Review of Neonicotinoid Use, Registration, and Insect Pollinator Impacts in Minnesota

August 2016

Minnesota Department of Agriculture

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Executive summary

Neonicotinoid insecticides are currently one of the most widely used insecticides in the world because of their properties including potent broad-spectrum toxicity possessing contact, oral, and systemic activity. They are effective at very low concentrations, are less toxic to mammals, and are not cross-resistant to other classes of insecticides including carbamates, organophosphates, and synthetic pyrethroids. However, recent research has suggested potential toxicity concerns for neonicotinoids to various life stages of honey bees, native bees, as well as other pollinating insects. Pollinators are essential in the reproduction of 90% of the world's flowering plants and 30% of the food human's consume. Many plants such as alfalfa, apple, blueberry, sunflower and canola, cannot reproduce without the help from insect pollinators. The pollination services offered by insect pollinators also play a crucial role in the maintenance of biodiversity and ecological balances in natural ecosystems by providing important food and habitat for other wildlife species. Managed honey bees (*Apis mellifera*) alone pollinate more than $17 billion worth of crops in the U.S. each year and are regarded as the most important managed pollinator. Over the last 50 years, honey bees have been faced with a number of stressors that impact their health and survivorship including a number of pests and diseases, fewer flowering plants available to meet their nutritional needs, and a wide variety of pesticides that can be toxic.

Pesticides have long been suspected as a potential cause of contemporary honey bee declines. Honey bees are exposed to pesticides and other chemicals commonly used in agriculture and landscapes via numerous pathways including direct exposure, exposure through the pollen and nectar of plants treated with contact or systemic pesticides and pesticides used by beekeepers themselves. Although many insecticides have been shown to affect honey bees, the attention has focused on neonicotinoid insecticides in recent years. The concern over the use of neonicotinoid insecticides in relation to insect pollinators led the Minnesota State Legislature to request that the Minnesota Department of Agriculture (MDA) report on the process and criteria to be used in a review of neonicotinoid use in Minnesota currently and in the future. Consequently, the Commissioner of Agriculture directed MDA staff, on November 5, 2013, to initiate a special review of neonicotinoid insecticides.

The MDA is the lead state agency for pesticide and fertilizer environmental and regulatory functions in Minnesota under the Pesticide Control Law (Minn. Stat. Chapter 18B). In addition to functions related to pesticide registration and monitoring, the MDA carries out in-depth reviews of pesticides to better understand Minnesota-specific issues related to pesticides. The scope of these special registration reviews varies depending on the potential education, outreach, and enforcement needs identified by the Department. As such, these reviews are not intended to be redundant of analyses and decisions reached by the United States Environmental Protection Agency (USEPA). Rather, these reviews result in a greater understanding of federal registration concerns and provide a variety of Minnesota specific opportunities for action.

In order to conduct the current review, the MDA followed a pre-established process to develop the criteria MDA would use to conduct a variety of in-depth pesticide reviews. The MDA has also previously reviewed several neonicotinoids of concern as part of its emerald ash borer insecticide review (including concerns about pollinator exposure). Following the pre-established process, the MDA developed a scoping document after soliciting input from the public and a number of interested stakeholders, including beekeepers, academics, citizens, farmers and their suppliers, and pesticide registrants. In addition, the MDA collaborated with the Minnesota Board of Water and Soil Resources (BWSR), the Minnesota Department of Natural Resources (DNR), the Minnesota Pollution Control Agency (MPCA), and the University of Minnesota (U of M). Based on the scoping document, the review was categorized into six broad criteria including:

- Neonicotinoid background, chemistry, and mode of action;
- Federal, state, and other neonicotinoid registration policies and initiatives;
- Neonicotinoid use and sales;
- Neonicotinoid applications and movement in the environment;
- Risks of neonicotinoid use; and
- Benefits of neonicotinoid use.

Each criterion was explored in relation to Minnesota-specific concerns and opportunities for action.

Neonicotinoid background, chemistry, and mode of action:

Neonicotinoids are used on nearly 140 agricultural crops and in many other uses including garden, turf, residential, and animal use. In the United States, six neonicotinoid insecticides: acetamiprid, clothianidin, dinotefuran, imidacloprid, thiacloprid, and thiamethoxam with potential pollinator impacts were registered for controlling agricultural and urban insect pests. Thiacloprid registration has been cancelled voluntarily by the registrants and will no longer be available after 2016. Neonicotinoids are systemic insecticides with a structure and mode of action similar to nicotine, a naturally occurring plant alkaloid compound toxic to humans. Contact and oral exposures of neonicotinoids target the acetylcholine receptors (nAChR) on the insect nerve cells within an insect nervous system. However, neonicotinoids vary from nicotine in their affinity to different nAChR subtypes, with nicotine showing selective toxicity to vertebrates whereas neonicotinoids are highly selective to insect nAChRs. Their action causes excitation of the insect nerves that lead to trembling, shaking and eventual paralysis, which can lead to death depending on the dose and exposure duration. Neonicotinoids bind at a receptor site specific to insect nerve cells, therefore, they are less toxic to mammals. All neonicotinoid insecticides show similar broad spectrum insecticidal activity but vary in their biological and physicochemical properties such as photolytic stability, soil degradation, metabolism in plants and insects, and toxicity to different animals.

