used to support the modeling of decline curves in these matrices. Such modeling enables residues to be extrapolated (or interpolated) across different times after application where measured data are not available. Furthermore, this modeling enables variability in kinetic parameters (k , C_{initial}) to be incorporated into model results, which facilitates the derivation of residue decline curves with specified probabilities (e.g., 50th, 90th).

Based on Monte Carlo analysis of the residue dissipation rate constant (k) and the C_{initial} values presented in **Table 6-20** and **Table 6-21** and methods described in **Section 4.5.5**, the 50th and 90th percentile dissipation curves for neonicotinoid residues in nectar of blueberry and cranberry are presented in **Figure 6-40**. The same curves are presented for pollen in **Figure 6-41**.

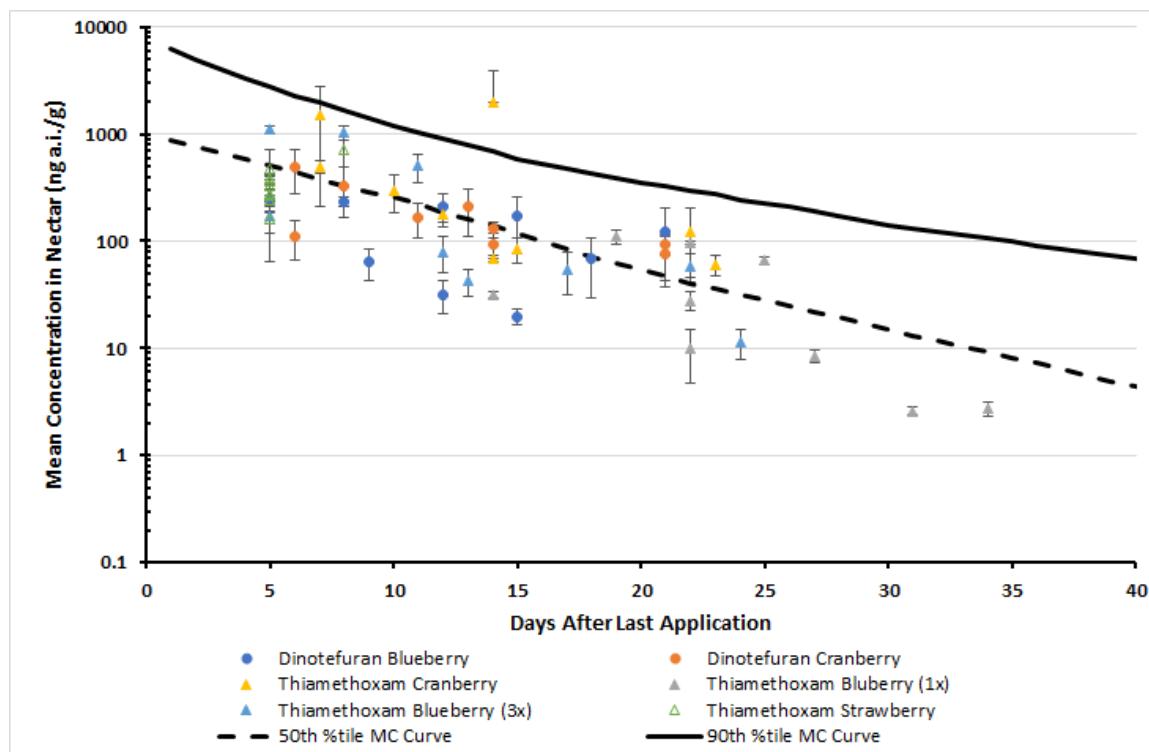


Figure 6-40. Dissipation curves and mean residues (with 95% confidence intervals) of neonicotinoids in nectar of berries following pre-bloom, foliar applications. Dashed line = 50th and solid line = 90th percentile residue decline curves derived from Monte Carlo analysis of residue kinetic parameters (k and C_{initial}). Residues are normalized to 0.1 lb a.i./A; Thiamethoxam expressed as clothianidin equivalents.

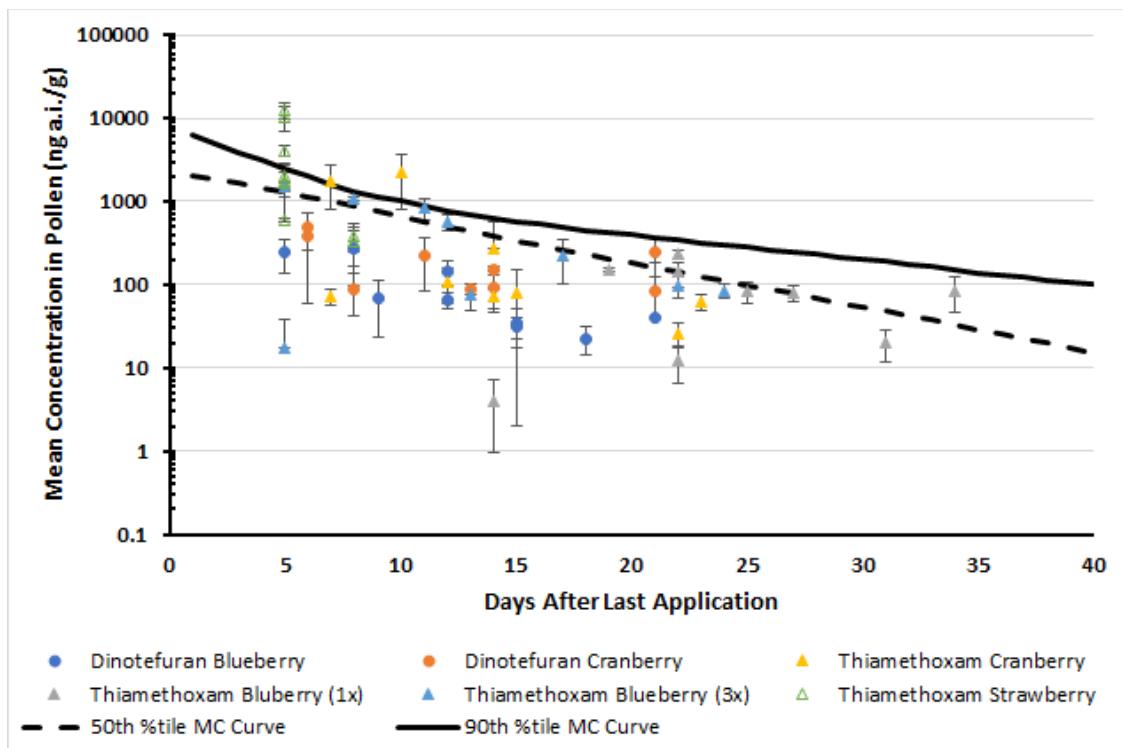


Figure 6-41. Dissipation curves and mean residues (with 95% confidence intervals) of neonicotinoids in pollen of berries following pre-bloom, foliar applications. Dashed line = 50th percentile and solid line = 90th residue decline curves derived from Monte Carlo analysis of residue kinetic parameters (k and $C_{initial}$). Residues are normalized to 0.1 lb a.i./A; Thiamethoxam expressed as clothianidin equivalents.

On the basis of nectar equivalents (*i.e.*, sum of concentrations in nectar + pollen/20; Attachment 1), the 50th and 90th percentile dissipation curves for neonicotinoid residues expressed as nectar equivalents in for berry crops are presented in **Figure 6-42**. These modeled dissipation curves in nectar and pollen are intended to be used as a line of evidence for characterizing the oral risk of the neonicotinoids to bees associated with their use on berries.

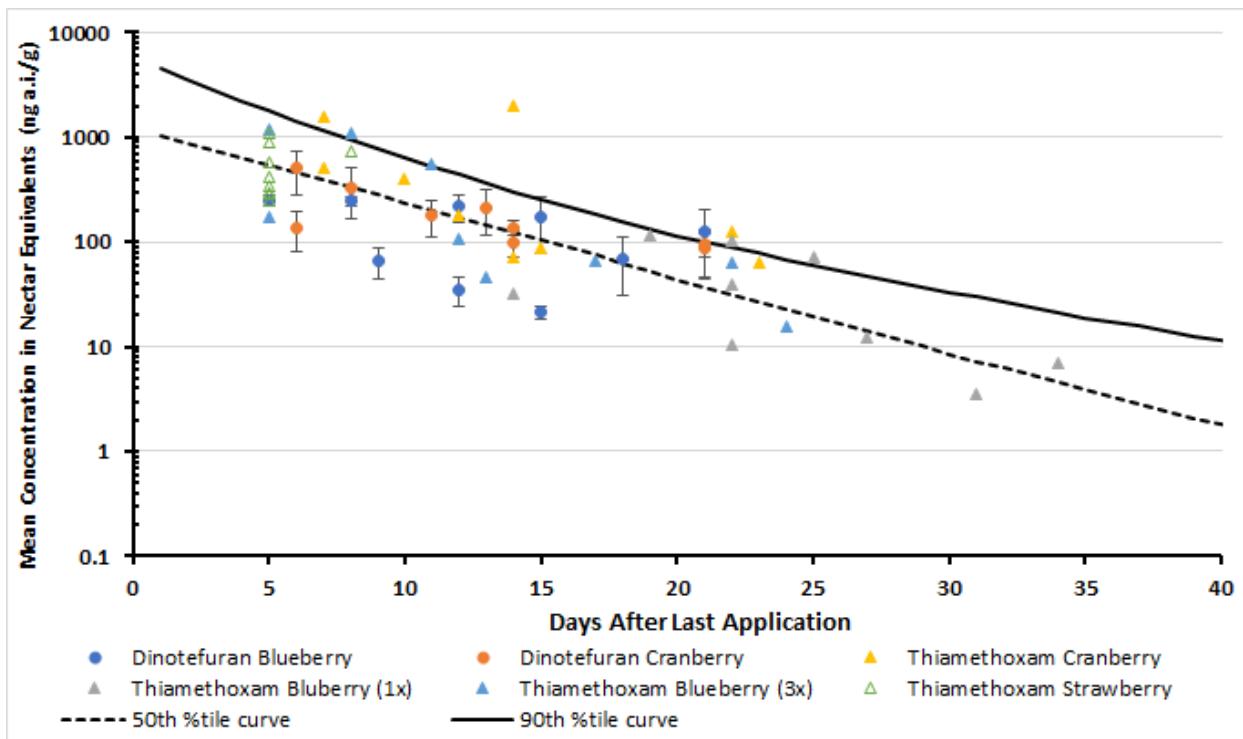


Figure 6-42. Dissipation curves and mean residues (with 95% confidence intervals) of neonicotinoids in berries (expressed as nectar equivalents) following pre-bloom, foliar applications. Dashed line = 50th percentile and solid line = 90th residue decline curves derived from Monte Carlo analysis of residue kinetic parameters (k and $C_{initial}$). Residues are normalized to 0.1 lb a.i./A; Thiamethoxam expressed as clothianidin equivalents.

6.2.3 Soil Applications

6.2.3.1 Summary of Label Rates/Restrictions

Registrations for soil applications for the four neonicotinoids are similar to foliar registrations. Imidacloprid is registered for pre- and post-bloom applications on strawberry and grape, though strawberry requires a 10-d pre-bloom interval. Bushberries and caneberries are registered for post-bloom applications only. Clothianidin is registered for post-bloom applications to bushberries and caneberries; applications to grapes are not restricted. Thiamethoxam is registered for all types of berries and small fruits with no restrictions. Dinotefuran is only registered for soil applications on small vines, but there are no application restrictions. The maximum rates for pre- and post-bloom foliar applications of these four chemicals are included in **Table 6-23**.

Table 6-23. Soil application rates (in lb a.i./A) and number of applications ($\times n$) for neonicotinoids on berry and small fruit crops (based on current labels).

Berry and Small Fruit Crop Group	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
Pre-bloom Applications				
Bushberries	NR	NR	0.16 \times 1	NR
Caneberries	NR	NR	0.16 \times 1	NR
Low growing berries	0.5 \times 1	NR	0.16 \times 1	NR
Small vines	0.5 \times 1	0.2 \times 1	0.2 \times 1	0.34 \times 1

Berry and Small Fruit Crop Group	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
Post-bloom Applications				
Bushberries	0.5 x 1	0.2 x 1	0.16 x 1	NR
Caneberries	0.5 x 1	0.2 x 1	0.16 x 1	NR
Low growing berries	0.5 x 1	NR	0.16 x 1	NR
Small vines	0.5 x 1	0.2 x 1	0.2 x 1	0.34 x 1

*Application rates expressed as clothianidin-equivalents.

NR = not registered

6.2.3.2 Available Residue Data

Pollen and nectar data are available for imidacloprid, clothianidin, and thiamethoxam from 3 studies, representing 3 crops within the berry and small fruit crop group (**Table 6-24**). Mean residues in nectar and pollen of berry crops following pre-bloom soil applications are shown in **Figure 6-43** and **Figure 6-44**, respectively, while those following post bloom applications are shown in **Figure 6-45** and **Figure 6-46**, respectively. Unlike with pre-bloom foliar applications, a distinct declining trend over time is not observed with the combined data sets of residues from soil applications to berries/small vines.

Table 6-24. Residue studies for berry and small fruit crops with foliar applications of clothianidin, thiamethoxam, or dinotefuran.

Crop	Chemical	# of sites (Location)	Matrix	Appl. Rate, #	Appl. Timing	# of Seasons	# Sampling events	MRID	Classification
Blueberry	Imidacloprid	3 (IL, MI, NY)	Pollen, Nectar	0.5 x 1	Post-bloom	2	2-5	49535602	Acceptable
Grape	Clothianidin	3 (CA, OR, CAN-Ontario)	Pollen, Nectar	0.2 x 1	Pre-bloom	1	3	50154305	Acceptable
Strawberry	Thiamethoxam	3 (CA, FL)	Pollen	0.188 x 1 0.129 x 1	Pre-bloom	1	3	50266001	Acceptable

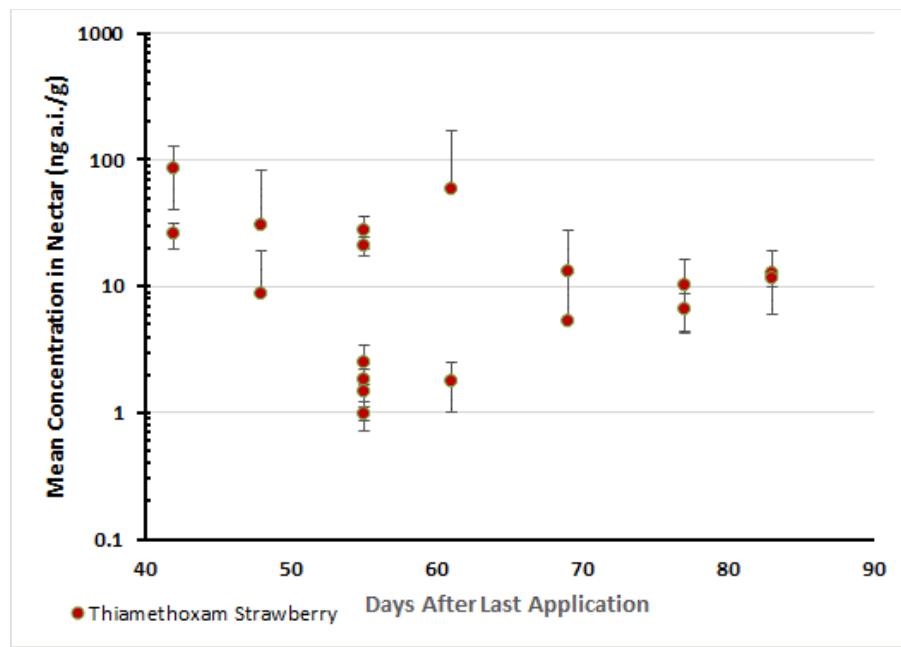


Figure 6-43. Mean residue of thiamethoxam (expressed as clothianidin equivalence) in pollen from pre-bloom soil applications to strawberry and grape. Values are normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

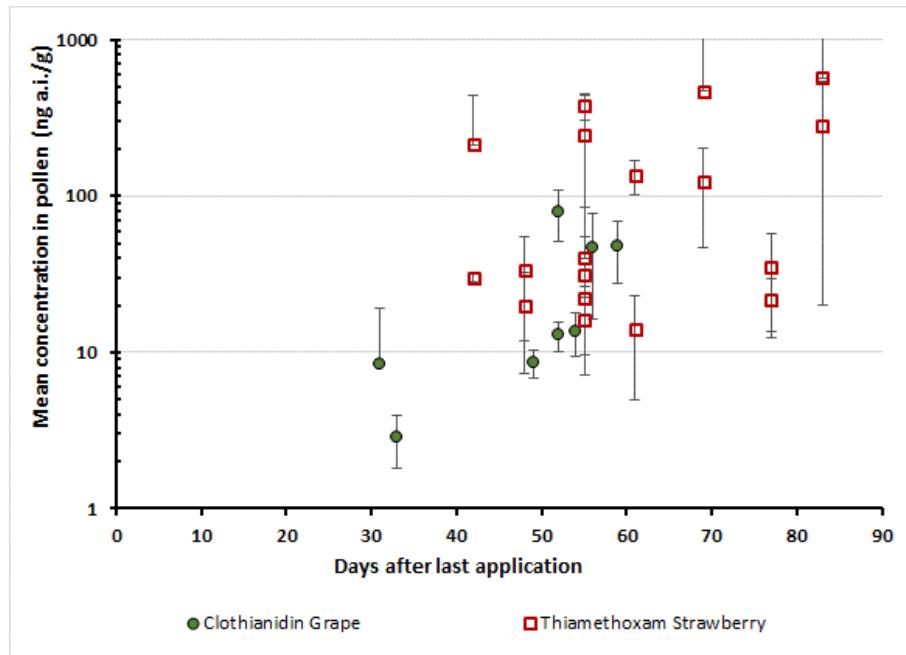


Figure 6-44. Mean residues applications of clothianidin and thiamethoxam (expressed as clothianidin equivalents) in pollen from pre-bloom soil applications to grape and strawberry. Values are normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

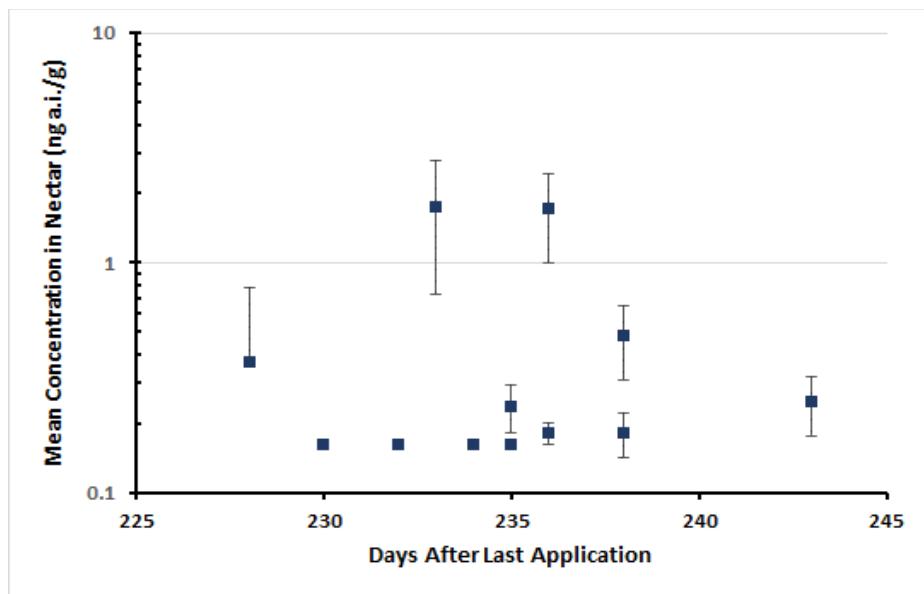


Figure 6-45. Mean residues of imidacloprid (expressed as total imidacloprid) in nectar from post-bloom soil applications to blueberry. Values are normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

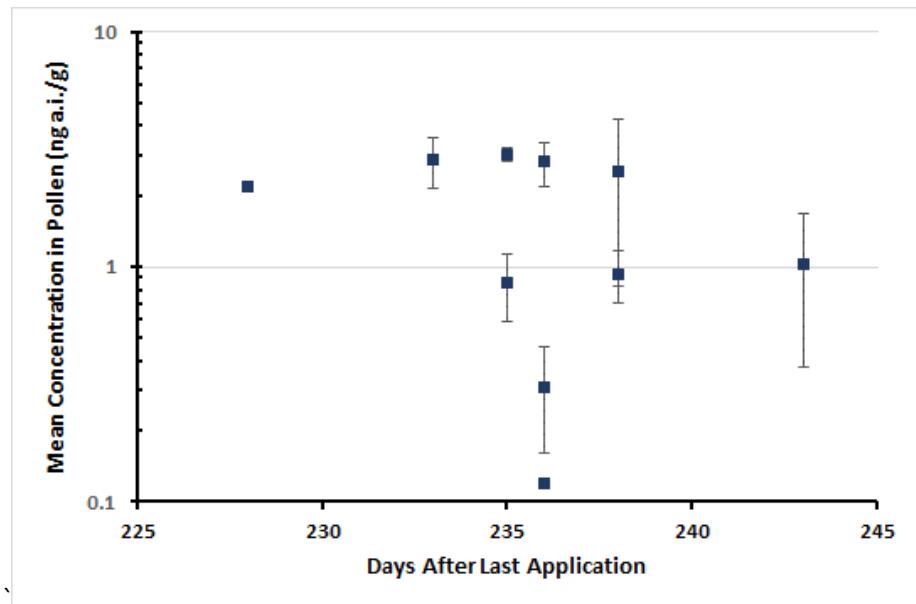


Figure 6-46. Mean residues of imidacloprid (expressed as total imidacloprid) in pollen from post-bloom soil applications to blueberry. Values are normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

6.2.3.3 Bridging needs (gaps)

For pre-bloom soil applications no residue data are available for imidacloprid applications to low growing berries or small vines. In addition, no residues are available for thiamethoxam or dinotefuran applications to bushberries, caneberries, or small vines (**Table 6-25**). For post-bloom applications, residue data are only available for imidacloprid applications to bushberries. **Table 6-25** summarizes the

available studies by crop group and chemical and identifies areas where bridging is needed (*i.e.*, indicated by “No data”). The analyses below considers options for bridging the available data to address these gaps.

Table 6-25. Identification of data gaps for registered soil pre- and post-bloom applications of neonicotinoids on berry and small fruit crops

Berry/Small Fruit Crop Group	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Pre-bloom Applications				
Bushberries	NR	NR	No data	NR
Caneberries	NR	NR	No data	NR
Low growing berries	No data	NR	Strawberry MRID 50266001	NR
Small vines	No data	Grape MRID 50154305	No data	No data
Post-bloom Applications				
Bushberries	MRID 49535602	No data	No data	NR
Caneberries	No data	No data	No data	NR
Low growing berries	No data	NR	No data	NR
Small vines	No data	No data	No data	No data

NR = not registered

6.2.3.4 Influence of Sampling Day (Time) on Residue Values

For pre-bloom soil applications, all but a few trials are not suitable for kinetic modeling or do not produce reliable estimates of kinetic parameters using the SFO model. Flat or increasing residue values over time were indicated in most of the trial specific data. This may be related to the nature of the application method, whereby pesticide in treated soil continues to become available for uptake in plants weeks or months after application. Therefore, as with soil applications to orchards, a kinetic analysis was not conducted for soil applications to berries/small vines.

Table 6-26 lists the range of mean residue values in pollen and nectar of berry and small fruit crops with different time periods between bloom and soil application. Residues in pollen are generally higher than those in nectar. Residues from pre-bloom applications tend to increase over time, with the highest concentrations in pollen and nectar measured between 61 and 70 days after last application. Pre-bloom applications yield residues in pollen and nectar that are 2-3 orders of magnitude greater than residues measured from post-bloom applications (which take place >228 days after last application). This analysis also suggests that timing of application (*i.e.*, pre- vs. post-bloom) likely influences residue concentrations, with pre-bloom applications resulting in higher residues in bee relevant matrices.

Table 6-26. Range of mean values for berry and small fruit crops following soil application of with neonicotinoids. Ranges broken out by different times between bloom and application date. Concentrations in ng a.i./g, normalized to a total rate of 0.1 lb a.i./A .

Days before bloom when application was made	Concentration in nectar		Concentration in pollen	
	Pre-bloom	Post-bloom	Pre-bloom	Post-bloom
30-40	1.9-19	NA	1.9-19	NA
41-50	2.9-122	NA	7.0-445	NA

Days before bloom when application was made	Concentration in nectar		Concentration in pollen	
	Pre-bloom	Post-bloom	Pre-bloom	Post-bloom
51-60	0.87-103	NA	9.3-501	NA
61-70	0.62-170	NA	5.2-1199	NA
71-85	4.4-19	NA	14-659	NA
228-235	NA	0.16-3.2	NA	0.62-4.4
236-254	NA	0.16-1.16	NA	0.12-1.36

NA = not applicable

6.2.3.5 Effect of Year and Site on Residue Values

Very limited data are available to inform year-to-year variability in neonicotinoid residues measured at the same site and variability among sites, with post-bloom soil applications of imidacloprid to blueberries being the only study available with multiple years of data (MRID 49535602). However, this study reported a high frequency of non-detects in this study (0.16 ng a.i./g for total imidacloprid), which limits the precision of the comparisons. With nectar, mean residues at the MI site in 2013 (**Figure 6-47** left panel, solid green squares) are within 10X of those measured at the same site in 2014 (left panel, open green circles). Mean nectar residues of total imidacloprid measured in the NY site in 2013 and 2014 were near or below levels of detection. With pollen, mean residues of total imidacloprid were similar (within 2X) at the MI site in 2013 and 2014. (**Figure 6-47**, right panel, green symbols), while those measured at the NY site were between 0.3 – 1.0 ng a.i./g in 2014 but not detected in 2013. With respect to site-to-site differences, the limited data shown in **Figure 6-47** indicates that mean residues of total imidacloprid can vary up to 10X among sites when comparisons are made at similar time points.

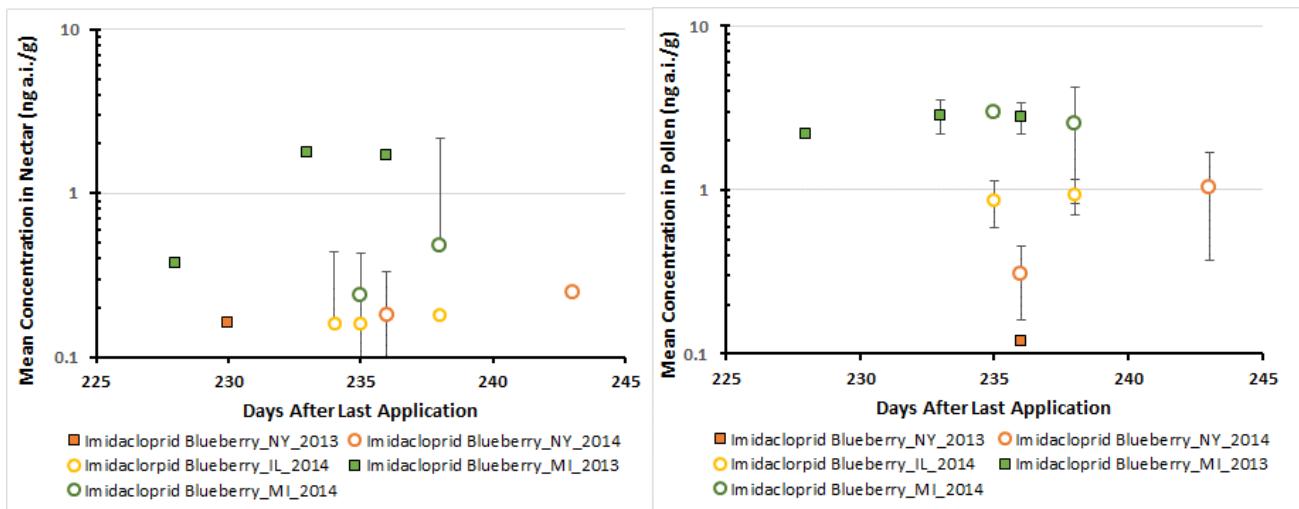


Figure 6-47. Mean imidacloprid residues in nectar (top) and pollen (bottom) from blueberries treated post-bloom (MRID 49535602). Residues reflect total imidacloprid and are normalized to a total rate of 0.1 lb a.i./A.

Data are available to inform the influence of site on concentrations of thiamethoxam (expressed as clothianidin equivalents) in nectar and pollen after pre-bloom soil applications of thiamethoxam (**Figure 6-48**). This study also used different application rates at the same site (0.129 and 0.188 lb a.i./A and therefore residues are normalized to 0.1 lb a.i./A. For the same site and DALA, mean residues of thiamethoxam (expressed as clothianidin equivalents) in nectar and pollen from trials with different

application rates are typically within 3X (open vs. solid symbols of the same color in **(Figure 6-48)**), but vary by 10X at some sites (e.g., FL site 2 with nectar and pollen). The source of this variation is not known.

With respect to differences among sites, mean residues measured at all 3 sites at the same point in time (55 DALA). Results indicate that mean residues in nectar and pollen at 2 of the 3 sites are very similar (within 2X) but are 10X different at 1 site with nectar (FL Site 1) and pollen (CA Site 1).

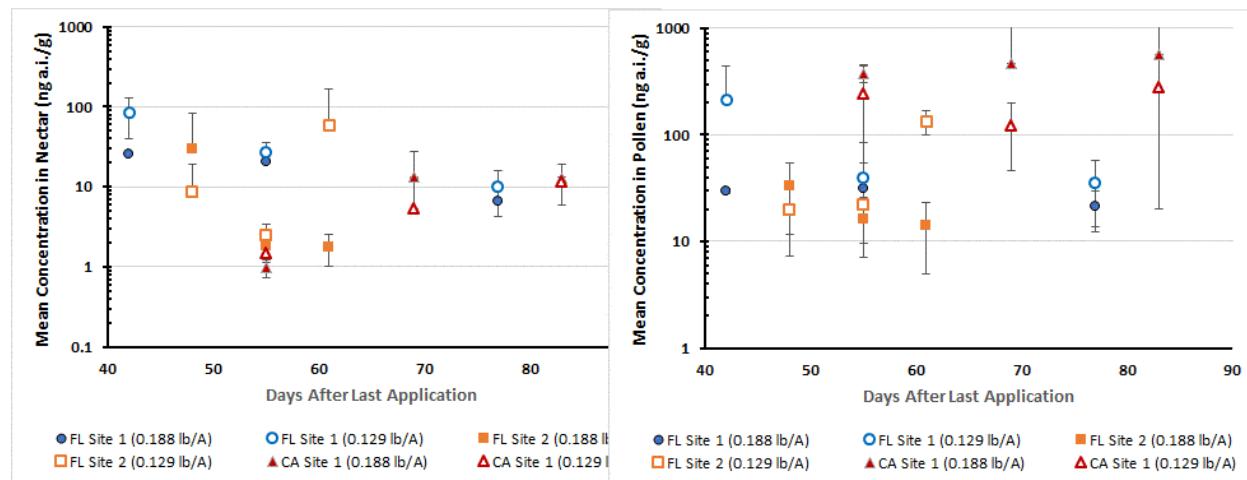


Figure 6-48. Mean thiamethoxam residues (expressed as clothianidin residues) in nectar (left) and pollen (right) from strawberries treated pre-bloom (MRID 50266001). Residues are normalized to a total rate of 0.1 lb a.i./A.

With pre-bloom soil applications of clothianidin to grape, mean residues measured from 55-60 DALA are within a factor of 10X, although confidence intervals do not always overlap suggesting these differences are statistically significant.

In summary, the limited data available for soil applications of neonicotinoids to berries indicates that differences in residues measured at similar times after application can vary by up to 10X, with some sites having similar mean residues (within 2X) while others can vary by 10X. Notably, mean residues varied by 10X at some sites when applied at different application rates, even after residues were normalized to a common application rate. This finding suggests that variability in residues within a site can be comparable to those observed across sites and highlights the relatively high degree of inherent variability that exists in the neonicotinoid residue data.

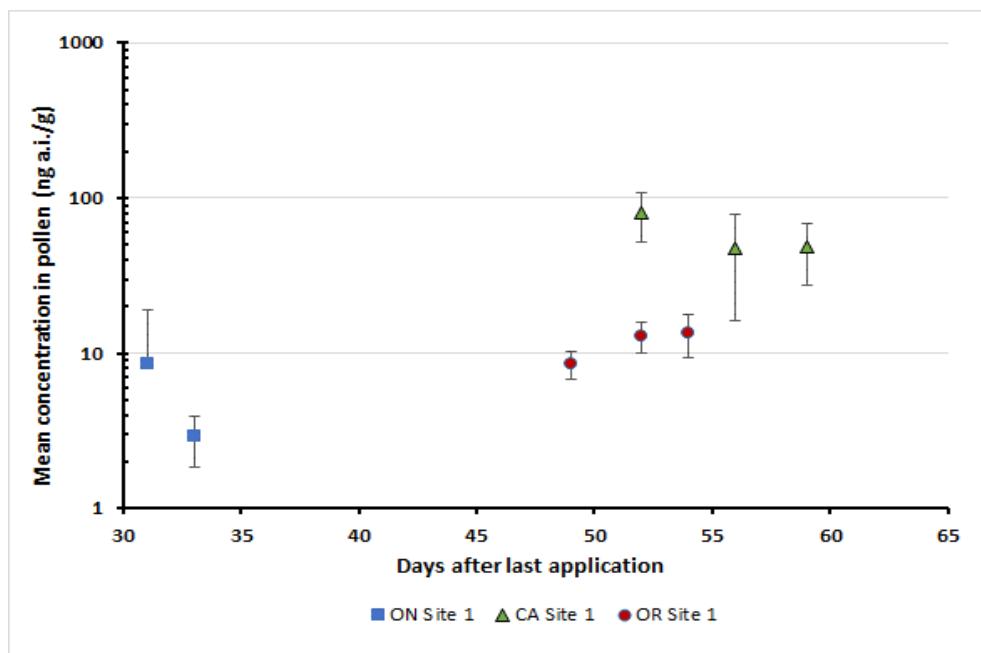


Figure 6-49. Mean residues of clothianidin in pollen of grapes treated via pre-bloom soil applications. Residues are normalized to a total rate of 0.1 lb a.i./A

6.2.3.6 Effect of Crop, Chemical, and Matrix on Residue Values

Available residue data for soil applications of neonicotinoids to berries/small vines are not sufficient to evaluate the individual impact of crop or chemical on residue concentrations. However, mean concentrations at similar timepoints in pollen after pre-bloom soil applications of clothianidin to grape or thiamethoxam to strawberry (Figure 6-44 above) are within an order of magnitude, with 95% confidence intervals overlapping for some trials. This suggests that chemical and crop may not matter.

The only data available to evaluate the effect of matrix on residue concentrations is thiamethoxam on strawberry (MRID 50266001), as much of the residue data from post-bloom applications of imidacloprid to blueberries were below detection. **Table 6-27** shows the mean residue concentrations in nectar (green triangles) and pollen (orange circles). Note that the pollen and nectar samples were taken on the same series of days for each trial. In general, the range of concentrations in pollen are higher than those in nectar, although 95% confidence limits overlap at 2 of the 3 trials.

Table 6-27. Comparison of mean residues of thiamethoxam in pollen and nectar of strawberries following pre-bloom soil application.

Chemical, Application (Crop)	Site (Year)	Nectar Site Mean (95% CL)	Pollen Site Mean (95% CL)
Thiamethoxam, Pre-Bloom, Soil (Strawberry)	FL Site 1 (2015)	29.2 (± 13.8)	61.6 (± 46.1)
	FL Site 2 (2015)	17.3 (± 19.7)	39.7 (± 21.3)
	CA Site 1 (2015)	7.9 (± 3.5)	338 (± 150)

6.2.3.7 Bridging Recommendations

For soil applications to berries/small vines, residue data are insufficient to evaluate the influence of chemical or crop on neonicotinoid residue in pollen and nectar. In the absence of data, it is assumed that residue data for soil applications can be bridged across the neonicotinoids. Cross-chemical bridging recommendations for foliar applications to berries and those made for other crop groups with sufficient data available (*e.g.*, orchards) provide support for this assumption.

With respect to crop, the current analysis indicates that residue data can be bridged among berry crops, but residue data for grapes should not be bridged among all berry crops. The residue data also suggest that matrix (pollen, nectar) influences residues, which supports the recommendation for assessing residues in pollen and nectar separately for risk assessment purpose. Although pre-bloom residues in pollen and nectar from soil application are substantially higher than those from post-bloom application, these data originate from different crops and chemicals which introduces uncertainty into this comparison. In the absence of conclusive data to suggest otherwise, it is recommended that residues in pollen and nectar pre-bloom and post-bloom soil applications be evaluated separately for risk characterization.

For foliar post-bloom or soil applications, residues in pollen and nectar were highly variable over time and do not support kinetic analyses and the development of residue decline curves. For these uses, it is recommended that risk characterization rely on the measured residue data.

6.3 Cotton

6.3.1 Crops of Concern for Bees

The oil seed crop group contains many major crops which are attractive to bees; however, only cotton is registered for foliar application of the four neonicotinoids. Soil application to cotton is only registered for imidacloprid. According to the USDA guidance on crops attractive to honey bees and other bees (USDA 2017), cotton nectar is considered attractive to honey bees, but pollen is not considered attractive. Furthermore, cotton is used as a source of nectar by some commercial beekeepers. Cotton is also considered attractive to non-*Apis* bees, including bumble bees and solitary bees. Therefore, exposure to bees from cotton will be considered in the neonicotinoid bee assessments for registered uses of these crops.

6.3.2 Foliar Applications

6.3.2.1 Summary of Label Rates/Restrictions

Foliar spray applications to cotton are registered for all four neonicotinoids (**Table 6-28**). The maximum seasonal application rates are similar among the chemicals (0.2 – 0.3 lb a.i./A), while the maximum single rates can vary by a factor of 2 (0.06 to 0.134 lb a.i./A). Imidacloprid has the lowest single application rate, but it is registered for up to 5 applications per season. The overall application intervals are also similar among the four chemicals. Regarding restrictions of application relative to bloom, only thiamethoxam is restricted for applications during bloom.

Table 6-28. Foliar application rates and number of applications for neonicotinoids on cotton (based on current labels).

Chemical	Max Appl. Rate x No. Apps. (lb a.i./A)	Total Seasonal Rate (lb a.i./A)	Minimum Interval (d)	Bloom Restrictions
Imidacloprid	0.06 x 5	0.3	7	No restrictions
Clothianidin	0.10 x 2	0.2	7	No apps. during bloom
Thiamethoxam	0.063 x 2	0.13	7	No restrictions
Dinotefuran	0.134 x 2	0.27	5	No restrictions

Cotton is considered an indeterminant blooming crop with a long bloom period (45 days or longer). 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 remains open for only 1 day. This differs from other crops (e.g., stone fruit) where all blossoms develop and bloom at a similar time. Thus, residues of neonicotinoids measured over time in cotton pollen and floral nectar reflect the development of new flowers and incorporation of translocated neonicotinoids at each sampling point. This may impact the nature of residue kinetics relative to crops which flower at approximately the same time. Cotton also produces nectar at various vegetative plant parts outside of the flower via epidermal glands and is referred to as extrafloral nectar. Extrafloral nectar is considered a potential source of pesticide exposure for bees, although the extent to which bees rely on this source relative to floral nectar is uncertain.

6.3.2.2 Available Residue Data

Residue data for pollen, floral nectar and extrafloral nectar following foliar application are available for all four neonicotinoids (**Table 6-29**). In all five studies, final applications were made just prior to bloom or during the beginning of bloom. The number of sites in each study ranged from 3 to 9. Most residue trials were conducted in two states (MO and CA). Given that all four neonicotinoids are represented by residue data from a single crop (cotton), these data appear particularly useful for evaluating the influence of chemical on residues in bee relevant matrices.

Table 6-29. Residue studies for cotton treated with foliar applications of neonicotinoids

Chemical	Variety	# sites (Locations)	Appl. Rate x No. Apps (interval)	Appl. Timing	# Seasons	# sampling events / season)	MRID (Classification)
Imidacloprid	Pima	3 (MO)*	0.06 lb a.i./A x 5 (5-8 d)	Inflorescence to first bloom	2	3-5	Acceptable (49511702)
Clothianidin	Pima	3 (MO, TX, CA)	0.085 x 1**	Inflorescence to first bloom	1	5	Supplemental (49904901)
Clothianidin	Pima & Acala	3 (CA)	0.1 x 2 (7 d)	Immediately prior to bloom	1	7	(49733302)
Thiamethoxam	Pima & Acala	9 (CA)	0.063 x 2 (5 d)	12 days prior to significant bloom	2	1	(49686801)
Dinotefuran	Pima & Acala	6 (CA)	0.09 x 2 & 0.134 x 2 (7 d)	Inflorescence to first bloom	1	5***	Acceptable (50198501)

* Two side-by-side trials were conducted in the first year (2012) at all three sites.

** includes trials with seed treatment, which results in negligible residues at bloom

*** Includes one sample between 1st and 2nd application

Figure 6-50 summarizes the neonicotinoid residues measured in cotton floral nectar (Panel A) and extrafloral nectar (Panel B), respectively, from all of five of the aforementioned studies. Mean values of neonicotinoids in cotton pollen from the same studies are shown in **Figure 6-51**. To facilitate comparisons, these residue values have been normalized to 0.1 lb a.i./A based on total application rate from each study.

A clear trend in decreasing concentrations with increasing time after the last foliar application is seen with mean residues of neonicotinoids in both floral and extrafloral nectar. It is also evident that mean normalized residue values overlap among chemicals as indicated by the proximity of different shaped symbols. Nonetheless, mean residue values among the neonicotinoids in floral and extrafloral nectar vary by up to 100X at similar time points after application. For the clothianidin, there is some indication that normalized floral nectar residues are lower than other chemicals from day 12 onward ("X" symbols, **Figure 6-50-A**). All of these residue values originated from the study with a single foliar application (MRID 49904901, 1 x 0.085 lb a.i./A). Residues of clothianidin in floral nectar measured before 12 days after application are comparable to dinotefuran and thiamethoxam (imidacloprid was not measured sooner than 13 days after application). Normalized residue values in extrafloral nectar (**Figure 6-50-B**) appear to be overlapping among the chemicals throughout the measurement period. Mean residues in cotton pollen show distinct differences among the neonicotinoids with the highest normalized residues observed for dinotefuran shortly after application and the lowest for imidacloprid. Since pollen is not considered attractive to honey bees, the subsequent analyses will focus primarily on floral nectar and extrafloral nectar.

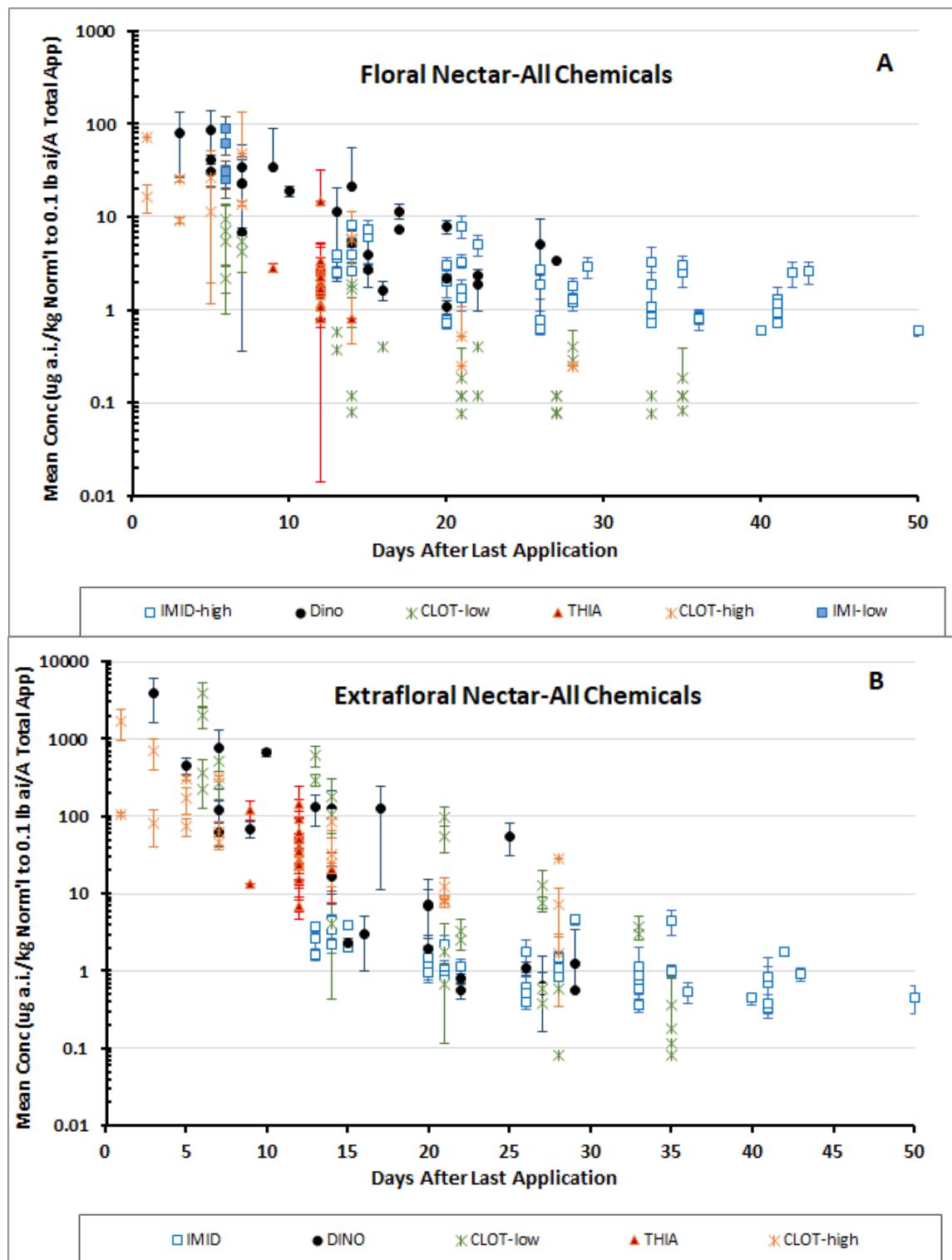


Figure 6-50. Mean concentration of neonicotinoids in floral nectar (A) and extrafloral nectar (B) following pre-bloom foliar applications to cotton. Values normalized to total application rate of 0.1 lb a.i./A. Imid = imidacloprid; Thia = thiamethoxam, Clot = clothianidin, Dino = dinotefuran. Thiamethoxam residues are expressed as clothianidin equivalents and imidacloprid residues reflect total imidacloprid. Error bars = 95% confidence interval.

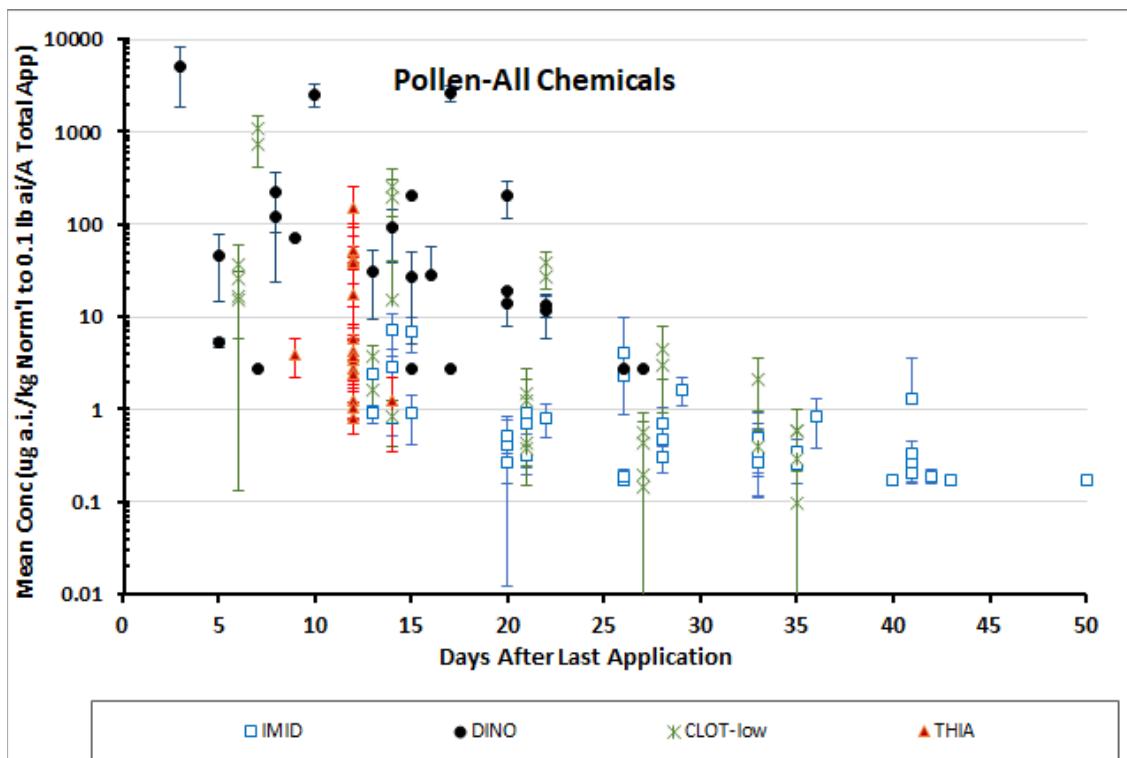


Figure 6-51. Mean concentration of neonicotinoids in pollen following pre-bloom foliar applications to cotton. Values normalized to total application rate of 0.1 lb a.i./A. Imid = imidacloprid; Thia = thiamethoxam, Clot = clothianidin, Dino = dinotefuran. Note that thiamethoxam residues are expressed as clothianidin equivalents imidacloprid reflect total imidacloprid. Error bars = 95% confidence interval.

6.3.2.3 Bridging Needs (Gaps)

All four neonicotinoids are represented by residue data for bee-relevant matrices (floral nectar, extrafloral nectar, and pollen). Furthermore, the neonicotinoids are only registered for foliar applications to one crop in the oil seed group (*i.e.*, cotton). Finally, cotton pollen is not considered attractive to honey bees. Therefore, the need for bridging among chemicals with cotton is not as relevant compared to the bridging needs for other crop groups where no data exist for some chemicals. However, there are noticeable differences in the temporal coverage among the four chemicals. The temporal coverage of each chemical for nectar and extrafloral nectar is as follows:

- Dinotefuran: Day 3-22;
- Imidacloprid: Day 13-50;
- Clothianidin: Day 1-35; and,
- Thiamethoxam: Day 9-14.

In addition, the temporal coverage of the thiamethoxam study is very limited, since it contained a single sampling event per trial. For the purposes of risk characterization, it is useful to evaluate the expected decline in residues over time for each neonicotinoid. The relationship between residues and time can be used to evaluate the expected amount of time a given toxicity threshold is exceeded. Therefore, analyses of the effect of factors described previously for other crop groups (*e.g.*, application rate, time,

site, year, and chemical) are evaluated below for cotton. In particular, this analysis is intended to add to the weight of evidence supporting bridging among the four neonicotinoids.

6.3.2.4 Influence on Residues of Application Rate and Number of Applications

Evaluation of the effect of application rate and number of applications on residues in bee-relevant crop matrices is most effectively done within a given study and site since factors such as location and year of application can confound interpretation of the residue data. For cotton, only one study evaluated residues following different application rates at the same location (dinotefuran, MRID 50198501 with foliar nectar only). At the Chula, GA site of this study, residues were measured in two plots. In plot B, residues in nectar were measured after two applications of 0.09 lb a.i./A, 7 days apart (total application = 0.18 lb a.i./A). In plot C, residues in nectar were measured after two applications of 0.13 lb a.i./A 7 days apart (total application = 0.26 lb a.i./A). This represents a 1.5X increase in the single and total application rate at plot C relative to plot B.

The residue profile from plots B and C from this study are shown in **Figure 6-52**. Only one sampling event was included in for plot C with the 1.5X higher application rate (day 5). On this day, it is evident that mean residues in nectar are 2X greater at plot C compared to plot B. Although this comparison is based on limited data, it suggests that residues of dinotefuran in floral nectar increase approximately in proportion to the foliar application rate. This finding is consistent with results from neonicotinoid applications to other crops summarized in this document.

No data were available to evaluate the impact of the number of applications in cotton residues measured at the same study site.

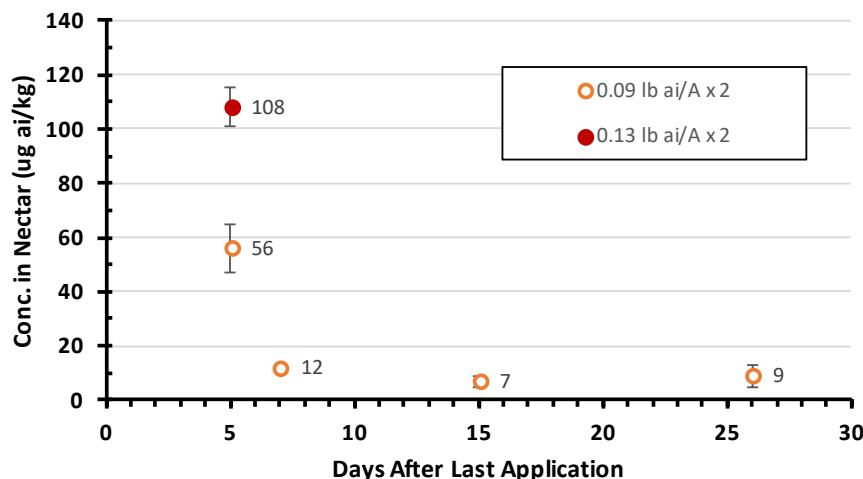


Figure 6-52. Effect of application rate on dinotefuran residues in nectar (MRID 50198501). Symbols = mean, error bars = max & min. Error bars = 95% confidence interval.

6.3.2.5 Influence of sampling day (time) on residue values

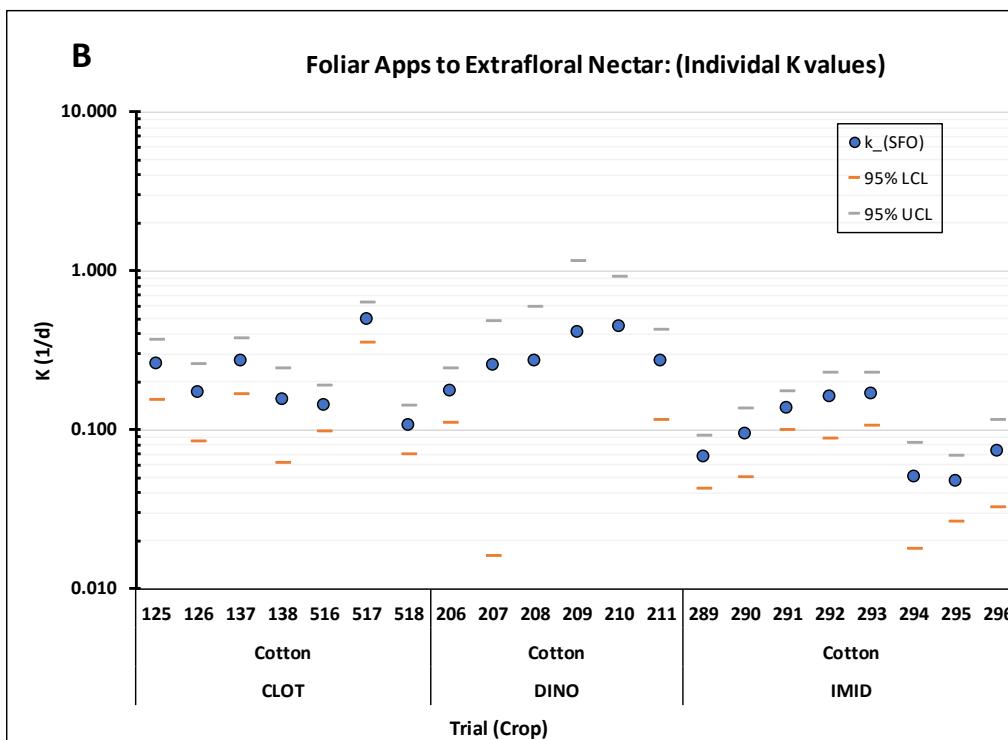
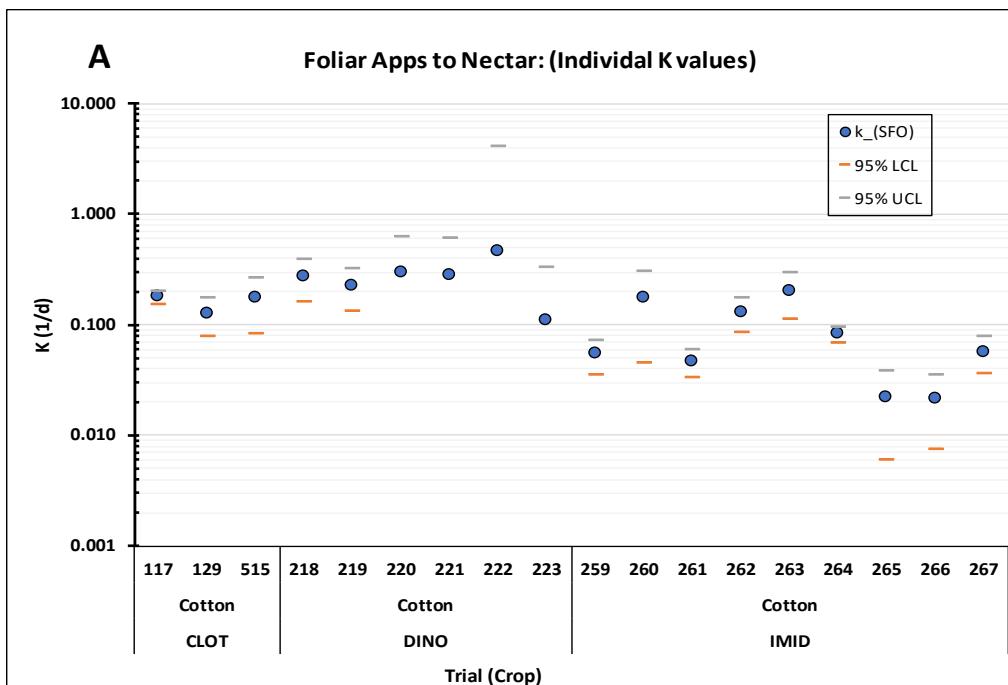
The influence of time after last application on the magnitude of residues in floral and extrafloral nectar was evaluated two ways. First was to quantify the magnitude of residues within various time periods after application. The second was to quantify the dissipation rate constants among chemicals and matrices.

Following the first approach, the mean and range of residues in cotton floral and extrafloral nectar within 10-d sampling periods after the last foliar application are shown in **Table 6-30**. Mean residues measured 1-10 d after application decline by an order of magnitude by 11-20 days after application for both floral nectar and extrafloral nectar. Beyond 20 days, mean residues in floral nectar approach the level of quantification (~ 1 ng a.i./g), while those in extrafloral nectar approach the LOQ after 31 days. Within each 10-d sampling window, the range in daily mean residue values span 2 orders of magnitude. Overall, mean residues in extrafloral nectar are about an order of magnitude greater than those in floral nectar.

Table 6-30. Effect of sampling time (days after last application) on daily mean neonicotinoid residues in cotton nectar and extrafloral nectar. Concentrations in ng a.i./g, normalized to 0.1 lb a.i./A rate.

Days After Last Application	Concentration in nectar (ng a.i./g / 0.1 lb a.i./A)		Concentration in extrafloral nectar (ng a.i./g / 0.1 lb a.i./A)	
	Mean	Min-Max	Mean	Min-Max
1-10	29.1	2.2-89	677	13-3,900
11-20	3.8	0.08-21	53	1.0-620
21-30	1.5	0.08-7.9	9.5	0.08-99
31-40	1.0	0.08-3.3	1.2	0.08-4.4
41-50	1.4	0.59-2.6	0.8	0.38-1.8

With the second approach for evaluating the effect of time on neonicotinoid residues, data from individual trials were analyzed to determine whether the single first order (SFO) dissipation rate constants (*k*) could be reliably quantified according to methods and screening criteria described in **Section 4.5.5**. Among the four neonicotinoids, reliable estimates of “*k*” could be calculated only with imidacloprid, clothianidin, and dinotefuran, since thiamethoxam did not contain sufficient sampling events over time. Results from the analysis of dissipation rates of these three chemicals in foliar nectar, extrafloral nectar and pollen are shown in **Figure 6-53 (panels A-C)**. Detailed summary statistics for the kinetic analysis of neonicotinoid residues in cotton floral nectar, extrafloral nectar and pollen are provided in **Tables B-1 to B-3 of Appendix B**.



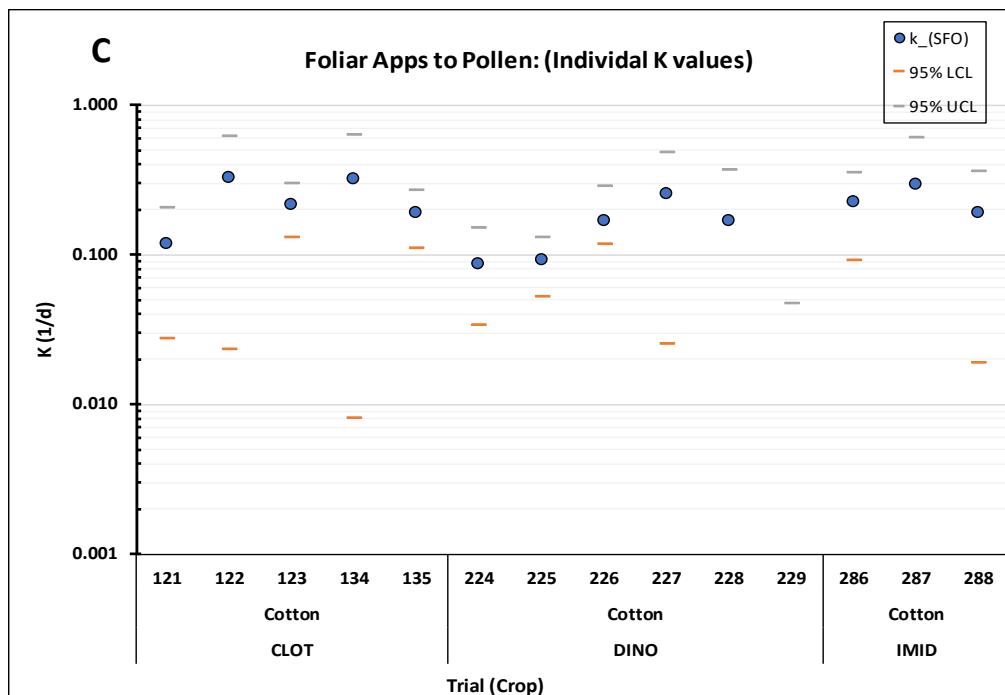


Figure 6-53. Individual dissipation rate constants (k) of clothianidin (CLOT), dinotefuran (DINO), and imidacloprid (IMID) in cotton floral nectar (A), extrafloral nectar (B), and pollen (C) from different residue trials. Dashes indicate upper and lower 95% confidence limits of k.

Dissipation rate constants for floral nectar are statistically similar among clothianidin and dinotefuran, as indicated by overlapping 95% confidence limits. However, 5 of the 9 trials with imidacloprid (259, 261, 265-267) produced distinctly lower k values (**Panel A of Figure 6-53**). A similar pattern is seen with extrafloral nectar, with values of k for imidacloprid below 0.1 d^{-1} (DT_{50} values > 7 days) for several trials while those for clothianidin and dinotefuran are at or above 0.1 d^{-1} (**Panel B**). With cotton pollen, no obvious distinction can be made among the neonicotinoids with respect to dissipation rate constants (**Panel C**).

Summary statistics for the dissipation rate constants among matrices and chemicals are shown in **Table 6-31**. These statistics are consistent with the trends observed in **Figure 6-53**. Although the mean DT_{50} of imidacloprid in cotton nectar and extrafloral nectar (7-8 days) is about 2X longer than either clothianidin or dinotefuran (2-3 days), these half-life values are fast relative to the bloom duration of cotton (~45 days).

Table 6-31. Summary statistics of dissipation rate constants (k) for neonicotinoids in cotton matrices.

Chemical	Mean K (1/d)	DT_{50} (d)	Std	Min	Max	n	Min 95% LCL	Max 95% UCL
Extrafloral Nectar								
CLOT	0.228	3.0	0.132	0.106	0.495	7	0.062	0.636
DINO	0.303	2.3	0.102	0.175	0.445	6	-0.331	1.145
IMID	0.099	7.0	0.049	0.047	0.168	8	0.018	0.229
All 3 Chemicals	0.200	3.5	0.127	0.047	0.495	21	-0.331	1.145
Nectar								
CLOT	0.243	2.9	0.158	0.127	0.423	3	0.078	0.525

Chemical	Mean K (1/d)	DT ₅₀ (d)	Std	Min	Max	n	Min 95% LCL	Max 95% UCL
Extrafloral Nectar								
DINO	0.276	2.5	0.115	0.109	0.462	6	-3.140	4.063
IMID	0.088	7.9	0.067	0.021	0.203	9	0.006	0.306
All 3 Chemicals	0.176	3.9	0.132	0.021	0.462	18	-3.140	4.063
Pollen								
CLOT	0.232	3.0	0.088	0.118	0.321	5	0.008	0.629
DINO	0.122	5.7	0.090	0.000	0.252	6	-0.047	0.478
IMID	0.234	3.0	0.051	0.190	0.290	3	-0.027	0.607
All 3 Chemicals	0.185	3.7	0.096	0.000	0.321	14	-0.047	0.629

6.3.2.6 Effect of Year, Site and Matrix on Residue Values

The effect of year (growing season), site and matrix on neonicotinoid residues in bee relevant matrices is best examined within a study, since analytical methods, sampling procedures and study design elements are similar within a study vs. among studies. Two approaches were used: 1) a qualitative comparison of residue values (and 95% confidence limits) based on plots of the data; and 2) comparison of residue concentrations adjusted to a common day after application using kinetic parameters summarized previously.

Imidacloprid

Figure 6-54 displays the concentration of total imidacloprid residues (sum of parent, imidacloprid olefin and 5-hydroxy imidacloprid) in cotton floral nectar (Panel A) and extrafloral nectar (Panel B) at three sites in MO (MRID 49511702) normalized to a total application rate of 0.1 lb a.i./A. The design of this study is unique among neonicotinoids in that two trials were conducted in neighboring plots in 2012 (open symbols labeled 2012 A&B); whereas, the 2013 trial was conducted on one plot (2013A, solid symbols). Overall, mean residues in floral and extrafloral nectar vary by up to 1 order of magnitude among trial sites and years when compared at similar days after the last application (DALA).

With respect to the impact of trial year on mean residues in floral and extrafloral nectar (open vs. closed symbols in **Figure 6-54 A & B**), differences among years of up to 10X occur depending on the trial site. For example, mean residues of total imidacloprid in floral nectar measured at the Malden, MO site in 2013 are approximately 10X greater than those measured in 2012 at similar DALA, with non-overlapping 95% confidence limits. This same pattern occurred in extrafloral nectar at the Malden, MO site.

When comparing differences in residues among sites in the same year (different symbol shapes in **Figure 6-54**), differences in residues among study years can equal or exceed those observed among study sites. This suggests that “year” can have a larger impact on residues compared to site (at least in those used in this study). Overall, mean residues in floral nectar vary by **3X** during the first sampling event. Subsequently, the overall range in imidacloprid residues in floral nectar varies by up to **10X** among sites and years. This increasing range in floral nectar residues with time appears to be a function of differential dissipation rates among trials, particularly at the Glennonville, MO site where residues declined rapidly after the first sampling event in 2012 (open orange squares) compared to 2013 (solid orange squares; Panel A).

Trends in site-to-site and year-to-year variation in imidacloprid residues in extrafloral nectar (panel B) are similar to those described previously for floral nectar (panel A).

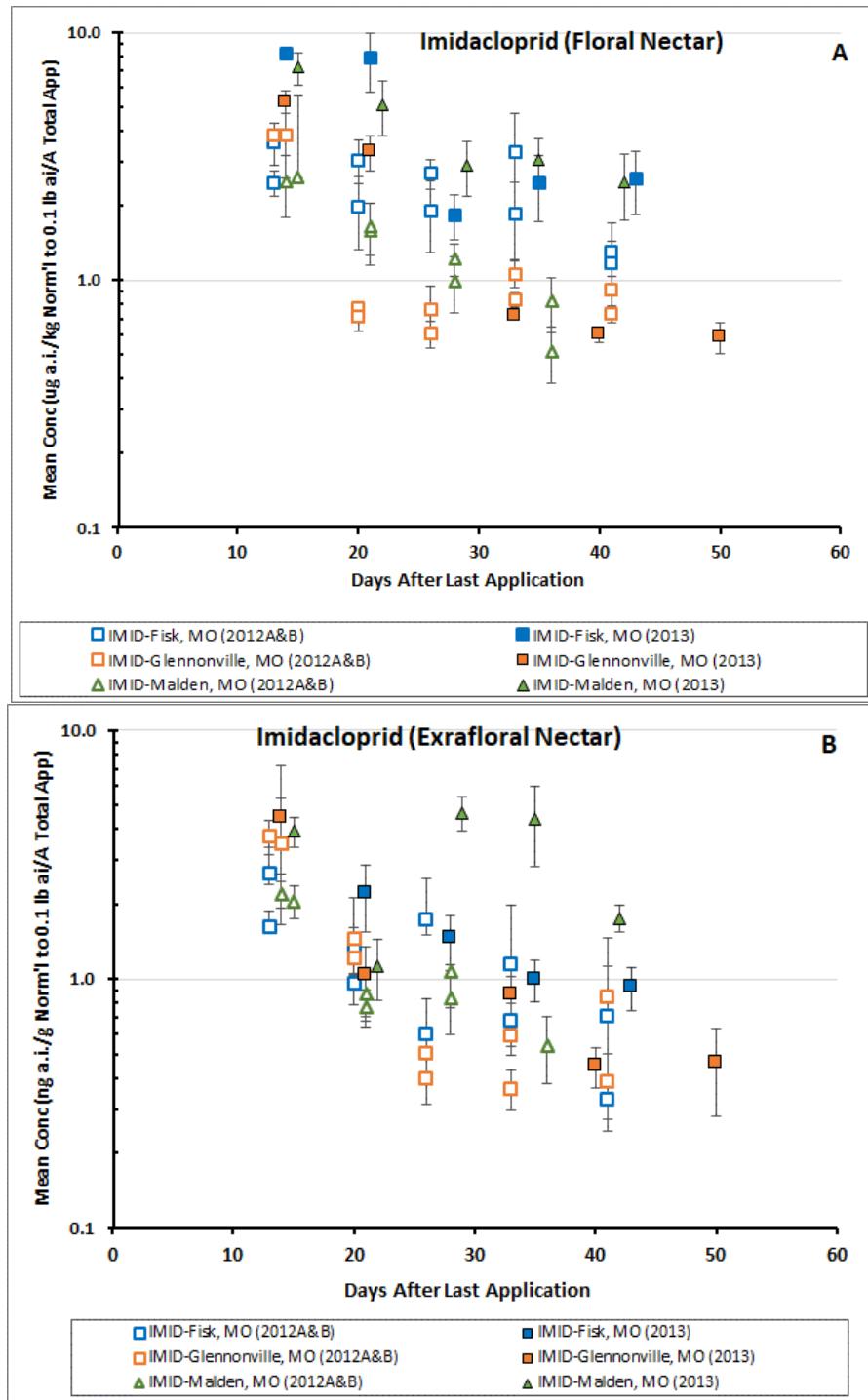


Figure 6-54. Total imidacloprid residues in floral nectar (panel A) and extrafloral nectar (panel B) from foliar applications to cotton (MRID 49511702). Values normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

A second approach evaluated the effect of site, year and matrix on neonicotinoid residues in cotton matrices using the k values from the individual trials presented in **Tables B-1 and B-2 of Appendix B**. Here, the initial measured concentrations (C_{Initial}) in floral and extrafloral nectar from each residue trial with a valid "k" estimate were adjusted to 15 days after last application using the following equation:

$$C_{\text{initial SFO (Day 10)}} = C_{\text{initial SFO (Day X)}} e^{(k \times [X - 15])}$$

where,

$C_{\text{initial SFO (Day 15)}}$ =	Concentration adjusted to day 15 using SFO model
$C_{\text{initial SFO (Day X)}}$ =	Concentration estimated on the initial sampling day (X) using SFO model
k =	Dissipation rate constant (1/d) estimated using SFO model
X =	Day of initial sampling from the residue trial

The adjustment was made to 15 days since this time point fell within the range of measured data for most of the trials. In all cases, residue values were normalized to a common total application rate of 0.1 lb a.i./A

A summary of the C_{Initial} estimates (normalized to 0.1 lb a.i./A) adjusted to DALA 15 with imidacloprid are shown in **Figure 6-55** for all 3 matrices and among sites and years. With extrafloral nectar, estimates of C_{Initial} vary by a factor of 3X across site and year (from 1.3 to 4.0 ng a.i./g per 0.1 lb ai/A) with an overall average of 2.8 ng a.i./g. The mean C_{Initial} estimates for floral nectar (4.5 ng a.i./g per 0.1 lb ai/A) is within 2X of extrafloral nectar, and also varies about 3X among sites and years (range: 2.4 – 8.3 ng a.i./g). Mean C_{Initial} estimates for pollen are only available for 2 trials and fall within a similar range as that of the other two matrices (2.4-6.8 ng a.i./g per 0.1 lb a.i./A). Therefore, the analysis of C_{Initial} adjusted to a common DALA among trials suggests the impact of site and year on imidacloprid residues is about 3X, which smaller than qualitative comparisons made previously based on results at similar DALA (up to 10X). The analysis of C_{Initial} adjusted to a common DALA also suggests that residues of imidacloprid among the 3 matrices are relatively similar (within 3X). It is noted, however, that estimating C_{Initial} also involves uncertainty associated with the k-values which is not reflected in these estimates.

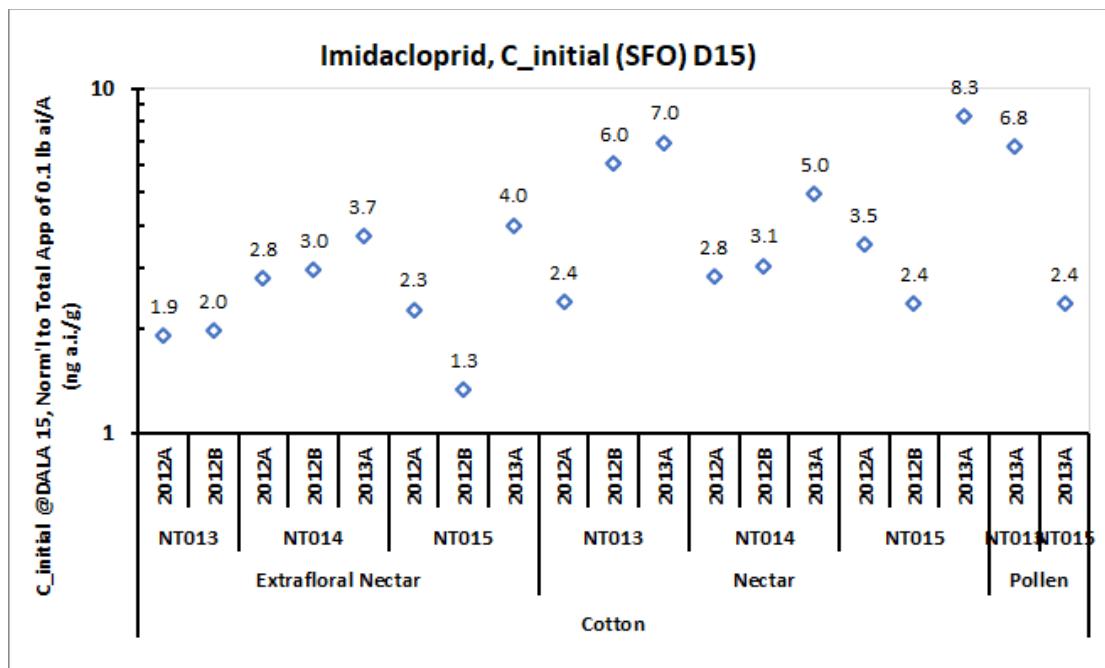


Figure 6-55. Initial concentrations of total imidacloprid in floral nectar, extrafloral nectar and pollen of cotton adjusted to DALA 15 using each trial-specific dissipation rate constant (MRID 49511702). Values normalized to total application rate of 0.1 lb a.i./A

Dinotefuran

The effect of site on concentrations of dinotefuran in floral and extrafloral nectar is shown in **Figure 6-56**, Panels A and B, respectively. With floral nectar, data are available from 8 sites and show an obvious decline with increasing DALA within each site. For some sites and sampling events, wide variation among sample replicates is indicated by the large 95% confidence intervals. Similar to that described previously with imidacloprid, residues in floral nectar measured at the initiation of each trial are not distinguishable based on non-overlapping 95% confidence limits. Later on in the trial, mean residue values are distinct from site to site in several cases.

Dinotefuran concentrations in extrafloral nectar are about 10X greater than those in floral nectar (panel B of **Figure 6-56**) in the first two weeks after application. Distinguishing the effect of site is problematic with the extrafloral data based on comparing observed residues since measurements are often not made during the same DALA. In the cases where samples were measured on the same DALA among 2 or more trials (DALA 7, 14, 20, 22, 27), mean concentrations range from about 2X (DALA 7 and 22) to approximately 100X (DALA 20).

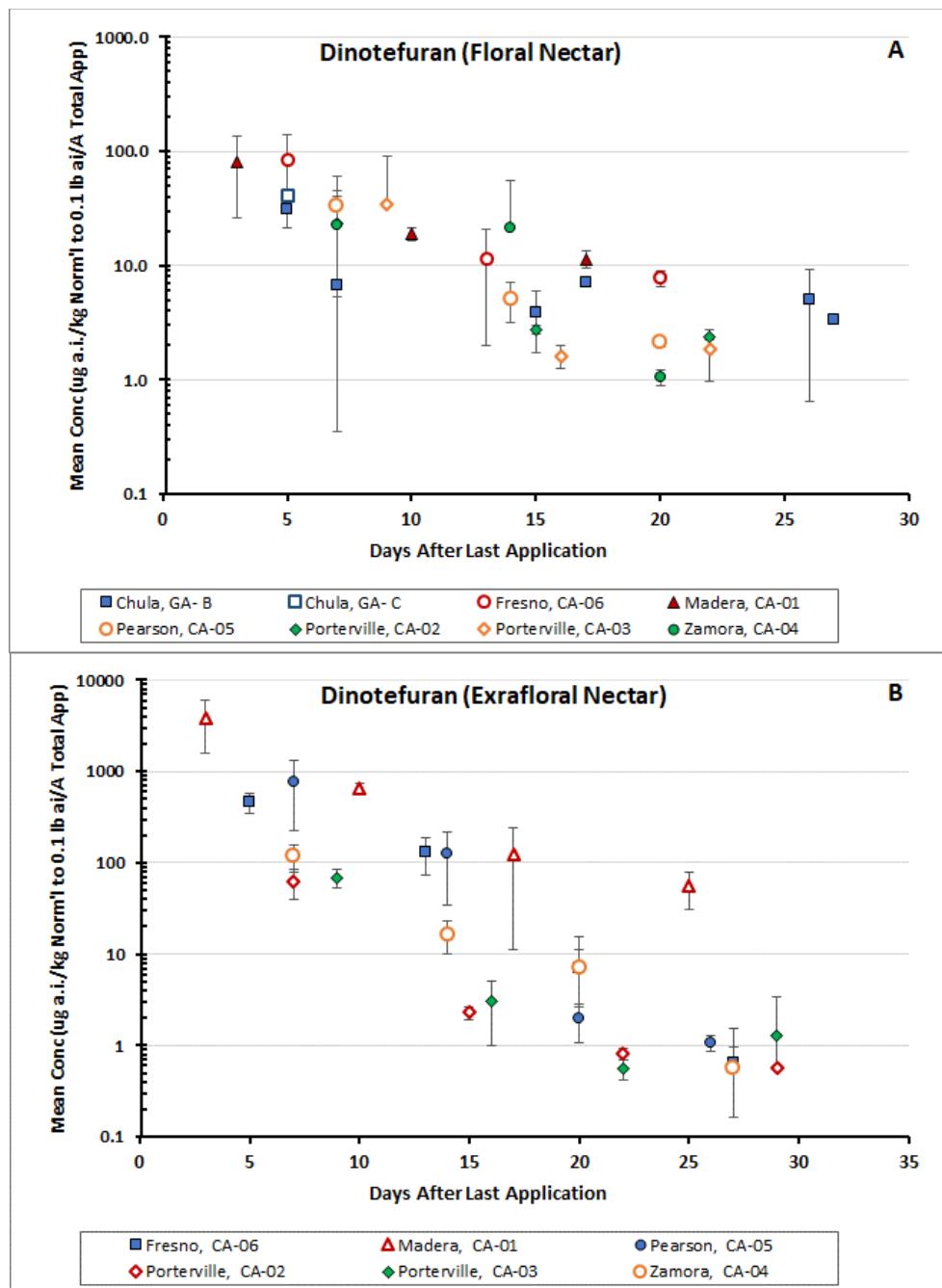


Figure 6-56. Mean dinotefuran residues in floral nectar (panel A) and extrafloral nectar (panel B) from foliar applications to cotton (MRID 50198501). Values normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

Since some of the dinotefuran trials contained reliable estimates of the dissipation rate constant (k), the SFO-estimated concentration estimated at the first sampling day of each trial (C_{Initial}) was adjusted to DALA 15 to facilitate cross-site comparisons as described previously with imidacloprid. Results from this analysis are shown in **Figure 6-57**. Although fewer trials were amenable to determining the DALA 15-adjusted concentrations, these data support the previous observations with the unadjusted residue data. Specifically, the range in DALA 15-adjusted concentrations in extrafloral nectar approach 40X

among the four trials. For floral nectar, a smaller range is seen (2X-4X) although only three trials were available for the analysis. Residues in pollen vary by nearly 100X among trials. This analysis suggests that site can have a substantial (>10X) on dinotefuran residues depending on matrix.

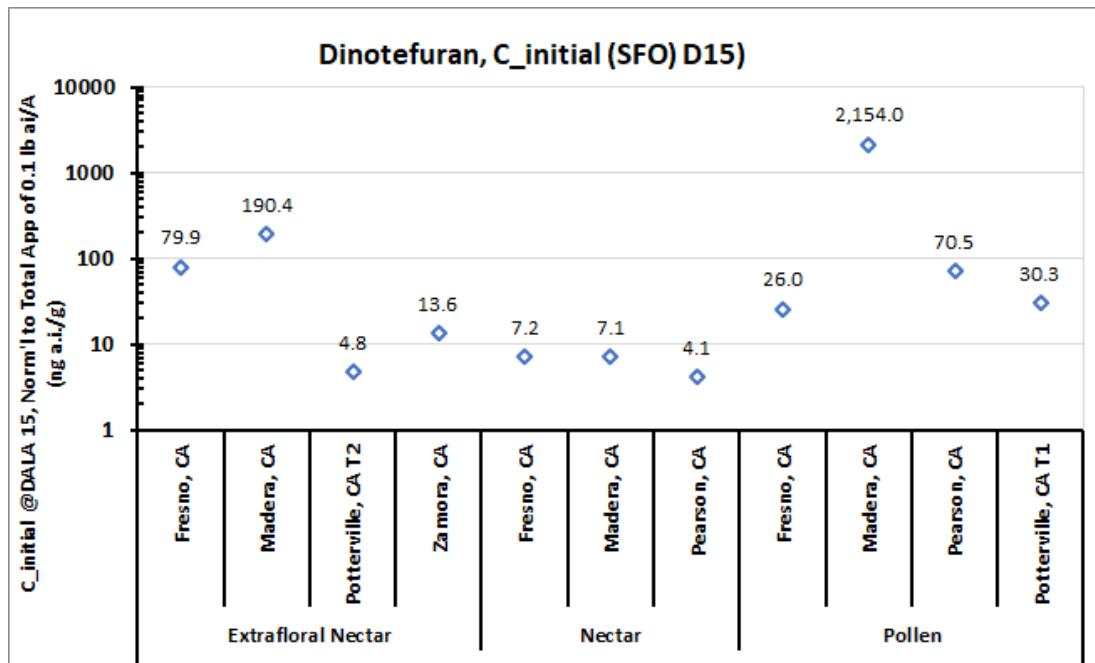


Figure 6-57. Initial concentrations of dinotefuran in floral nectar, extrafloral nectar and pollen of cotton adjusted to DALA 15 using each trial-specific dissipation rate constant (MRID 50425902). Values normalized to total application rate of 0.1 lb a.i./A.

Clothianidin

The effect of site on concentrations of clothianidin in floral and extrafloral nectar is shown in **Figure 6-58**, Panels A and B, respectively. Symbols with the same color reflect trials of foliar application of 0.086 lb a.i./A (open symbols) while those with solid symbols are trials that also had seed treatment applications (about 0.04 lb ai/A). Residue value below 1 ng ai/g are below the LOQ. Seed treatment application does not make a significant contribution to residue concentrations from combined seed treatment + foliar application in floral or extrafloral nectar, as indicated by overlapping 95% confidence intervals.

As seen with imidacloprid and dinotefuran, concentrations of clothianidin in floral nectar are not distinguishable at the first sampling day (panel A). At later sampling times during the trials, the effect of site cannot be determined due to concentrations being below the LOQ. In contrast, with extrafloral nectar, site-to-site differences in clothianidin concentrations are evident throughout the trials. In particular, the trial in TX resulted in 10X greater concentrations compared to trials in MO and CA.

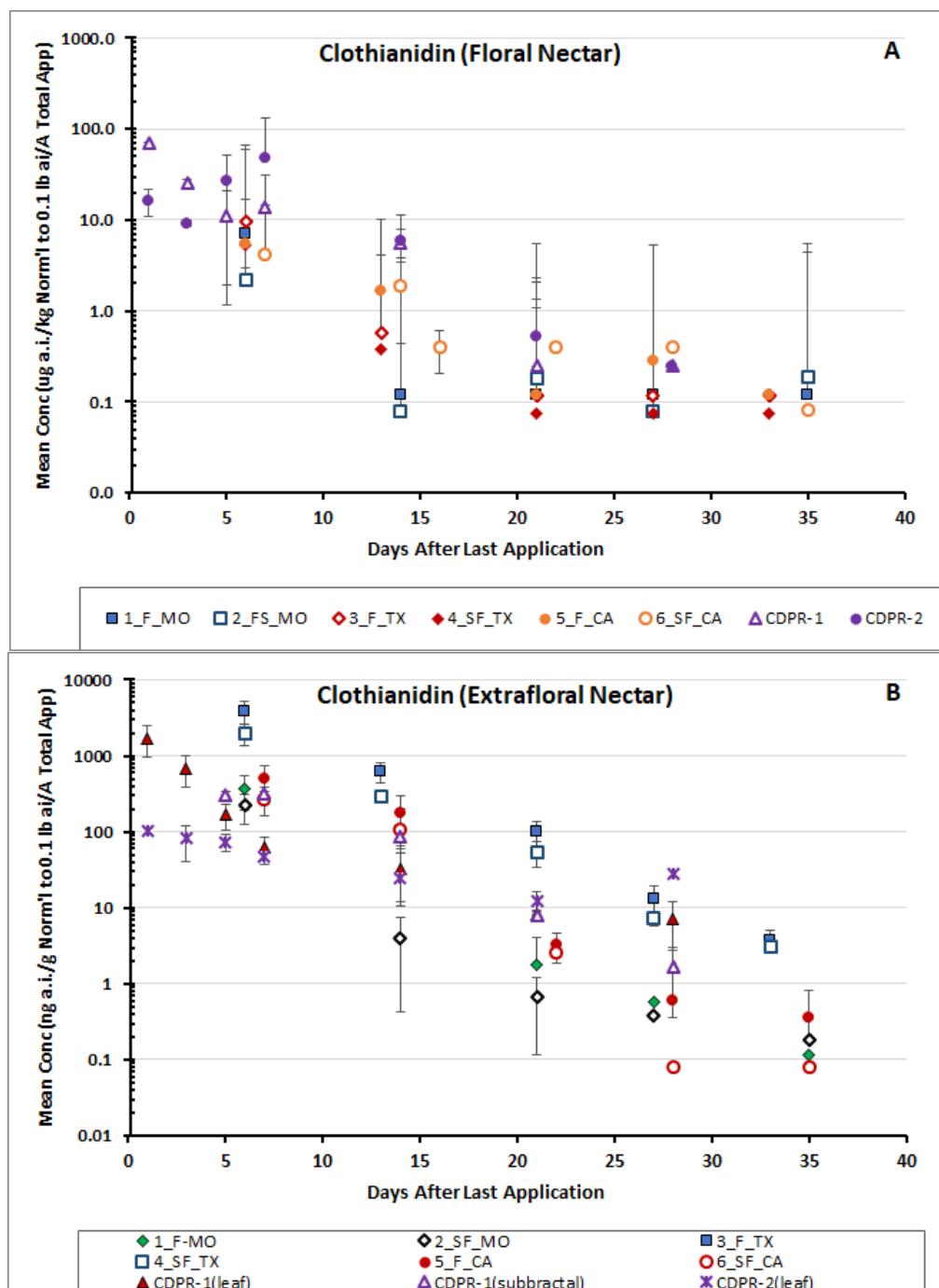


Figure 6-58. Mean clothianidin residues in floral nectar (panel A) and extrafloral nectar (panel B) from foliar applications to cotton (MRID 49904901 & 49733302). Values normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

Since some of the clothianidin trials contained reliable estimates of the dissipation rate constant (k), the SFO-estimated concentration estimated at the first sampling day of each trial (C_{Initial}) was adjusted to DALA 15 to facilitate cross-site comparisons as described previously with imidacloprid. Results from this analysis are shown in **Figure 6-59**. Specifically, the range in DALA 15-adjusted concentrations in extrafloral nectar is up to 200X among the 7 trials (mean = 130 ng a.i./g per 0.1 lb a.i./A). For floral

nectar, a smaller range is seen (5X) although only three trials were available for the analysis. The mean $C_{initial}$ of clothianidin in floral nectar is 2.6 ng a.i./g per 0.1 lb a.i./A, which is 100X lower than the mean in extrafloral nectar. Residues in pollen also vary by nearly 100X among trials with a mean of 75 ng a.i./g per 0.1 lb a.i./A. This analysis suggests that both site and matrix can have a substantial (>10X) on clothianidin residues depending on matrix.