Federal, state, and other neonicotinoid registration policies and initiatives

Both federal and state laws govern the registration and use of neonicotinoid insecticides in Minnesota. The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) of 1972, amended by the Food Quality Protection Act of 1996, and the Pesticide Registration Improvement Act of 2003, requires all pesticides sold or distributed in the United States (including imported pesticides) to be registered by USEPA. The USEPA registers a pesticide after determining that the pesticide meets the statutory standard and there are no outstanding data requirements. The law requires USEPA to review each pesticide registration at least once every 15 years. Registration reviews for the six neonicotinoid insecticides were initiated between 2008 and 2012 and are expected to be completed between 2016 and 2019. The USEPA released the preliminary imidacloprid, pollinator specific review for agricultural and horticultural crops in January 2016. Work plans for neonicotinoids identified numerous ecological information gaps on toxicity and exposure to honey bee life stages and/or full colonies on acute or chronic exposure basis.

Historically, the USEPA's testing paradigm for pollinators relied on qualitative evaluations rather than precise quantitative measurements. The process relied primarily on developing an understanding of the types of effects that might be caused by the pesticide (hazard characterization), based on toxicity studies using honey bees as surrogate species. In 2012, the USEPA in collaboration with Health Canada's Pest Management Regulatory Agency (PMRA) and the California Department of Pesticide Regulation (CalDPR) developed a new risk assessment framework for bees. The new framework takes into account multiple lines of evidence including registrant-submitted data, open literature, and ecological incident data. The USEPA has acknowledged some uncertainties with initial registration of neonicotinoid insecticides regarding their potential environmental fate and effects, particularly as they relate to pollinators. Considering these uncertainties, the USEPA amended label language to clarify the risk some of the neonicotinoid products may have to non-target insect pollinators. One of the major changes USEPA made to neonicotinoid insecticide products approved for outdoor foliar uses, is the addition of a "Protection of Pollinators" box. This box visually alerts the user of application restrictions when bees are present by displaying a bee icon, near important information, and accenting key phrases in red "Application Restrictions" and "This product can kill bees and other insect pollinators." The "Protection of Pollinators" box further describes how foliar applications of these insecticides can result in pollinator exposure, and provides steps an applicator can take to reduce non-target impacts. However, there remains criticism of the ability of these label amendments to reduce impacts on pollinators. In addition, some states and communities around the United States have decided to minimize any potential impacts of neonicotinoids on insect pollinators through ordinances or commitments to minimize their use on city, township, or university/school district property. In Minnesota, 16 cities, townships, or school districts including Minneapolis and Saint Paul currently have some ordinance limiting the use of neonicotinoid insecticides on the land they own.

Canada's providence of Ontario implemented new laws beginning July 1, 2015 that aim to reduce prophylactic use of neonicotinoid treated corn and soybean seed, through requiring farmers to demonstrate that a pest problem exists before allowing the sale of treated seed. The goal is to reduce the number of acres planted with neonicotinoid treated corn and soybean seed by 80% by 2017. The plan requires farmers to ensure that neonicotinoid-treated corn and soybean seeds are used only when there is a demonstrated pest problem. In addition, Canada added a new seed packaging label with updated advisories and is requiring farmers to use Bayer's new seed lubricant call Fluency Agent that may reduce the amount of active ingredient abraded from seeds. Claims of abrasion reductions has been variable in the US and Canada ranging from 0, 55, and 65%. The European Union member countries have been restricting neonicotinoid use on certain crops since 1999. More recently, the EU as a whole, enacted a moratorium (December 1, 2013 – December 1, 2015) applying to imidacloprid, clothianidin, and thiamethoxam seed, soil and foliar treatments to bee-attractive crops and cereal grains. Updated risk evaluations are proposed to be completed by January 2017. At present, and despite high use of neonicotinoids on the Australian continent, honey bee populations are generally not considered to be in decline and insecticide impacts to pollinators are not considered a highly significant issue.

Neonicotinoid use and sales:

In the global insecticide market, neonicotinoids accounted for 24% of total insecticide use in 2008. The seed treatment market, initially dominated by insecticides from the carbamate family, was 80% comprised of neonicotinoid insecticides by 2008. Neonicotinoid insecticides, used primarily as seed treatments, accounted for more than 98% of the annual average 133 million acres of corn, soybean, wheat, cotton, and sorghum acres farmers treated in North America.

In Minnesota, there were 510 registered neonicotinoid products in 2015 to control soil (wireworms, seedcorn maggot, corn rootworm, white grubs, etc.) and foliar insect pests (corn earworm, flea beetles, aphids, armyworms, plant bugs, leaf hoppers, grasshoppers, etc.). With the introduction of soybean aphid in 2004, use of neonicotinoids has increased significantly in soybean in Minnesota through seed treatments or foliar applications. In addition to crop protection, applications of neonicotinoid insecticides in non-agricultural fields such as urban household, lawn and garden and animal health have also expanded in recent years. Total sale of neonicotinoid products in Minnesota from 2010 to 2013 was 381.30 thousand pounds. The bulk (>99%) of neonicotinoid products sold from 2010 to 2013 in Minnesota comprised of clothianidin, thiamethoxam, and imidacloprid. In comparison to all pesticides (pounds sold of all chemistries including nonagricultural pesticide products), neonicotinoids accounted for 0.05, 0.12, 0.06, and 0.09% of all pesticide products sold in Minnesota in 2010, 2011, 2012, and 2013, respectively. Because, the State does not have the authority to regulate the sale and use of pesticide treated seeds, almost all corn seed and about 20% of soybean seed treated outside of Minnesota's borders and shipped into the state for planting is not tracked by the MDA. Gross sales and revenues from neonicotinoids and all pesticides in Minnesota showed wide variation from 2010 to 2013 and may not be related to pounds sold each year because price of the same pesticide can vary from year to year and also from seller to seller (manufacturers/retailer). The MDA collected $332,480 from registration of neonicotinoid products (pesticide fee+ AACRA fee + registration fee), which was 3.7% of total revenue for all pesticide registration in 2013.