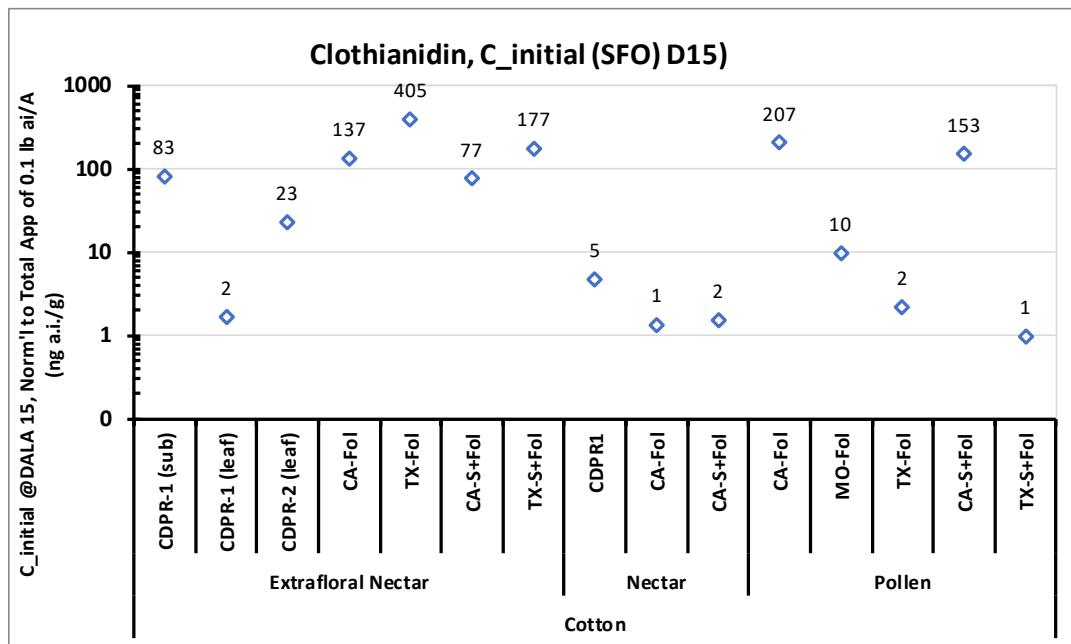


Figure 6-59. Initial concentrations of clothianidin in floral nectar, extrafloral nectar and pollen of cotton adjusted to DALA 15 using each trial-specific dissipation rate constant (MRID 49904901 & 49733302). Values normalized to total application rate of 0.1 lb a.i./A.

Thiamethoxam

With thiamethoxam (expressed as clothianidin equivalents), residue data are available from one study of 9 different sites in California (**Figure 6-60**); however, measurements were made at a single time point in most trials (DALA 12). The two trials with measurements at DALA 9 and 14 represent different years. As with dinotefuran and clothianidin, concentrations in extrafloral nectar (Panel B) are about 10X greater than those in floral nectar (Panel A). In general, however, thiamethoxam concentrations among sites are within 3X for 8 or the 9 sites and 10X for all 9 sites. With extrafloral nectar, variation due to site is about 20X overall. The effect of year on floral and extrafloral nectar concentrations appears modest for the two sites where multiple years were sampled (*i.e.*, within 3X).

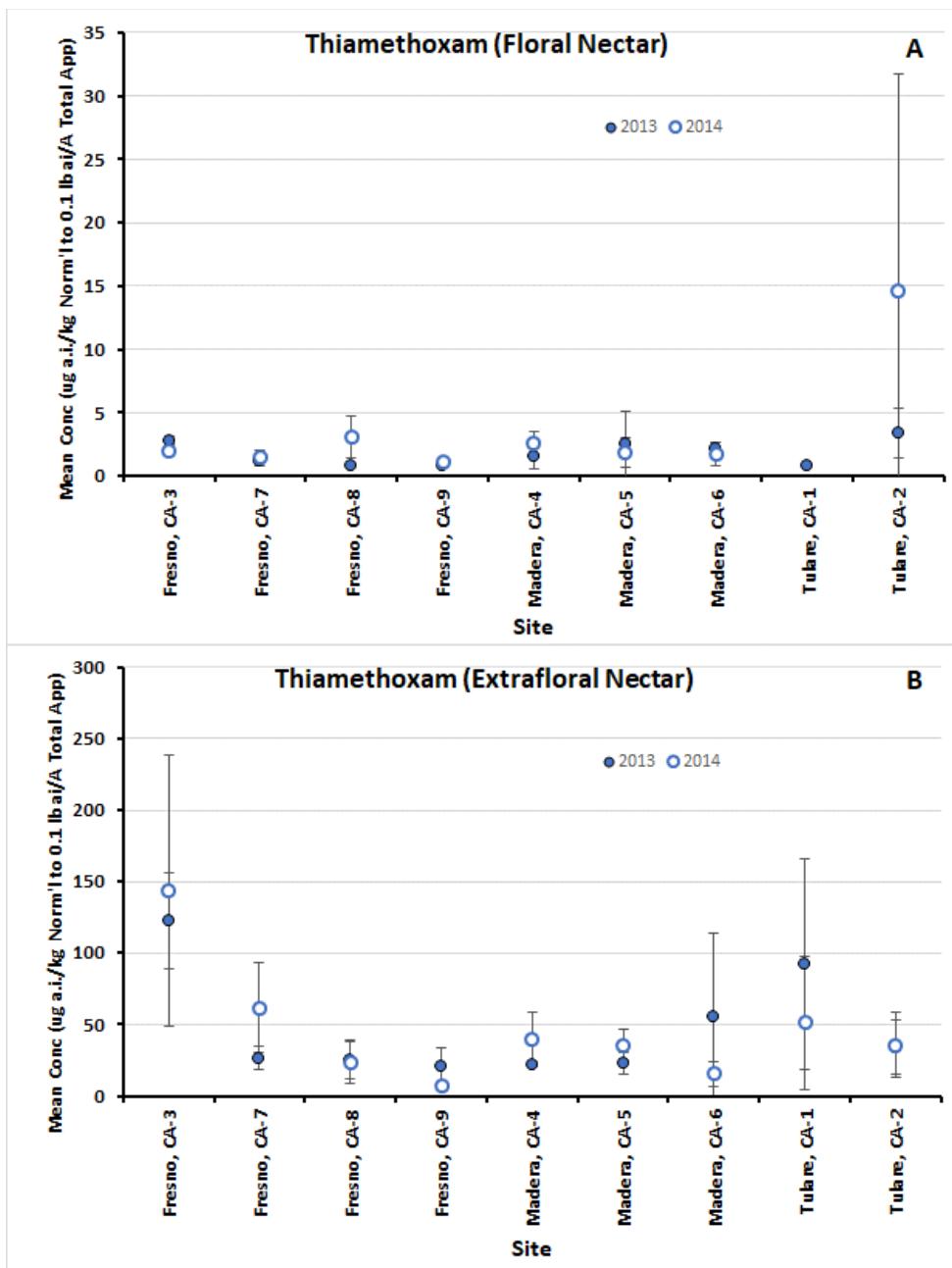


Figure 6-60. Mean thiamethoxam residues (as clothianidin equivalents) in floral nectar (panel A) and extrafloral nectar (panel B) from foliar applications to cotton (MRID 49686801). Values normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

6.3.2.7 Effect of crop and application timing

Since all studies were conducted with cotton, an evaluation of the effect of crop is not applicable. Similarly, all applications were made at the onset of bloom. Therefore, the impact of differential application times on residues could not be evaluated with cotton.

6.3.2.8 Effect of chemical on residue values

Figure 6-61 summarizes the daily mean residues of all 4 neonicotinoids in cotton floral nectar (Panel A) and extrafloral nectar (Panel B) normalized to 0.1 lb a.i./A based on the total application rate. For clothianidin, a distinction is made between the higher rate study (0.1 lb a.i./A x 2) and the lower rate study (0.08 lb a.i./A x 1). In interpreting these figures, it is important to recognize that a significant portion of the variation in residue data likely comes from the influence of study site and season of application. As discussed previously, the effect of site or season alone can result in a 10X to 100X difference among residue values in various matrices. Since no study involved application of multiple chemicals simultaneously, it is not possible to remove the influence of site or season when considering chemical-specific influences on residue values. For this reason, a regression line based on all log-transformed residue values is shown in order to help identify chemical-specific biases in the residue data.

Another important consideration when interpreting **Figure 6-61** is that the LOQ among the four neonicotinoids is approximately 1 µg ai/kg. When normalized to an application rate of 0.1 lb a.i./A, this LOQ equates to 0.3 µg ai/kg per 0.1 lb ai/A for imidacloprid; 0.4 µg ai/kg per 0.1 lb ai/A for dinotefuran; 0.5 – 1.2 µg ai/kg per 0.1 lb ai/A for clothianidin (high and low rate, respectively) and 0.8 µg ai/kg per 0.1 lb ai/A for thiamethoxam. Therefore, residue values in these figures which are at or below 1.0 µg ai/kg per 0.1 lb ai/A are subject to greater uncertainty due to assumptions made for analytical purposes (e.g., assuming < LOQ = ½ LOQ).

With floral nectar, the chemical-specific residue values overlap up to approximately 20 DALA (Panel A). One exception are residue data from the “low rate” clothianidin study, whereby residue values are commonly below the LOQ (1.2 µg ai/kg per 0.1 lb ai/A) beginning around DALA 14. Beyond DALA 20, greater differences are observed among the different chemicals, which may reflect differences in dissipation rates among other factors.

With extrafloral nectar, all four chemicals have overlapping residue values through 35 DALA. Overall variation is less than that observed with floral nectar. With the exception of a comparatively slower decline in imidacloprid residues over time, the influence of chemical on the normalized extrafloral residue values is not obvious based on **Figure 6-61**.

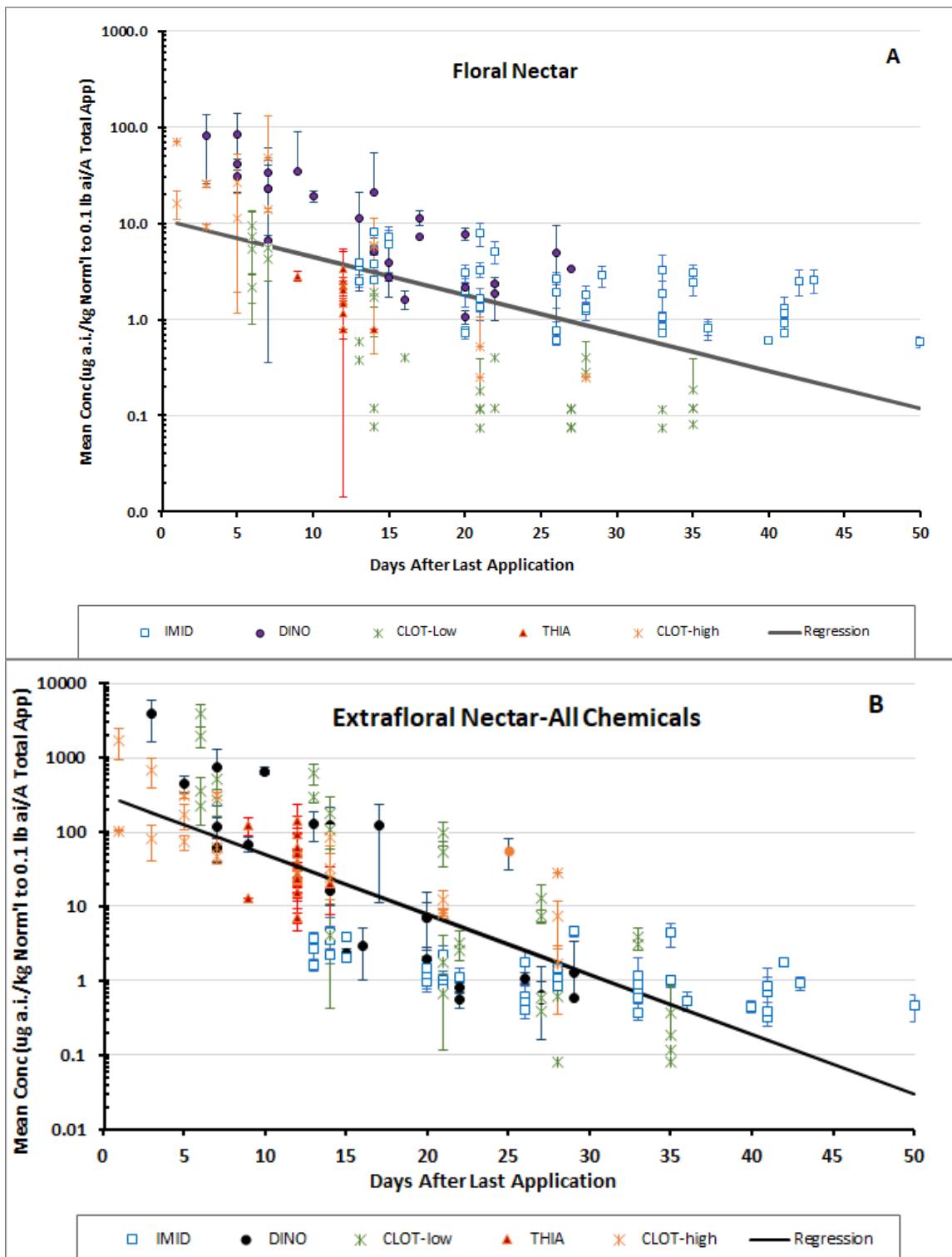
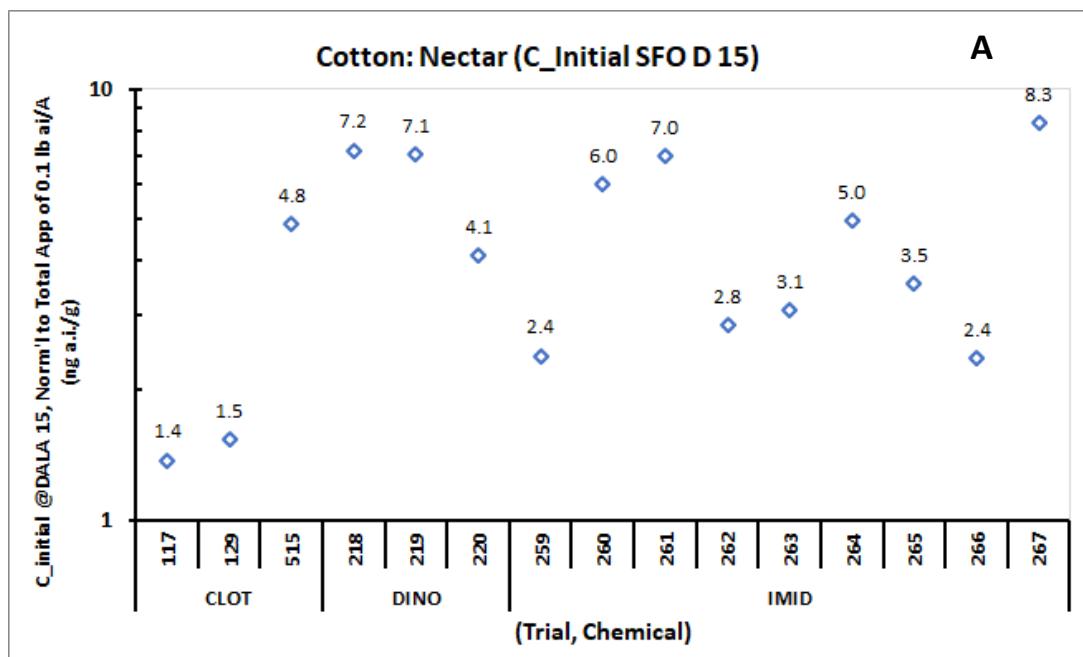


Figure 6-61. Mean neonicotinoid residues in cotton floral nectar (A) and extrafloral nectar (B) normalized to 0.1 lb a.i./A based on total foliar application. For clothianidin, a distinction is made between the higher rate study (0.1 lb a.i./A x 2) and the lower rate study (0.08 lb a.i./A x 1). The line represents least square regression on the log transformed residue data ($r^2 = 0.34$ for floral nectar and 0.65 for extrafloral nectar). Error bars = 95% confidence interval.

One of the difficulties of the approach shown in **Figure 6-61** is addressing the influence of time on the residue values, which may differ not only among chemicals, but among trials within a chemical. As discussed earlier, one approach for addressing the influence of time on residue values is to adjust the initial measured concentrations to a common DALA using the trial-specific dissipation rate constant (k). For the cotton residue studies, a DALA of 15 was chosen due to overlapping measurements at this time among the studies.

Figure 6-62 displays residue values for clothianidin, dinotefuran and imidacloprid C_{Initial} values adjusted to DALA 15 for floral nectar (Panel A) and extrafloral nectar (Panel B). These values are also normalized to 0.1 lb ai/A based on total application rates for comparative purposes. With floral nectar (Panel A), the time-adjusted residues among the three neonicotinoids with reliable estimates of “ k ” generally vary by an order of magnitude. This is a similar amount of variation seen with the influence of site and application season on residue values.

With extrafloral nectar (Panel B), the time-adjusted C_{Initial} values are 10X to 100X lower for imidacloprid compared to the other two chemicals. This may reflect chemical specific attributes of imidacloprid and suggests that bridging residues in extrafloral nectar should not be conducted across all chemicals. It is also worth noting that the imidacloprid data reflect three sites in relatively close proximity to one another (*i.e.*, Missouri).



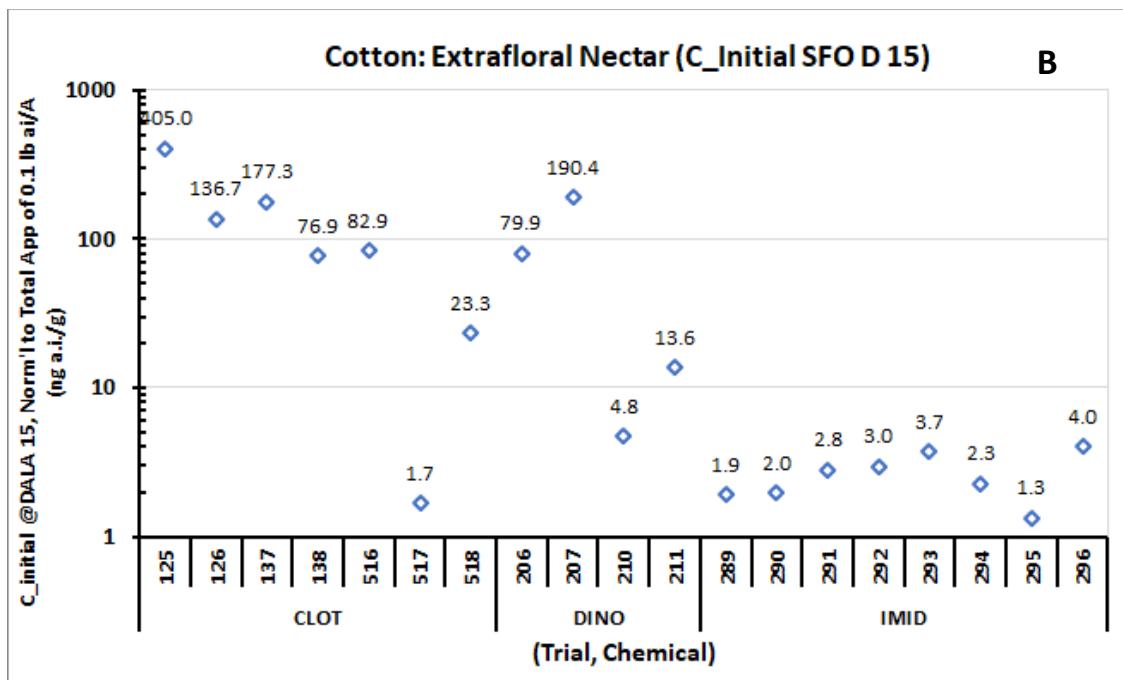


Figure 6-62. Initial concentration of neonicotinoids expressed as “C_{initial}” (adjusted to DALA 15) and normalized to 0.1 lb ai/A based on the last application (blue diamonds) and the total application rate (orange squares). Numbers represent different residue trials.

6.3.2.9 Bridging recommendations

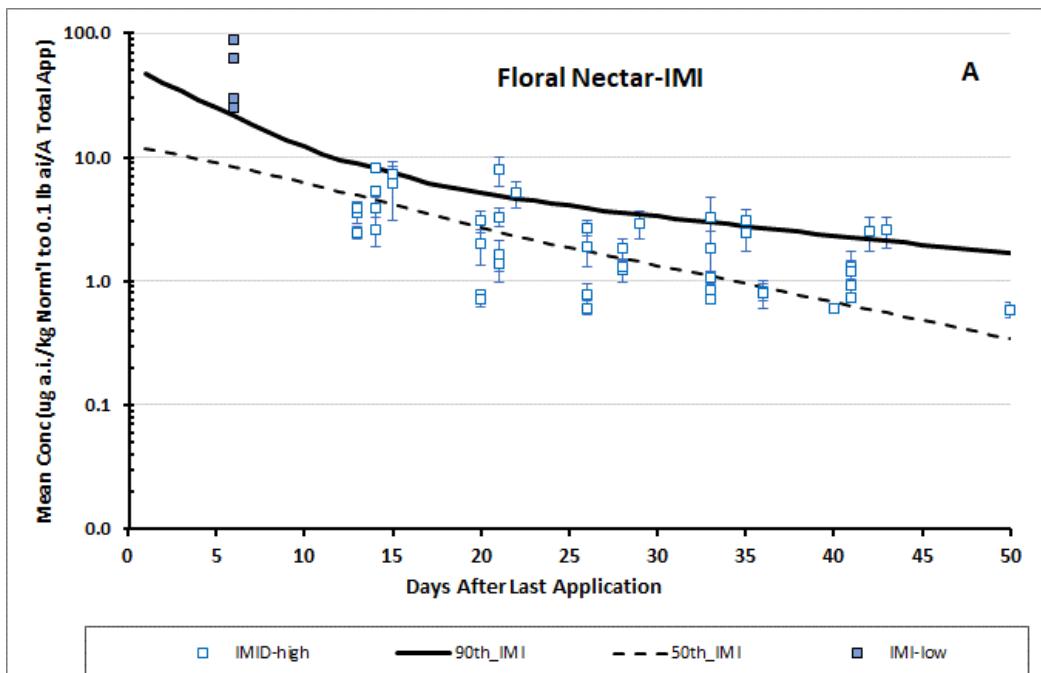
In summary, the previous analysis indicates that neonicotinoid residues in bee-relevant matrices of cotton following pre-bloom foliar applications can vary by up to two orders of magnitude due to differences associated with the study site or application season. The limited data available support the assumption that residues in cotton scale in proportion to application rate, which is consistent with results with other crop groups. With respect to the effect of chemical on residues, this analysis suggests that residues in floral nectar of cotton are comparable among imidacloprid, dinotefuran and clothianidin when adjusted to a common DALA, however, those in extrafloral nectar vary by up to 40X for these same chemicals. In addition, dissipation rate constants for imidacloprid appear to be substantially slower compared to dinotefuran or clothianidin. Given the differences observed in dissipation rate constants and C_{initial} values between imidacloprid, dinotefuran and clothianidin, it is recommended that the floral nectar and extrafloral nectar residues not be combined (bridged) among these three chemicals with cotton. Given the very limited available data for thiamethoxam and the similarity in its residues compared with clothianidin, it is recommended that residues in floral and extrafloral nectar be bridged with these two chemicals for risk assessment purposes.

In addition to evaluating oral risk to bees based on observed (measured) residue values in cotton floral nectar and extrafloral nectar, the aforementioned kinetic analysis of these residues can be used to support the modeling of decline curves in these matrices. Such modeling enables residues to be extrapolated (or interpolated) across different times after application where measured data are not available. Furthermore, this modeling enables variability in kinetic parameters (k, C_{initial}) to be incorporated into model results, which facilitates the derivation of residue decline curves with specified probabilities (e.g., 50th, 90th).

Based on Monte Carlo analysis of the residue dissipation rate constant (k) and the C_initial values presented in **Table 6-32** and methods described in **Section 4.5.5**, the 50th and 90th percentile dissipation curves for neonicotinoid residues in floral and extrafloral nectar of cotton are presented in **Figure 6-63** (for imidacloprid), **Figure 6-64** (for dinotefuran) and **Figure 6-65** (for clothianidin and thiamethoxam). These modeled dissipation curves in floral and extrafloral nectar are intended to be used as a line of evidence for characterizing the oral risk of the neonicotinoids to bees associated with their use on cotton.

Table 6-32. Summary statistics for dissipation rate constants (k) and initial concentrations (C_initial) of neonicotinoids in cotton nectar and extrafloral nectar adjusted to DALA 15 for use in Monte Carlo modeling of residue decline curves.

Chemical	K (1/d)				C_initial @ D15 (ng a.i./g per 0.1 lb a.i./A)			
	Mean	Std Dev.	Min-Max	n	Mean	Std Dev.	Min-Max	n
Extrafloral Nectar								
Imidacloprid	0.099	0.049	0.047-0.168	8	2.6	0.9	1.3-4.0	8
Dinotefuran	0.303	0.102	0.175-0.445	6	72.2	86	4.8-190	4
Thiamethoxam + Clothianidin	0.228	0.132	0.106-0.495	7	129	136	1.7-405	7
Floral Nectar								
Imidacloprid	0.088	0.067	0.021-0.203	9	4.5	2.2	2.4-8.3	9
Dinotefuran	0.276	0.115	0.109-0.462	3	6.1	1.7	4.1-7.2	3
Thiamethoxam + Clothianidin	0.160	0.029	0.127-0.178	3	2.6	2.0	1.4-4.8	3



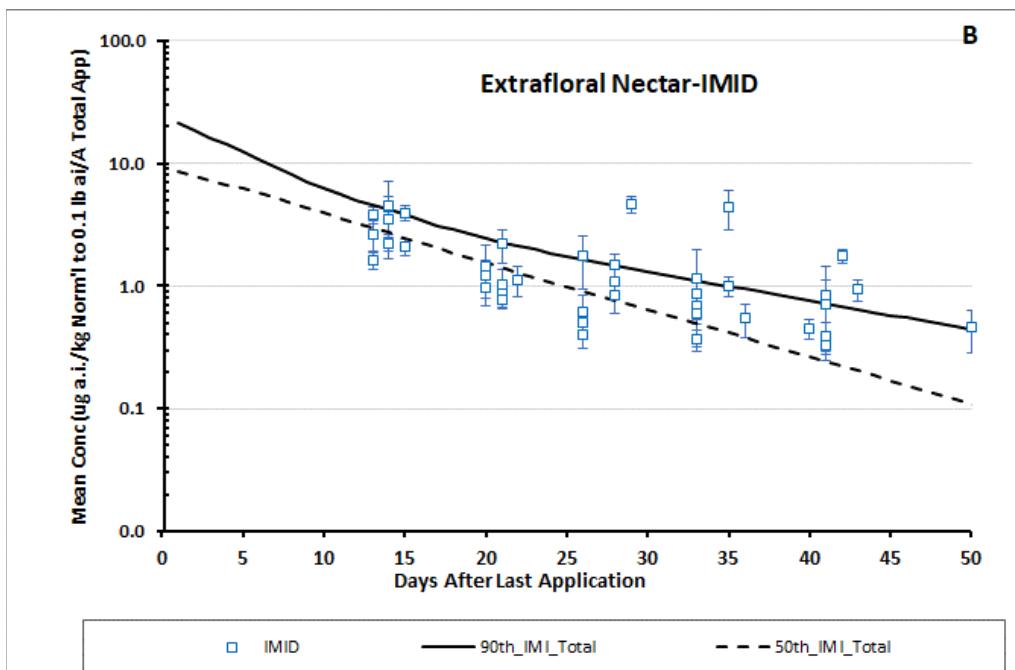
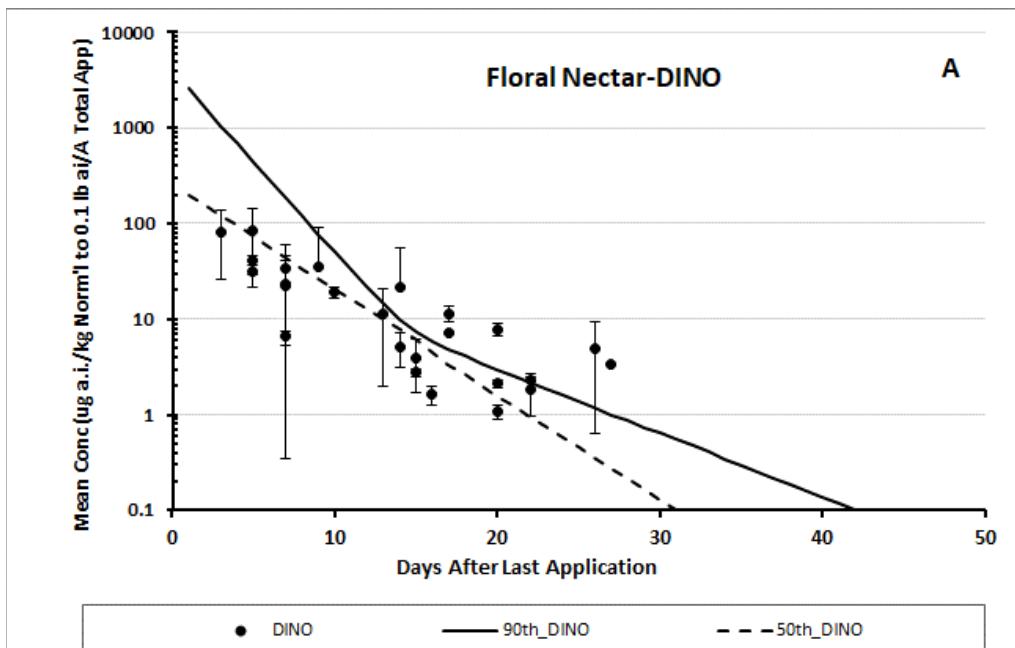


Figure 6-63. Dissipation curves and mean residues (with 95% confidence intervals) of total imidacloprid in floral nectar (A) and extrafloral nectar (B) of cotton following pre-bloom, foliar applications. Dashed line = 50th and solid line = 90th percentile residue decline curves derived from Monte Carlo analysis of residue kinetic parameters (k and $C_{initial}$). Residues are normalized to 0.1 lb a.i./A.



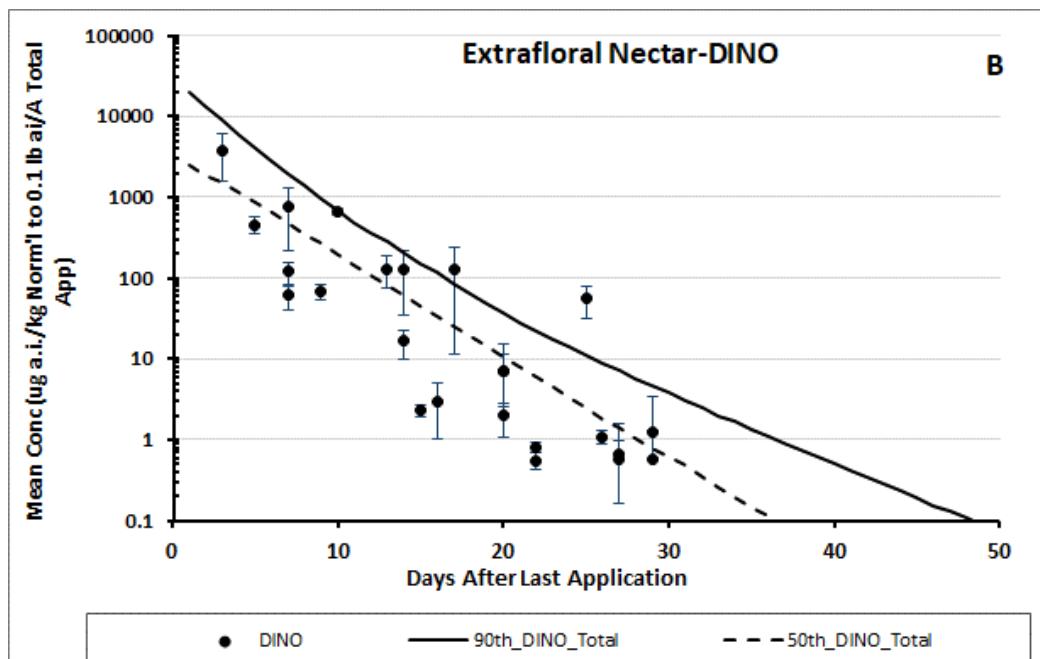
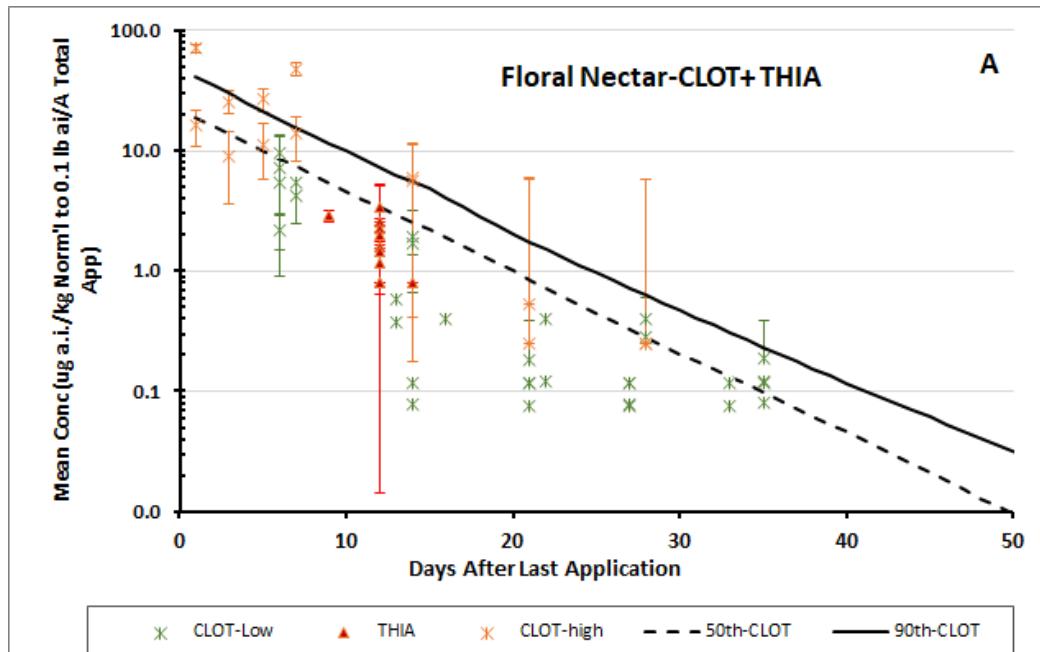


Figure 6-64. Dissipation curves and mean residues (with 95% confidence intervals) of dinotefuran in floral nectar (A) and extrafloral nectar (B) of cotton following pre-bloom, foliar applications. Dashed line = 50th and solid line = 90th percentile residue decline curves derived from Monte Carlo analysis of residue kinetic parameters (k and $C_{initial}$). Residues are normalized to 0.1 lb a.i./A.



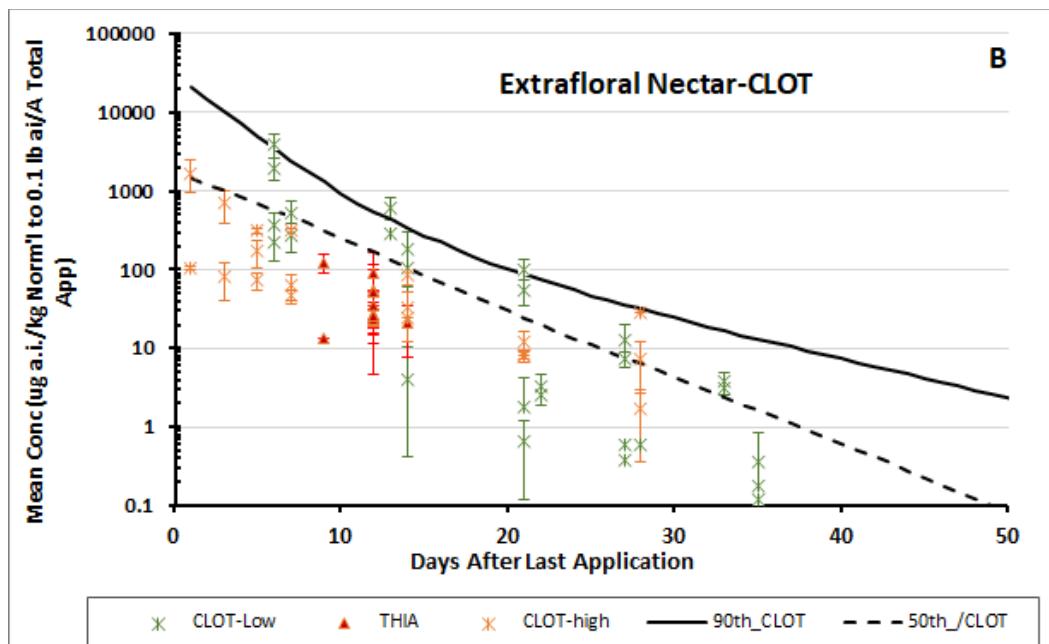


Figure 6-65. Dissipation curves and mean residues (with 95% confidence intervals) of clothianidin and thiamethoxam in floral nectar (A) and extrafloral nectar (B) of cotton following pre-bloom, foliar applications. Dashed line = 50th and solid line = 90th percentile residue decline curves derived from Monte Carlo analysis of residue kinetic parameters (k and $C_{initial}$). Residues are normalized to 0.1 lb a.i./A. CLOT=clothianidin, THIA = Thiamethoxam (expressed as clothianidin equivalents).

6.3.3 Soil Applications

With the four neonicotinoids under consideration, soil applications to oil seed crops (cotton) are only registered for imidacloprid. Therefore, a bridging analysis was not conducted with residue data from soil applications to cotton.

6.4 Root and Tuber Crops

6.4.1 Crops of Concern for Bees

According to USDA (2017), the following root and tuber crops are considered attractive to honey bees but are either not harvested prior to bloom (sweet potato) or there is no indication on the harvest relative to bloom (Jerusalem artichoke, edible burdock, dasheen and horseradish).

6.4.2 Considerations of Crop Biology/Physiology

Many of the vegetables in the root and tuber group are not considered attractive to honeybees or they are harvested prior to bloom (unless used in seed production). Potatoes (the crop for which residue data are available) do not produce nectar, and the pollen they produce is considered attractive to both bumblebees and solitary bees but not honeybees.

6.4.3 Foliar Applications

6.4.3.1 Summary of label rates/restrictions

All four neonicotinoids are registered for use on the root and tuber crop group, with varying use restrictions. There are no use restrictions on imidacloprid, while clothianidin, dinotefuran, and thiamethoxam restrict some applications at bloom (*e.g.*, applications of thiamethoxam are allowed after all petals have fallen; 100% petal drop). The maximum rates for foliar applications of these chemicals are included in **Table 6-33**.

Table 6-33. Foliar application rates (in lb a.i./A) and number of applications (x n) for neonicotinoids on root and tuber vegetables (based on current labels).

Root and Tubers	Imidacloprid	Clothianidin	Thiamethoxam* ⁹	Dinotefuran
Root and Tuber (except below)	0.04 x3	0.05 X 4	0.043 X 2	0.068 X 3
Potato (Irish)	0.05 X 4	--	0.043 X 2	0.068 X3 (0.198 seasonal)
Sugar beet	--	--	0.053 X 2	0.068 X 3 0.203

*Expressed as clothianidin equivalents.

6.4.3.2 Available residue data

Anther and pollen residue data are available for foliar spray applications of clothianidin on potatoes (**Table 6-34**). Pre-bloom foliar applications were made in June/July of 2015 at a nominal application rate of 0.05 lbs a.i./A. Soils were characterized as coarse-textured, moderate coarse-textured, or medium-textured. After the application and throughout the bloom duration, leaves and flowers were collected and analyzed for residue concentrations. Flowers were harvested to obtain anthers and nectar. Anthers are considered here as a surrogate for pollen when pollen specific residues are not available.

Table 6-34. Residue studies with foliar applications of clothianidin to potatoes.

Crop	Chemical	# sites (Locations)	App. Rate x # of apps (interval)	# Seasons	# sampling events (per season)	MRID (Classification)
Potato	Clothianidin	4 (ND, CA, OR-1, OR-2)	0.05 lb a.i./A X 1 (NA)	1	3	49705902 (Acceptable)

A summary of clothianidin residue data for pollen/anthers is presented in **Figure 6-66**. In this study, 16/47 (34%) of the samples were below the limit of detection and limit of quantification (LOD/LOQ) and were confined to two sites in North Dakota and Oregon. When normalized to the 0.1 lb a.i./A, residue

⁹ Clothianidin is a major degradate of thiamethoxam forming in plants. Residue studies based on thiamethoxam application measured both a.i.s in relevant matrices. To account for residues from both chemicals, measured thiamethoxam residues were converted a clothianidin equivalent based on the molecular weight ratio and residues from both chemicals were summed to obtain the final residue value. This applies to all thiamethoxam residue values.

concentrations in pollen/anthers generally decrease over time but these trends are not readily distinguished as the pollen and anther data are variable and limited. The North Dakota site had no residues above the LOD, and one site in Oregon had only one time point (*i.e.*, the earliest) above the LOD.