Neonicotinoid applications and movement in the environment:

Neonicotinoid insecticides are widely used for seed treatment on various crops. Studies of the uptake for each neonicotinoid seed dressing chemistry into a target crop suggest that between 1.6 and 20% of the active ingredient is absorbed by the plant, depending on the chemistry, while the remainder enters the soil. As with any other pesticide, the behavior of neonicotinoids in soils, and hence their bioavailability and transfer to other environmental compartments (i.e. atmosphere, water bodies, etc.), is governed by a variety of complex dynamic physical, chemical, and biological processes, including adsorption–desorption, volatilization, chemical, photo and biological degradation, uptake by plants, run-off, and leaching. The rate and magnitude of transport of pesticides to environmental compartments is also influenced by factors like properties of the pesticide (water solubility, adsorption, chemical structure, acid dissociation constant, etc.) and soil (bulk density, organic matter, texture, pH, etc.), the soil hydrologic cycle, how the pesticide was applied, proximity to sensitive aquatic resources (streams, rivers, etc.), and environmental conditions surrounding the application. These processes directly control the transport of pesticides within the soil and their transfer from the soil to water, air or food. The relative importance of these processes varies with the pesticide compound and the properties of the soil. The high water solubility and low Koc for neonicotinoids indicate low tendency for adsorption to soil particles. Laboratory and field studies have produced a wide range of values for soil dissipation half-lives (7 to 6,931 days) of neonicotinoid compounds. In general, half-lives have been reported to be longer for N-nitroguanidines (imidacloprid, thiamethoxam, clothianidin, and dinotefuran) than N-cyanoamidines (acetamiprid and thiacloprid). However, the highest and lowest values may not represent typical half-life values under Minnesota-specific conditions. Neonicotinoid half-life in soils will vary with soil type, climate, soil pH, moisture, temperature, light intensity, use of organic fertilizers, presence or absence of ground cover, etc. For example, the half-life for imidacloprid is estimated to be longer in temperate regions than in the mid and higher latitudes, because of fewer sun hours, lower sun light intensity, and lower average seasonal temperatures.

Chemicals applied to the soil or plant surfaces may be transported to groundwater or surface water through leaching, runoff, and drift. Presence of pesticides in water poses a concern for humans relying on groundwater as a source of drinking water, and for aquatic communities of invertebrates, fish, and plant life. Owing to high water solubility, some neonicotinoid insecticide compounds may be more prone to leaching into groundwater or running off into surface water. Both thiamethoxam and imidacloprid have been shown to be highly mobile in soils with a high potential to leach downward through the soil profile or laterally through soil flow paths to contaminate surface and groundwater. The persistence of neonicotinoids in aqueous environments depends upon its exposure to sunlight, the soil or water's pH and temperature, the composition of microorganisms and other biotic communities, the concentration of the pesticide in a given water resource, and the pesticide's product formulation. For example, imidacloprid and thiamethoxam have been shown to degrade more rapidly in alkaline media than in acidic or neutral conditions.

MDA regularly monitors groundwater and surface water for presence of neonicotinoids in Minnesota. When a pesticide is detected frequently and benchmarks are reached, it triggers regulatory agencies to take additional actions to mitigate future exposure to the pesticide of concern. To date, the detected neonicotinoid insecticide concentrations in groundwater samples have been below the Minnesota Department of Health (MDH) drinking water guidance values of concern. Clothianidin, imidacloprid, and thiamethoxam detected in 4.3% (71 out of total 1,644 samples) of groundwater samples collected in Minnesota in 2014. The highest concentration for clothianidin, imidacloprid, and thiamethoxam in groundwater was 391, 59, and 14.8 times below the drinking water level of concern concentrations, respectively. There were no detections in urban areas and private drinking water wells.

In surface water, neonicotinoids insecticides were detected in up to 4.5% of surface water samples (58 out of total 1,284 samples) in 2014. No neonicotinoids have been found in any lake samples; however, they are being detected in rural and some urban river and stream sites, and in wetland water and sediment samples. The maximum values for clothianidin and imidacloprid was 22.23% and 44.5% of EPA's chronic aquatic life benchmarks for invertebrates, respectively.

Risk of neonicotinoid use:

For an insecticide to become lethal to an organism, the organism must be exposed to a sufficient amount of active ingredient for a sufficient period of time. Bees and other insect pollinators can be exposed to insecticides primarily through contaminated plant parts (pollen and nectar) and through unintended, exposure pathways like insecticide drift and abraded seed dust generated during planting. Pollinators may also be exposed to pesticides via plant guttation droplets, contaminated surface water, or soil. However, the extent to which bees may be exposed via direct contact with guttation, surface water, or soil is considered uncertain. Exposure from contaminated plant parts depends upon factors such as attraction or frequency of visitation to the pollen or nectar source, concentration of residue in plant parts collected and daily amount of pollen and nectar consumed by a pollinator. Insecticide residues can vary greatly in their concentration at an exposure point and are a function of the type and amount of active ingredient applied, application methods used, and ability of the plant to uptake the active ingredient. In addition, there are factors that influence an active ingredient's rate of degradation and movement in the soil thus impacting the amount of residues available to the plant for uptake at a given time. The complexity of these interacting factors makes it difficult to anticipate the environmental exposure to pollinators over a period of time.

Wide variation has been reported in neonicotinoid residue concentrations in various exposure points. Review of several studies revealed that, foliar or soil treatments closer to blooming resulted in higher concentrations of active ingredients in pollen and nectar of plants as compared to the seed treatments. For example, in one study, it was shown that residue concentrations in pollen from seed treated with ≤ 1 mg imidacloprid resulted in an average of 2.1 ppb imidacloprid in corn pollen (5.4% of a honey bees oral LD_{50}). While, foliar treatments of pumpkin at 96 g thiamethoxam/ha resulted in up to 127 ppb thiamethoxam in the pollen (2.5 times a honey bees oral LD_{50}).

Abraded dust when released into the air during planting, can contain insecticide concentrations toxic to bees. Bees could be directly 'powdered' by insecticides if their flight path went through airborne planter dust or bees may be exposed to the vegetation on which planting dust has settled during planting. In addition to amount and type of active ingredient applied on seed, concentration of residues in treated seed planting dust may depend upon the type of planter and seed lubricant used, application distance from bee hives/nesting sites and abiotic factors such as temperature, relative humidity, and wind. In one study where honey bees presumably flew through dust abraded from the seed during planting, individuals were exposed to an average of 5,700 ppb and up to 12,400 ppb clothianidin. These levels far exceed clothianidin's honey bee acute contact LD_{50} value.

It is important to note that many pesticides, not just neonicotinoids, can make their way into honey bee colonies and possibly result in adverse effects on honey bee colony health and behavior. Field experiments studying pesticide residue accumulation in wax, pollen, water, and individual honey bees, showed colonies located near high intensity agricultural areas accumulated many pesticides in a single sample. For example, residues of up to 39 different pesticides were detected from one sample of the wax of brood comb, while analysis of bees revealed residues of up to 25 different pesticides on or within their bodies.

Based on acute LD_{50} values, four of the six neonicotinoids (clothianidin, dinotefuran, imidacloprid, thiamethoxam) are highly toxic to insect pollinators. Typically, lethal effects to insect pollinators are considered on an acute (single) exposure basis, however, chronic (multiple or duration-based) exposures to an insecticide at levels below an organism's acute LD_{50} can also cause mortality in insect pollinators. There are several ways in which sublethal concentrations of neonicotinoid residues might adversely affect honey bees or other pollinators such as by impacting their orientation, learning, memory, feeding, movement, foraging, reproduction, or colony health. However, there have been relatively few field studies that confirm or invalidate the findings associated with these adverse sublethal effects found in laboratory studies. Further research is needed to identify sublethal exposure thresholds according to standardized protocols that can be reproducible across all pesticide chemistries.

Although this review was scoped to evaluate the impacts of neonicotinoids on insect pollinators, neonicotinoid concentrations can persist, and possibly accumulate under certain soil, water, and sediment conditions and may pose a risk to other taxa (mammals, birds, fish, arthropods, etc.) living in these environments. In general, neonicotinoids pose low to moderate risks (acute or chronic) to mammals and birds. Relative toxicity of neonicotinoids to fish and amphibians varies from practically nontoxic to moderately toxic. However, chronic exposure to neonicotinoids at sublethal concentrations could be a concern to various taxa.

Benefits of neonicotinoid use:

Neonicotinoid insecticides have some distinct advantages over other classes of insecticides such as organophosphates, carbamates, pyrethroids, and chlorinated hydrocarbons. They provide very effective control of piercing and sucking insect pests and some difficult-to-control foliage- and root-feeding insects, such as Colorado potato beetles, termites and white grubs, which have developed resistance to other classes of insecticides. Neonicotinoids show distinct advantages in pest control including efficacy against boring insects and root-feeding insects, both of which cannot easily be controlled using foliar sprays of non-systemic compounds. Neonicotinoids are also known to suppress the secondary spread of insect-transmitted plant pathogens in various crops such as barley yellow dwarf virus in cereal crops. Seed treatment provides efficient and prolonged control of insect pests at low dosages when plants are small and most vulnerable to pests. Seed treatment applications also, generally limit non-target organism direct exposure, or field runoff from foliar, or soil-applied liquid and granular products. Neonicotinoids were registered by USEPA as "reduced risk" pesticides due to their low mammalian toxicity, thus protecting applicators and farm workers from adverse impacts. Several of the alternatives (older chemistries) are considered to be more toxic to bees, mammals, birds, and aquatic organisms than neonicotinoids. In addition, pest management programs that rely on fewer chemical choices and foliar applications may result in the evolution of resistance in insect populations.

Based on the review, the MDA identified several opportunities for action to minimize the impact of neonicotinoids on pollinators.