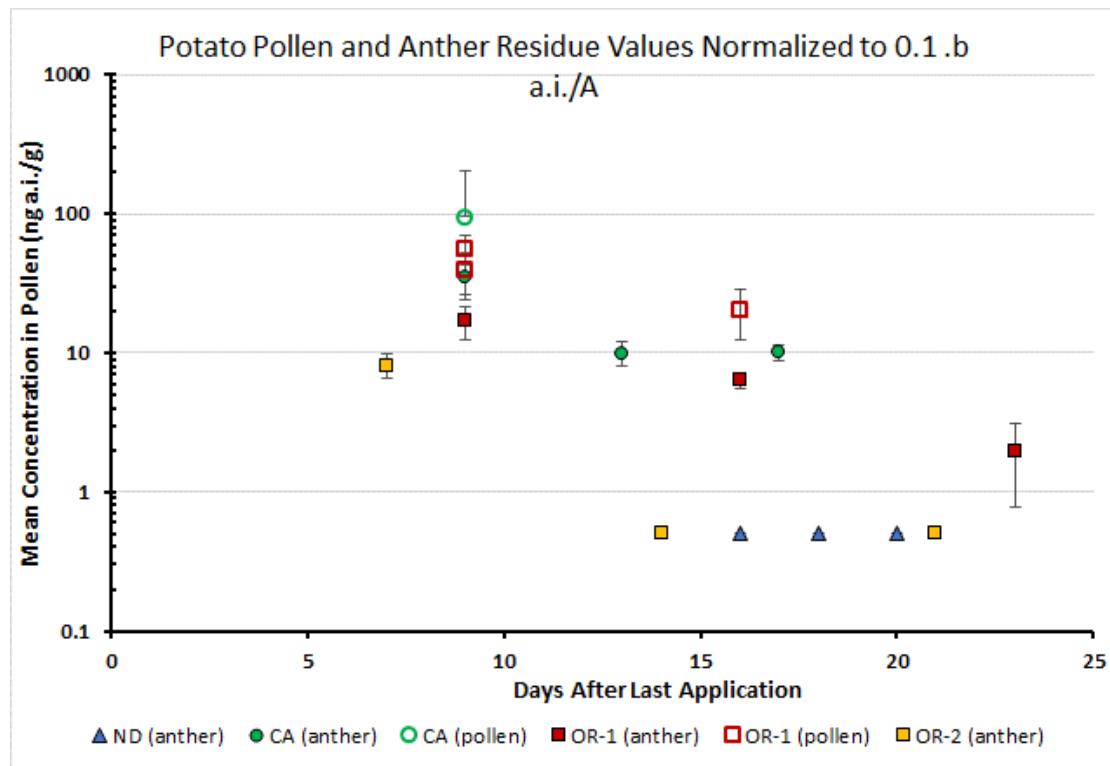


Figure 6-66. Clothianidin residues in pollen (open symbols) and anthers (closed symbols) following foliar application to potatoes in California (CA), Oregon (OR) and North Dakota (ND). Residues were normalized to a total application rate of 0.1 lb a.i./A. Error bars = 95% confidence interval.

6.4.3.3 Bridging needs (gaps)

Table 6-35 identifies data gaps for registered foliar applications of neonicotinoids on root and tuber vegetables that are attractive to bees. Clothianidin use on Potato were the only respective chemical and crop for which residues resulting from foliar spray data were available. Other potential uses relevant to honeybees include bridging conclusions to sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish. One major limitation of the available study is a lack of nectar concentration data.

Table 6-35. Residue data gaps for neonicotinoid foliar applications to root and tuber crop group.

Root and Tuber	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
sweet potato, Jerusalem artichoke, edible burdock, dasheen and horseradish	No data	Potato (MRID 49705902)	No data	No data

6.4.3.4 Influence of Sampling Day (Time), Site, Crop and Chemical on Residue Values

The influence of crop and chemical on neonicotinoid residues in root/tuber crops following foliar applications cannot be evaluated since data are available for only one chemical (clothianidin) and one

crop (potato). Regarding the effect of time on residue values, there appears to be some general declining trend within a site with increasing number of days after application. However, data are too limited to conduct a robust analysis of residue kinetics as was done for other crops (*e.g.*, cotton, berries, cucurbits). Regarding the influence of site, mean residues of clothianidin in potato pollen/anthers vary by up to 10X when compared on the same day after application (DALA 9 and 16; **Figure 6-66**).

6.4.3.5 Bridging Recommendations

Residue data resulting from foliar applications for the root and tuber crop group only are available for potatoes. The utility of extrapolating these residues to other members of the group is uncertain. This uncertainty is driven by the number of samples with residues below the LOD, the limited number of crops, and limited sample size. Furthermore, potatoes do not produce nectar; however, other root/tuber crops produce nectar (*e.g.*, sweet potatoes). Therefore, utilizing data on pollen alone to characterize exposure from residues in both pollen and nectar is an uncertainty which suggests the need for additional lines of evidence to more fully characterize exposure for this group. Consequently, it is recommended that residue data from other herbaceous crop groups (including cucurbits, oilseeds, and legumes) be used to characterize potential exposure from pre-bloom foliar applications of the neonicotinoids to root and tuber crops.

6.4.4 Soil Applications

6.4.4.1 Summary of label rates/restrictions

Like foliar spray use, clothianidin, dinotefuran, imidacloprid, and thiamethoxam are all registered for use as a soil application to root and tuber vegetables. The maximum rates for soil applications of these chemicals are included in **Table 6-36**.

Table 6-36. Soil application rates (in lb a.i./A) and number of applications (x n) for neonicotinoids on roots and tuber crop group (based on current labels).

Root and Tubers	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
Root and Tuber (except below)	0.38 X 1	0.2 X 1	0.16 X 1	0.34 X 1
Potato	0.18 X 1	--	--	--
Sugar beet	0.31 X 1	--	--	--

*Expressed as clothianidin equivalents.

6.4.4.2 Available residue data

Data are available for clothianidin and dinotefuran from 2 studies of potato **Table 6-37**. The clothianidin in-furrow soil applications were made at planting (in 2015) using the maximum annual application rate of 0.2 lbs ai/A at the same sites used in the aforementioned foliar application study. Dinotefuran was applied via soil application (in 2015) at 0.34 lbs ai/A. Flowers were harvested and used to collect anthers during early, mid, and late bloom to examine residue decline.

Table 6-37. Residue studies for root and tuber crops with soil applications of clothianidin and dinotefuran in California (CA), North Carolina (NC), North Dakota (ND), and Missouri (MO).

Crop	Chemical	# sites (Locations)	Appl. Rate x # of apps (interval)	# Seasons	# sampling events (per season)	MRID (Classification)
Potato	Clothianidin	4 (ND, CA, OR-1, OR-2)	0.02 lb a.i./A X 1 (NA)	1	3	49705902 (Acceptable)
	Dinotefuran	3 (NC, MO, CA)	0.34 lb a.i./A X 1 (NA)	1	3	49841001 (Acceptable)

A summary of the pollen/anther residue data from soil applications to potato normalized to 0.1 lb a.i./A based on total application rate is provided in **Figure 6-67**. Among the two neonicotinoids, sites and matrices, mean residues vary by 2 orders of magnitude, from 0.2 to 46 ng a.i./g per 0.1 lb a.i./A. A decline trend of residues with increasing sampling day is seen at one site (OR-1) with clothianidin, but not for other sites or with dinotefuran. The lack of a consistent declining trend with increasing time after application with soil applications to potato is consistent with results from soil applications to other crops (*e.g.*, cucurbits, orchard crops).

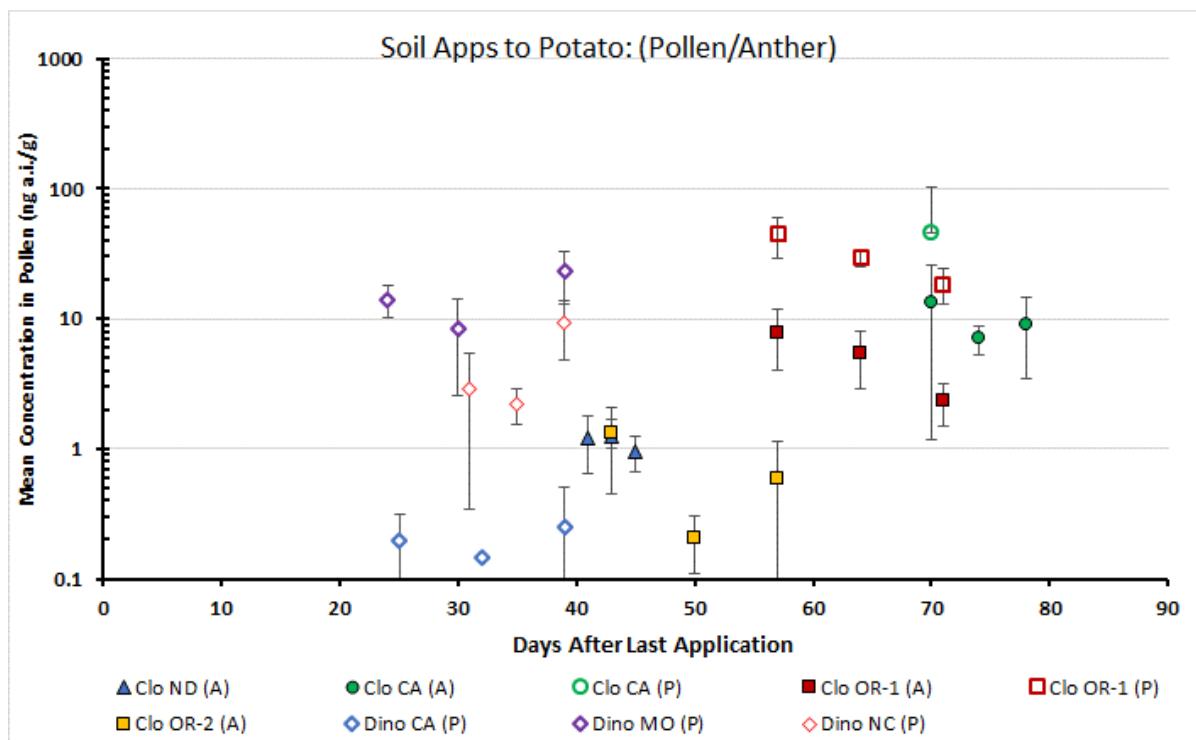


Figure 6-67. Summary of mean anther (closed markers)/pollen (open markers) residues ($\mu\text{g}/\text{kg}$) of clothianidin and dinotefuran in potatoes (normalized to total app. rate of 0.1 lb a.i./A) sampled in California (CA), Missouri (MO) North Dakota (ND) and Oregon (OR). Error bars = 95% confidence interval.

5.1.4.3 Bridging needs (gaps)

Table 6-38 Identifies data gaps for registered soil applications of neonicotinoids on root and tuber crop group. Potato data are available for clothianidin and dinotefuran; however, similar data are not available for imidacloprid and thiamethoxam. There are gaps for residues in potential uses relevant to honeybees including: sweet potato, Jerusalem artichoke, edible burdock, dasheen, and horseradish.

Table 6-38. Residue data gaps for neonicotinoid soil applications to root and tuber crop group.

Root and Tubers	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Sweet potato, Jerusalem artichoke, edible burdock, dasheen, horseradish	No data	Potato (MRID 49705902)	No data	Potato (MRID 49841001)

6.4.4.3 Influence of Sampling Day (Time), Site, Crop and Chemical on Residue Values

The available residue data for soil applications to root/tuber crops are limited in quantity and scope and therefore, do not support a robust evaluation of dissipation kinetics similar to that conducted for other crops (*e.g.*, berries, cotton, cucurbits, orchard crops). Therefore, no formal analysis of the influence of sampling day on the residue values was conducted. Similarly, with respect to the influence of crop, no analysis was conducted since data were available for only one crop (potato).

The influence of site on residue values is evident within each of the chemicals represented (**Table 6-39**). Mean residues in pollen/anther among sites vary by up to 100X for clothianidin and dinotefuran. Since no consistent trend with residue values and time after application, comparison of mean values among sites/trials is reasonable. Based on mean normalized values among sites, clothianidin residues in potato pollen/anther (11.7 ng a.i./g) are within 2X of those for dinotefuran (7.2 ng a.i./g). Furthermore, the overall range in residue values for the two chemicals among sites is similar.

Table 6-39. Summary statistics for neonicotinoid residues in pollen/anthers in potato following soil applications at various sites. Values are normalized to a total app. rate of 0.1 lb a.i./A.

Chemical/Site	Concentration in pollen/anther (ng a.i./g per 0.1 lb a.i./A)			n
	Mean	Min	Max	
Clothianidin	11.7	0.1	93.8	47
California	19.0	4.6	93.8	12
North Dakota	1.1	0.6	1.7	9
Oregon 1	17.9	1.7	57.0	17
Oregon 2	0.7	0.1	1.5	9
Dino	7.2	0.1	30.5	28
California	0.2	0.1	0.5	9
Missouri	15.2	4.1	30.5	9
North Carolina	4.8	1.5	13.1	9
Oregon 1	20.5	20.5	20.5	1

6.4.4.4 Bridging Recommendations

Residue data resulting from soil applications to the root and tuber crop group are available only for potatoes treated with clothianidin and dinotefuran. Similar to foliar applications, the utility of extrapolating these residues to other members of the crop group is uncertain. There are only a limited number of species within this crop group that are not harvested prior to bloom and/or produce pollen/nectar that is considered attractive to honeybees. Thus, the likelihood of exposure to honeybees from use of neonicotinoids on root and tuber is limited to a small subset of crops including sweet potato, Jerusalem artichoke, edible burdock, dasheen, and horseradish.

When normalized to the same application rate, residue concentrations generally appear similar across sampling events and are not remarkably distinguishable between chemicals as they all overlap in magnitude. Since these data come from different sites, it is not possible to distinguish the potential contribution of site from chemical on the residue values in potato pollen. However, it is apparent that chemical does not contribute an overriding influence on residue values within the context of differences among sites.

Based on the available data and since the studies were conducted on a single crop (*i.e.*, potato) and within a single year, it is not possible discern if crop or year influence the expression of residues in pollen within root and tuber crops. Due to the limited data for potatoes (a non-nectar producing crop), it is recommended that data from other herbaceous crops (cucurbits, cotton, and legumes) be used to characterize exposure to residues from soil treatments of bee-attractive root and tuber crops with the four neonicotinoids.

6.5 Legumes

6.5.1 Crops of Concern for Bees

Soybeans are part of the legume crop group and are considered attractive to bees as a source of both attractive pollen and nectar; however, bees are not required for soybean pollination (USDA 2017). Some members of the legume crop group including broad beans and snap beans are considered highly attractive to bees and require bee pollination. Consequently, exposure is expected for bees on treated crops within this group.

6.5.2 Foliar Applications

6.5.2.1 Summary of label rates/restrictions

Three neonicotinoids (clothianidin, imidacloprid, and thiamethoxam) are registered for use on this crop group with varying restrictions. There are no restrictions on imidacloprid, while clothianidin and thiamethoxam restrict application at bloom (thiamethoxam no apps until all petals have fallen). Foliar applications are registered for soybean only for thiamethoxam and clothianidin, while imidacloprid is registered for other legume vegetables. The maximum rates for foliar applications of these chemicals are included in **Table 6-40**.

Table 6-40. Foliar application rates (in lb a.i./A) and number of applications (x n) for neonicotinoids on legumes (based on current labels).

Legumes	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Soybean	0.04 X 3	0.05 X 4	0.043 X 2	NR
Other legumes	0.04 X 3	NR	NR	NR

NR = not registered

6.5.2.2 Available residue data

A total of 3 studies are available which quantified residues of thiamethoxam or imidacloprid of bee-relevant matrices following foliar application to soybeans (**Table 6-41**). With the thiamethoxam study (MRID 50265503), two foliar applications were made 12 and 5 days prior to bloom at two sites (Iowa, Louisiana) and at 17 and 10 days prior to bloom at one site (North Carolina). Pollen collection was attempted using bees (*i.e.*, corbicular pollen) but this was unsuccessful. Residues in anther were therefore used as a surrogate for pollen based on the inter-tissue extrapolation analysis presented in **Section 5.4**. Nectar was also collected from foraging bee honey stomachs as attempts to collect nectar from combs were unsuccessful. Residue samples were taken between 5 and 20 days after application depending on the site.

The two imidacloprid studies had identical study designs but were conducted in different years (2014 and 2015). In each study, three replicate plots of soybeans at one site in Brazil were treated with two foliar applications (10 days apart) prior to bloom. Samples of bee-collected and comb-collected pollen and nectar were taken at 4 time periods after the last foliar application. Honey bee colonies were tented during the sample collection portion of the study.

Table 6-41. Residue studies for soybean foliar applications of thiamethoxam and imidacloprid.

Crop	Chemical	# sites (Locations), Timing	Appl. Rate, # of apps (interval)	# Seasons	# sampling events (per season)	MRID (Classification)
Soybean	Thiamethoxam	3 (NC, LA, IA), Pre-bloom	0.063 lb a.i./A X 2 (7 d)	1	3	50265503 (Acceptable)
	Imidacloprid	1 (Brazil), Pre-bloom (2014)	0.089 lb a.i./A X 2 (10 d)	1	4	50025901 (Supplemental)
		1 (Brazil), Pre-bloom (2015)	0.089 lb a.i./A X 2 (10 d)	1	4	50025902 (Supplemental)

Results from the thiamethoxam study are summarized in **Figure 6-68**. Overall, thiamethoxam residues in anthers and bee-collected nectar (expressed as clothianidin equivalents and normalized to 0.1 lb a.i./A) are relatively low (< 10 ng c.e./g for anthers and < 1 ng c.e./g for nectar). Residues in anthers show a declining trend with increasing days after application while those in bee-collected nectar were relatively stable; but many are below the LOD or LOQ.

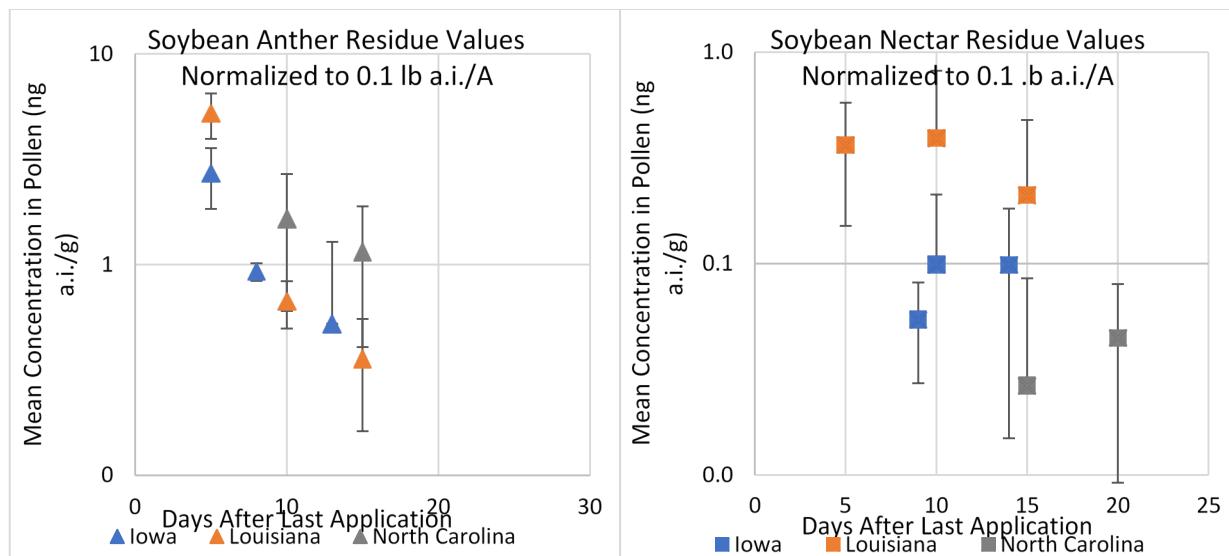


Figure 6-68. Summary of mean anther and bee-collected nectar residues of thiamethoxam (Thia) and in soybeans (normalized to 0.1 lb a.i./A) from Iowa (IA), Louisiana (LA) and North Carolina (NC).

Results for the two imidacloprid studies are summarized in **Table 6-42** and also indicate low levels in bee-collected pollen and nectar. Residues in bee-collected pollen and nectar from the 2014 study were all below the level of detection. A few detections were reported for the 2015 study, but most values were below the LOQ/LOD.

Table 6-42. Summary of imidacloprid residues (normalized to 0.1 lb a.i./A) in soybean matrices following foliar application.

MRID	DALA	Total Imidacloprid (ng a.i./g per 0.1 lb a.i./A)		n
		Mean	Min-Max	
Nectar from Bees				
50025901	16-18, 22, 25	< LOD/LOQ*	NC	15
50025902	26, 27, 33	< LOD/LOQ	NC	9
	29	1.4	< LOD-2.8	3
Pollen from Bees/Trap				
50025902	33	1.9	NC	1

* LOD and LOQ for total imidacloprid (sum of parent, imidacloprid olefin and 5-hydroxy imidacloprid) are 0.8 and 0.45 ng/g

NC = not calculated due to non-detects

6.5.2.3 Bridging needs (gaps)

Table 6-43 identifies data gaps for registered foliar applications of neonicotinoids on legumes. Soybean data are available for thiamethoxam and imidacloprid. Other potential uses of imidacloprid on honey bee-attractive legumes include other peas, beans, and peanuts.

Table 6-43. Residue data gaps for neonicotinoid foliar applications to legume crop group.

Legumes	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Soybean	MRIDs 50025901, 50025902	No data	MRID 50265503	NR
Other legumes	No data	NR	NR	NR

NR = not registered

6.5.2.4 Influence of Sampling Day (Time), Site, Crop and Chemical on Residue Values

The available residue data for legumes are very limited in quantity and scope and therefore do not support a robust evaluation of dissipation kinetics similar to that conducted for other crops (e.g., berries, cotton, cucurbits, orchard crops). Therefore, no formal analysis of the influence of sampling day on the residue values was conducted. Similarly, with respect to the influence of crop, no analysis was conducted since data were available for only one crop (soybean).

Regarding the influence of site, results from the thiamethoxam study indicate that residues in anthers vary within an order of magnitude among sites sampled at similar times after foliar application. Results from the imidacloprid studies were all conducted at one site and are mostly below LOD/LOQ and thus, are not applicable for evaluating site-to-site differences.

Evaluating the effect of chemical is uncertain given the paucity of data available. With both thiamethoxam and imidacloprid, residues in anthers/pollen are < 10 ng a.i./g per 0.1 lb a.i./A and those for bee-collected nectar are < 1.4 ng a.i./g per 0.1 lb a.i./A.

6.5.2.5 Bridging Recommendations

Residue data resulting from foliar applications for the legume crop group are available for soybean, which is the only crop within the legume group that is registered for use of thiamethoxam and clothianidin. Imidacloprid is registered for foliar applications to the entire legume crop group; therefore, there is a need to quantify exposure from imidacloprid to the legumes. The utility of extrapolating these residues to other members of the group is uncertain because no data are available to allow comparisons across different legume crops. Based on the available data it is uncertain to reliably tell if there is a chemical specific difference for soybean crops. For both imidacloprid and thiamethoxam, residues are relatively low, and many were below levels of detection or quantitation. For assessing risks associated with clothianidin applications to soybean, it is recommended that the thiamethoxam data be bridged to clothianidin. For assessing risks of imidacloprid to bee-attractive legumes, it is recommended that the imidacloprid and thiamethoxam data be bridged.

6.5.3 Soil Applications

There are no data for soil applications of neonicotinoids to legumes. Imidacloprid is the only chemical with registered soil applications to legumes. In the absence of data risks will be bridged from the analysis done for soil applications to other herbaceous crops, including cucurbits, oilseeds, and fruiting vegetables.

6.6 Fruiting Vegetables

6.6.1 Crops of Concern for Bees

According to the USDA crop attractiveness guidance (USDA 2017), the majority of crops that fall within the fruiting vegetable group are not attractive to honey bees. Many are attractive to other bees, such as bumble bees (*Bombus* spp). The following fruiting vegetable crops are considered attractive to honey bees:

- okra and roselle (producing pollen and nectar)
- chilis and peppers (producing pollen only).

6.6.2 Foliar Applications

6.6.2.1 Summary of label rates/restrictions

Imidacloprid is registered for pre-and post-bloom applications on fruiting vegetables, while, thiamethoxam is registered for applications after petal fall (i.e., no pre-bloom or at bloom applications). Dinotefuran is registered for pre- and post-bloom applications only. Clothianidin is not registered for any crops in the fruiting vegetable group. The maximum rates for foliar applications of these chemicals are included in **Table 6-44**.

Table 6-44. Foliar application rates (in lb a.i./A) and number of applications (x n) for neonicotinoids on fruiting vegetables (based on current labels).

Fruiting Vegetables	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
All Crops	0.08 X 3	NR	0.075 X 2	0.179 X1 and 0.09 X1 (total 0.27)

*expressed as clothianidin equivalents

NR = not registered

6.6.2.2 Available residue data

Residue data associated with foliar applications to fruiting vegetables are available for two chemicals (thiamethoxam and dinotefuran) with one crop (tomato; **Table 6-45**). Only pollen residue data are available for tomato since they do not produce nectar. Although tomatoes are not attractive to honey bees, bumble bees are used for commercial pollination of tomatoes in greenhouses. With the thiamethoxam study, residues are also available for flowers. Since two members of the honey bee attractive fruiting vegetables produce nectar (okra, roselle), there is a need to assess exposure via nectar. Therefore, based on the inter tissue analysis presented in **Section 5.5**, residue data for flowers are used as a surrogate for nectar based on multiplication by a factor of 0.3.

With the thiamethoxam study, two pre-bloom foliar applications were made to tomato plants in 2015 at a nominal application rate of 0.075 lbs ai (c.e)/A at 3 sites: Kansas, Alabama, and California. With the dinotefuran study, application rates 0.089 and 0.180 lb a.i./A were used for the first and second foliar applications, respectively. The first application was made approximately 9 days prior to first flower opening.

Table 6-45. Residue studies for tomato crops with foliar applications of thiamethoxam or dinotefuran.

Crop	Chemical	# sites (Locations)	Application information (rate x # of apps & interval)	# Seasons	# sampling events (per season)	MRID (Classification)
Tomato	Thiamethoxam	3 (KS, AL, CA)	0.075 lb a.i./A X 2 (5)*	1	3	49804101 (Acceptable)
	Dinotefuran	3 (NC, MO, CA)	0.089 lb a.i./A X 1, 0.180 lb a.i./A X 1 (7)	1	3	49841004 (Acceptable)

*expressed as clothianidin equivalents

6.6.2.3 Bridging needs (gaps)

Table 6-46 Identifies data gaps for registered foliar applications of neonicotinoids on tomato. Tomato was the only crop for which foliar data were available. Other potential uses relevant to honeybees include bridging conclusions to chili peppers, okra, and roselle.

Table 6-46. Residue data gaps for neonicotinoid foliar applications to fruiting vegetables.

Fruiting Vegetables	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Non-honey bee attractive crops	No data	NR	Tomato (MRID 49804102)	Tomato (MRID 49841004)
Okra, Chili Peppers, and Roselle	No data	NR	No data	No data

NR = not registered

Daily mean residue values of thiamethoxam (expressed as clothianidin equivalents) and dinotefuran in tomato pollen following pre-bloom foliar applications are shown in **Figure 6-69**. These residue values are normalized to 0.1 lb a.i./A based on the last application rate. For each chemical, a general declining trend in mean residue values with increasing time after application is both within a site (trial) and among sites. Between 4 and 10 DALA, mean residue values of thiamethoxam and dinotefuran vary between 1,000 and 10,000 ng a.i./g when normalized to 0.1 lb a.i./A. By 10-22 DALA, mean residues vary from about 5 to 370 ng a.i./g.

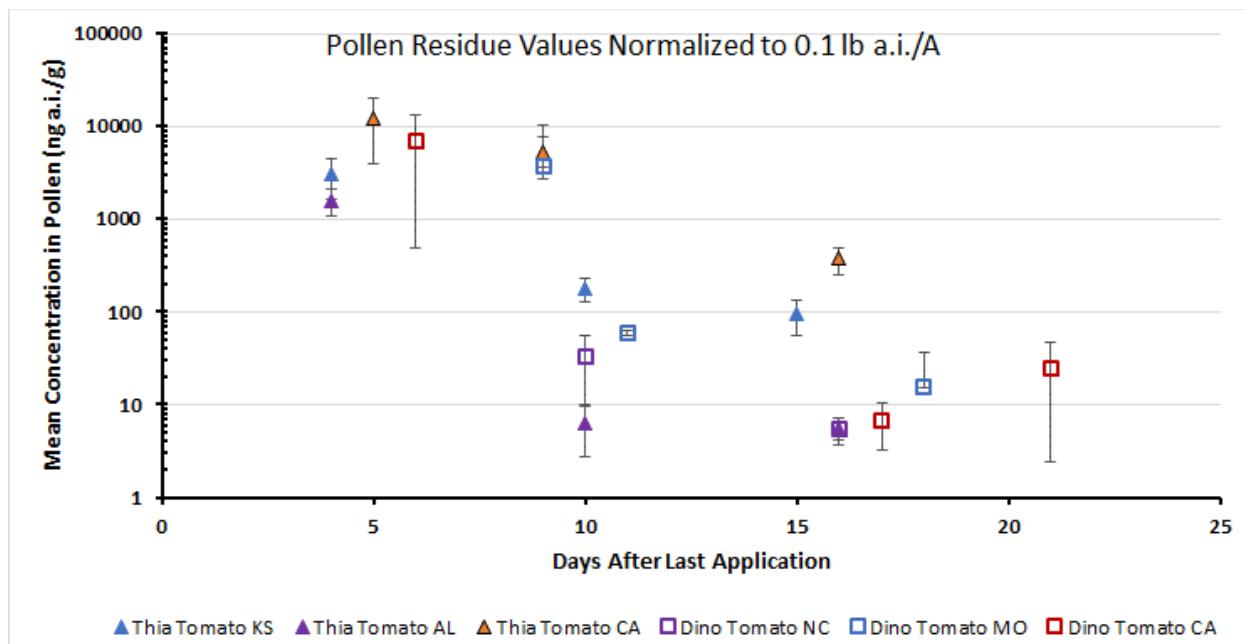


Figure 6-69. Summary of mean (+/- 95% CL) pollen residue concentrations of thiamethoxam (triangles) and dinotefuran (squares) in tomatoes (normalized to 0.1 lb a.i./A) sampled in Alabama (AL), California (CA), Kansas (KS), Missouri (MO), and North Carolina (NC). Thiamethoxam residues are expressed as clothianidin equivalents.

Daily mean residue values of thiamethoxam (expressed as clothianidin equivalents) in tomato flowers following pre-bloom foliar applications are shown in **Figure 6-70**. These residues have been multiplied by 0.3 to provide an estimate of expected concentrations in nectar, as described in **Section 5.5**. Again, a general declining trend is seen over the 12-d sampling period. However, the initial residue measurements on DALA 4 are about 10X lower than those measured in pollen.

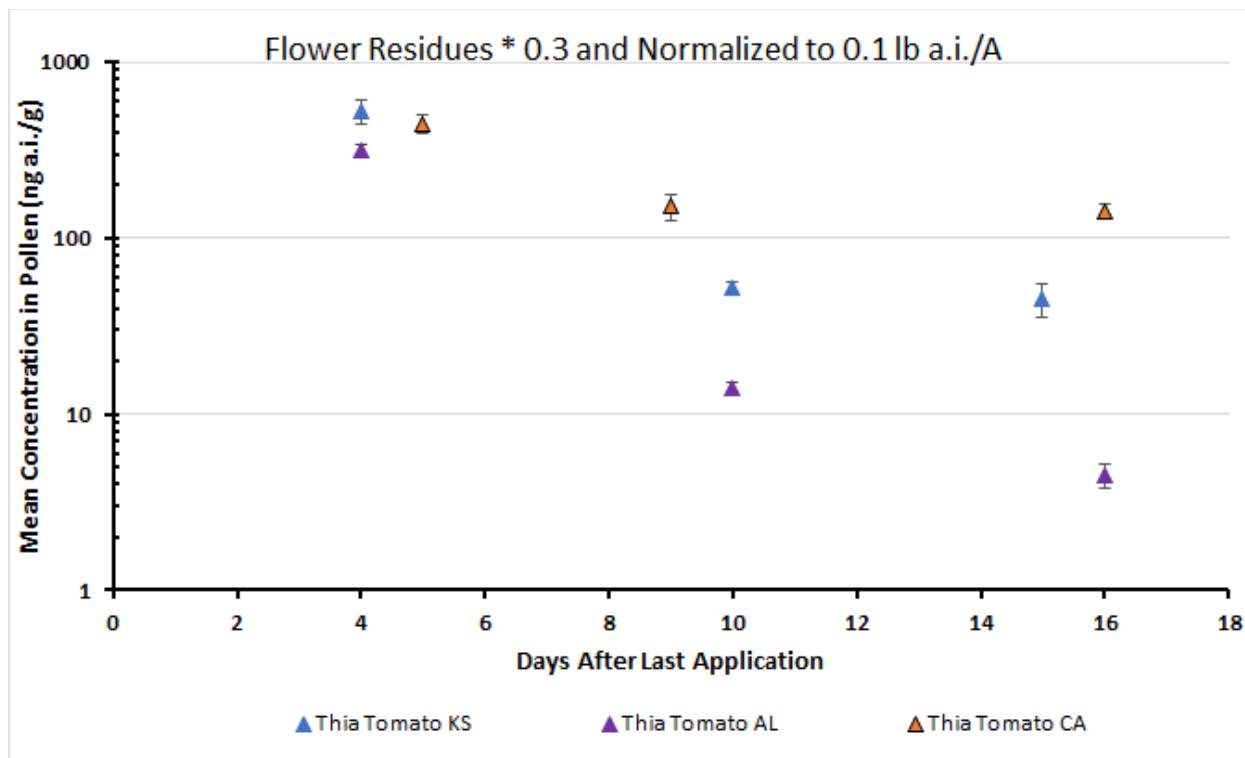


Figure 6-70. Summary of mean (+/- 95% CL) flower residue concentrations (multiplied by 0.3) in thiamethoxam used as a surrogate for nectar of thiamethoxam and dinotefuran in tomatoes (normalized to 0.1 lb a.i./A) sampled Alabama (AL), California (CA), and Kansas (KS). Thiamethoxam residues are expressed as clothianidin equivalents.

6.6.2.4 Influence of Sampling Day (Time), Site, Crop and Chemical on Residue Values

Given the consistent decreasing trends in residue values over time with the tomato data, the residue decline kinetics were evaluated in accordance with **Section 4.5.4**. Data were screened to eliminate trials with high variability across replicates and trials with stable dissipation curves (LCL of $k < 0$, $R^2 < 0.2$, and $P > 0.1$). A summary of data evaluated for the single first order dissipation rate constant (k) for all trials with sufficient data is presented in **Table 6-47**. Some sites did not have sufficient data for k analysis (*i.e.*, thiamethoxam AL – pollen; dinotefuran NC). Of the 5 trials with reliable estimates of ‘ k ’, residue values declined rapidly over time with half-lives less than 4 days. Half-life values in pollen are comparable to those in flowers; however, reliable estimates of ‘ k ’ could not be calculated with dinotefuran. This prevented a cross-chemical comparison of dissipation rates constants.

Table 6-47. Summary of dissipation rate information of thiamethoxam and dinotefuran in tomato pollen after foliar applications (normalized to 0.1 lb a.i./A).

Chemical	Crop	Location	k (95% CI)	Half-life (d)	R ²	P	First measurement (DALA)	Reliable k?	Comments
Thiamethoxam	Tomato	AL (flower)	0.52 (0.32-0.717)	1.3	0.99	<0.01	4	Y	
		CA (flower)	0.18 (0.085-0.28)	3.9	0.83	<0.01	5	Y	
		KS (flower)	0.36 (0.20-0.52)	1.9	0.97	<0.01	4	Y	
		CA (pollen)	2.06 (0.41-0.50)	0.3	0.68	<0.01	9	Y	Only 1 sampling point with residues >LOD.
		KS (pollen)	0.60 (0.28-0.57)	1.2	0.60	<0.01	6	Y	
		MO (pollen)	0.18 (-0.04-0.50)	3.9	0.62	0.04	5	N	
		CA (pollen)	0.36 (-0.38-1.32)	1.9	0.84	0.12	4	N	
Dinotefuran									

Regarding the influence of site on residue values in tomato pollen, comparison of residue data measured at the same time after application (DALA, 10 and 16 of **Figure 6-69**) indicate that mean residues can vary up to 10X across sites for each chemical. A similar range is seen with residues in flowers (**Figure 6-70**).

The influence of chemical on mean normalized residue values can only be estimated using the pollen data. Comparisons of mean residues measured on DALA 10 and 16 indicate differences up to 10X between dinotefuran and thiamethoxam. Since these data come from different sites, it is not possible to distinguish the potential contribution of site from chemical on the residue values in tomato pollen. However, it is apparent that chemical does not contribute an overriding influence on residue values within the context of differences among sites. No evaluation of the influence of crop could be conducted for foliar applications to fruiting vegetables since data are available for only one crop.

6.6.2.5 Bridging Recommendations

Residue data resulting from foliar applications for the fruiting vegetable group are available for tomatoes for two chemicals across three sites. While tomatoes are not considered attractive to honeybees, they are considered as a surrogate for the purposes of this analysis, to members of the fruiting vegetables that are honeybee attractive. Residues in pollen were generally higher than those for flowers (surrogate for nectar). Of the crops that are considered attractive to honeybees in this group (*i.e.*, chili pepper, okra, and roselle) okra and roselle are the only ones that produce nectar.

When normalized to the same application rate, residues generally decrease in pollen over time and are not remarkably different across the chemicals. Similarly, residue values for both chemicals at similar time points do not suggest a difference in chemical over time. There is uncertainty in relying on a single crop to compare foliar applications with respect to being representative of all fruiting vegetables, and there is uncertainty in using flowers as a nectar surrogate. However, as mentioned previously, there are relatively few crops that are considered honeybee attractive, and of those okra, and roselle, are the only ones that produce nectar. Looking at residue concentrations following soil applications (for which several crops are available; see section below), there was no distinguishable pattern in residue expression in the different crops. This is an additional line of evidence that tomato residues (utilizing flowers as a nectar surrogate) would be a reasonable surrogate for crops in the honey bee attractive members of the fruiting vegetable group. Consequently, it is recommended that residue data for tomato be used to bridge to all fruiting vegetable that are honey bee attractive (including using flower residues where appropriate) when evaluating risk from foliar treatments of neonicotinoids.

6.6.3 Soil Applications

6.6.3.1 Summary of label rates/restrictions

Like foliar spray applications, dinotefuran, imidacloprid, and thiamethoxam are all registered for use as a soil application to fruiting vegetables while clothianidin is not registered for any crops in the fruiting vegetable group. The maximum rates for foliar applications of these chemicals are included in **Table 6-48**.

Table 6-48. Soil application rates (in lb a.i./A) and number of applications (x n) for neonicotinoids on fruiting vegetable crops (based on current labels).

Fruiting Vegetables	Imidacloprid	Clothianidin	Thiamethoxam*	Dinotefuran
All crops	0.33 X 1 (total 0.54)	NR	0.15 X 1	0.3 X 1, 0.2 X1 (total 0.5)

NR = Not registered

*Expressed as clothianidin equivalent (c.e.) rate

6.6.3.2 Available residue data

Data are available for imidacloprid, clothianidin, and thiamethoxam from 5 studies, representing 3 crops within the fruiting vegetable crop group (**Table 6-49**), including tomatoes, bell, and chili peppers. For imidacloprid, nine trials (all in CA) representing all three soil texture categories (fine, medium, and coarse) included soil drip application 5-7 days after tomato transplanting at 0.38 lb a.i./A. For dinotefuran, tomato soil applications (2015) were made post-emergence at 0.206 lb ai/A and 0.330 lb ai/A., while thiamethoxam used single soil application (2016) at two application rates, 0.11 lb c.e.¹⁰/A and 0.15 lb c.e./A either at or one day after transplanting. Pepper residue data were also available. Dinotefuran used bell pepper (not honeybee attractive) while thiamethoxam used three varieties of chili peppers which are considered honeybee attractive. Chili peppers were treated (2015) at planting using a rate of 0.15 lb c.e./A while bell peppers were treated (2016) as soil drench treatments at application rates of 0.206 lbs ai/A (first application) and 0.330 lbs ai/A (second application 7-day interval). Applications were made to bell pepper plants ca. 28 days before early flowering.

Table 6-49. Residue studies for fruiting vegetable crops with soil applications of dinotefuran, imidacloprid and thiamethoxam.

Crop	Chemical	# sites (Locations)	Application information (rate x # of apps, (interval))	# Seasons	# sampling events (per season)	MRID (Classification)
Tomato	Thiamethoxam	3 (KS, IL, CA)	0.11 X 1 (NA) 0.15 X 1 (NA)	1	3	50265507 (Acceptable)
	Imidacloprid	9 (CA)	0.38 X 1 (NA)	2	4	49665201 (Supplemental)
	Dinotefuran	3 (NC, MO, CA)	0.206 x1 and 0.33 x 1 (7)	1	3	49841004 (Acceptable)
Chili pepper	Thiamethoxam	3 (KS, AL, CA)	0.15 X 1 (NA)	1	3	49804103 (Acceptable)
Bell pepper	Dinotefuran	3 (NC, GA, CA)	0.206 x1 and 0.33 x 1 (7)	1	3	50145702 (Acceptable)

NA = Not applicable

Figure 6-71 summarize residues in pollen for 3 chemicals (thiamethoxam, dinotefuran and imidacloprid) and 3 fruiting vegetable crops (tomato, chili pepper and bell pepper). These residue values have been normalized to 0.1 lb a.i./A based on the last application rate. Within the dinotefuran/chili trials, mean

¹⁰ c.e. = clothianidin equivalents

residues in pollen generally show a decreasing trend from 20-35 days after soil applications (closed circles, **Figure 6-71**). With imidacloprid (diamonds) and thiamethoxam (squares), an overall declining trend in mean residue values with increasing time after soil application is not apparent. Among crops and chemicals, most residue values fall between 1 and 100 ng a.i./g per 0.1 lb a.i./A. One notable exception are residues of dinotefuran in tomato pollen from two sites (MO, CA, open circles) which range from 300 to 2000 ng a.i./g.

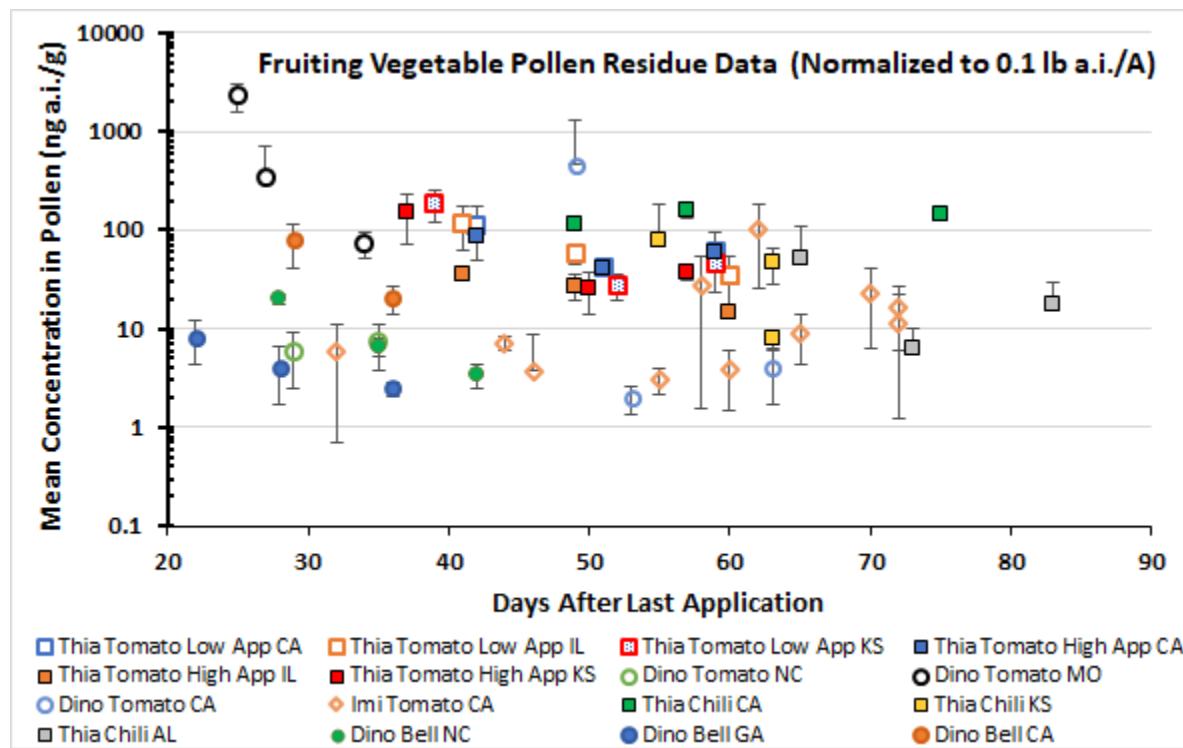


Figure 6-71. Summary of mean (+/- 95% CL) pollen residues of thiamethoxam (squares), dinotefuran (circles) and imidacloprid (diamonds) in tomatoes, chili peppers, and bell peppers (normalized to 0.1 lb a.i./A). Thiamethoxam residues are expressed as clothianidin equivalents.