Proposed action steps regarding use of neonicotinoids

1. Pursue the creation of a Treated Seed program (requires legislative action):
   A Treated Seed program would provide the State with the authority to regulate seeds treated with pesticides, fund research to develop need based recommendations for the use of seed treatments, and may require that untreated seeds and seeds treated at lower pesticide application rates are available in the market.
2. Pursue the creation of a dedicated pollinator protection account (requires legislative action):
   The dedicated pollinator protection account would support activities related to pollinators including evaluating and supporting research on economic thresholds, development of an educational campaign on the use of pesticides and development of stewardship materials.
3. Require formal verification of need prior to use of neonicotinoid pesticides, where appropriate:
   The MDA will work with the U of M and other stakeholders to develop pest thresholds and acceptable IPM criteria. Once pest thresholds and IPM criteria are established, the MDA will ensure that pesticide applicators understand the verification process and requirements. The MDA will ensure that applications of neonicotinoids are made only when a qualified individual verifies that there is a demonstrated pest problem and there is a need for neonicotinoid pesticide use. The MDA will develop a formal process for verification of need by a trained and approved individual prior to the use of neonicotinoid pesticides on crops.
4. Develop an educational campaign for homeowners and residential users of insecticides:
   An educational campaign, with an emphasis on neonicotinoids, will educate homeowners and other residential users of the appropriate and safe use of insecticides and emphasize practices related to the creation of pollinator habitat.
5. Review product labels for appropriate use of neonicotinoids for homeowners and residential users:
   On an ongoing basis, the MDA will review product labels for appropriate urban and suburban uses and restrictions of neonicotinoids to minimize the impact to pollinators.
6. Develop Minnesota specific pollinator stewardship materials:
   The MDA will work with pesticide registrants to develop a Minnesota-specific stewardship program to promote practices targeted at minimizing non-target exposure to pollinators in Minnesota.
7. Increase use inspections for insecticides that are highly toxic to pollinators:
   The MDA will increase use inspections for insecticides that are classified as highly toxic to pollinators on acute exposure basis.
8. Review label requirements for individual neonicotinoid products:
   The MDA will review product labels for enforceable language and appropriate requirements. After reviewing and identifying the language, steps may be taken to clarify and revise the label language.

1 Introduction and background

The Minnesota Department of Agriculture (MDA) has conducted a special review of neonicotinoid use, registration, and insect pollinator impacts in Minnesota. The MDA is the lead state agency for pesticide and fertilizer environmental and regulatory functions in Minnesota under the Pesticide Control Law (Minn.Stat. Chapter18B). One of those functions is state-level registration of pesticide products approved by the U.S. Environmental Protection Agency (USEPA). In 2006, and in response to a Minnesota Legislative Auditor's report, the MDA initiated an effort to broaden state-level review of pesticide registrations by routinely learning more about new registrations and conducting expanded, in-depth reviews to better understand Minnesota-specific registration issues. The scope of these special registration reviews varies depending on the potential education, outreach, and enforcement needs identified by the Department.

Prior to the 2006 Auditor's report, the MDA conducted special pesticide reviews while carrying out many of its statutory responsibilities. The MDA's first formal review in response to the Auditor's recommendations was for the corn herbicide atrazine; a multi-agency review comprised of five agency-specific technical assessments addressed human health, the environment, costs and benefits, water quality monitoring, and product labels. Subsequent in-depth reviews have addressed insecticide active ingredients used to control emerald ash borer (which included a review of two neonicotinoids and noted a concern for pollinator impacts), and a special review of insecticide use related to bed bug control. All of these in-depth reviews led MDA, its collaborators, and stakeholder groups to a greater understanding of the risks and benefits of pesticide product use or generated various voluntary and enforcement-related educational and outreach materials related to human health and environmental protection. For more information on these reviews visit Pesticide Special Registration Review Information.

In addition to the in-depth reviews, the MDA also reviews new active ingredients recently approved by USEPA as well as currently registered pesticides that have significant new uses or have undergone a major label change (21 reviews in 2012-2015). In the process of completing these shorter reviews, the MDA explores a variety of human health and ecological risk issues, and assesses laboratory analytical concerns for tracking potential misuse and non-target impacts. Information on projected pesticide use and efficacy is gathered from University Extension, user groups, and others. Reviews may also include communication with USEPA or the registrant to request more information about identified concerns.

The concern over the use of neonicotinoid insecticides in relation to insect pollinators led the legislature to request that MDA report on the process and criteria to be used in a review of neonicotinoid use and impact in Minnesota currently and in the future.

1.1 Process

The basic process and criteria that MDA uses to conduct a variety of pesticide reviews has already been established, and MDA previously reviewed several neonicotinoid concerns as part of its emerald ash borer insecticide review (including concerns about pollinator exposure). For these reasons, the Commissioner of Agriculture (the Commissioner) directed MDA staff on November 5, 2013, to initiate a special review of neonicotinoid insecticides on insect pollinators.

An in-depth, special review is conducted to provide stakeholders and the Commissioner with more information about Minnesota-specific pesticide products and issues. As such, these reviews are not intended to be redundant of analyses and decisions reached by USEPA during federal registration. Rather, these reviews result in a greater understanding of federal registration concerns and provide a variety of opportunities for action.

The MDA has a history of reviewing Minnesota-specific enforcement data and other data related to pesticide use and insect pollinators, including that related to endangered pollinator species (Karner blue butterfly) or candidate species (Dakota skipper butterflies and Poweshiek skipper). As noted above, the MDA's special review of insecticide active ingredients used to control emerald ash borer included a review of two neonicotinoids (imidacloprid and dinotefuran) and noted concerns about potential pollinator impacts. As an outgrowth of that review, the MDA has been collecting and reviewing a significant amount of information and peer-reviewed research related to neonicotinoids and pollinators. Building off of this information, and in order to conduct the current review, the MDA solicited input from number of interested stakeholders, including beekeepers, academics, citizens, farmers and their suppliers, and pesticide registrants. In addition, the MDA collaborated with the Department of Natural Resources (DNR), the Minnesota Pollution Control Agency (MPCA), the Minnesota Board of Water and Soil Resources (BWSR) and the University of Minnesota (U of M) to develop a scoping document to be used in conducting the review.

The MDA made the draft scoping document available for public comment on March 3, 2014 in order to provide an opportunity for public comment regarding the proposed scope so that interested parties had an understanding of the criteria to be used in conducting the review. The comments were accepted through May 2, 2014. The MDA received 24 unique and 419 general comments. The MDA responded to relevant comments and modified the scoping document appropriately. The final scoping document and the response to comments were posted to MDA website www.mda.state.mn.us/chemicals/pesticides/regs/scopingneonics.aspx. During the course of the review MDA continued to provide information about review-related topics through a public listserver.

1.2 Criteria

The scoping document identified the underlying criteria to be used in conducting the review. As with previous in-depth special reviews of pesticides, the scope of the neonicotinoid review included an overview of federal and state pesticide programs, roles and responsibilities related to the registration and use of neonicotinoids in Minnesota.

The review was carried out using the following six broad criteria:

- Neonicotinoid background, chemistry, and mode of action;
- Federal, state, and other neonicotinoid registration policies and initiatives;
- Neonicotinoid use and sales;
- Neonicotinoid applications and movement in the environment;
- Risks of neonicotinoid use; and
- Benefits of neonicotinoid use.

Minnesota-specific concerns are based on an evaluation of each criterion and the subsequent identification of potential opportunities for action. Before evaluating each criterion, a general overview of insect pollinators and pesticides is presented to provide context for the remainder of the review.

1.3 Insect pollinators and pesticides

More than one third of all plants or plant products consumed by humans are directly or indirectly dependent on insects for pollination. Pollination, the process of transferring pollen from a flower anther to a stigma for fertilization, can occur by an estimated 200,000 pollinator species worldwide, including insects, birds, bats, and other animals. Many plants such as almond, apple, blueberry, sunflower, clover, and canola, cannot reproduce without the help from insect pollinators. The pollination services offered by insect pollinators also play a crucial role in the maintenance of biodiversity and ecological balances in natural ecosystems by providing important food and habitat for other wildlife species. Managed honey bees (*Apis mellifera*) alone pollinate more than $17 billion worth of crops in the U.S. each year and are regarded as the most important pollinator (Calderone, 2012). Native insects, primarily native bees, contribute more than $8.7 billion of pollination services in the U.S. each year (Calderone, 2012). While native bees, beetles, flies, butterflies, moths, and wasps are some other insects known to pollinate flowers, the number and species of other insects that act as pollinators in the U.S. and in Minnesota is unknown.

Honey bee colonies are managed for honey production and are moved around the country for pollination of our nation's almond, fruit, and vegetable crops. The United States Department of Agriculture (USDA) statistics report that there were just over 2.74 million managed colonies of honey bees in the U.S., in 2014 (USDA, 2015a). Over the last 50 years, honey bees have been faced with a number of stressors that impact their health and survivorship. They have been confronted by a number of pests and diseases, fewer flowering plants available to meet their nutritional needs, and a wide variety of pesticides that can be toxic. In the 1980s, two parasitic mites were introduced into the United States. One mite, *Varroa destructor*, has caused very serious declines of honey bees and remains a serious pest that is extremely difficult to control. Beginning in 2006, honey bee colonies began declining throughout the US in unprecedented numbers. The term Colony Collapse Disorder (CCD) was used to describe these losses, because no single factor could account for the high bee population decline. CCD was described as the abrupt disappearance of worker bees from a colony of the European honey bee with no dead bees present in or around the hive. Often colonies which experienced CCD still had stored honey, pollen, and immature bees (brood) present in the hive (USDA, 2014). Occasional, unexplained honey bee losses have been reported as early as 1880; however, the average mortality of honey bee colonies across the nation has been over 30% each year since 2007 (USDA, 2014), and general colony health and the average annual honey production has also decreased. The general consensus among researchers has been to attribute losses and diminished colony health to multiple factors, including biotic stresses such as pathogens, parasites, and pests; abiotic stresses such as climate change, pollutants, and pesticides; and resource factors such as reduced availability of foraging and nesting sites due to habitat fragmentation and loss (Blacquiere et al., 2012). For more information on managed bee stressors see appendix 1. Unexplained, mass bee die-offs and losses of both managed and native pollinators have been documented in North America and Europe throughout recorded history, with major declines in some species dating as far back as the years 950, 992, 1443 in Ireland, and 1903 in Utah, U.S. (Oldroyd, 2007). While the challenges faced by managed honey bee colonies has been recorded and tracked, little is known about the population levels and habitat requirements of native insect pollinators (Biesmeijer et al., 2006; Cameron et al., 2011; Potts et al., 2010).

Pesticides have long been suspected as a potential cause of contemporary honey bee declines. Honey bees are exposed to pesticides and other chemicals commonly used in agriculture via numerous pathways including direct exposure, exposure through the pollen and nectar of plants treated with systemic pesticides and the pesticides used by beekeepers themselves. A number of studies have shown that insecticides and some fungicides may have sub-lethal effects on bees, not killing them outright but instead impairing their development, behavior and immunity to parasites and diseases (Mullin et al., 2010). Although many insecticides such as cyhalothrin, deltamethrin, fipronil and parathion have also been shown to affect honey bees, the attention has focused on neonicotinoid insecticides in the recent years (Mullin et al., 2010).

Because of the concerns outlined above, there has been growing scientific and public interest in further understanding the impact of neonicotinoids on insect pollinators. Non-profit advocacy groups and others have initiated a number of legal actions against USEPA, other federal agencies, individual US states, and registrants for the alleged harm that neonicotinoids have on populations of honey bees and other insect pollinators, urging a precautionary approach (via restrictions or cancellations) until more is known. Meanwhile, as USEPA continues to carry out its Registration Review of neonicotinoids, which includes generation and collection of additional toxicity and exposure data for various pollinator life stages, registrants filed lawsuits in Europe that challenge the European Union's two-year moratorium on certain uses of neonicotinoids, citing insufficient scientific evidence to support such action.