Mean residues in nectar (dinotefuran) and flower (thiamethoxam) in tomatoes, chilis and bell pepper are shown in **Figure 6-72**. The flower residues have been multiplied by 0.3 to provide an estimate of expected concentrations in nectar, as described in **Section 5.5**. As with pollen, the nectar and flower residue values have been normalized to 0.1 lb a.i./A based on the last application rate. While some declining trends are indicated within some of the residue trials (i.e., within a crop/location), these trends are not consistent among the trials.

With dinotefuran, mean normalized residues in nectar of bell pepper are low (~ 1 ng a.i./g and lower) which is about 10X lower than those in bell pepper pollen. Mean normalized residues of thiamethoxam in tomato flowers (multiplied by 0.3 to estimate residues in nectar) are mostly between 10 and 100 ng a.i./g, which is similar to those found in tomato pollen.

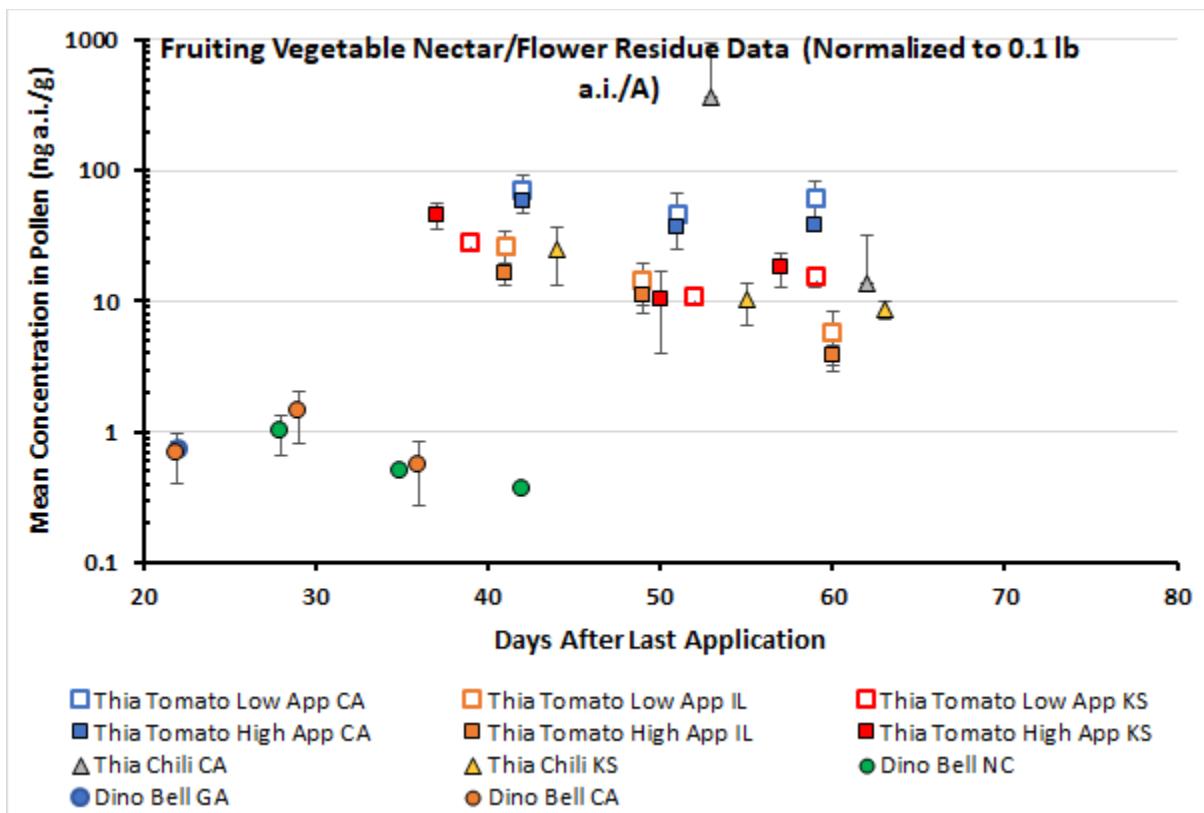


Figure 6-72. Summary of mean (+/- 95% CL) nectar residues (chili and bell pepper) and flower residues (tomato, multiplied by 0.3) in fruiting vegetables (normalized to 0.1 lb a.i./A). Thiamethoxam residues are expressed as clothianidin equivalents.

6.6.3.3 Bridging needs (gaps)

Table 6-50 identifies data gaps for registered soil applications of neonicotinoids on fruiting vegetables. Tomato data are available for all three chemicals while data on chili pepper are available for thiamethoxam; data on bell pepper are available for dinotefuran. Fruiting vegetables considered attractive to honey bees include chilis, peppers, okra, and roselle (USDA 2017).

Table 6-50. Residue data gaps for neonicotinoid soil applications to fruiting vegetables.

Fruiting Vegetables	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Non-honeybee attractive crops	49665201 (tomato)	NR	49804102 (tomato)	49841004 (tomato) 50145702 (bell pepper)
Chilis & Peppers, Okra, Roselle	No data	NR	49804103 (chili pepper)	No data

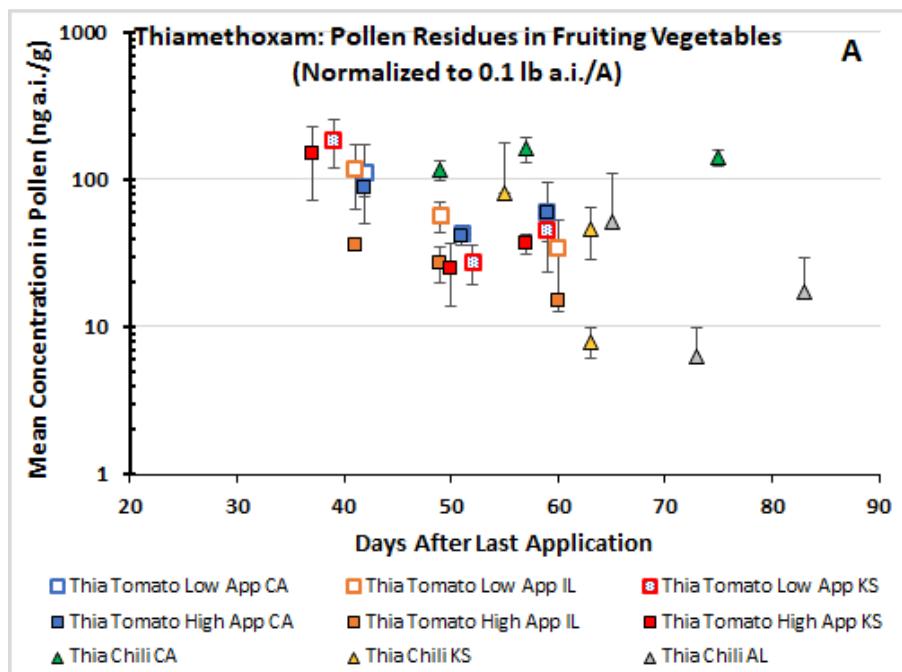
NR = not registered

6.6.3.4 Influence of Sampling Day (Time), Site, Crop and Chemical on Residue Values

The available residue data for soil applications of neonicotinoids to fruiting vegetable crops are limited in quantity and scope (most trials have just 3 sampling events) and do not show consistent trends with time after application across crops and trials. This latter finding is similar to those from soil applications of neonicotinoids to other crops. Therefore, a robust evaluation of dissipation kinetics similar to that

conducted for other crops (*e.g.*, berries, cotton, cucurbits, orchard crops) is not presented for soil applications to fruiting vegetables.

Figure 6-73 presents the application rate-normalized thiamethoxam residues in pollen of tomato and chilis, expressed as clothianidin equivalents (**Panel A**). Regarding the effect of site on residues within a crop, mean values for tomato (different color squares) and chilis (different color triangles) vary by up to 10X at similar times after soil application. Mean residues of dinotefuran in pollen of tomato and bell pepper are shown in **Figure 6-73 (Panel B)**. With tomato, mean residues of dinotefuran among sites at similar time points (DALA 27-29 & 34-35) also vary by an order of magnitude (solid circles of different colors). A similar impact of site is indicated for dinotefuran in pollen of bell peppers. With imidacloprid, residues were measured in pollen of tomatoes at 7 sites among different years in California (**Figure 6-74**). Within the same year, residue values were within an order of magnitude across sites. Normalized residue values measured in different seasons (years) are also within 10X, with most being within 3X. Notably, values in this figure were only measured at different times after application (32-76 DALA), so there is the potential of measurement time to contributed to the observed variability in imidacloprid in tomato pollen.



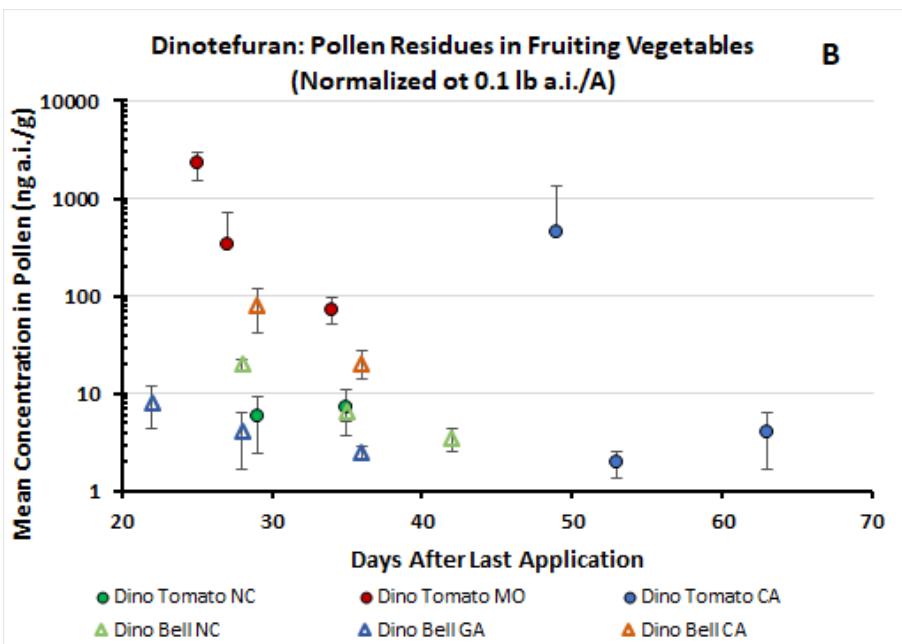


Figure 6-73. Mean (+/- 95% CL) residues in pollen of fruiting vegetables for thiamethoxam (A) and dinotefuran (B) following soil applications. Values are normalized to 0.1 lb a.i./A based on the last application and thiamethoxam residues are expressed as clothianidin equivalents.

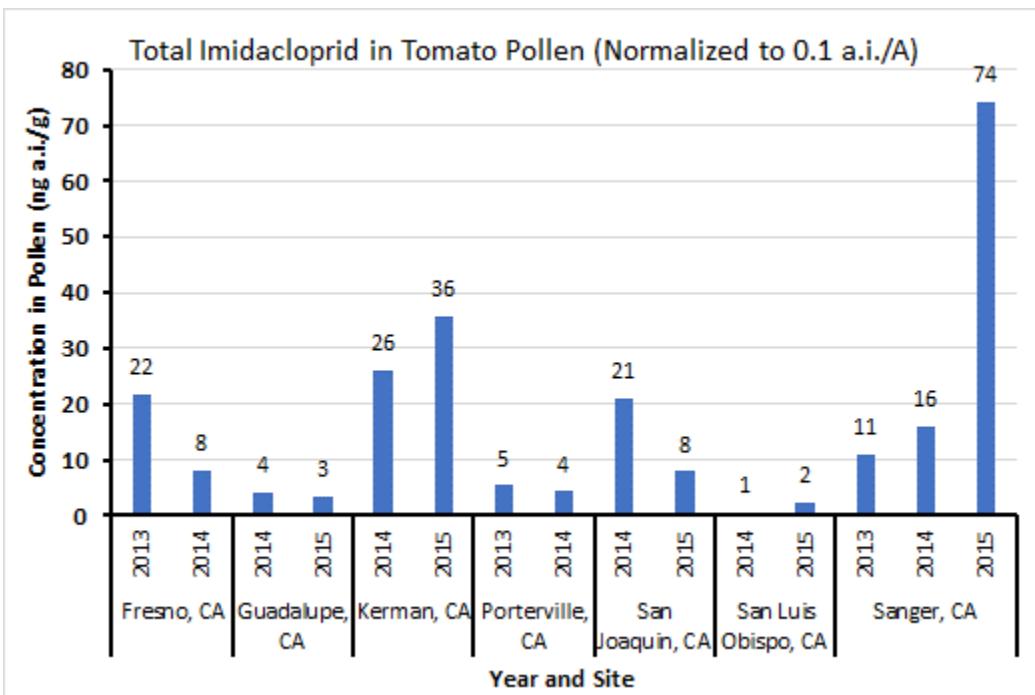


Figure 6-74. Residues of total imidacloprid in tomato pollen among sites and years following soil applications. Values are normalized to 0.1 lb a.i./A based on the last application.

The effect of chemical or crop on residue values in fruiting vegetables cannot be separated from the effect of site, since trials with different chemicals and crops were conducted at different sites. However,

it is instructive to evaluate whether differences across crop or chemicals are similar to or greater than those associated with site.

The most complete data set for evaluating the effect of chemical on residues in fruiting vegetables is for tomato (**Figure 6-75**). At similar time points after application, mean normalized residues in tomato tend to overlap among the chemicals. Very large residue values are seen for dinotefuran in pollen less than 30 DALA, but no other chemicals have data for comparison at this sampling time. It is important to note that the imidacloprid residue data reflect 1 or 2 replicates at a time point and therefore, these values are more uncertain compared to the other chemicals. This may be why there is greater variability seen for the imidacloprid data. Based on these data, the effect of chemical on pollen residues is not evident within the context of the variability that exists among sites.

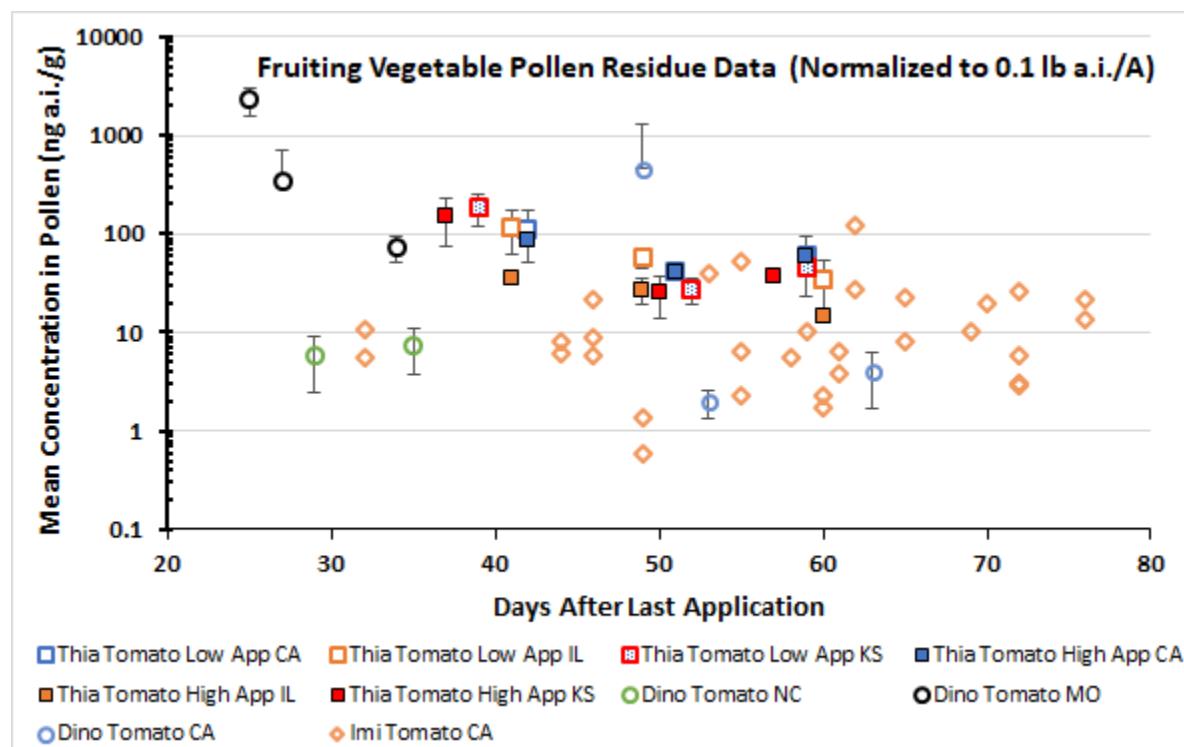


Figure 6-75. Mean (+/- 95% CL) residues of thiamethoxam (expressed as clothianidin equivalents) in nectar of chilis and flowers of tomato (multiplied by 0.3) following soil applications. Values are normalized to 0.1 lb a.i./A based on the last application

Regarding the effect of crop on pollen residues, mean residues of dinotefuran in tomato among sites and sampling times are about 20X much larger than those in bell pepper (**Table 6-51**). However, dinotefuran residues in tomato pollen were exceptionally high at one site (MO), while those for the other sites (NC and CA) were comparable those in bell pepper (**Figure 6-73 Panel B**). For thiamethoxam, mean residues in chilis and tomato are similar (within 2X). Based on these data, the effect of crop on pollen residues is not evident within the context of the variability that exists among sites.

Similar comparisons of residues in nectar or flower could not be conducted due to the combination of different in crops or matrices among chemicals.

Table 6-51. Summary statistics of mean residues of neonicotinoids in pollen of fruiting vegetables following soil application. Values are normalized to 0.1 lb a.i./A.

Chemical / Crop	Mean (ng a.i./g)	Min (ng a.i./g)	Max (ng a.i./g)	n
Dinotefuran				
Bell Pepper	18	2.5	79	8
Tomato	396	2.0	2280	8
Imidacloprid				
Tomato	19.5	3.0	102.8	11
Thiamethoxam				
Chili	70	6.4	161	9
Tomato	64	15	186	18

6.6.3.5 Bridging Recommendations

Residue data in pollen resulting from soil applications to crops within the fruiting vegetable group are available for tomatoes, bell, and chili peppers. There are relatively few members of this crop group that produce pollen/nectar attractive to honeybees, so exposure of bees to this group is generally limited to non-*Apis* species (e.g., *Bombus*) used in pollination services for crops like greenhouse tomato.

Soil residue data variability is generally higher than that observed for foliar applied. Additionally, the effect of sampling time on residue in pollen or nectar following soil application was variable among trials and chemicals. Therefore, the soil residue data were not amenable to dissipation curve analysis due to measurement gaps and general trends of the data. When normalized to the same application rate, residues in pollen among crops and chemicals overlap at similar times after soil application. The variability observed across chemical and crops is not distinguishable from that observed among sites. Nectar data were not amenable to a robust analysis of the effects of chemical or crop.

Therefore, it is recommended that available residue data for tomatoes, chili peppers, and bell peppers be bridged within a matrix to all chemicals in the risk assessment for fruiting vegetables. Based on the previous results from inter-tissue extrapolations of residue values, the tomato flower data are recommended for use as a surrogate for nectar producing fruiting vegetable crops (with the application of the 0.3 factor) in addition to the nectar data for chili and bell pepper.

6.7 Cucurbits

6.7.1 Crops of concern for pollinators

According to the USDA guidance on crops attractive to honey bees and other bees, all cucurbit crops evaluated therein (e.g., cucumbers, pumpkins, melons, etc.) are considered attractive to bees. Therefore, exposure to bees from applications to cucurbits will be considered in the neonicotinoid bee assessments for registered uses of these crops.

6.7.2 Foliar Applications

6.7.2.1 Summary of label rates/restrictions

All neonicotinoids being assessed, except for imidacloprid, are registered for foliar applications to cucurbit vegetables. Generally, pre-bloom restrictions are not on labels, though some labels (e.g., 59639-150 for clothianidin) specify that applications cannot be made after early development (e.g. BBCH 14: up to four true leaves unfolded on main stem). **Table 6-52** includes the maximum single and annual application rates by chemical.

Table 6-52. Max foliar application rates (in lb a.i./A) and number of applications (x n) for curcurbits by neonicotinoid compound.

Crop Group	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Cucurbits	NR	0.1 x 2	0.075 x 2	0.179 (x 1) + 0.091 (x 1)

NR = not registered

6.7.2.2 Available residue data

Pollen, nectar and/or whole flower residue data are available for clothianidin, thiamethoxam, and imidacloprid from 5 studies, representing 3 crops within the cucurbit crop group and 12 different sites (**Table 6-53, Figure 6-76 and Figure 6-77**). Although the squash/cucumber subgroup is well represented (4 studies), the melon subgroup is limited with only a single study on a single (non-US) site. No data are available to inform year-to-year variability on the same site. The analysis below considers influences of site and chemical on residues in pollen and nectar. Available flower residue data for whole flowers (for one thiamethoxam study on cucumber and imidacloprid study on watermelon) are discussed above in **Section 5.5 and 5.6** for comparisons with nectar and pollen residues, respectively. A study with dinotefuran on cucumbers (MRID 49841003) was considered qualitative due to insufficient quantities of pollen and nectar being collected for reliable residue analysis. Quantitative data from a Brazilian study applying imidacloprid to watermelon (MRID 50357101) were considered, despite the lack of U.S. registration for foliar applied imidacloprid to cucurbits. This tented field study used foraging honey bees to gather the pollen and nectar; however, residues in pollen were not available for the concurrent nectar samples. Given the relative contribution of nectar versus pollen residues to colony level exposures (see **Attachment 1** to the neonicotinoid risk assessments), the nectar data from this study are primarily used in considering overall exposures from imidacloprid applications. In-hive residues (from comb) from this study were not used in this analysis as they may have degraded and/or been mixed with other honey bee products.

In addition to these studies, there was also residue data available from one dinotefuran study (MRID 50145703) involving two foliar applications to pumpkins. Pollen and nectar samples were taken but were sometimes taken from within the hive rather than from foraging bees or from fresh pollen collected from pollen traps affixed to the hive. Nectar and pollen residues from in-hive samples may have degraded and/or been mixed with other honey bee products and it was often unclear from the study report which samples were from within the hive versus which were from foragers/pollen traps. Therefore, data from this study was not used to inform the residue bridging strategy.

Table 6-53. Residue studies of cucurbit crops treated with foliar applications of neonicotinoids.

Crop	Chemical	# sites (Locations)	App. Rate, # of apps (interval)	# Sampling events (per season)	MRID	Classification
Pumpkin	Clothianidin	2 (ON, Canada)	0.0935 lb a.i./A x 2 (2-4 d interval)	5	49602802	Supplemental ^{2,3}
Pumpkin	Clothianidin	3 (ND, CA, OR)	0.1 lb a.i./A x 1	3-5	49910601	Supplemental
Pumpkin	Thiamethoxam	3 (CA, MO, NC)	0.01978 lb a.i./A ¹ x 2 (5d) 0.07396 lb a.i./A ¹ x 2 (5d)	5	50265506	Acceptable
Cucumber	Thiamethoxam	3 (GA, NC, CA)	0.073-0.074 ¹ lb a.i./A x 2 (5d)	3	49804105	Acceptable
Watermelon	Imidacloprid	1 (Brazil)	0.1875 lb a.i./A x 3	1-3	50357101	Supplemental

¹Clothianidin-equivalent rates

²Quantitative data not available from 3 sites.

³Less than 3 samples taken per sampling event

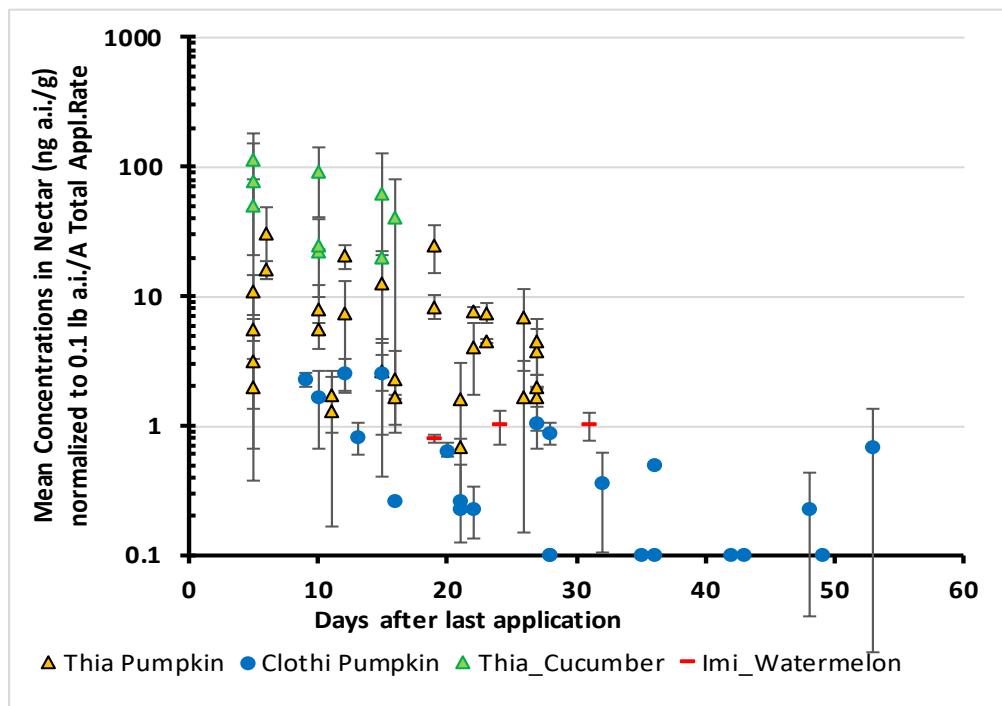


Figure 6-76. Mean concentrations in nectar following foliar applications to cucurbit crops. Error bars represent 95% confidence interval. Values normalized to total application rate of 0.1 lb a.i./A. Imi = imidacloprid; Thia = thiamethoxam, Clothi = clothianidin, Dino = dinotefuran. Note that thiamethoxam residues are expressed as clothianidin equivalents.

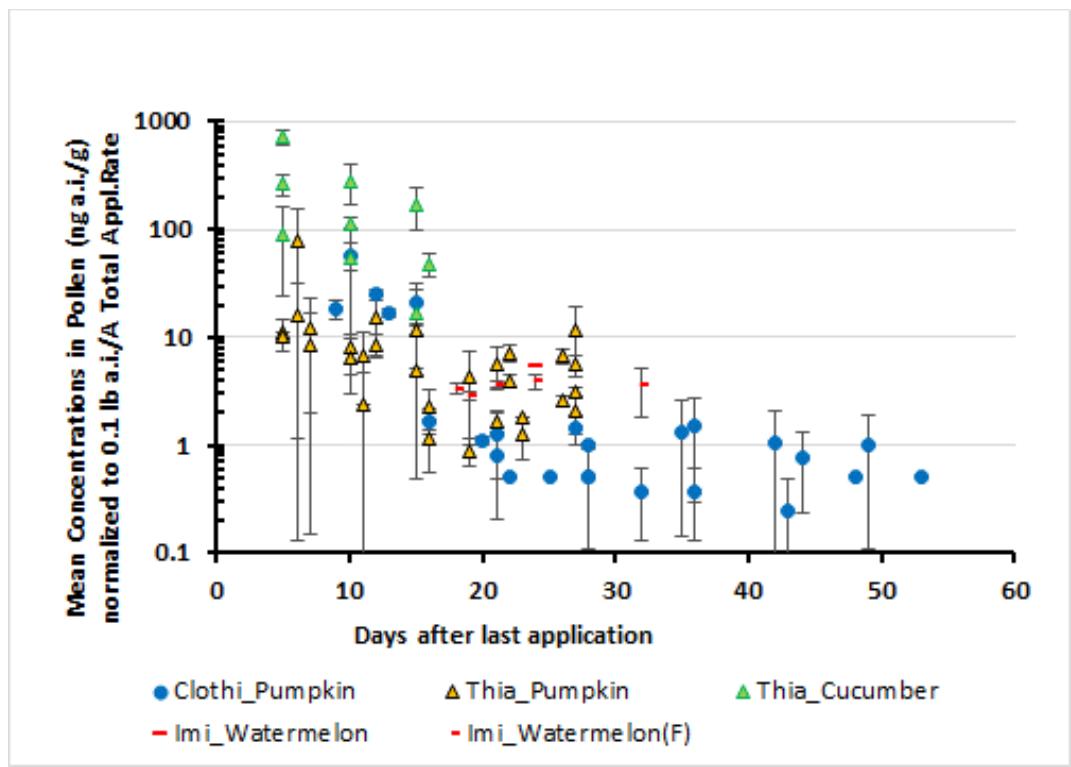


Figure 6-77. Mean concentrations in pollen following foliar applications (pre- and post-bloom) to cucurbit crops. Error bars = 95% confidence interval. Values normalized to total application rate of 0.1 lb a.i./A. Imi = Imidacloprid, Thia = thiamethoxam, Clothi = clothianidin, Dino = dinotefuran. Note that thiamethoxam residues are expressed as clothianidin equivalents and Imi residues in pollen are estimated from flower.

6.7.2.1 Bridging Needs (Gaps)

Limited quantitative data are available for the melon sub-group, where only one study is available with from a single non-U.S. site, using a neonicotinoid (imidacloprid) that is not registered for foliar applications on cucurbits in the U.S (**Table 6-54**). As no data are available for the melon sub-group of cucurbits across multiple active ingredients, there is greater uncertainty when considering bridging the melon sub-group to the squash/cucumber subgroup.

Table 6-54. Studies with quantitative residues in pollen, nectar, and/or flowers from foliar applications to cucurbits by active ingredient and cucurbit crop subgroup.

Crop	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Cucurbits: Melon Sub-group	NR Melon (MRID 50357101)	No Data	No Data	No Data
Cucurbits: Squash/cucumber Subgroup	NR	Pumpkin (MRIDs 49602802, 49910601)	Pumpkin (MRID 50265506) Cucumber (MRID 49804105)	No Data

NR = Not Registered

6.7.2.2 Influence of application rate on residues

One study is available to evaluate the influence of variable thiamethoxam application rates on residues in pollen and nectar following foliar application to pumpkins. In this study, thiamethoxam was applied to pumpkins with two foliar applications at either 0.0198 or 0.0740 lb a.i./A (clothianidin equivalents; 5-D application interval; MRID 50265506). **Figure 6-78** and **Figure 6-79** depict residues in pollen and nectar (respectively) collected from pumpkins treated at the different rates. For both figures, the graph on the left represents the mean residues from the study while the right graph represents residues normalized to the same total application rate (0.1 lb a.i./A).

When residues are not normalized, mean residues from the high application rate are generally higher (as expected) than residues from the low application rate, particularly during the earlier sampling times (*i.e.*, before DALA 15). When residues were normalized to the same total application rate, there is no clear pattern to whether residues from either application rate will be higher in either pollen or nectar (though there was considerably more scatter from the normalized concentrations in nectar in the low rate trial and generally normalized residues from one site {California} were higher in the low rate trial than they were in the high rate trial following normalization). For pollen, there is one value at 6 days after the last application that appears to drive the mean residues at the low treatment rate substantially higher than the high treatment rate; however, the confidence limits indicate that this is driven by a single sample value that is >10x the other two samples. Overall, the data support normalization of residue concentrations by application rate.

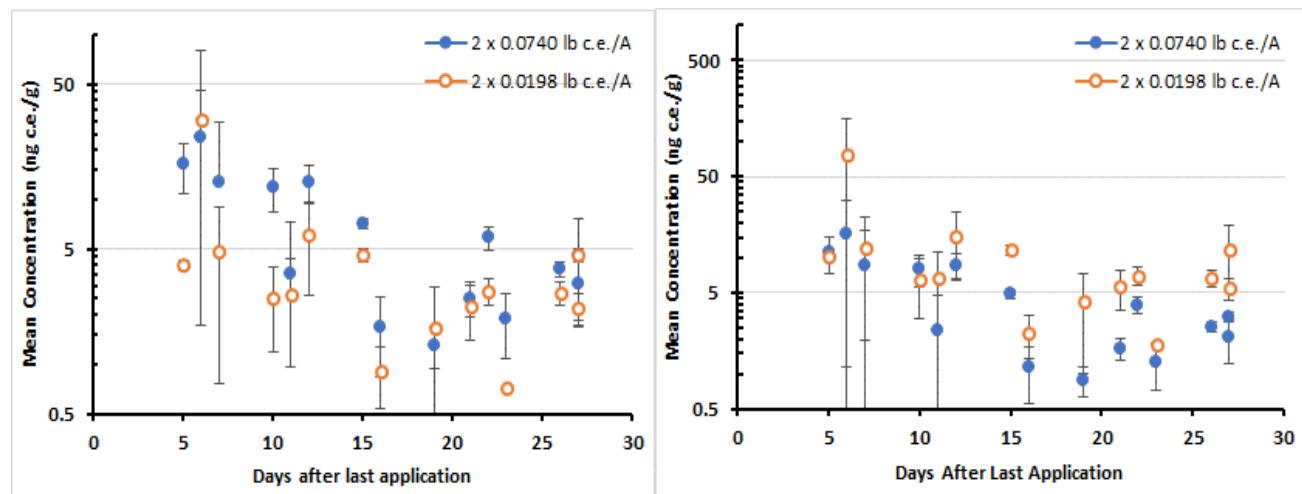


Figure 6-78. Mean residues (expressed as clothianidin equivalents; ng c.e./g +/- 95% CL) in pollen following thiamethoxam foliar applications to pumpkin (MRID 50265506). Left graph depicts unadjusted residues. Right graph depicts residues normalized to total application rate.

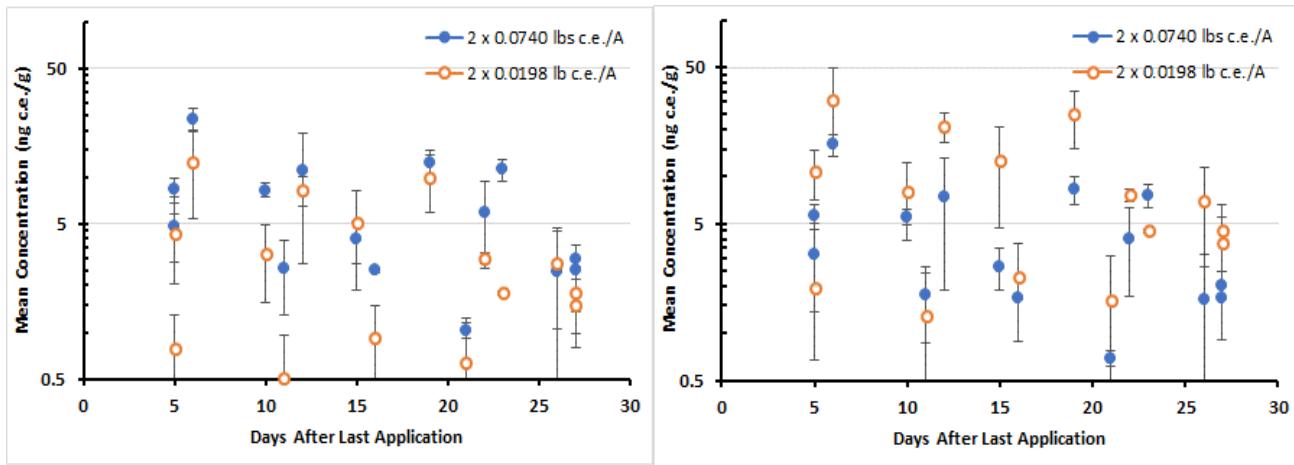


Figure 6-79. Mean residues (expressed as clothianidin equivalents; ng c.e./g) in nectar following thiamethoxam foliar applications to pumpkin (MRID 50265506). Left graph depicts unadjusted residues. Right graph depicts residues normalized to total application rate of 0.1 lb c.e./A. Error bars = 95% confidence interval.

6.7.2.3 Influence of sampling day (time) on residue values

Figure 6-78 and **Figure 6-79** above depict individual mean values for nectar and pollen, respectively for each cucurbit study following neonicotinoid foliar application. Residues in pollen are generally higher but are still within an order of magnitude of those in nectar. Applications made within 15 days of bloom yield residues in pollen and nectar that are 1-2 orders of magnitude greater than residues measured after >30 days following applications, indicating a strong temporal trend in the data. Table 6-55 lists the range of mean residue values for pollen and nectar from cucurbit crops with different time periods between bloom and application.

Table 6-55. Concentrations of neonicotinoids in cucurbit nectar and pollen over time after normalizing to a total application rate of 0.1 lbs a.i./A (thiamethoxam application rate and concentrations expressed in clothianidin equivalents; c.e.).

Days before bloom when application was made	Concentration in nectar (ng a.i./g)	Concentration in pollen (ng a.i./g)
1-5	<LOQ-154	<LOQ-968
6-10	<LOQ-125	<LOQ-386
11-15	<LOD-86	1.4-233
16-20	1.3-56	<LOQ-66
21-30	<LOD-7.6	<LOQ-12
31-40	<LOD-<LOQ	<LOQ-1.5
41-55	<LOD-0.7	<LOQ-1.1

6.7.2.4 Differences in dissipation rates (k)

Effect of chemical, crop, matrix on k

Residue data from individual trials were analyzed to determine whether the single first order (SFO) dissipation rate constants (k) could be reliably quantified according to methods and screening criteria

described in **Section 4.5.5**. Dissipation rate constants were calculated from trials with at least three sampling time points containing residues greater than the LOQ (**Table 6-56** and **Table 6-57** for nectar and pollen, respectively). Reliable k values were calculated from the clothianidin pumpkin studies (2 sites in Ontario, Canada and sites in three U.S. States). Reliable k values were also determined from thiamethoxam pumpkin and cucumber studies in several states. The imidacloprid and dinotefuran studies did not produce reliable k values due to either residues below the LOQ or lack of declining monotonic responses. Flower data from the thiamethoxam cucumber and pumpkin studies also produced reliable k values (**Table 6-58**).

Table 6-56. Dissipation rate constants derived for residues in nectar from foliar, pre-bloom applications to cucurbit group crops.

Chemical	Crop	Location (trial)	k (95% CI)	Half-life (d)	R ²	P	First Measurement (DALA)	Reliable k?	Comments
Clothianidin	Pumpkin	Cambridge, ON	0.058 (0.008-0.11)	11.9	0.46	0.03	9	Y	
		Rockville, ON	0.19 (0.026-0.37)	3.6	0.49	0.03	10	Y	
		Grand Forks, ND	NA	NA	NA	NA	32	N	Most samples <LOQ
		Fresno, CA	NA	NA	NA	NA	21	N	Most samples <LOQ
		Clackamas, OR	NA	NA	NA	NA	22	N	Most samples <LOQ
Thiamethoxam	Pumpkin	Woodland, CA-(Low Rate)	0.028 (-0.009-0.064)	24.9	0.21	0.062	5	N	Variable
		Woodland, CA-(High Rate)	0.042 (0.015-0.064)	16.6	0.5	0.003	5	Y	
		Fisk, MO-(Low Rate)	0.064 (0.019-0.11)	10.9	0.5	0.004	6	Y	
		Fisk, MO-(High Rate)	0.063 (0.03-0.093)	11.1	0.64	<0.001	6	Y	
		Belvidere, NC-(Low Rate)	NA	NA	NA	NA	5	N	Non-monotonic
		Belvidere, NC-(High Rate)	0.056 (0.009-0.10)	12.5	0.34	0.012	5	Y	
	Cucumber	Fresno, CA	0.12 (-0.13-0.36)	5.9	0.15	0.15	5	N	Poor fit
		Jeffersonville, GA	0.11 (-0.008-0.23)	6.4	0.46	0.032	5	Y	
		Mebane, NC	0.044 (-0.14-0.23)	15.9	0.05	0.30	5	N	Poor fit, variable
Imidacloprid	Watermelon	Triunfo, Brazil	NA	NA	NA	NA	19	N	Non-monotonic

k = decline constant; R² = Regression fit; P = Regression Model Statistical Probability; DALA = Days after Last Application; LOQ = Level of Quantification; NA = Not Applicable

Table 6-57. Dissipation rate constants derived for residues in pollen from foliar, pre-bloom applications to cucurbit group crops.

Chemical	Crop	Location	k (95% CI)	Half-life (d)	R ²	P	First measure (DALA)	Reliable k?	Comments
Clothianidin	Pumpkin	Cambridge-ON	0.094 (0.019-0.17)	7.3	0.61	0.024	9	Y	
		Rockville-ON	0.434 (0.32-0.54)	1.6	0.97	<0.001	10	Y	
		Grand Forks, ND	NA	NA	NA	NA	25	N	Most samples <LOQ
		Fresno, CA	NA	NA	NA	NA	21	N	Most samples <LOQ
		Clackamas, OR	NA	NA	NA	NA	22	N	Most samples <LOQ
Thiamethoxam	Pumpkin	Woodland, CA-(Low Rate)	0.019 (-0.004-0.041)	37.2	0.21	0.05	5	N	Variable
		Woodland, CA-(High Rate)	0.071 (0.046-0.096)	9.8	0.80	<0.001	5	Y	
		Fisk, MO-(Low Rate)	0.25 (-0.25-0.75)	2.7	0.33	0.15	6	N	Variable
		Fisk, MO-(High Rate)	0.13 (0.024-0.24)	5.3	0.55	0.01	6	Y	
		Belvidere, NC-(Low Rate)	0.052 (-0.016-0.12)	13.3	0.16	0.06	7	N	Variable
		Belvidere, NC-(High Rate)	0.23 (-0.11-0.57)	3.0	0.29	0.08	7	N	Variable
	Cucumber	Fresno, CA	0.16 (0.097-0.23)	4.3	0.89	<0.001	5	Y	
		Jeffersonville, GA	0.14 (-0.051-0.33)	5.0	0.41	0.06	5	N	Variable
Imidacloprid	Watermelon	Triunfo, Brazil	NA	NA	NA	NA	18	N	Non-monotonic

k = decline constant; R² = Regression fit; P = Regression Model Statistical Probability; DALA = Days after Last Application; LOQ = Level of Quantification; NA = Not Applicable

Table 6-58. Dissipation rate constants derived for residues in flowers from foliar, pre-bloom applications to cucurbit group crops.

Chemical	Crop	Location (-trial)	k (95% CI)	Half-life (d)	R ²	P	First Measurement (DALA)	Reliable k?	Comments
Thiamethoxam	Pumpkin	Woodland, CA-(Low Rate)	0.086 (0.046-0.13)	8.1	0.70	<0.001	5	Y	
		Woodland, CA-(High Rate)	0.14 (0.088-0.19)	5.0	0.86	<0.001	5	Y	
		Fisk, MO-(Low Rate)	0.11 (0.088-0.13)	6.5	0.95	<0.001	6	Y	
		Fisk, MO-(High Rate)	0.091 (0.06-0.12)	7.6	0.84	<0.001	6	Y	
		Belvidere, NC-(Low Rate)	0.093 (0.057-0.13)	7.4	0.76	<0.001	5	Y	
		Belvidere, NC-(High Rate)	0.27 (0.032-0.51)	2.6	0.71	0.015	5	N	Non-monotonic, wide confidence limits
	Cucumber	Fresno, CA	0.18 (0.14-0.22)	3.8	0.97	<0.001	5	Y	
		Jeffersonville, GA	0.15 (0.11-0.20)	4.6	0.94	<0.001	5	Y	
		Mebane, NC	0.19 (0.17-0.21)	3.6	0.99	<0.001	5	Y	
Imidacloprid	Watermelon	Triunfo, Brazil	NA	NA	NA	NA	18	N	Non-monotonic

k = decline constant; R² = Regression fit; P = Regression Model Statistical Probability; DALA = Days after Last Application; LOQ = Level of Quantification; NA = Not Applicable

The subsequent analysis only considers SFO-derived k values from the screened “reliable” trials. For cucumber, the effect of matrix (flower, nectar, pollen) on k values following thiamethoxam application appears minimal (**Figure 6-80; Table 6-60**). Similarly, k values for pumpkin also do not vary greatly by matrix or chemical (**Figure 6-81; Table 6-59**). One clothianidin pollen trial (#86) has a relatively high value for k, while the other two trials appear to have k values consistent with the other trials. Although the clothianidin dataset that passed the screen is much smaller than that for thiamethoxam, the mean values for k are similar with highly overlapping 95% confidence intervals. The effect of crop on k was also considered (**Table 6-61**). Although cucumber seems to have a higher k value than pumpkin, the sample size is too low to make confident conclusions (n of 1 for cucumber nectar and pollen, n of 3 for flowers). Table 9 and Table 10 also suggest that nectar k may be slightly slower than flower or pollen, but this is not likely statistically significant (average k of 0.067 for nectar versus average k of 0.121/0.146 for pollen and flower, respectively). Taken together, the data support bridging foliar “k” values across chemicals and matrices for cucurbit floral parts.