This review is a summary of the various issues, lines of evidence, and activities related to neonicotinoid impacts on insect pollinators. Without being redundant of USEPA Registration Review or conducting a unique risk assessment for pollinator exposure to neonicotinoids, the goal of the review is to present relevant information and identify Minnesota-specific concerns that might be addressed by specific regulatory or non-regulatory activities.

2 Neonicotinoid background, chemistry, and mode of action

Neonicotinoids are a relatively new class of insecticides with large-scale applications in agriculture, home-landscape, and animal production. The name "neonicotinoids" literally means new nicotine-like and hence they are chemically similar to the botanical insecticide nicotine. Nicotine is an alkaloid compound found in several plants of the Solanaceae (nightshade) family. The family Solanaceae includes tobacco, ornamentals such as petunia and several edible plants such as potato, pepper, tomato, and eggplant. In addition, this plant family also includes some common ornamental plant species such as petunia and some weed species such as black nightshade and jimsonweed.

Neonicotinoids are potent broad-spectrum insecticides affecting insects through contact and oral exposures and are effective at very low concentrations. All neonicotinoid insecticides are classified in Group 4A in the Insecticide Resistance Action Committee (IRAC) Mode of Action (MoA) scheme. Structurally, neonicotinoids can be classified into N-nitroguanidines (imidacloprid, thiamethoxam, clothianidin and dinotefuran), nitromethylenes (nitenpyram), and N-cyano-amidines (acetamiprid and thiacloprid). Neonicotinoids can also be classified into cyclic (imidacloprid, thiacloprid, thiamethoxam) and noncyclic compounds (nitenpyram, acetamiprid, clothianidin). Irrespective of structural classification, all neonicotinoid insecticides show similar broad spectrum insecticidal activity but vary in their biological and physicochemical properties such as photolytic stability, soil degradation, metabolism in plants and insects, and toxicity to different animals (Jeschke and Nauen, 2008).

Like nicotine, neonicotinoids target the acetylcholine receptors (nAChR) within an insect nervous system and act as agonists on nAChRs by opening cation channels (Jeschke and Nauen, 2008). Normally, acetylcholine binds to the receptors for few milliseconds to transmit signals and then, is broken down by the enzyme acetylcholinesterase to terminate the signals from these receptors resulting in short and controlled nerve stimulation. However, acetylcholinesterase cannot break down neonicotinoids for longer periods (minutes or longer) resulting in nerve hyper-stimulation. This mode of action causes excitation of insect nerves that can lead to trembling and shaking and eventual paralysis, which can lead to death depending on the exposure duration and dose (acute, short-term effects at high exposure concentrations or chronic, longer-term effects at lower exposure concentrations, and potentially no deleterious effects at even lower exposure concentrations). Voltage-gated calcium channels are also involved in their insecticidal activity (Tomizawa and Casida, 2003). Although the botanical insecticide nicotine acts on the same target as the neonicotinoids, these compounds vary in their affinity to different nAChR subtypes, with nicotine showing selective toxicity for vertebrates whereas neonicotinoids are highly selective for insect nAChRs. In addition, nicotine is less effective as an insecticide because of positively charged nitrogen molecules in its molecular structure in aqueous solution. Two more insecticide classes, sulfoxamines and butenolide, function similarly to neonicotinoids; however, these classes are considered chemically distinct from neonicotinoids (Jeschke et al., 2015; Sparks et al., 2013) and hence, these classes are not a part of this review.

Neonicotinoids are applied in a variety of ways, including as foliar sprays, soil applications, seed treatments, and as trunk injections in trees. Consequently, they are now used worldwide on nearly 140 agricultural crops and in many non-agricultural uses. They are among the most effective insecticides available for control of sucking insect pests such as aphids, white flies, leaf- and plant-hoppers, thrips, some Lepidopteron (caterpillar), and a number of Coleopteran (beetle) pests. When used to control plant pests, they are absorbed by plant parts and move systemically within plant tissues connected to the plant's vascular system.

2.1 Commercially available neonicotinoids

Currently, there are eight neonicotinoid insecticides (acetamiprid, clothianidin, dinotefuran, imidacloprid, thiacloprid, nitenpyram, nithiazine, and thiamethoxam) available commercially for use in crop or animal agriculture, urban landscapes and domestic settings. Imidacloprid was the first commercially registered neonicotinoid insecticide in the US in the early 1990s, followed by clothianidin and thiamethoxam in the early 2000s (Jeschke and Nauen 2008). Another neonicotinoid insecticide, nithiazine, was discovered in 1970s. However, nithiazine was not registered until 1995 because of its limited efficacy and rapid degradation under hydrolytic and photolytic conditions. Nitenpyram is used for controlling dog and cat insect pests only, while nithiazine has a limited use as fly abatement strips. Use of these two neonicotinoids is unlikely to affect insect pollinators, therefore, these two insecticides are not part of this review. In addition, the registration for thiacloprid has been voluntarily cancelled by the registrants and will no longer be available for use on crops after the year 2016. Below is a description of six neonicotinoid active ingredients addressed in this review (Table 1). Included is the first date of US registration, general information about its control of pests on certain crops, the number of Minnesota-registered products containing the active ingredient, and its relative toxicity to pollinators.

Table 1. Biological profile of six commercially available neonicotinoid insecticides.