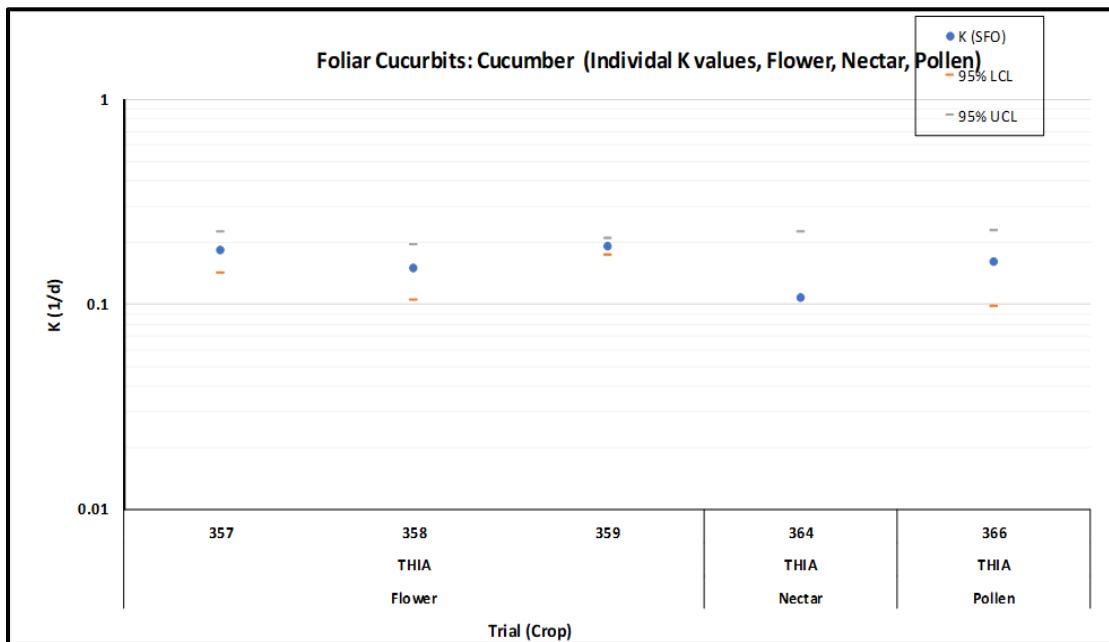


Figure 6-80. Cucumber k values by matrix for Thiamethoxam

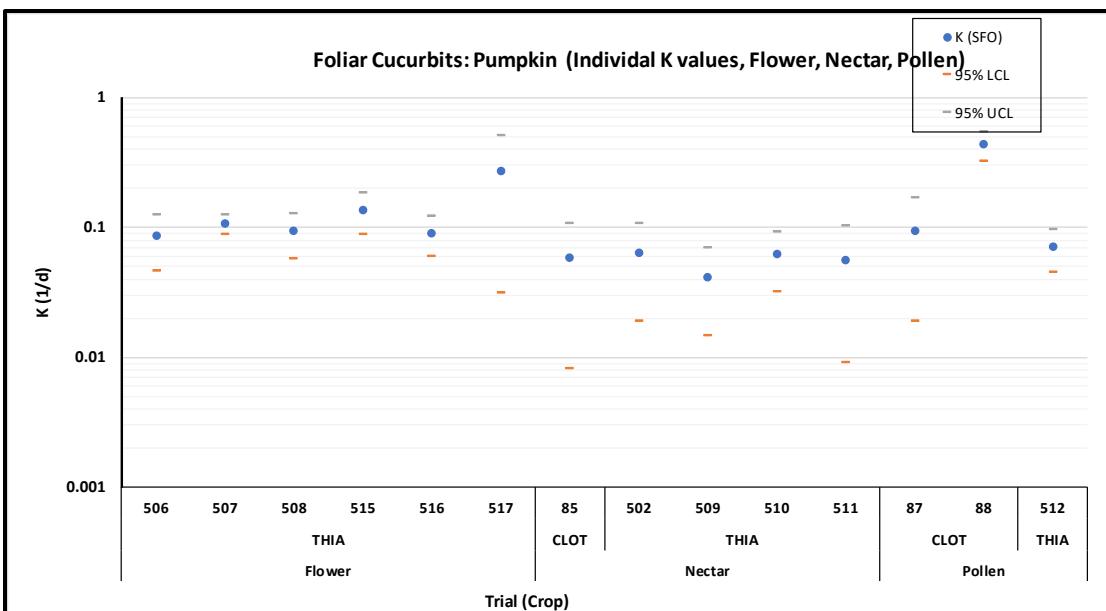


Figure 6-81. Pumpkin k values by matrix for clothianidin and thiamethoxam

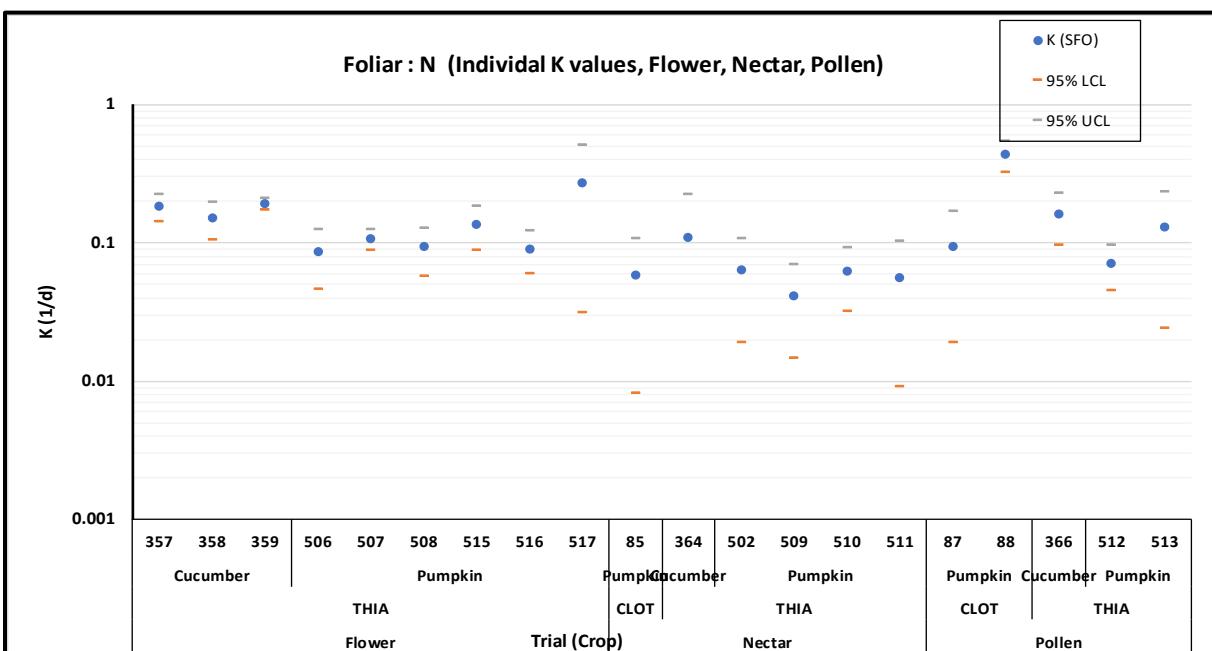


Figure 6-82. Cucurbit k values across crop, floral matrix and chemical.

Table 6-59. Comparison of dissipation rate constants (k) values by active ingredient following foliar applications.

Chemical	Mean K (SFO) (1/d)	Std. Dev of K (1/d)	n	95% LCL (1/d)	95% UCL (1/d)
CLOT	0.195	0.207	3	0.008	0.544
THIA	0.117	0.062	16	-0.008	0.512
Geometric Mean	0.130	0.094			

K = decline constant; SFO = Single First Order Model; LCL/UCL = Lower and Upper Confidence Limits

Table 6-60. Comparison of dissipation rate constants (k) values by floral matrix following foliar applications

Matrix	Mean K (SFO) (1/d)	Std. Dev of K (1/d)	Min K (1/d)	Max K (1/d)	n	Min 95% LCL (1/d)	Max 95% UCL (1/d)
Flower	0.146	0.062	0.086	0.272	9	0.031	0.512
Nectar	0.065	0.023	0.042	0.109	6	-0.008	0.225
Pollen	0.178	0.147	0.071	0.434	5	0.019	0.544
All Matrices	0.130	0.094	0.042	0.434	20	-0.008	0.544

Table 6-61. Comparison of dissipation rate constants (k) values by crop following foliar applications of thiamethoxam to cucurbits

Matrix/ Crop	Mean K (SFO) (1/d)	Std. Dev of K (1/d)	Min K (1/d)	Max K (1/d)	n	Min 95% LCL (1/d)	Max 95% UCL (1/d)
Flower							
Cucumber	0.176	0.022	0.151	0.191	3	0.106	0.225
Pumpkin	0.131	0.071	0.086	0.272	6	0.031	0.512
Flower Total	0.146	0.062	0.086	0.272	9	0.031	0.512
Nectar							
Cucumber	0.109	N/A	0.109	0.109	1	-0.008	0.225
Pumpkin	0.056	0.010	0.042	0.064	4	0.009	0.108
Nectar Total	0.067	0.025	0.042	0.109	5	-0.008	0.225
Pollen							
Cucumber	0.163	N/A	0.163	0.163	1	0.097	0.228
Pumpkin	0.100	0.042	0.071	0.130	2	0.024	0.236
Pollen Total	0.121	0.046	0.071	0.163	3	0.024	0.236

Based on these data and analyses, the following parameters in **Table 6-62** are recommended for modeling the dissipation of neonicotinoid residues in nectar and pollen resulting from foliar applications to cucurbits. These parameters reflect combined analysis among chemicals and matrices (nectar, pollen, flower) and are intended for use in the Monte Carlo modeling of residue decline curves as described in **Section 4.5.5**.

Table 6-62. Kinetic parameters recommended for use in the Monte Carlo analysis of neonicotinoid residues in cucurbits following foliar application

Statistic	Final Combined Foliar Cucurbit Dissipation Rate (k) in d ⁻¹
-----------	--

Mean	0.130
STD	0.091
Min	0.042
Max	0.434
n	20

6.7.2.5 Effect of chemical, crop, matrix and location on residue values

For those residue trials with reliable estimates of kinetic parameters (k , C_{initial}), the effect of chemical, crop, matrix and site on residues in pollen and nectar was further evaluated. With these trials, residue values can be adjusted to reflect a common day after last application (DALA) so that the influence of elapsed time on neonicotinoid concentrations can be minimized.

Figure 6-83 shows the range of initial measured values (C_{initial}) in nectar and pollen for pumpkin and cucumber by chemical. For both nectar and pollen, there is high variability in the measured concentrations, varying by factors of one order of magnitude (~20x) for nectar and roughly two orders of magnitude (~65x) for pollen, with the highest concentrations generally correlated with the shortest sampling intervals after application (5-10 days after last application) suggesting an adjustment for time is relevant.

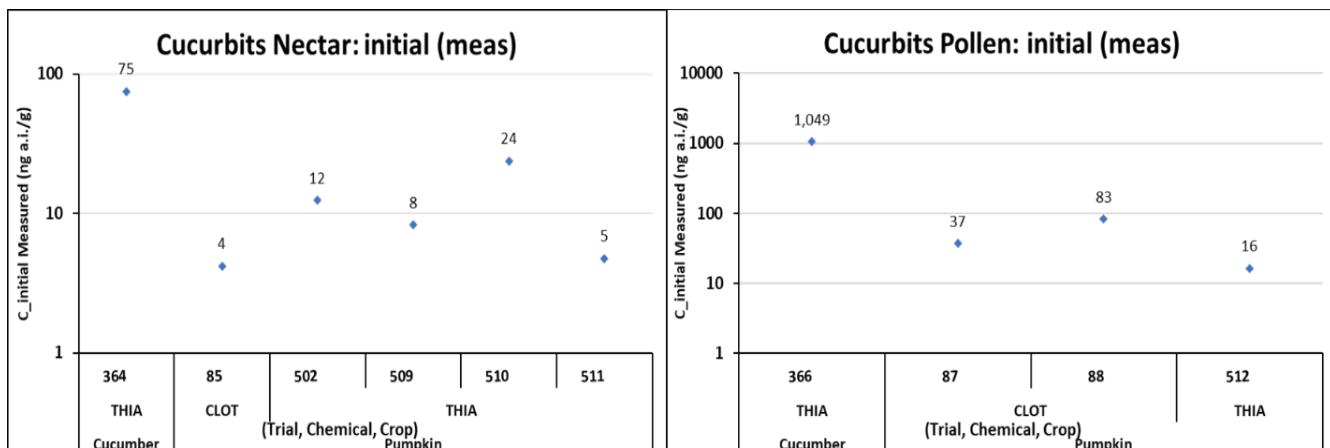


Figure 6-83. Average initial neonicotinoid measured concentrations (ng a.i./g) in nectar (left) and pollen (right) across trial, chemical and crop. CLOT = clothianidin, THIA = thiamethoxam. Thiamethoxam residues expressed in clothianidin equivalents.

Using the k values from the individual trials presented in **Table 6-56** and **Table 6-57** to estimate declining residues over time, initial measured concentrations (C_{initial}) in nectar and pollen were adjusted to 10 days after last application using the following equation:

$$C_{\text{initial SFO (Day 10)}} = C_{\text{initial SFO (Day X)}} e^{(k \times [X - 10])}$$

where,

- $C_{\text{initial SFO (Day 10)}}$ = Concentration adjusted to day 10 using SFO model
- $C_{\text{initial SFO (Day X)}}$ = Concentration estimated on the initial sampling day (X) using SFO model
- k = Dissipation rate constant (1/d) estimated using SFO model

X =

Day of initial sampling from the residue trial

Adjusted concentrations in nectar and pollen for cucurbits are presented in **Figure 6-84**. For nectar, normalizing by sampling interval reduces the range in values only slightly. For pollen, normalizing to Day 10 reduces the range in values by approximately 2X.

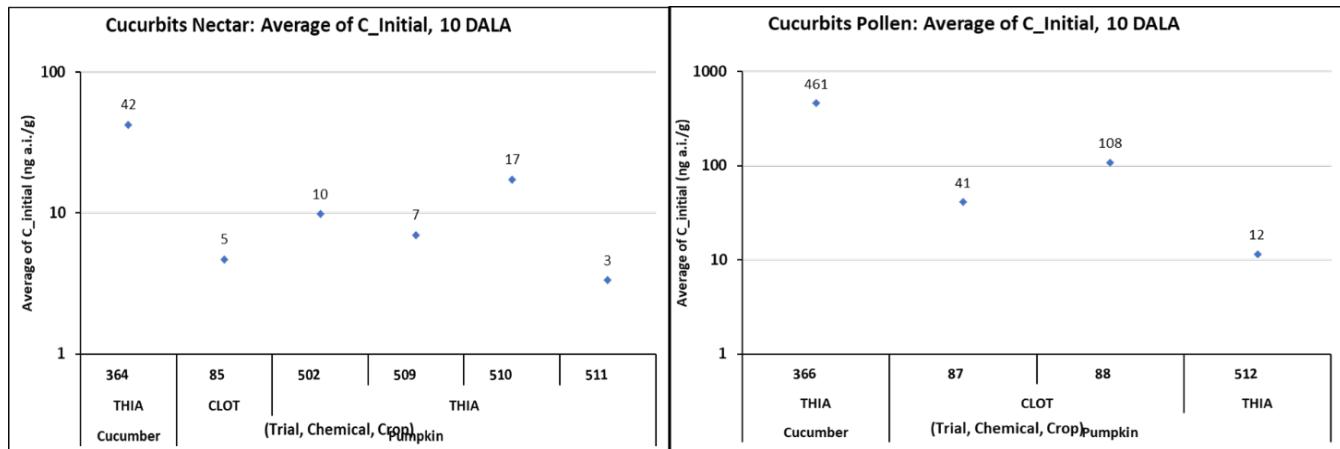


Figure 6-84. Average initial neonicotinoid measured concentrations (ng a.i./g) normalized to sampling day (10 DALA) in nectar (left) and pollen (right) across chemical and crop. CLOT = clothianidin. THIA = thiamethoxam. Thiamethoxam residues expressed in clothianidin equivalents.

To account for the potential variability caused by application rate, residues were further normalized to a rate of 0.1 lb a.i./A, based on either the last application or total application. For nectar (**Figure 6-85**), the range of concentrations decreases to approximately 10x, regardless of whether normalizing by last or total application rate. The nectar data are very limited for evaluating the impact of chemical or crop on residue values, since time-normalized residue values are only available from one trial and crop with clothianidin and 5 trials (2 crops) with thiamethoxam. Residues of clothianidin in pumpkin nectar are within same range as that observed with thiamoxam for pumpkin. Similarly, residues of thiamethoxam in cucumber nectar are within the range of those observed for pumpkin, regardless of normalization by last or total application rate.

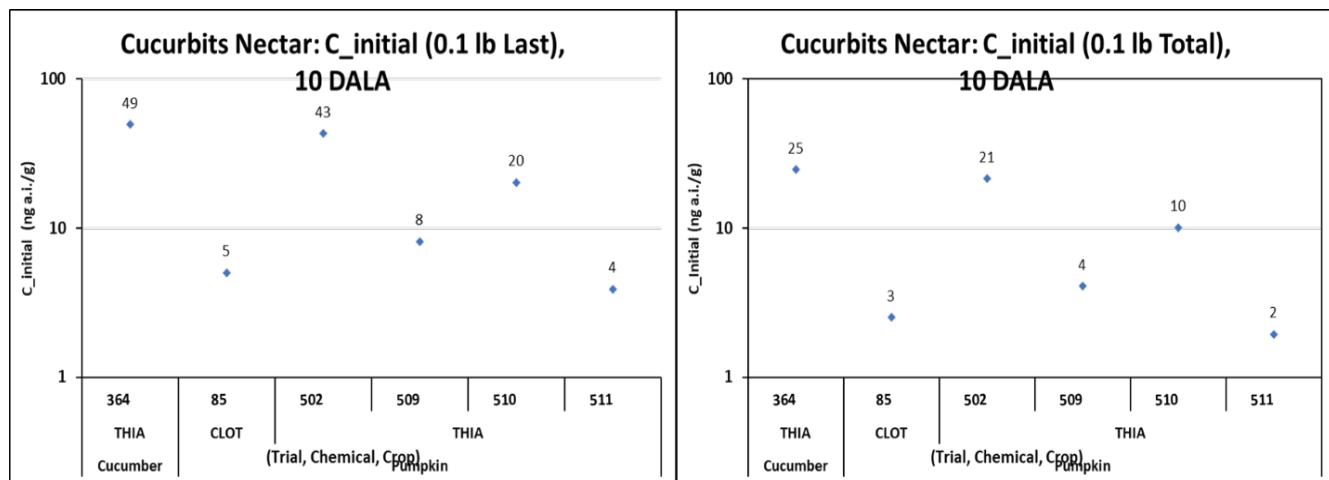


Figure 6-85. Average initial neonicotinoid measured concentrations (ng a.i./g) in nectar normalized to sampling day and 0.1 lb a.i./A for the last (left) and total (right) application rate across chemical and crop. CLOT = clothianidin. THIA = thiamethoxam. Thiamethoxam residues expressed in clothianidin equivalents.

for pollen (Figure 6-86), normalizing by the application rate does not greatly reduce the range of concentrations beyond the ~2X reduction already described above when normalizing by sampling interval (~approximately 40x range in pollen concentrations, regardless of whether normalizing by last or total application rate). Notably, residues of thiamethoxam in cucumber pollen (normalized to DALA 10) are about 40X those in pumkin pollen. This may indicate the potential effect of crop on thiamethoxam residues or possibly the effect of site, since these trials were conducted at different sites.

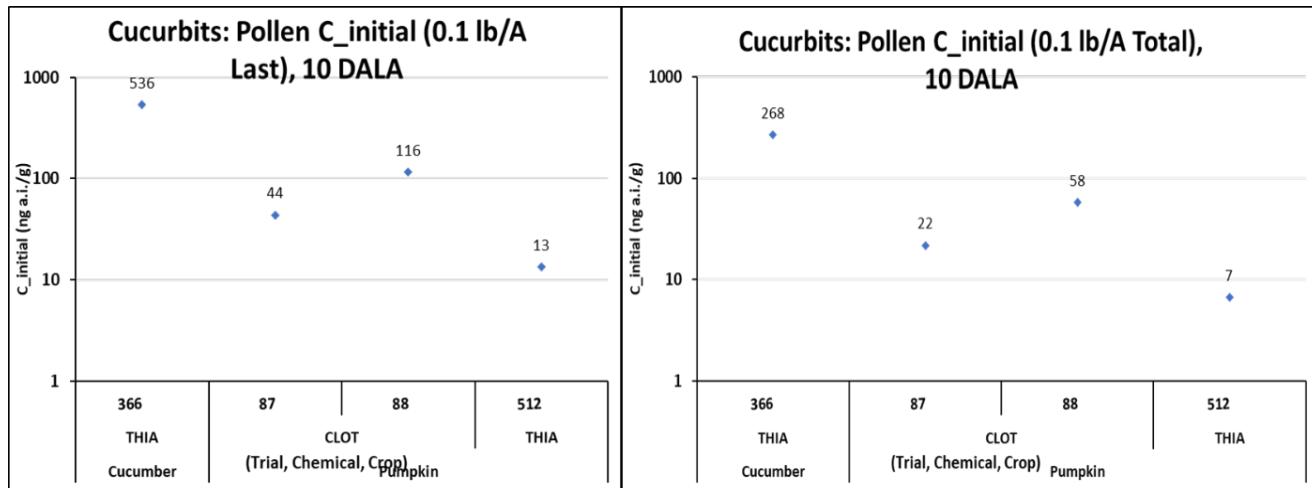


Figure 6-86. Average initial neonicotinoid measured concentrations (ng a.i./g) in pollen normalized to sampling day and 0.1 lb a.i./A for the last (left) and total (right) application rate across chemical and crop. CLOT = clothianidin. THIA = thiamethoxam. Thiamethoxam residues expressed in clothianidin equivalents.

6.7.2.6 Effect of site on residue values

The effect of site (trial location) on residue values can be evaluated for three studies: clothianidin (pumpkin) and thiamethoxam (pumpkin and cucumber). With clothianidin residues in pumpkin nectar and pollen, the range in mean residues measured at similar DALA are within 1 order of magnitude when normalized to a common application rate (**Figure 6-87**). Similarly, mean residues of thiamethoxam in pumpkin vary by 1 order of magnitude among the trial sites when compared at similar DALA (**Figure 6-88**). The 95% confidence intervals associated with mean residues in pumpkin nectar from the Fisk, MO site generally do not overlap with those from the Belvidere, NC site, suggesting a potential influence of site. However, while the thiamethoxam cucumber nectar data also do not suggest a strong influence of site (based on generally overlapping confidence intervals), the cucumber pollen residue data had significantly higher residues in the California site (**Figure 6-89**, green triangles) than in the Georgian site (**Figure 6-89**; orange diamonds) with residues in pollen in North Carolina always being intermediate to the other two sites.

In summary, the majority of comparisons suggest that residues are within 10X between sites within the same study as a result of foliar applications to cucurbit crops, although data are limited to two chemicals and crops. There is some evidence that residues measured at different sites can be substantially different based on non-overlapping 95% confidence limits. Such differences may result from multiple factors that can impact the bioavailability and translocation of neonicotinoids (*e.g.*, weather, soil properties). Therefore, based on the limited data available, the impact of site and year on neonicotinoid residues appears to be modest in most cases, but cannot be dismissed as a potentially important factor influencing pollen and nectar residues from pre-bloom applications to cucurbits crops.

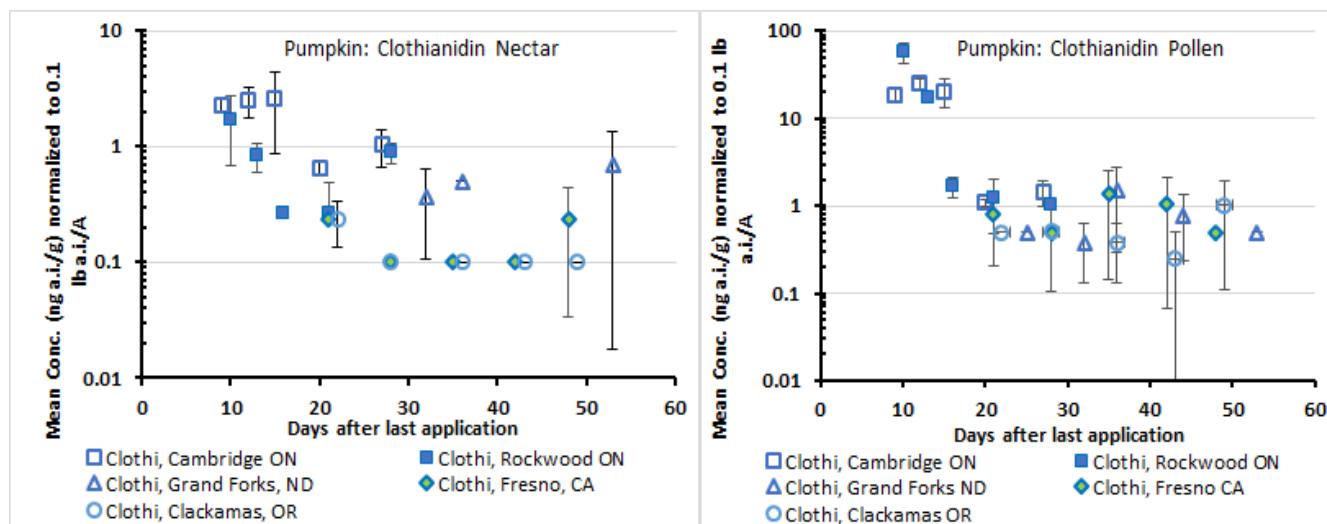


Figure 6-87. Mean measured clothianidin concentrations by site in nectar (left) and pollen (right) following foliar applications to pumpkin. Error bars = 95% confidence intervals.

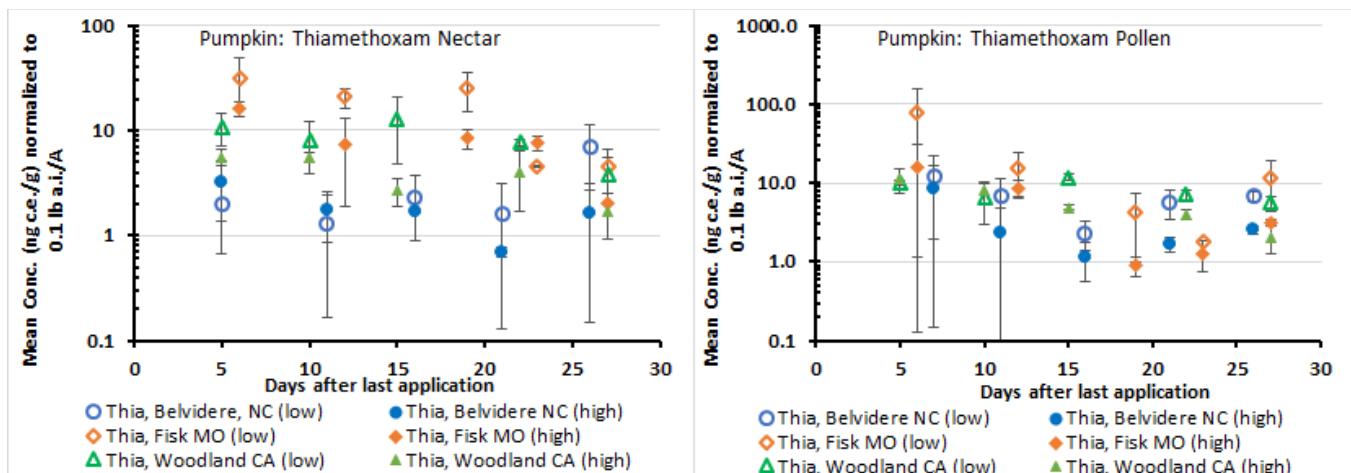


Figure 6-88. Mean measured thiamethoxam concentrations (in clothianidin equivalents) by site in pumpkin nectar (left) and pollen (right) after foliar applications. “Low” and “high” refer to different application rates. Error bars = 95% confidence intervals.

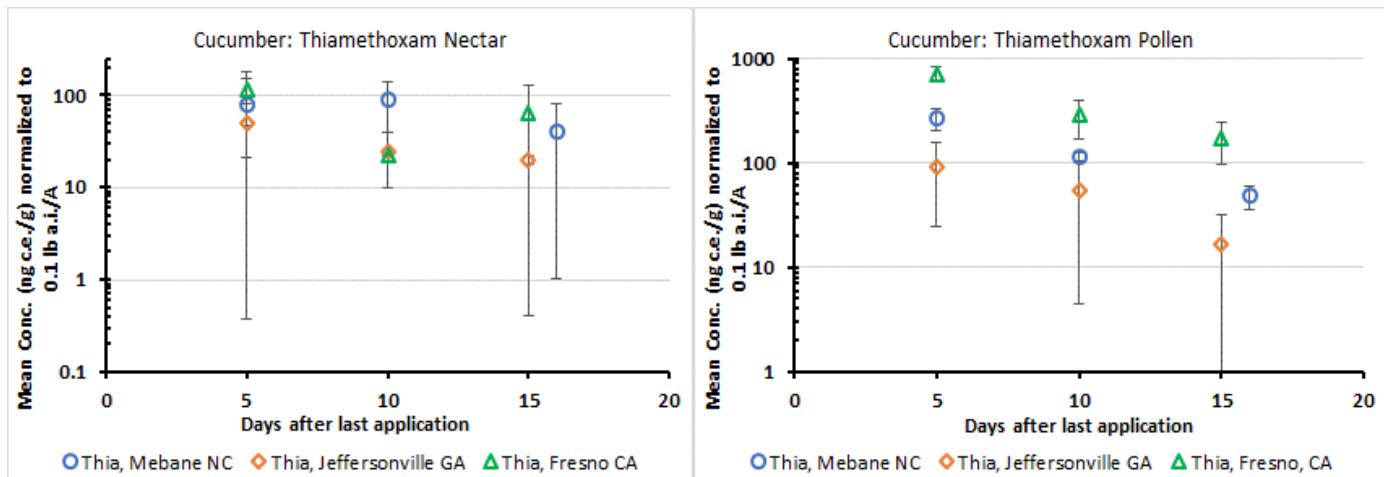


Figure 6-89. Mean measured thiamethoxam concentrations (in clothianidin equivalents) by site in cucumber nectar (left) and pollen (right) after foliar applications. Error bars represent 95% confidence intervals.

6.7.2.7 Effect of crop on residue values

For foliar applications to cucurbits, thiamethoxam data are available for two different crops (pumpkin and cucumber) with overlaps in sampling timing between 5 and 16 DALA (Figure 6-90) below depicts nectar on the left and pollen on the right in clothianidin equivalents). When compared, the normalized residues suggest that the cucurbit crop tested may have an influence on overall residues, with consistently higher residues in cucumber with some non-overlapping 95% confidence limits with pumpkin for some sites. In some cases, mean residues in cucumber nectar or pollen exceed those measured in the corresponding pumpkin matrices by about 100X when compared at similar DALA, depending on site. Since the effect of site on mean residues within a study was found to vary by up to 10X, this suggests that residues of thiamethoxam in cucumber pollen and nectar may reflect crop-specific attributes in addition to site.

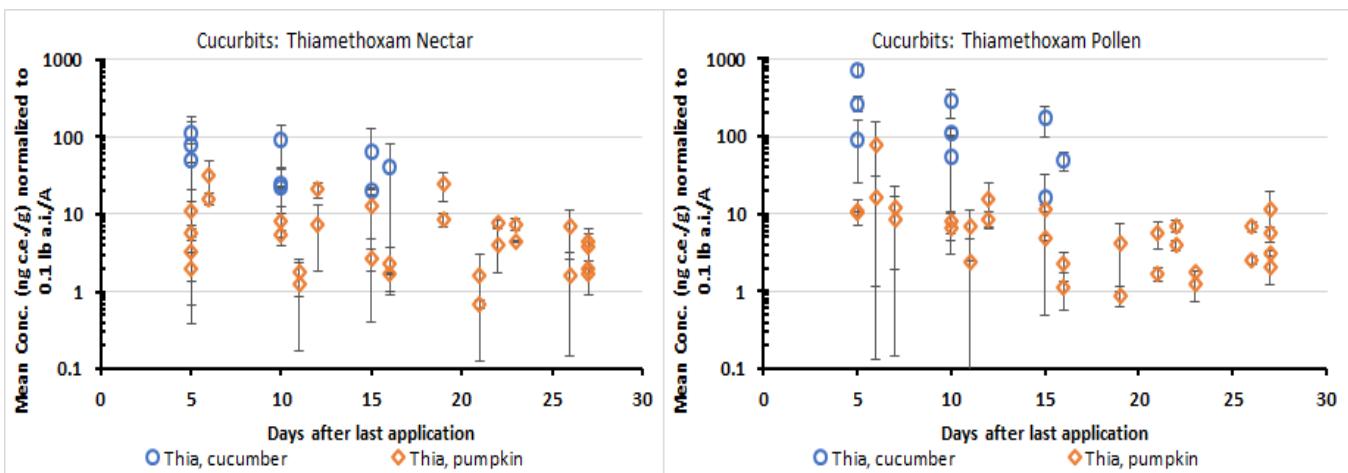


Figure 6-90. Mean normalized residue concentrations of thiamethoxam (in clothianidin equivalents; ng ce/g) in nectar (left) and pollen (right) of cucurbit crops over similar sampling times following bloom. Error bars = 95% confidence intervals.

6.7.2.8 Effect of chemical on residue values

Data are available for different chemicals and the same crop for foliar applications to pumpkins (clothianidin and thiamethoxam; **Figure 6-91**). The thiamethoxam and clothianidin pumpkin data had overlaps in their sampling times between approximately 10 and 30 DALA. No obvious influences of chemical can be observed, though thiamethoxam residues (in clothianidin equivalents) in nectar trend somewhat higher than clothianidin, they are generally within an order of magnitude at the same sampling time period. It is noted that thiamethoxam and clothianidin residue values in pollen and nectar were found to vary by up to 10X based on site. Therefore, within the context of variability in residues among sites, this analysis suggests that chemical does not have an overriding influence on neonicotinoid residues in pollen and nectar measured after foliar applications to pumpkin.

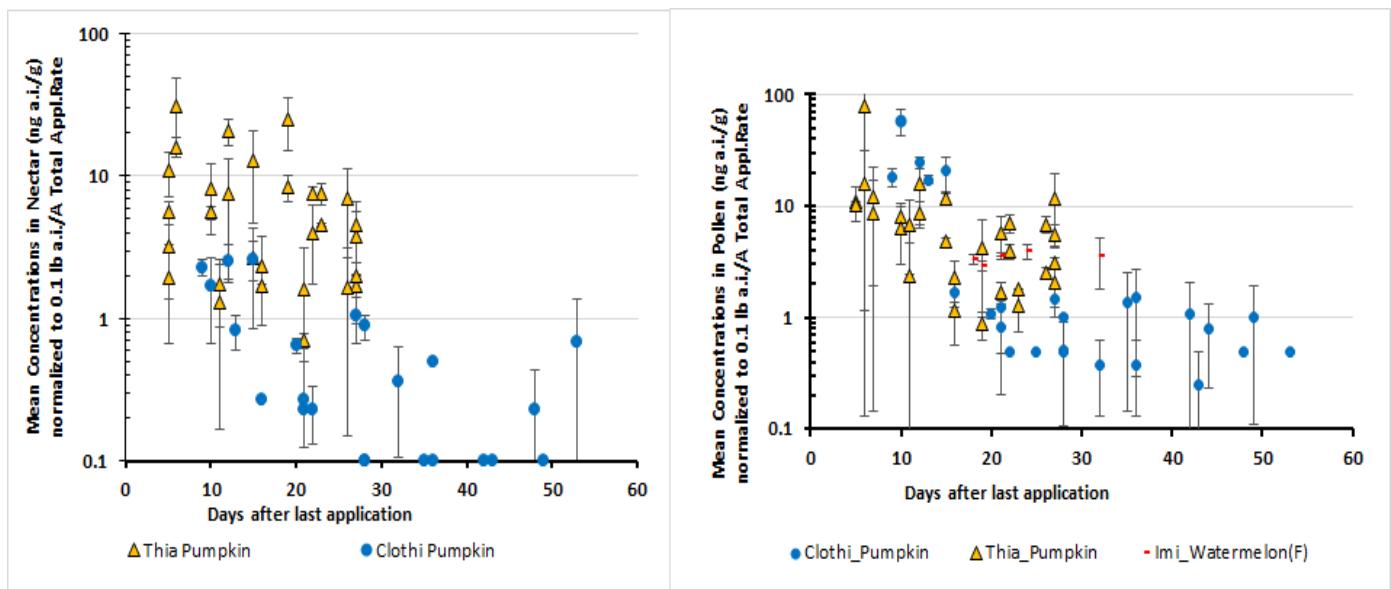


Figure 6-91. Mean normalized residues of clothianidin and thiamethoxam (in clothianidin equivalents; ng ce/g) in pumpkin nectar and pollen at similar sampling times. Error bars = 95% confidence intervals.

6.7.2.9 Bridging recommendations

While the available data are limited to two chemicals and cucurbit crops, the previous analysis of the available pollen and nectar residue data suggests that neither chemical nor crop have a consistent or overriding influence on neonicotinoid residues following foliar applications to cucurbit crops. The majority of comparisons indicated residues are within an order of magnitude among sites, although there is evidence that site can have a substantial impact on residues in some situations (*e.g.* thiamethoxam cucumber pollen residue data for Fresno, CA compared to Jeffersonville, GA). Residues in pollen and nectar generally display a consistent declining trend over time.

As discussed previously in this section, the most robust data for neonicotinoid residues in cucurbits is for clothianidin (pumpkin) and thiamethoxam (pumpkin and cucumber) while less data is available for dinotefuran and imidacloprid and for other cucurbit species such as squash and melon. The sparseness of data for imidacloprid is not considered a main data gap, given its lack of registered foliar uses in the U.S. For foliar applications, the main data gaps that remain are for:

- Applications of dinotefuran to any cucurbit crop
- Applications of clothianidin to crops other than pumpkin
- Application of any neonicotinoid to the melon sub-group

Given the lack of obvious influences of chemical and crop on residue data, it is recommended that the available data for clothianidin, imidacloprid and thiamethoxam can be bridged across cucurbit crops and neonicotinoids. Similarly, the analysis supports bridging for “K” across crops and chemicals. However, cucurbit crop may influence the magnitude of residues including $C_{initial}$. Uncertainties associated with this approach include: lack of data on the melon sub-group and lack of reliable data for imidacloprid and dinotefuran for comparison.

6.7.3 Soil Applications

6.7.3.1 Summary of label rates/restrictions

All four neonicotinoids being assessed are registered for soil applications to cucurbits (**Table 6-63**). Maximum single application rates vary from 0.15 to 0.38 lb a.i./A while total seasonal rates vary from 0.15 to 0.54 lb a.i./A.

Table 6-63. Soil application rates (in lb a.i./A) and number of applications for neonicotinoids on cucurbit crops (based on current labels).

Chemical	Max Appl. Rate x No. Apps. (lb a.i./A)	Total Seasonal Rate (lb a.i./A)	Minimum Interval (d)
Imidacloprid	0.38 x 1	0.38	N/A
Clothianidin	0.2 x 1	0.2	N/A
Thiamethoxam	0.15 x 1	0.15	N/A
Dinotefuran	0.33 x 1	0.54	7

N/A = not applicable

6.7.3.2 Available residue data

Residue data for pollen, nectar and/or whole flower are available for soil applications of clothianidin, thiamethoxam, dinotefuran and imidacloprid from 12 studies, representing 4 crops within the cucurbit crop group and >30 different sites (**Table 6-64**). Residue data are also available for whole flowers for one thiamethoxam study of cucumber and an imidacloprid study on watermelon. Therefore, the relationships between anthers and pollen and flowers and pollen/nectar are considered, as described in Section 5. A study with dinotefuran on cucumbers (MRID 49841003; qualitative) was not considered due to insufficient quantities of pollen and nectar collected for residue analysis. Additional qualitative data for dinotefuran on pumpkin, cucumber, melon and squash (MRID 50145704) were also not considered as pollen and nectar samples were taken but were sometimes taken from within the hive rather than from foraging bees or from fresh pollen collected from pollen traps affixed to the hive. Nectar and pollen residues from in-hive samples may have degraded and/or been mixed with other honey bee products and it was often unclear from the study report which samples were from within the hive versus which were from foragers/pollen traps. Therefore, data from this study was not used to inform the residue bridging strategy. Quantitative data from a Brazilian study applying imidacloprid to watermelon (MRID 50357101) were considered. This study used honey bees to gather the pollen and nectar; however, residues in pollen were not available for concurrent nectar samples (*i.e.* pollen and nectar samples were not taken at the same time).

Table 6-64. Residue studies for cucurbit crops treated with soil applications of neonicotinoids.

Crop	Chemical	# sites (Locations)	App. Rate, # of apps (interval)	# Seasons	# sampling events (per season)	MRID (Classification)
Pumpkin	Clothianidin	1 (Fresno, CA)	0.2 lb a.i./A x 1	1	5	49705901 Supplemental ²
Pumpkin	Clothianidin	3 (Grand Forks ND Fresno CA Clackamas OR)	0.2 lb a.i./A x 1	1	3-5	49910601 (Supplemental)
Pumpkin	Clothianidin	9 (California sites)	0.2 lb a.i./A x 1	3	1	49602801 (Acceptable)
Pumpkin	Thiamethoxam	3 (Woodland CA Fisk MO Belvidere NC)	0.107 lb a.i./A ¹ x 1 (low) 0.147 lb a.i./A ¹ x 1 (high)	1	5	50265501 (Acceptable)
Pumpkin	Dinotefuran	3 (Belvidere NC Fisk MO Northwood ND)	0.185 lb a.i./A x 1 + 0.297 lb a.i./A x 1 (7-18d)	1	3	49852701 (Acceptable)
Pumpkin	Dinotefuran	1 (Sanger, CA)	0.206 lb a.i./A x 1 + 0.33 lb a.i./A x 1 (7d)	1	3	50145704 (Supplemental) ⁴
Cucumber	Clothianidin	1 (Fresno, CA)	0.2 lb a.i./A x 1	1	3-4	49705901 (Supplemental) ^{2,3}
Cucumber	Thiamethoxam	2 (Sanger CA San Louis Obispo CA)	0.172 ¹ lb a.i./A x 1	1	1	49550801 (Acceptable)
Cucumber	Dinotefuran	1 (Sanger CA)	0.206 lb a.i./A x 1 + 0.33 lb a.i./A x 1 (7d)	1	3	50145704 (Supplemental) ⁴
Cantaloupe	Clothianidin	1 (Fresno, CA)	0.2 lb a.i./A x 1	1	3-4	49705901 (Supplemental) ^{2,3}

Crop	Chemical	# sites (Locations)	App. Rate, # of apps (interval)	# Seasons	# sampling events (per season)	MRID (Classification)
Cantaloupe	Clothianidin	3 (Paso Robles CA Jeffersonville GA Mebane NC)	0.2 lb a.i./A	1	5	50154306 (Acceptable)
Muskmelon	Thiamethoxam	3 (Woodland CA Fisk MO Belvidere NC)	0.147 lb a.i./A ¹ x 1	1	5	50265501 (Acceptable)
Watermelon	Imidacloprid	1 (Brazil)	0.187 lb a.i./A x 1	1	3-4	50357101 (Supplemental)
Melon	Imidacloprid	10 (California sites)	0.28-0.38 lb a.i./A x 1	2	1	49090501 (Supplemental)
Melon (cantaloupe)	Dinotefuran	3 (Cedar Grove NC Jeffersonville GA Sanger CA)	0.206 x 1 + 0.33 x 1 (7d)	1	3	50145701 (Supplemental) ⁴
Squash (Yellow Crookneck)	Clothianidin	1 (Fresno, CA)	0.2 lb a.i./A x 1	1	5	49705901 (Supplemental) ^{2,3}
Squash	Thiamethoxam	3 (Woodland CA Fisk MO Belvidere NC)	0.147 lb a.i./A ¹ x 1	1	5	50265501 (Acceptable)
Squash (Butternut and Yellow Crookneck)	Dinotefuran	1 (Sanger, CA)	0.206 x 1 + 0.33 x 1 (7d)	1	3	50145704 (Supplemental) ⁴

¹Clothianidin-equivalent rates

²Quantitative data not available from 3 sites.

³Less than 3 samples taken per sampling event

⁴Some samples were taken within tented bee colonies as residues in bee bread or in-hive nectar. These residues may be lower due to degradation over time or potential mixing with other bee products.

Based on the aforementioned studies, mean residue values in nectar and pollen resulting from soil applications of neonicotinoids to cucurbits are shown in **Figure 6-92** and **Figure 6-93**, respectively.

Unlike residues associated with foliar applications to cucurbits, those resulting from soil applications do not display a distinct declining trend with time after application, at least when data are combined across neonicotinoids and crops. When compared at similar time points after application, mean residue values range up to 100X among neonicotinoids and crops.

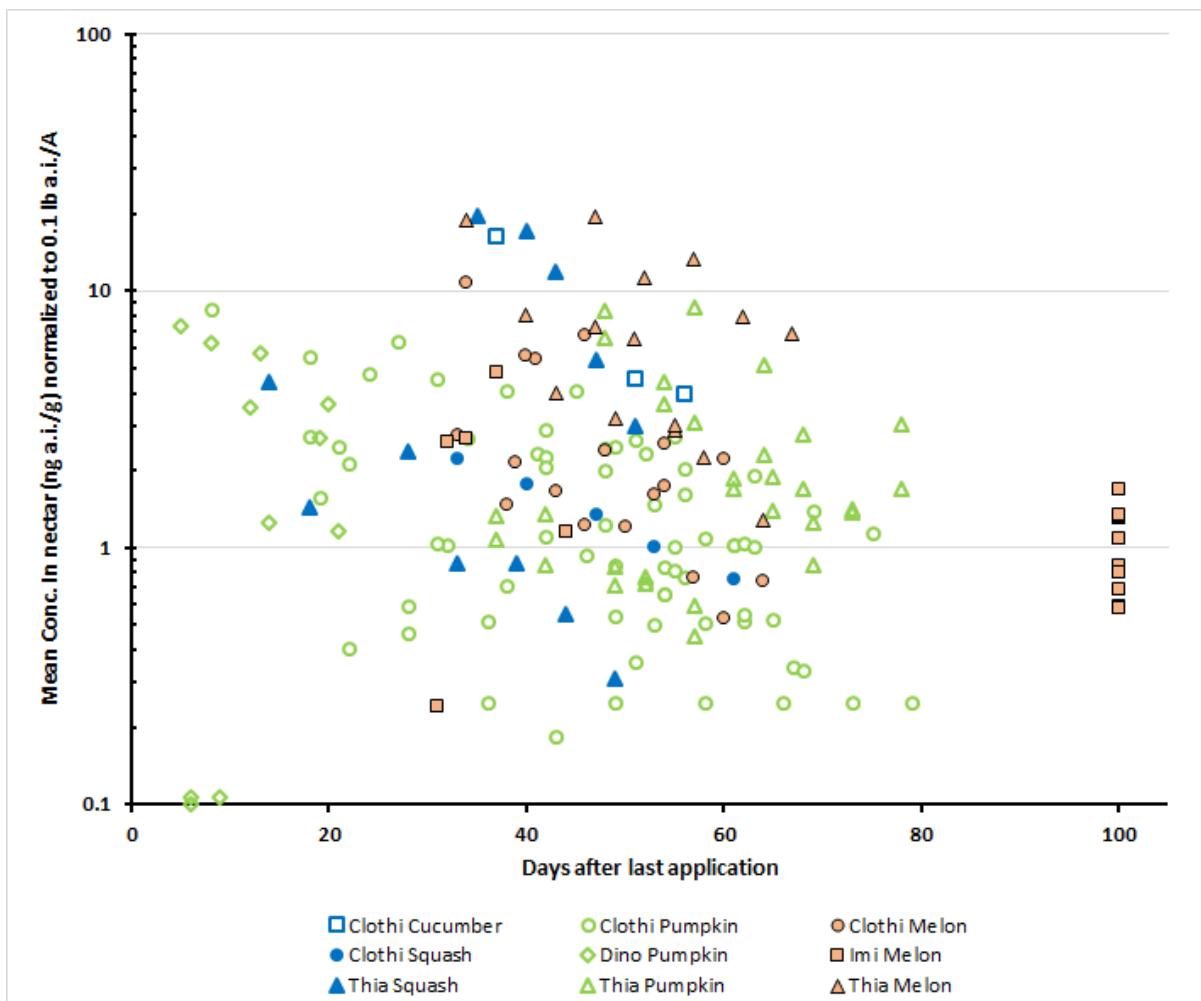


Figure 6-92. Mean concentrations in nectar following soil applications to cucurbit crops. Values normalized to total application rate of 0.1 lb a.i./A. Imi = imidacloprid; Thia = thiamethoxam, Clothi = clothianidin, Dino = dinotefuran. Thiamethoxam residues are expressed as clothianidin equivalents.

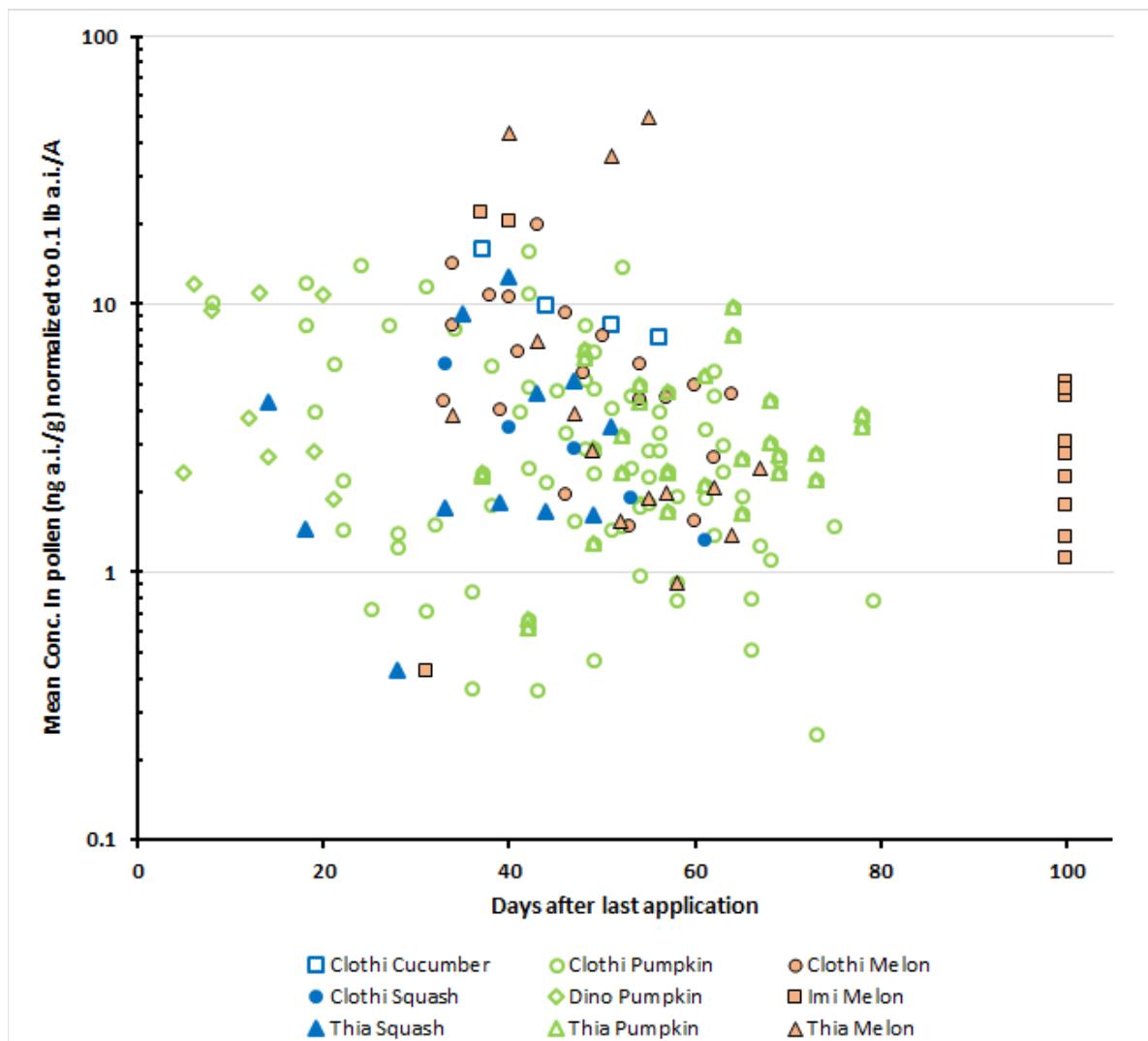


Figure 6-93. Mean concentrations in pollen following soil applications to cucurbit crops. Values normalized to total application rate of 0.1 lb a.i./A. Imi = imidacloprid; Thia = thiamethoxam, Clothi = clothianidin, Dino = dinotefuran. Thiamethoxam residues are expressed as clothianidin equivalents.

6.7.3.3 Bridging needs (gaps)

All the compounds, with the exception of imidacloprid, have some data on multiple crops within the cucurbit crop group, including data for both cucurbit sub-groups. For imidacloprid, there is a question of whether having only melon data is sufficient to serve as a reasonable surrogate for all cucurbit crops. Further, the quality of the imidacloprid dataset is limited (e.g., MRID 49090501 only has 1 sampling period per year per site, while MRID 50357101 only has data for one location in Brazil, with fairly limited replication) compared to the overall quality of the cucurbit data for other neonicotinoids). Two dinotefuran studies (MRIDs 50145701 and 50145704) were excluded from the analysis due to their nectar measurements having been sampled from in-hive matrices while in pollen samples were a combination of bee collected (from pollen traps or bee bread) and by hand. Although the hives were tented in these studies, residues in hive nectar and bee bread may be lower due to degradation over time or potential mixing with other bee products. The available colony feeding studies for the

neonicotinoids provide additional data demonstrating that residues in sucrose outside the hive (which is what the colony level endpoints are based on) are significantly different than the stored nectar and bee bread residues within the hive.

Based on these considerations, the residue data bridging needs with soil applications to cucurbits are shown in **Table 6-65**.

Table 6-65. Identification of data gaps for registered soil applications of neonicotinoids on cucurbits¹

Crop	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Cucurbits: Melon Sub-group	NR Watermelon (MRID 50357101) Melon (MRID 49090501)	Canteloupe (MRIDs 49705901 50154306)	Muskmelon (MRID 50265501)	No Data
Cucurbits: Squash/cucumber subgroup	No Data	Pumpkin (MRIDs 49705901, 49910601 & 49602801) Cucumber (MRID 49705901) Squash (MRID 49705901)	Pumpkin (MRID 50265501) Cucumber (MRID 49550801) Squash (MRID 50265501)	Pumpkin (MRID 49852701)

NR = not registered. Assessment

¹ Residue data include acceptable or supplemental studies considered appropriate for quantitative use in risk assessment.

6.7.3.4 Influence of application rate on residues

One study is available to evaluate the influence of varying application rates on residues in pollen and nectar following a soil application to pumpkins. In this study, thiamethoxam was applied to pumpkins with one soil application at either 0.107 or 0.147 lb a.i./A (clothianidin equivalents; MRID 50265501).

Figure 6-94 and **Figure 6-95** depict residues in nectar and pollen, respectively, collected from pumpkins treated at the different rates. For both figures, the graph on the left represents the mean residues from the study while the graph on the right represents residues normalized to an application rate of 0.1 lb a.i./A. When residues are normalized to the same total application rate, there is no clear pattern to regarding the influence of application rate on residue concentrations in either pollen or nectar.

However, the difference in the application rates used in this analysis is fairly small (<50%) and its effect on residues may be masked by other factors resulting in variability in the data.

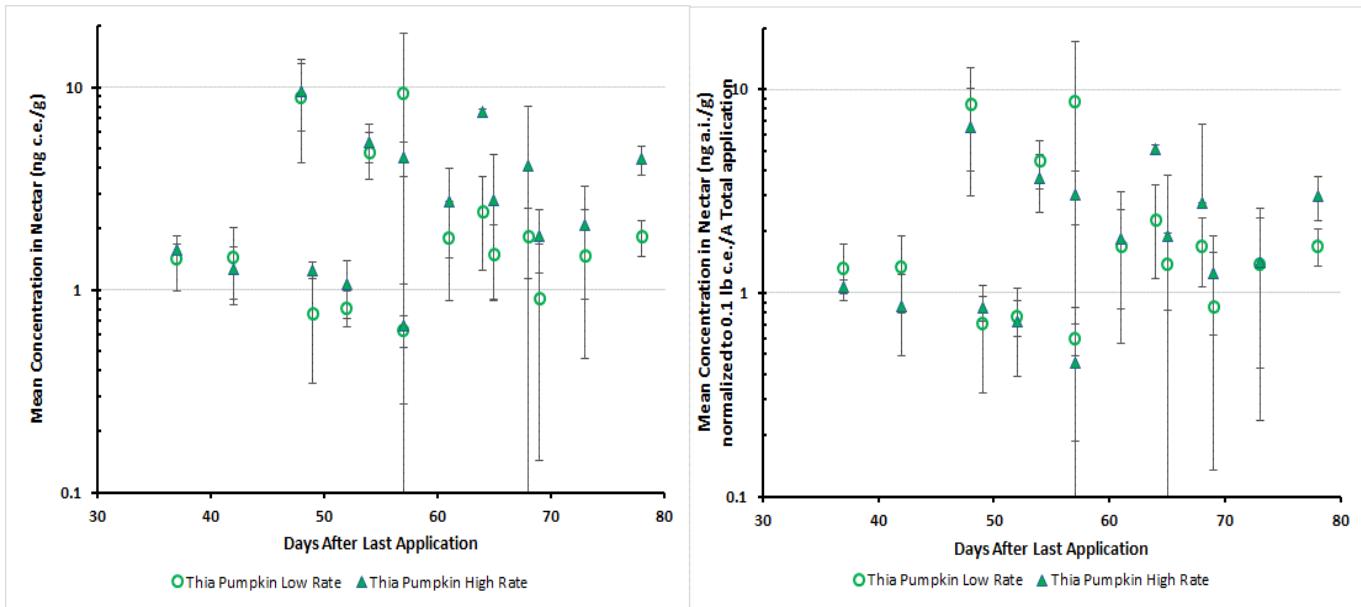


Figure 6-94. Mean residues in nectar (expressed as clothianidin equivalents; ng c.e./g) following soil applications of thiamethoxam to pumpkin (MRID 50265506). Low applications (hollow triangles) were made at 0.107 lbs c.e./A while high applications (solid triangles) were made at 0.147 lbs c.e./A. Left graph depicts unadjusted residues. Right graph depicts residues normalized to application rate of 0.1 lb a.i./A. Error bars = 95% confidence intervals.

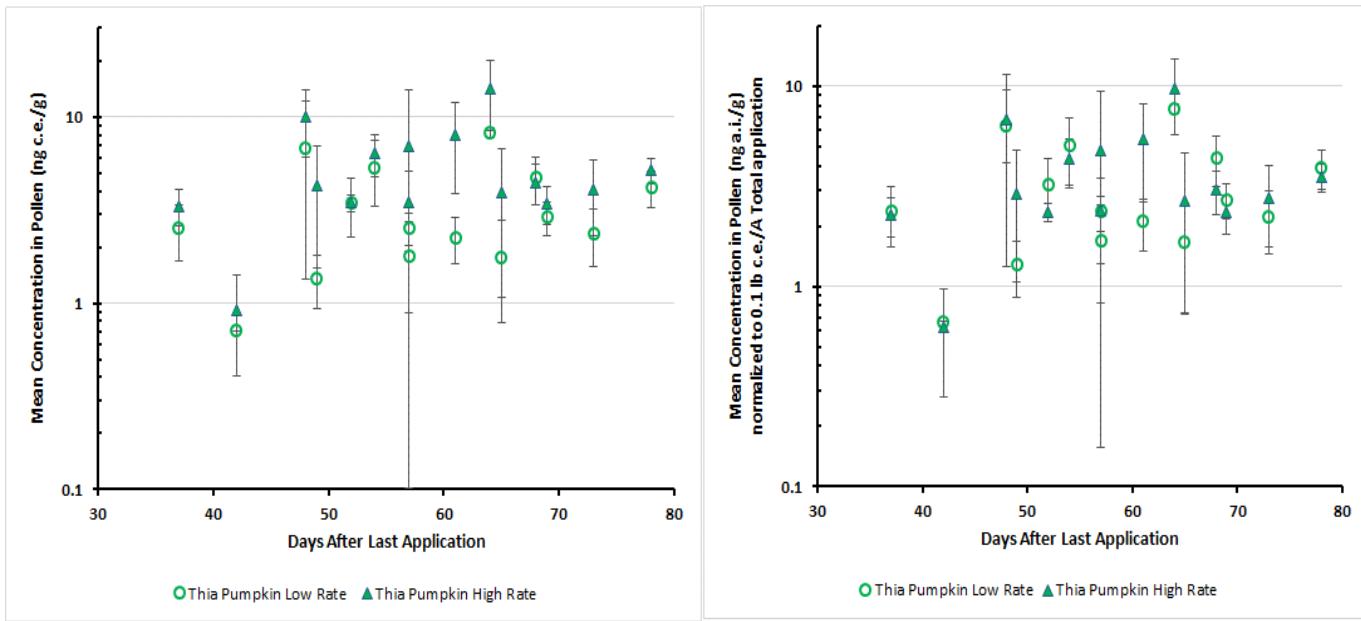


Figure 6-95. Mean residues (expressed as clothianidin equivalents; ng ce/g) in pollen following soil applications of thiamethoxam to pumpkin (MRID 50265506). Low applications (hollow triangles) were made at 0.107 lbs c.e./A while high applications (solid triangles) were made at 0.147 lbs c.e./A. Left graph depicts unadjusted residues. Right graph depicts residues normalized to total application rate of 0.1 lb a.i./A. Error bars = 95% confidence intervals.

6.7.3.5 Influence of sampling day (time) on residue values

For soil applications, all but a few trials are not suitable for kinetic modeling or do not produce reliable estimates of kinetic parameters using the SFO model. Flat or increasing residue values over time were indicated in most of the trial specific data. This may be related to the nature of the application method, whereby pesticide in treated soil continues to become available for uptake in plants weeks or months after application. Therefore, a kinetic analysis was not conducted for soil applications to cucurbits.

Table 6-66 below lists the range of mean residue values for pollen and nectar from cucurbit crops following soil applications with different time periods between bloom and application. Residues in pollen are generally higher than those of nectar, but typically within an order of magnitude. There are no obvious trends regarding the magnitude of residues over time, although the highest mean concentrations tend to occur between 30 and 60 DAA. However, this may also have been a function of the greater number of samples taken during this time.

Table 6-66. Ranges of mean thiamethoxam residues (expressed as clothianidin equivalents normalized to 0.1 lb a.i./A total application) in cucurbit nectar and pollen by days since application.

Days before bloom when application was made	Concentration in nectar ng ce/g	Concentration in pollen ng ce/g
1-10	<LOD-8.5	2.5-13.7
11-20	1.3-6.0	1.4-18.9
21-30	<LOQ-6.4	<LOQ-16.6
31-40	<LOQ-19.5	<LOQ-43.8
41-50	<LOQ-11.9	<LOQ-210
51-60	<LOQ-8.7	<LOQ-49.5
61-70	<LOQ-5.1	0.5-9.7
71-100	<LOQ-3.0	<LOQ-5.2

6.7.3.6 Effect of site and year on residue values

For comparisons across multiple sites, data is available for clothianidin in pumpkin (MRIDs 49705901, 49910601, and 49602801) and melon (cantaloupe; MRIDs 49705901, 50154306), for thiamethoxam in pumpkin, melon (muskmelon) and squash (all three crops from MRID 50265501) and for dinotefuran in pumpkin (MRID 49852701). A brief summarization of these data with respect to site-to-site differences is provided below.

Clothianidin/Pumpkin. Data for clothianidin residues in pumpkin nectar and pollen (normalized to 0.1 lb a.i./A) following soil applications at 6 sites are shown in **Figure 6-96**. With nectar (left panel), most mean residue values are within 10X when compared at similar DALA, although some values approach 100X apart. It is evident from non-overlapping confidence limits that residues in pumpkin nectar from the Fresno, CA site (open blue circles) are consistently greater than those from the Clackamas, OR site (solid orange squares). Residues in pollen (right panel) followed a similar pattern as that described for nectar. Residues in the Californian sites did trend higher the closer to application, although there could also be an impact of whether the applications were made post-emergent (BBCH 14; in which most samples were taken within 40 days of treatment) or pre-emergent (in which most samples were taken >50 days following treatment). Other factors such as soil characteristics, agronomic practices and weather could contribute to these differences and are worthy of further investigation.

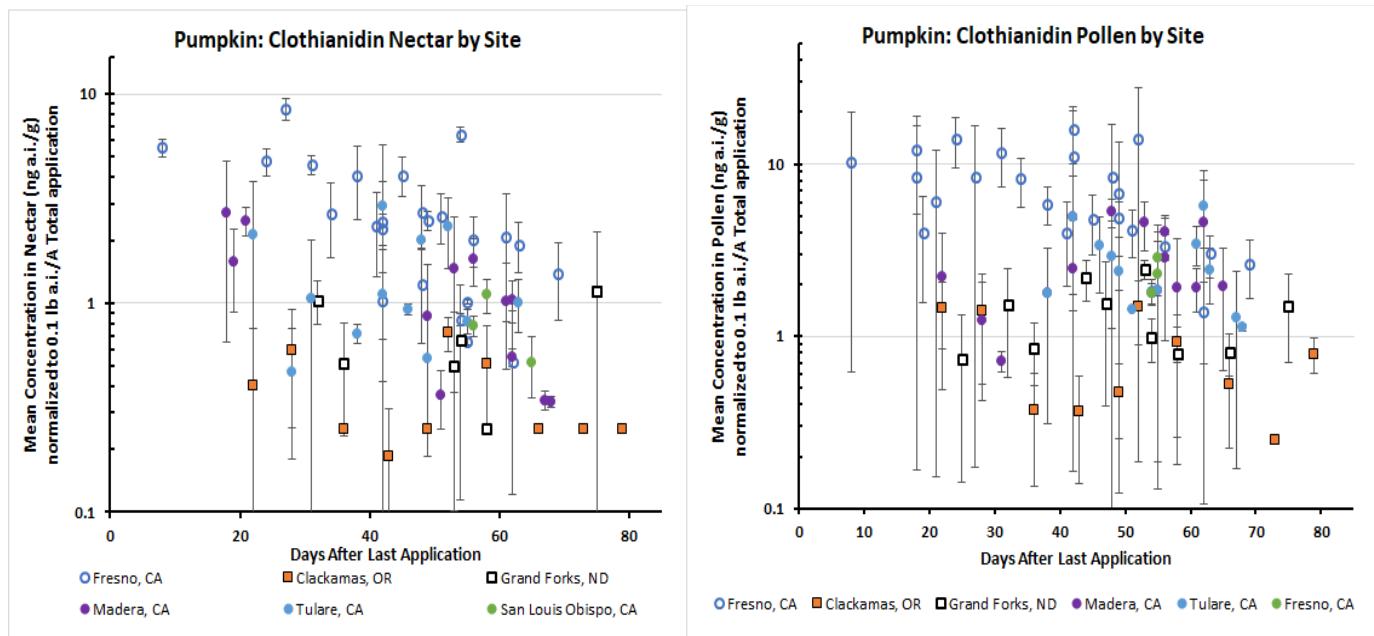


Figure 6-96. Mean clothianidin concentrations (ng a.i./g) normalized to 0.1 lb a.i./A total application among sites in pumpkin nectar (left) and pollen (right) following clothianidin soil applications to pumpkin. Error bars = 95% confidence intervals.

Clothianidin/Melon. Data for clothianidin residues in melon nectar and pollen (normalized to 0.1 lb a.i./A) following soil applications at 4 sites are shown in (Figure 6-97). With nectar, mean residues are within 10X at similar DALA and have overlapping confidence intervals (left panel). With pollen, the overall range in mean values is similar to that observed with nectar, however, residue values from the Jeffersonville, GA site are consistently lower than those of the other 3 sites with non-overlapping confidence intervals. The lack of consistent trend in apparent differences due to “site” among nectar and pollen residues suggests that site-related factors may be affecting residues in these two plant matrices differently. Some of the variability in the clothianidin melon data (for all sites except Fresno, CA) may be attributed to daily means including both bee-collected and hand-collected samples. Generally, hand-collected samples were higher than bee-collected samples, but replicate hand-collected samples were not taken at each time point.

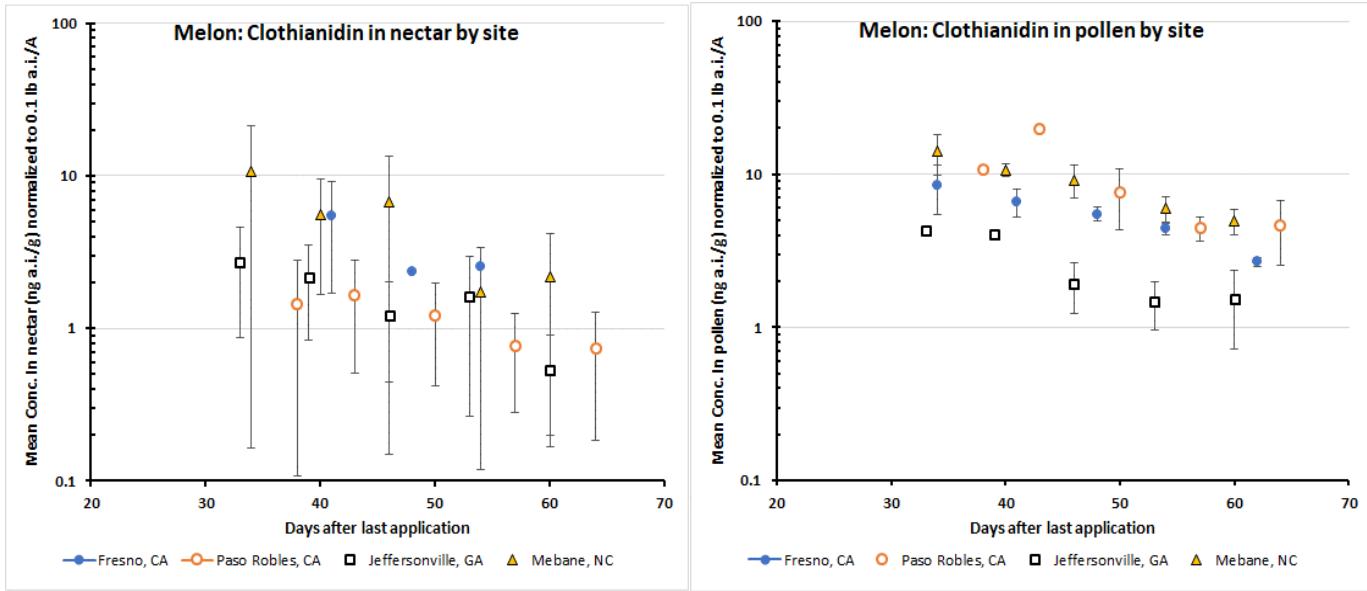


Figure 6-97. Mean normalized clothianidin concentrations (ng a.i./g) by site in melon nectar (left) and pollen (right) following soil applications of clothianidin. The Fresno, CA pollen residues represent residues in anthers. Error bars = 95% confidence intervals.

Thiamethoxam/Pumpkin. Data for thiamethoxam residues in pumpkin nectar and pollen (normalized to 0.1 lb a.i./A and expressed as clothianidin equivalents) following soil applications at 3 sites are shown in **Figure 6-98**. While the range in mean residues in nectar and pollen are both within 10X at similar DALAs, nectar residues at the Belvidere, NC site are consistently lower than those from the other two sites, with non-overlapping confidence intervals. This same pattern is not seen with residues in pollen.

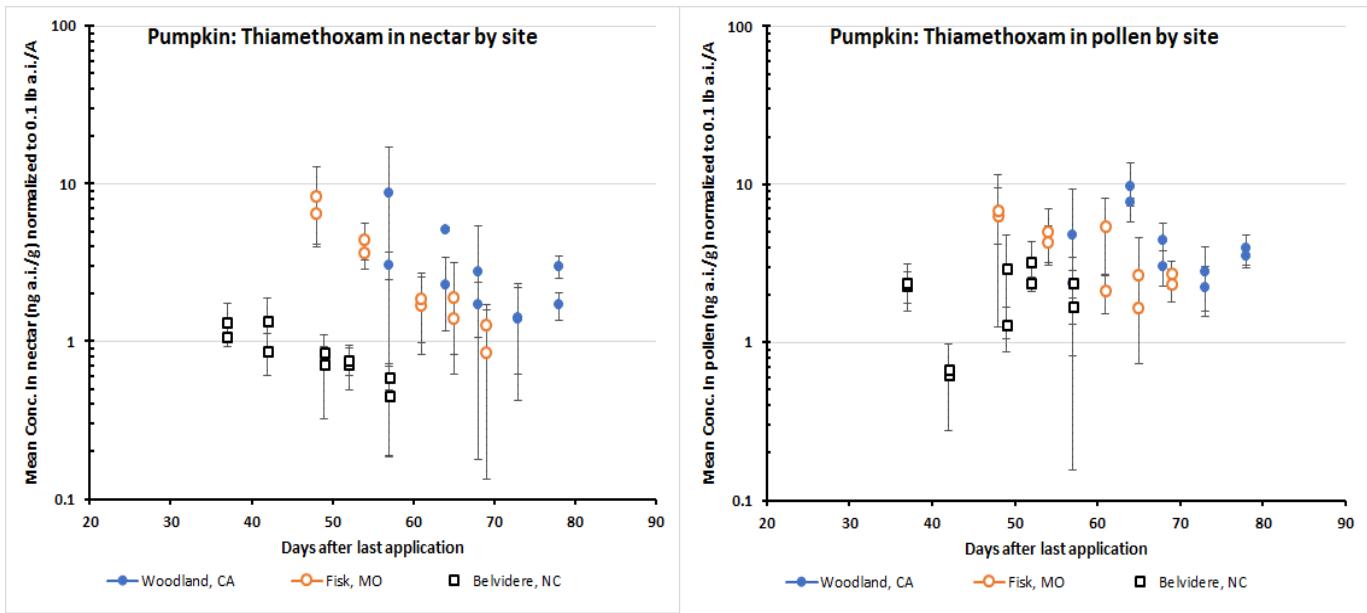


Figure 6-98. Mean normalized thiamethoxam concentrations (expressed as clothianidin equivalents; ng c.e./g) by site in pumpkin nectar (left) and pollen (right) following thiamethoxam soil application to pumpkin. Error bars = 95% confidence intervals.

Thiamethoxam/Melon. Data for thiamethoxam residues in melon nectar and pollen (normalized to 0.1 lb a.i./A and expressed as clothianidin equivalents) following soil applications at 3 sites are shown in **Figure 6-99**. As observed with the thiamethoxam pumpkin data, residues in melon nectar from the Belvidere, NC site tended to be lower than those from the other two sites with non-overlapping confidence intervals in several cases (left panel). However, this pattern was not evident with residues pollen (right panel). Mean residues were very high in the thiamethoxam melon pollen data for the Fisk, MO site, but were also associated with high variance as depicted in the wide confidence intervals.

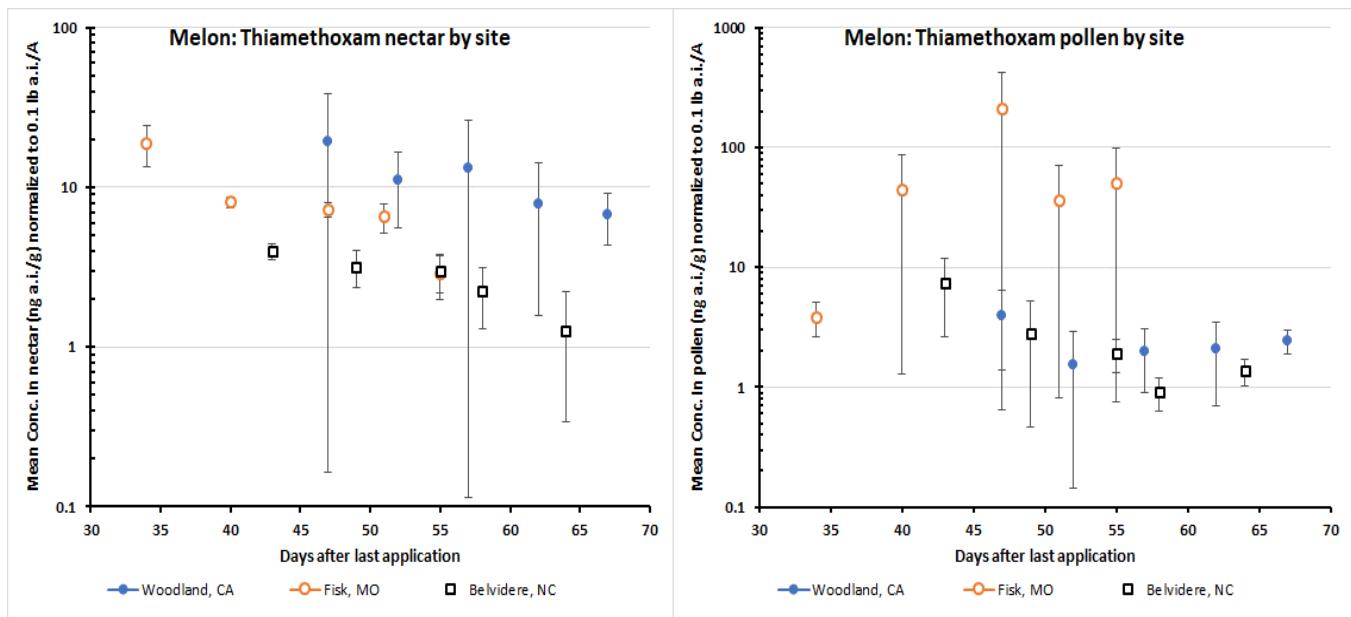


Figure 6-99. Mean normalized thiamethoxam concentrations (expressed as clothianidin equivalents; ng c.e./g) in muskmelon nectar (left) and pollen (right) by site. Error bars = 95% confidence intervals.

Thiamethoxam/Squash. Data for thiamethoxam residues in squash nectar and pollen (normalized to 0.1 lb a.i./A and expressed as clothianidin equivalents) following soil applications at 3 sites are shown in **Figure 6-100**. Mean residues in both the thiamethoxam squash pollen and nectar data are higher in the Fisk, MO site compared to the Woodland, CA site by about 10X, with non-overlapping confidence intervals.

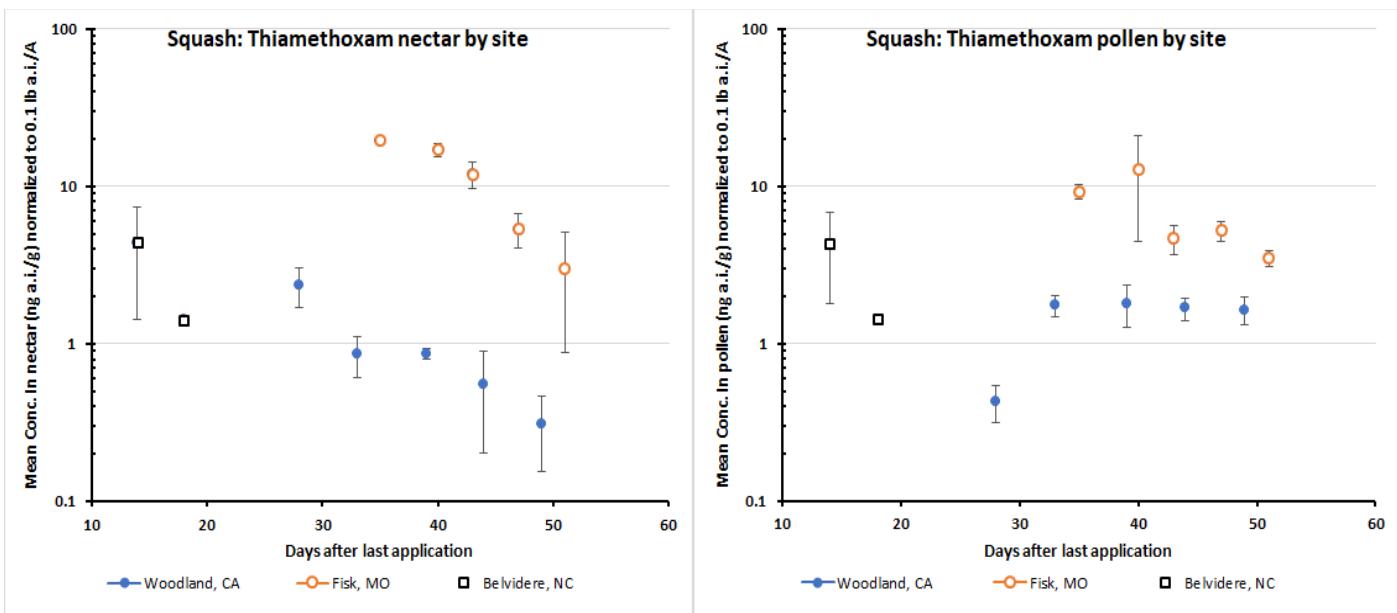


Figure 6-100. Mean normalized thiamethoxam concentrations (expressed as clothianidin equivalents; ng c.e./g) in squash nectar (left) and pollen (right) by site. Error bars = 95% confidence intervals.

Dinotefuran/Pumpkin. Data for dinotefuran in pumpkin nectar and pollen (normalized to 0.1 lb a.i./A) collected from 3 sites are shown in **Figure 6-101**. Mean values among sites are within 10X at similar DALA. Obvious site-specific differences are not indicated in most cases as evidenced by overlapping confidence intervals.

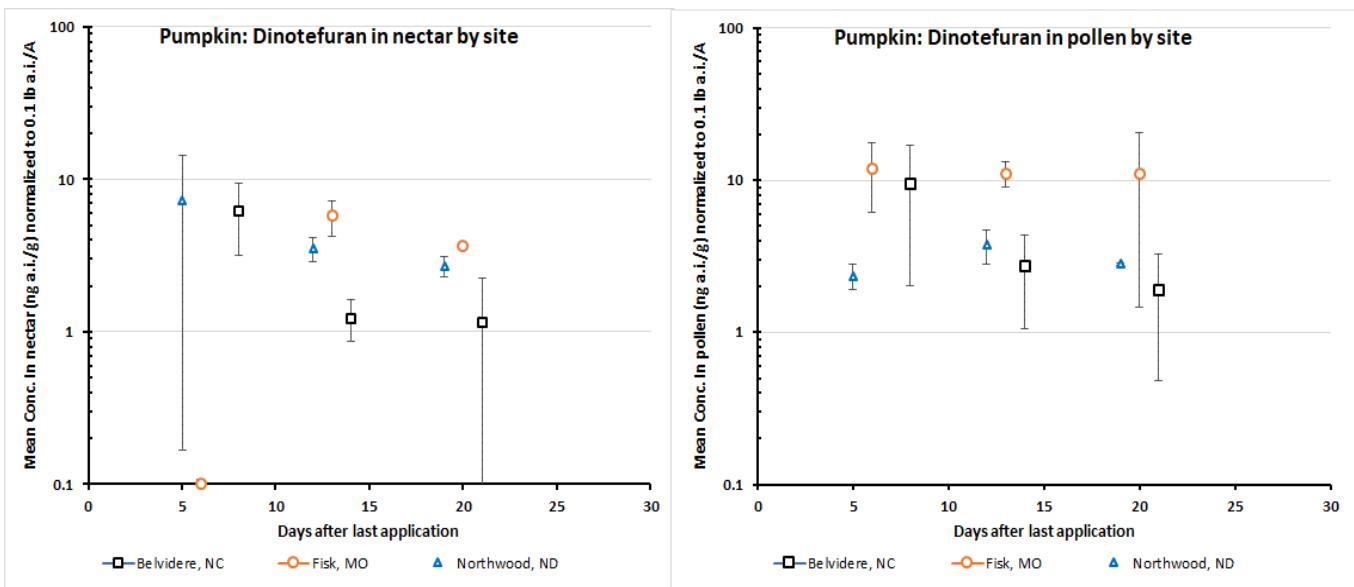


Figure 6-101. Mean normalized dinotefuran concentrations by site in pumpkin nectar (left) and pollen (right). Error bars = 95% confidence intervals.

Two studies were considered to evaluate the effect of year on residues. In a study with clothianidin on pumpkins in California (MRID 49602801), residues were measured in 9 sites over 3 years. However,

samples were only measured once per year. Further, the samples were taken at different days after last application in each year. Therefore, it was determined that this study lacked sufficient information to reliably consider the effect of year on residue values. In a study with imidacloprid on melons in California (MRID 49090501), residues were measured in 10 sites over 2 years. However, in this study measurements were also only made a single time in each year and were not made until 100 days after applications. Given the large time-frame between applications and measurements and the relatively low levels of residues observed at 100 DALA, the study was determined to provide insufficient data to develop reliable conclusions regarding the effect of year on residue values.

6.7.3.7 Effect of crop on residue values

For soil applications to cucurbits, clothianidin data are available for four crops (pumpkin, squash, melon, cucumber) with overlaps in sampling between 30 and 65 DAA among multiple studies and sites (**Figure 6-102**). The pumpkin and melon datasets are the most robust while cucumber and squash data were only available for one site. Clear effects of crop are difficult to discern given the wide variation in mean residues within a crop, presumably reflecting the influence of different sites and seasons. Most of the mean residue of clothianidin in pollen and nectar among crops at similar DALA are within 10X, but some approach 100X.

One study, however, measured residues in 4 cucurbits (pumpkin, melon, squash, and cucumber) at a single site (Fresno, CA) over the same growing season (MRID 49705901). This study is unique in that the effect of season and site on clothianidin residues are minimized when comparing results among crops. Results from this study are shown in **Figure 6-103**. The results from this study indicate that mean residues in nectar and pollen (normalized by application rate) are within 1 order of magnitude among crops. However, there is indication that residues in cucumber nectar and pollen are greater than those measured in other cucurbits based on non-overlapping confidence limits at multiple sampling times. These data suggest that crop can have a discernable influence on residues of clothianidin in pollen and nectar of cucurbit crops, although these differences are within the same single order of magnitude that was generally observed with residues for the same crop among multiple sites and seasons.

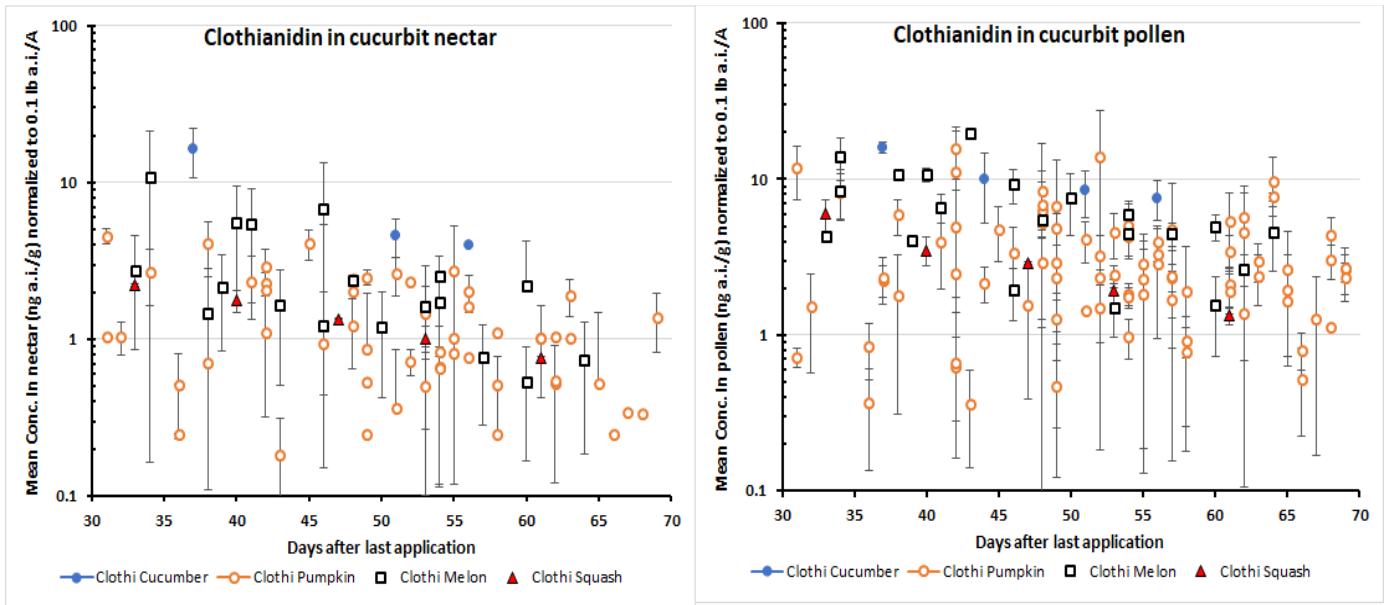


Figure 6-102. Mean normalized concentrations of clothianidin in nectar (left) and pollen (right) of cucurbit crops. Error bars = 95% confidence intervals. For some melon samples, anther residues data was used as a direct surrogate for pollen residues.

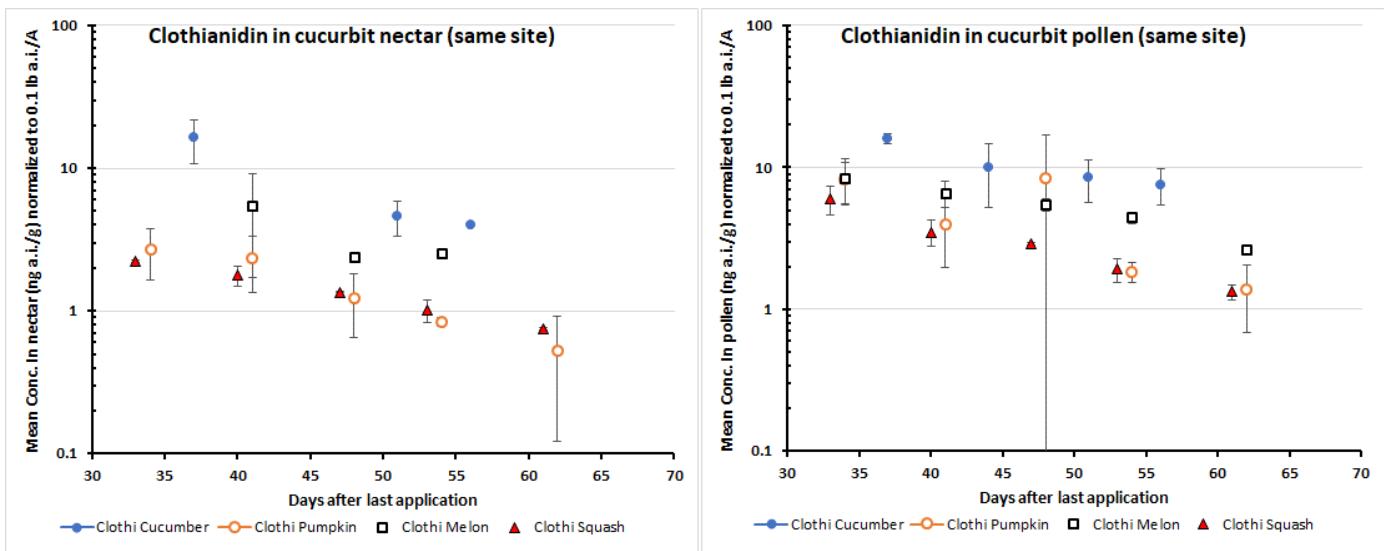


Figure 6-103. Mean normalized concentrations of clothianidin in nectar (left) and pollen (right) of cucurbit crops at a single site and season (MRID 49705901). Error bars = 95% confidence intervals. For some melon samples, anther residues data was used as a direct surrogate for pollen residues

With thiamethoxam, one study was available which evaluated residues in melon, pumpkin and squash at each of three sites (Woodland, CA; Fisk, MO; Belvidere, NC; MRID 50265501). Since residues were measured at the same sites among multiple cucurbits, these data are considered most appropriate for evaluating the influence of crop on thiamethoxam residues in nectar and pollen. Results from this study are shown for each of the three sites in **Figure 6-104**, with nectar residues shown on the left and pollen on the right. Residues are expressed as clothianidin equivalents.

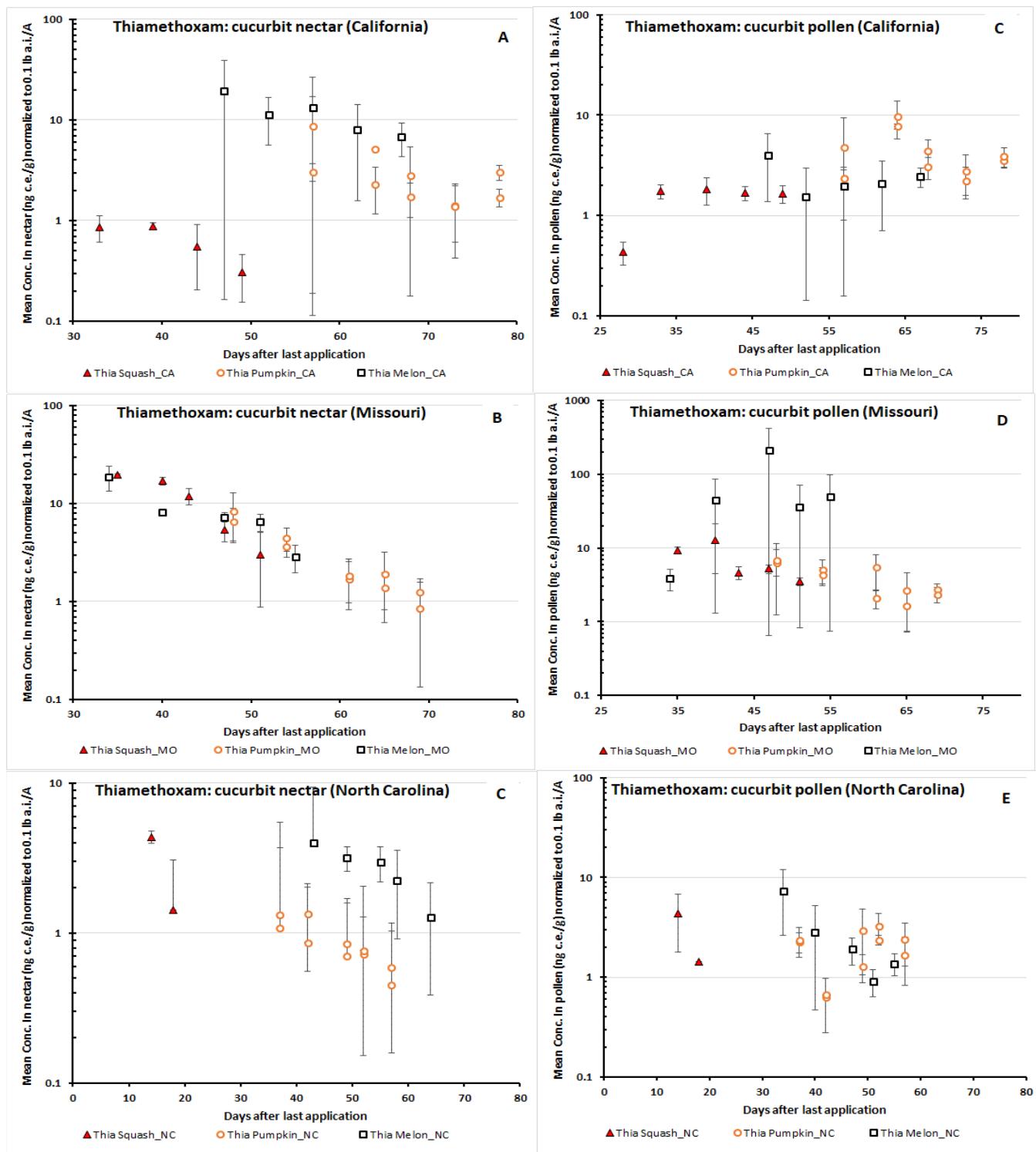


Figure 6-104. Mean normalized residues of thiamethoxam (in clothianidin equivalents; ng c.e./g) in nectar (left) and pollen (right) of cucurbit crops grown in 3 sites (MRID 50265501). Error bars = 95% confidence intervals.

For most comparisons, a consistent and distinct influence of crop on thiamethoxam residues in nectar and pollen is not evident, based on overlapping confidence intervals. Two possible exceptions include nectar residues from the California site (panel A) and the North Carolina site (panel B). Specifically, thiamethoxam residues in nectar of squash from the CA site are about 10X lower than those in melon at similar DALA. In contrast, it appears that thiamethoxam in nectar of melon and pumpkin from the NC site are different (by about 10X) with non-overlapping confidence intervals at similar DALA.

In summary, the results from the previous studies indicate that neonicotinoid residues among multiple species of cucurbit crops associated with soil applications vary by approximately 1 order of magnitude when data are compared for the same site and season. In most cases, differences in mean residues among crops are not significant, based on overlapping confidence intervals. In a few cases (*e.g.*, clothianidin in cucumber), crop-specific differences are evident, although these differences are still within an order of magnitude for the tested cucurbit crops.

6.7.3.8 Effect of chemical on residue values

In order to consider the effect of chemical on residue values in pollen and nectar, residues for different chemicals are compared for the same crop. For soil applications to pumpkins, residue data are available for clothianidin, thiamethoxam and dinotefuran (**Figure 6-105**). There is general overlap of clothianidin and dinotefuran sampling for applications shortly before bloom (*i.e.*, 7-20 DALA) while the overlap of clothianidin and thiamethoxam sampling occurs later (between 35 and 80 DALA). For neonicotinoid residues in pumpkin nectar and pollen, there are no clear differences based on chemical. Mean daily samples generally range between <LOQ-10 ng a.i./g in nectar and <1-15 ng a.i./g in pollen for each active ingredient, when normalized to 0.1 lb a.i./A total application rate. Within a chemical, residue values originate from different sites with as discussed previously, may result in variations of 10X among sites.

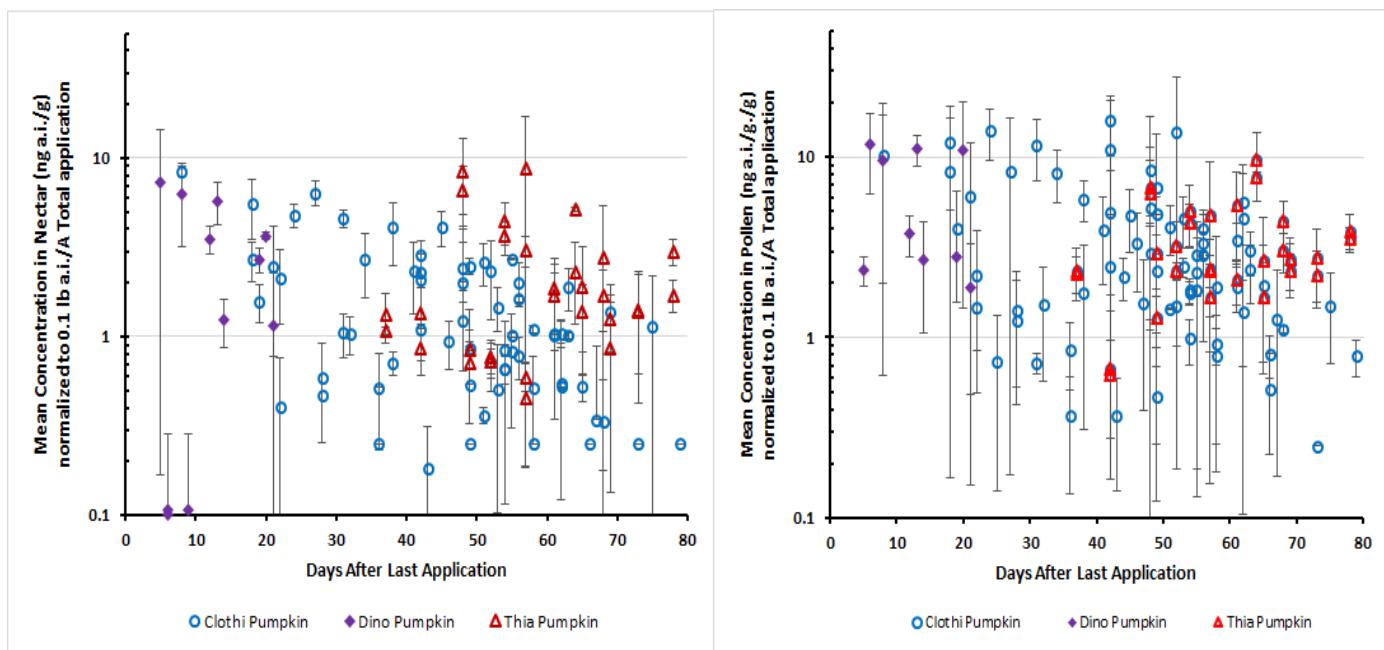


Figure 6-105. Mean normalized residues of clothianidin (circles), thiamethoxam (triangles; in clothianidin equivalents) and dinotefuran (diamonds) in pumpkin nectar (left) and pollen (right) at similar sampling times. Error bars= represent 95% confidence intervals.

For neonicotinoid soil applications to melons, data are available for clothianidin (cantaloupe), thiamethoxam (muskmelon), and imidacloprid (melon and watermelon). There is general overlap of clothianidin, imidacloprid (watermelon only) and thiamethoxam sampling times (the imidacloprid melon samplings were all later than the other samples, at DALA 100). Similar to the pumpkin data, the melon data presented in **Figure 6-106** also do not show any clear trends regarding the magnitude of residues between neonicotinoid compounds (mean normalized residues generally <10 ng a.i./g in nectar and <20 ng a.i./g in pollen) and although the highest residues detected in both nectar and pollen tended to be from thiamethoxam applications (up to 20 ng a.i./g in nectar and 210 ng a.i./g in pollen), their confidence intervals overlap with the other residue data. Additionally, the imidacloprid data and most of the clothianidin data were bee-collected, rather than hand-collected, while the thiamethoxam data was all hand-collected, which may contribute to any perceived differences.

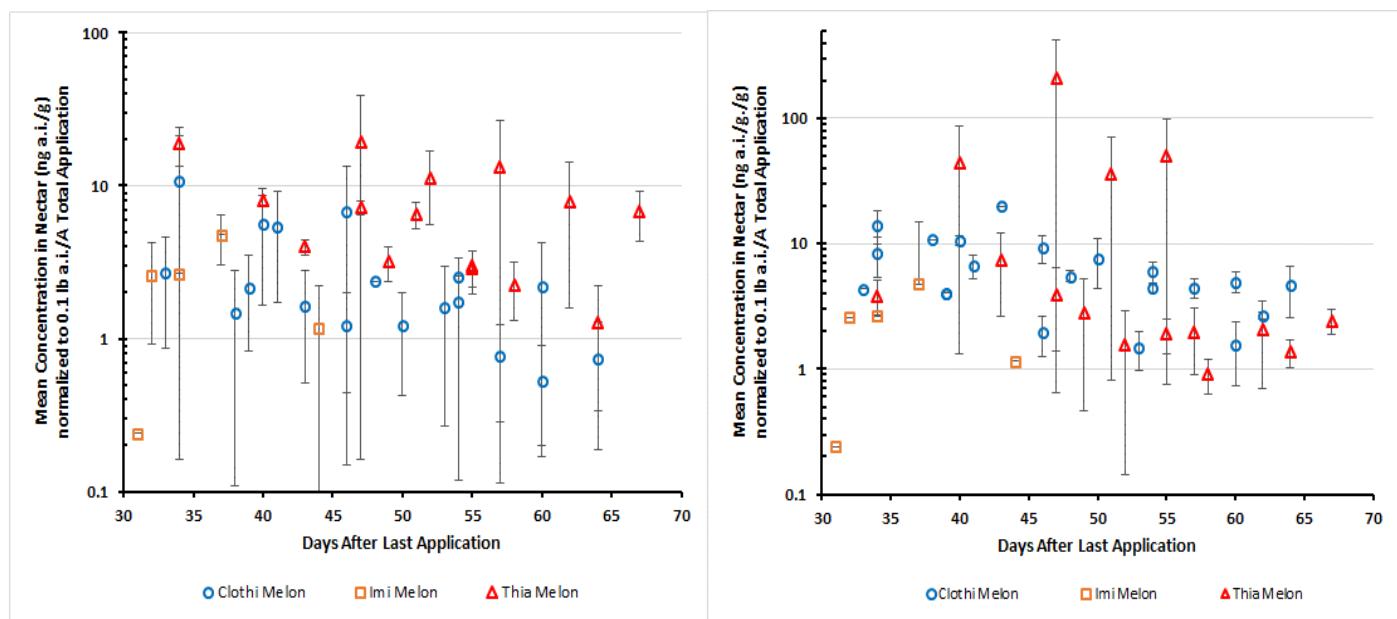


Figure 6-106. Mean normalized residues of clothianidin (circles), thiamethoxam (triangles; in clothianidin equivalents) and imidacloprid (squares) in melon (cantaloupe, muskmelon and watermelon) nectar (left) and pollen (right) at similar sampling times. Error bars = 95% confidence intervals.

For soil applications to squash (**Figure 6-107**), data are available for clothianidin and thiamethoxam with overlap between 35 and 60 DALA. Although there is limited overlap in confidence intervals surrounding the mean daily residues in the squash dataset, the higher thiamethoxam residues (up to 20 ng a.i./g in nectar and 13 ng a.i./g in pollen, compared to clothianidin residues <10 ng a.i./g in both matrices) can be considered associated more with location (see site analysis above, showing that the high thiamethoxam residues in squash were associated with the Fisk, MO site) than with chemical. This dataset is further limited in that the data for clothianidin squash residues are only for a single site.

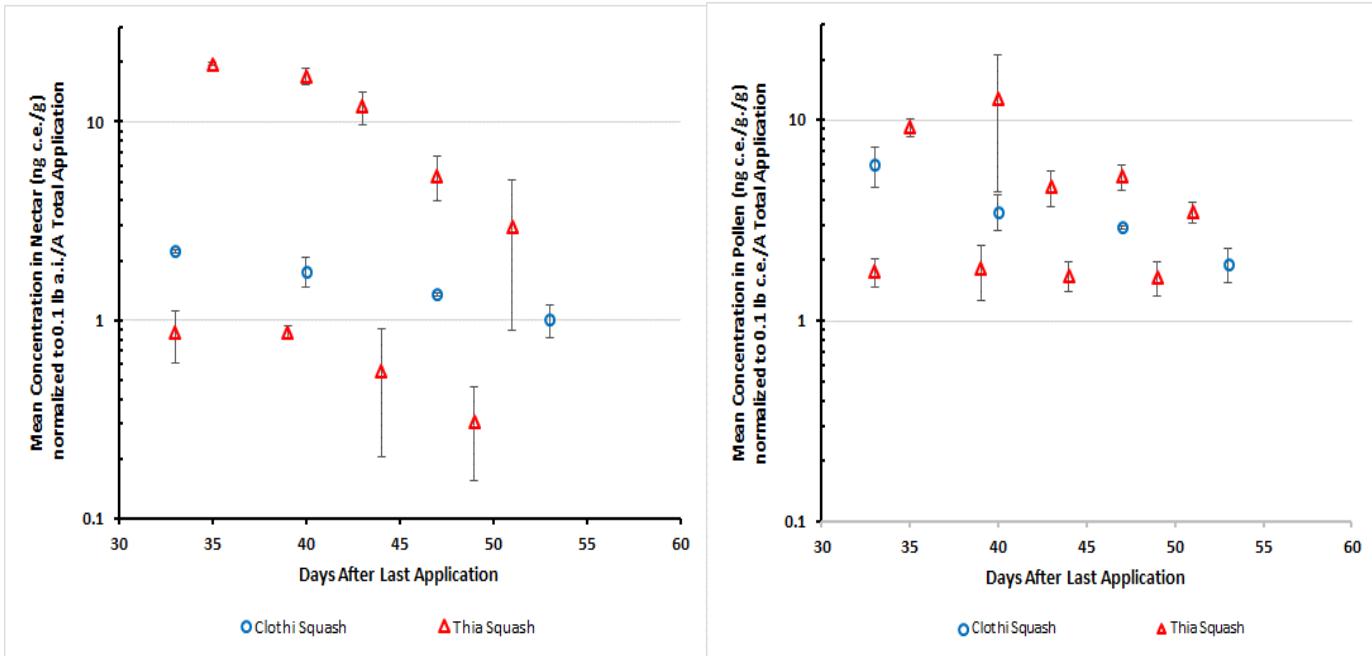


Figure 6-107. Mean normalized residues of clothianidin (circles) and thiamethoxam (triangles; in clothianidin equivalents) in squash nectar (left) and pollen (right). Error bars = 95% confidence intervals.

In summary, the preceding summary of residue data among neonicotinoids measured in the same crop and matrix do not indicate any consistent differences among chemical. While it is not possible to remove the potential influence of site on chemical residues, this analysis suggests that chemical does not have an overriding influence on neonicotinoid residues in pollen and nectar in cucurbit crops within the context of variability in residues among sites.

6.7.3.9 Bridging recommendations

Analysis of the available pollen and nectar residue data indicates that neither chemical nor crop have a consistent or overriding influence on neonicotinoid residues following soil applications to cucurbit crops. As observed with foliar applications to cucurbits, the majority of comparisons indicated residues are within an order of magnitude among sites, although there is evidence that site can have a substantial impact on residues in some situations (e.g. thiamethoxam squash data for Fisk, MO compared to data for squash in other sites or with other active ingredients). Therefore, consideration of the number of sites that underly the residue data is recommended for characterizing the robustness of risk conclusions based on residue data. Unlike residues in pollen and nectar resulting from foliar applications, those resulting from soil applications do not display a consistent declining trend over time, as residues appear to be relatively stable or even increasing over up to 2 months after application.

As discussed previously in this section, the most robust data for neonicotinoid residues in cucurbits is for clothianidin and thiamethoxam and specifically for residues in pumpkin and melon while less data is available for dinotefuran and imidacloprid and for other cucurbit species such as squash and cucumber. For soil applications, the main data gaps that remain are for:

- Applications of imidacloprid to multiple cucurbit crops
- Applications of imidacloprid at multiple sites

- Applications of imidacloprid at multiple time points
- Applications of dinotefuran to multiple cucurbit crops

Given the lack of obvious influences of chemical and crop on residue data, it is recommended that the available data for clothianidin, dinotefuran, imidacloprid and thiamethoxam can be bridged across cucurbit crops and neonicotinoids.

6.8 Other Crops Groups (with no residue data)

For several crops or crop groups including herbs and spices, hops, peanut, residue data were available for the neonicotinoids. 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.

7 SUMMARY AND CONCLUSIONS

Based on the results summarized in this Attachment, the following general conclusions can be made among the neonicotinoids:

- 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 for the neonicotinoid risk assessment, residues from foliar application be considered separately from those associated with soil application.
- 2. Influence of Application Rate.** The results from this 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 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 "site" in this analysis incorporates multiple factors that could influence residues including weather, soil characteristics, hydrology, agronomic practices and crop variety. These findings support the consideration of the number of sites upon which a given risk finding is based as one 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 7-1**.

Table 7-1. 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 are shown in **Table 7-2**. In general, bridging among chemicals and crops is recommended within a crop group. Residue bridging is not recommended between 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 7-2. 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

Crop Group	Method	Recommended Bridging Option:			
		Across Chemical?	Across Crop?	Across Pre- vs. Post-Bloom?	Use Modeled Residue Decline Curves?
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.

8 REFERENCES

- Bohaty, R. F. H., Eckel, W., Shamim, Spatz, D., White, K., and Young, D. F. 2015. *Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation*. March 23. Environmental Fate and Effects Division. Office of Pesticide Programs. United States Environmental Protection Agency, Washington DC.
- Bonmatin J., Giorio C., Girolami V., Goulson D., Kreutzweiser D., Krupke C., Liess M., Long E., Marzaro M., Mitchell E., Noome D., Simon-Delso N., Tapparo A. 2015. Environmental fate and exposure; neonicotinoids and fipronil. *Environ. Sci. Pollut. Res.* 22: 35-67.
- Briggs G., Bromilow R., Evans A., Williams, M. 1983. Relationship between lipophilicity and the distribution of non-ionised chemicals in barley shoots following uptake by roots. *Pest. Sci.* 14: 492-500.
- EFSA. 2013. Guidance on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus spp.* and solitary bees). EFSA Journal 2013;11(7):3295, 266 pp.
doi:10.2903/j.efsa.2013.3295.
- Gierer F., Vaughan S., Slater M., Thompson H., Elmore S., Girling R. 2019. A review of the factors that influence pesticide residues in pollen and nectar: Future research requirements for optimising the estimation of pollinator exposure. *Environ. Poll.* 249: 236-247.
- NAFTA. 2012. *Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media*. December 2012. NAFTA Technical Working Group on Pesticides
- Sappington, K., Mroz, R., Garber, K., Farruggia, F., Wagman, M., Blankenship, A., Koper, C. 2018. Quantifying sources of variability in neonicotinoid residue data for assessing risks to pollinators. *Julius-Kühn-Archiv*, 462:46-54.
- Sur, R., Stork, A. 2003. Uptake, translocation and metabolism of imidacloprid in plants. *Bull. Insectol.* 56(1): 35-40.
- Trapp S. 2004. Plant uptake and transport models for neutral and ionic chemicals. *Env. Sci. Poll. Res.* 11(1): 33-39.
- USDA. 2017. *Attractiveness of Agricultural Crops to Pollinating Bees for the Collection of Nectar and/or Pollen*. US. Department of Agriculture, Washington, DC.
(https://www.usda.gov/oce/opmp/Attractiveness%20of%20Agriculture%20Crops%20to%20Pollinating%20Bees%20Report-FINAL_Web%20Version_Jan%203_2018.pdf)
- USEPA. 2017. Preliminary Bee Risk Assessment to Support the Registration Review of Clothianidin and Thiamethoxam. Environmental Fate and Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington DC (<https://www.epa.gov/pesticides/epa-releases-four-neonicotinoid-risk-assessments-public-comment>)
- USEPA. 2016. Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid. Environmental Fate and Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington DC (<https://www.epa.gov/pesticides/epa-releases-four-neonicotinoid-risk-assessments-public-comment>)
- 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.
- USEPA. 2012. User's Guide T-REX Version 1.5 (Terrestrial Residue EXposure model). March 22, 2012. Environmental Fate and Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington, D.C.

APPENDIX A. PLANT LIFE HISTORY CHARACTERISTICS

Table A-1 provides a summary of the life history characteristics of the crops that may influence the magnitude or duration that pesticide residues may be present in bee-relevant plant matrices. The summary represents the Environmental Fate and Effects Division's interpretation of the characteristics as described in the compendium of source literature below and from information readily available on agricultural extension websites (e.g., flowering duration).

Table A-1. Plant Life History Characteristics that May Influence Residue Concentrations in Bee-Relevant Matrices

Crop Group	Crop	Life History	Habit	Level of Dormancy	Significant growth dormancy to bloom?	Flowering Window	BBCH ¹ Flowering Window	Peak Flowering Duration (Days)	Flowering Frequency	Single Flower Lifespan (days)
Root and Tuber	Potato	perennial	herb	annual	high	mid-season	61-97	60-90	successional	2-7
Legumes	Soybean	annual	herb	annual	high	mid-season	61-69	120	successional	2-7
Fruiting Vegetables	Tomato	annual	herb	annual	high	mid-season	61-97	60-90	successional	2-7
Cucurbits	Pepper	annual	herb	annual	high	mid-season	61-97	60-90	successional	2-7
	Watermelon	annual	vine	annual	High+	mid-late season	61-69	90	successional	1-3
	Squash	annual	vine	annual	high	mid-late season	61-69	90	successional	1-4
	Melon	annual	vine	annual	high	mid-late season	61-69	120	successional	1-4
	Pumpkin	annual	vine	annual	high	mid-late season	61-69	120	successional	1-4
	Cucumber	annual	vine	annual	high	mid-late season	61-69	90	successional	1-3
Citrus ²	Cantaloupe	annual	vine	annual	high	mid-late season	61-69	120	successional	1-3
	Orange	perennial	tree	evergreen	low	early Leafout	60-69	14-30	single	14

Crop Group	Crop	Life History	Habit	Level of Dormancy	Significant growth dormancy to bloom?	Flowering Window	BBCH ¹ Flowering Window	Peak Flowering Duration (Days)	Flowering Frequency	Single Flower Lifespan (days)
	Mandarin	perennial	tree	evergreen	low	early Leafout	60-69	14-30	single	14
	Grapefruit	perennial	tree	evergreen	low	early Leafout	60-69	14-30	single	14
	Lemon	perennial	tree	evergreen	low	early Leafout	60-69	14-30	single	14
Pome	Apple	perennial	tree	deciduous	moderate	early Leafout	60-69	14-21	Single	7
Stone	Cherry	perennial	tree	deciduous	low	pre-leafout	60-69	14-21	single	7
	Peach	perennial	tree	deciduous	low	pre-leafout	60-69	14-21	single	7
	Plum	perennial	tree	deciduous	low	pre-leafout	60-69	14-21	single	7
	Apricot	perennial	tree	deciduous	low	pre-leafout	60-69	14-21	single	7
Berry/Small Fruit	Blueberry	perennial	shrub	deciduous	low	early Leafout	60-69	14	single	14-21
	Grape	perennial	vine	deciduous	moderate	mid-season	61-69	8-14	Successional	2
	Cranberry	perennial	shrub	deciduous	low	early Leafout	60-69	30-45	single	14-21
	Strawberry	perennial	herb	deciduous	moderate	mid-late season	60-67	30-270 ³	successional	4-7
Tree Nut	Almond	perennial	tree	deciduous	low	pre-leafout	60-69	14-21	single	7
Oilseed	Cotton	annual	herb	annual	moderate	mid-season	60-69	30-45	successional	5-7

¹ BBCH- Biologische Bundesanstalt, Bundessortenamt, und CHemische Industrie

² Citrus notes: Some Citrus species may have multiple bloom periods throughout a year. Some Citrus crops (e.g., mandarin) are tented to prevent pollination for the production of seedless fruit.

³ Strawberry varietals may have a short bloom duration (~30-days) or may extend throughout the year. Long bloom durations are highly dependent upon climate, variety, and cultural practices.

Source Literature:

- Almekinders, C.J.M., P.C. Struik. Shoot development and flowering in potato (*Solanum tuberosum* L.). *Potato Research* 39: 581-607.
- Beasley, C.A. 1975. Developmental morphology of cotton flowers and seed as seen with the scanning electron microscope. *Amer. J. Bot.* 62(6): 584-592.
- Bernardello, G. A systematic survey of floral nectaries. In: S.W. Nicolson, M. Nepi, and E. Pacini (eds.), *Necatires and Nectar*, 129-166, Springer Publishing. Pages 19-128.
- Chwil, M., E. Weryszko-Chmielewska. 2011. Comparison of features of the epidermis and the size of the floral nectary in four species of the genus *Cotoneaster* Med. *Acta Agrobotanica*, 64(4): 47-58.
- Celis-Gamboa, B.C. 2002. The life cycle of the potato (*Solanum tuberosum* L.). Ph.D. Thesis, Wageningen University.
- Dixon, E., B. Strik, J. Fernandez-Salvador, L.W. Devetter. 2019. *Strawberry Nutrient Management Guide for Oregon and Washington*. Oregon State University Agricultural Extension Service.
- Garcia-Salazar, C. 2002. Crop timeline for blueberries in Michigan and Indiana. Michigan State University. Prepared for the U.S. Environmental Protection Agency.
- Hack et al. 2001. Growth stages of mono- and dicotyledonous plants. Second Edition. Uwe Mier (ed.). Federal Biological Research Center for Agriculture and Forestry, Berlin and Braunschweig.
- Nemes, Z., A. Baciu, D. Popa, L. Mike, A. Petrus-Vancea, O. Danci. 2008. The study of the potato's life-cycle phases important to the increase of the individual variability.
- Nepi, M., E. Pacini, M.E. M. Willemse. 1996. Nectary biology of *Cucurbita pepo*: ecophysiological aspects. *Acta Bot. Neerl.* 45(1): 41-54.
- Nepi, M. 2007. Nectary Structure and Ultrastructure. In: S.W. Nicolson, M. Nepi, and E. Pacini (eds.), *Necatires and Nectar*, 129-166, Springer Publishing. Pages 129-166.
- Peng, Y., Y. Li, Y. Hao, Z. Xu, S. Bai. 2004. Nectar production and transportation in the nectaries of the female *Cucumis sativus* L. flower during anthesis. *Protoplasma* 224: 71-78.
- Purcell, L.C., M. Salmeron, L. Ashlock. 2014. Soybean Growth and Development. *Arkansas Soybean Production Handbook*. Division of Agriculture Research and Extension, University of Arkansas. 1-8.
- Ritchie, G.L., C.W. Bednarz, P.H. Jost, S.M. Brown. 2007. Cotton growth and development. University of Georgia, Cooperative Extension.
- Srivastava, A.K., S. Singh, A.D., Huchche. 2000. An analysis on citrus flowering- a review. *Agric. Rev.* 21(1): 1-15.
- Vasconcelos, M.C., M. Greven, C.S. Winefield, M.C.T. Trought, V. Raw. 2009. The flowering process of *Vitis vinifera*: a review. *Am. J. Enol. Vitic.* 60(4): 411-434.
- Zhao, P., L. Zhao, Q. Sheng, S. Li, H. Peng. 2011. The days anthesis in relation to the floral shapes, pollen size, and S-RNase gene identifying in self-incompatibility of wild species. *African journal of Biotechnology* 10(65): 14319-14328.

APPENDIX B. KINETIC ANALYSIS OF NEONICOTINOID RESIDUES COTTON FLORAL NECTAR, EXTRAFLORAL NECTAR AND POLLEN

Table B-1. Summary statistics for first order dissipation rate constants (k) estimated for residues of imidacloprid, clothianidin, and dinotefuran in floral nectar of cotton after pre-bloom foliar applications

Chemical	Trial (Year)	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
Imidacloprid	Malden, MO (2012A)	0.05 (0.04-0.07)	12.8	0.74	<0.001	14	Y	Consistently decreasing
	Malden, MO (2012B)	0.18 (0.05-0.31)	3.9	0.61	0.006	15	Y	Flattens > 21 days
	Malden, MO (2013)	0.05 (0.03-0.06)	14.9	0.74	<0.001	15	Y	Consistently decreasing
	Glennonville, MO (2012A)	0.13 (0.08-0.18)	5.3	0.79	<0.001	13	Y	Flattens > 20 days
	Glennonville, MO (2012B)	0.20 (0.11-0.29)	3.4	0.78	<0.001	14	Y	Flattens > 20 days
	Glennonville, MO (2013)	0.08 (0.07-0.10)	8.4	0.95	<0.001	14	Y	Flattens > 33 days
	Fisk, MO (2012A)	0.02 (0.01-0.04)	31.4	0.29	0.005	13	Y	Consistently decreasing
	Fisk, MO (2012B)	0.02 (0.01-0.04)	32.8	0.33	0.002	13	Y	Consistently decreasing
	Fisk, MO (2013)	0.06 (0.04-0.08)	12.2	0.66	<0.001	14	Y	Flattens > 28 days
Dinotefuran	Fresno, CA	0.28 (0.16-0.39)	2.5	0.98	0.001	5	Y	Flattens > 15 days.
	Madera, CA	0.23 (0.13-0.32)	3.1	0.95	0.000	3	Y	Flattens > 15 days.
	Pearson, CA	0.30 (-0.03-0.63)	2.3	0.84	0.035	7	Y	Good fit all 3 time points. Kept in analysis
	Potterville, CA T1	0.28 (-0.05-0.61)	2.5	0.85	0.041	7	N	Only 3 time points, last 2 flat.
	Potterville, CA T2	0.46 (-3.1-4.1)	1.5	0.33	0.39	9	N	Only 3 time points, last 2 flat.
	Zamora, CA	0.11 (-0.11-0.33)	6.4	0.27	0.14	7	N	high variability @ 2 of 3 time points
Clothianidin	Fresno, CA (foliar)	0.18 (0.15-0.20)	3.9	0.98	<0.001	7	Y	Last 3 sample events < LOQ
	Fresno, CA (seed + foliar)	0.13 (0.08-0.18)	5.5	0.83	<0.001	7	Y	Last 3 sample events < LOQ
	Fresno, CA (Acala, CDPR-1)	0.17 (0.08-0.27)	4.0	0.83	0.004	3	Y	Omitted Day 1 outlier

Chemical	Trial (Year)	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
	Fresno, CA (Pima, CDPR-2)	0.05 (-0.07-0.18)	12.8	0.12	0.22	1	N	high variability among reps

* based on criteria described in Section 4.5.5; DALA = Day after last application; total imidacloprid = parent+ imidacloprid olefin + 5-hydroxy imidacloprid

Table B-2. Summary statistics for first order dissipation rate constants (k) estimated for residues of imidacloprid, clothianidin, and dinotefuran in extrafloral nectar of cotton after pre-bloom foliar applications

Chemical	Trial (Year)	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
Imidacloprid	Malden, MO (2012A)	0.07 (0.04-0.09)	10.4	0.71	<0.001	14	Y	Consistently decreasing
	Malden, MO (2012B)	0.09 (0.05-0.14)	7.4	0.71	<0.001	15	Y	Consistently decreasing
	Glennonville, MO (2012A)	0.14 (0.10-0.17)	5.1	0.88	<0.001	13	Y	Flattens > 26 days
	Glennonville, MO (2012B)	0.16 (0.09- 0.23)	4.4	0.80	<0.001	14	Y	Flattens > 26 days
	Glennonville, MO (2013)	0.17 (0.11-0.23)	4.1	0.88	<0.001	14	Y	Flattens > 21 days
	Fisk, MO (2012A)	0.05 (0.02-0.08)	13.8	0.49	0.002	13	Y	Consistently decreasing
	Fisk, MO (2012B)	0.05 (0.03-0.07)	14.8	0.55	0.000	13	Y	Flattens > 21 days
	Fisk, MO (2013)	0.07 (0.03-0.11)	9.5	0.48	0.001	14	Y	High replicate variability
Dinotefuran	Fresno, CA	0.18 (0.11-0.24)	4.0	0.94	<0.001	5	Y	Consistently decreasing
	Madera, CA	0.25 (0.02-0.49)	2.8	0.79	0.02	3	Y	Wide CL reflects sample spacing
	Pearson, CA	0.27 (-0.05-0.59)	2.6	0.72	0.05	7	N	Flattens > 20 days
	Potterville, CA T1	0.41 (-0.33-1.2)	1.7	0.91	0.12	7	N	Flattens > 20 days, wide sample spacing near K
	Potterville, CA T2	0.44 (-0.03-0.92)	1.6	0.96	0.03	9	Y	Good fit, wide CL wide sample spacing, kept in analysis
	Zamora, CA	0.27 (0.11-0.43)	2.6	0.92	0.002	7	Y	Good fit all 4 time points

Chemical	Trial (Year)	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
Clothianidin	Butler, MO (seed+foliar)	0.50 (-0.82-1.8)	1.4	0.89	0.26	6	N	Wide sample spacing
	Butler, MO (foliar)	0.35 (-2.85-3.55)	2.0	0.86	0.42	6	N	Wide sample spacing
	Willacy, TX (foliar)	0.26 (0.15-0.37)	2.7	0.92	<0.001	6	Y	Strong fit @ all 5 times
	Willacy, TX (seed+foliar)	0.27 (0.17-0.37)	2.6	0.94	<0.001	6	Y	Strong fit @ all 5 times
	Fresno, CA (foliar)	0.17 (0.08-0.26)	4.1	0.83	0.002	7	Y	last two sampling periods < LOQ
	Fresno, CA (seed + foliar)	0.15 (0.06-0.24)	4.5	0.80	0.01	7	Y	last two sampling periods < LOD
	Fresno, CA (Acala, CDPR-1 subbr.)	0.14 (0.10-0.19)	4.9	0.95	<0.001	5	Y	Good model fit
	Fresno, CA (Acala, CDPR-1 leaf)	0.50 (0.35-0.64)	1.4	0.93	<0.001	1	Y	Good model fit
	Fresno, CA (Pima, CDPR-2 leaf)	0.11 (0.07-0.14)	6.5	0.86	<0.001	1	Y	Good model fit

* based on criteria described in **Section 4.5.5**; DALA = Day after last application; total imidacloprid = parent+ imidacloprid olefin + 5-hydroxy imidacloprid

Table B-3. Summary statistics for first order dissipation rate constants (k) estimated for residues of imidacloprid, clothianidin, and dinotefuran in pollen of cotton after pre-bloom foliar applications

Chemical	Trial (Year)	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
Imidacloprid	Malden, MO (2013)	0.22 (0.09-0.36)	3.1	0.74	0.001	15	Y	Consistently decreasing
	Glennonville, MO (2013)	0.29 (-0.03-0.61)	2.4	0.71	0.035	14	N	Only 2 time points > LOD
	Fisk, MO (2013)	0.19 (0.02-0.36)	3.7	0.58	0.016	14	Y	Last 2 sampling points ~ LOD
Dinotefuran	Fresno, CA	0.09 (0.03-0.15)	8.1	0.76	0.004	5	Y	Consistently decreasing

Chemical	Trial (Year)	K (95% CI)	Half-life (d)	R ²	P-Value	First Sample Day (DALA)	Reliable k?*	Comments
	Madera, CA	0.09 (0.05-0.13)	7.6	0.79	0.001	3	Y	Decreasing
	Pearson, CA	0.17 (0.12-0.29)	4.2	0.93	<0.001	8	Y	3 time points
	Potterville, CA T1	0.25 (0.03-0.48)	2.8	0.88	0.017	7	Y	3 time points
	Potterville, CA T2	0.17 (-0.03-0.36)	4.2	0.57	0.045	9	N	High rep. variability
	Zamora, CA	0.00 (-0.05-0.05)	N.C.	0.09	0.500	8	N	Non-monotonic
	Butler, MO (foliar)	0.12 (0.03-0.21)	5.9	0.55	0.019	6	Y	Last 3 sampling points ~ LOD
	Willacy, TX (foliar)	0.32 (0.02-0.62)	2.2	0.78	0.039	6	Y	Last 3 sampling points ~ LOD
	Fresno, CA (foliar)	0.21 (0.13-0.30)	3.3	0.90	<0.001	7	Y	Consistently decreasing
	Willacy, TX (seed+foliar)	0.32 (0.01-0.63)	2.2	0.76	0.046	6	Y	Last 3 sampling points ~ LOD
	Fresno, CA (seed + foilar)	0.19 (0.11-0.27)	3.7	0.87	<0.001	7	Y	Consistently decreasing
	Butler, MO (seed+foliar)	0.36 (-0.39-1.1)	2.0	0.60	0.21	6	N	Wide sampling interval near k

* based on criteria described in **Section 4.5.5**; DALA = Day after last application; total imidacloprid = parent+ imidacloprid olefin + 5-hydroxy imidacloprid