Insecticide active ingredient	Year of initial registration	Primary registrant in the United States	Primary use type	Application methods	Number of crops registered	Common trade names[a]
Acetamiprid	2002	Bayer CropScience, DuPont, Gowan	Agriculture, household	Foliar, broadcast, seed treatment.	60	Assail, Chipco, Pristine, Tristar, Justice, Intruder
Clothianidin	2003	Bayer CropScience, Valent	Agriculture, household	Foliar, seed treatment, soil incorporation, tree injection.	40	Arena, Belay, Clutch, Poncho, Titan, NipsIt Inside
Dinotefuran	2004	Mitsui Chemicals Inc., Gowan, PBIGordon, Valent	Agriculture, household	Foliar, soil incorporation, bait application, tree injection.	35	Scorpion, Venom,
Imidacloprid	1992	Bayer CropScience	Agriculture, household, structural, animal	Foliar, seed treatment, soil incorporation, tree injection.	140	Admire, Gaucho, Provado, Macho, Imicide, Sepresto, Widow, Wrangler
Thiacloprid[b]	2003	Bayer CropScience, DuPont	Agriculture	Foliar	50	Calypso
Thiamethoxam	1999	Syngenta Crop Protection, LLC.	Agriculture, household	Soil incorporation, seed treatment, foliar application, bait application, spot treatment.	115	Actara, Adage, Centric, Cruiser, Platinum

[a] Trade names are used as examples only and are not inclusive of all products, nor do they imply any recommendation.

[b] All products comprising thiacloprid has been voluntarily cancelled by the registrants in the United States in August 2014.

Source: (Elbert et al., 2008)

2.1.1 Acetamiprid

Launched in Japan in 1995, acetamiprid, N-[(6-chloro-3-pyridyl) methyl]-N'-cyano-N-methyl-acetamidine, was registered conditionally in the US by Aventis Crop Science in 2002. Currently, it is registered for controlling sucking insect pests on more than 60 crops nationwide, including alfalfa, soybean, sweet corn, vegetables, fruits, turf, ornamentals, cotton, and citrus. Acetamiprid is also registered for use against household pests. Acetamiprid was an active ingredient (a.i.) in 20 registered products in Minnesota in 2015. Based on USEPA's LD_{50} value for honey bees (2 to 10.9 µg a.i./bee), acetamiprid is considered moderately toxic to pollinators.[1]

2.1.2 Clothianidin

Clothianidin, (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine, was launched by Sumitomo Chemical Takeda Agro Company and Bayer CropScience in 2002 and was registered conditionally in the US in 2003. Clothianidin is a breakdown product of another neonicotinoid insecticide thiamethoxam and was an active ingredient in 26 registered products in Minnesota in 2015. It is registered for use against a broad range of insects in residential areas and on more than 40 agricultural crops nationwide. Based on USEPA's LD_{50} value for honey bees (< 2 µg a.i./bee), clothianidin is considered highly toxic to pollinators.

2.1.3 Dinotefuran

Dinotefuran, 2-methyl-1-nitro-3-[(tetrahydro-3-furanyl) methyl] guanidine, was registered conditionally in the US by Mitsui Chemicals in 2004. Dinotefuran is registered for foliar use on more than 35 crops including leafy vegetables (except Brassica) turf and ornamentals. Dinotefuran is an active ingredient in 73 registered products in Minnesota in 2015. Dinotefuran is also registered for use on trees for emerald ash borer control in Minnesota. Emerald ash borer is a serious forest tree pest in Minnesota (www.mda.state.mn.us/emeraldashborer). Based on USEPA's LD_{50} value for honey bees (<2 µg a.i./bee), dinotefuran is considered highly toxic to pollinators.

2.1.4 Imidacloprid

Imidacloprid, N-[1-[(6-Chloro-3-pyridyl) methyl]-4,5-dihydroimidazol-2-yl]nitramide, was first registered for use in the US in 1994 by Bayer CropScience. Although it is now off patent, the primary manufacturer is still Bayer CropScience but it is also sold by others under many trade names. Currently, it is the most

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[1] A pesticide's initial classification as "moderately" or "highly" toxic to bees has no specific relationship to whether its actual use according to label instructions will result in exposure concerns of a magnitude leading to acute or chronic impacts to pollinators. Much depends on the way in which the pesticide is ultimately used, its application rate, and the likelihood that residues will be associated with honey bee oral or contact routes of exposure, as well as other exposures assessed under current USEPA guidance. USEPA risk assessments and final label use instructions are designed to limit pollinator exposure concentrations to levels below those which would result in acute toxicity to honey bees and/or lead to unreasonable adverse effects on adults, other life stages, or colonies. Current USEPA guidance on honey bee toxicity risk assessment is described in USEPA new risk assessment framework for pollinators. The median acute toxicity value for an organism is said to be the lethal dose to 50 percent of a population (the LD_{50}).

widely used insecticide in the world with approved use on more than 140 crops in more than 120 countries. Imidacloprid was an active ingredient in 344 registered products in Minnesota in 2015. More generic products based on imidacloprid have been registered since its patent expired in most countries in 2006. Based on USEPA's LD_{50} value for honey bees (<2 µg a.i./bee), imidacloprid is considered highly toxic to pollinators. The preliminary imidacloprid, pollinator specific review was released by USEPA in January 2016.

2.1.5 Thiacloprid

Thiacloprid, [(2Z)-3-[(6-Chloropyridin-3-yl) methyl]-1,3-thiazolidin-2-ylidene] cyanamide, was registered conditionally in the US in 2003 by Bayer CropScience for use on agricultural crops to control variety of sucking and chewing insects. In 2014, the manufacture voluntarily cancelled all products with thiacloprid as an active ingredient in the US, and products will be off retail shelves by the end of 2016 (USEPA, 2014a). Based on USEPA's LD_{50} value for honey bees (>11.9 µg a.i./bee), thiacloprid is considered practically non-toxic to pollinators.

2.1.6 Thiamethoxam

Thiamethoxam, 3-[(2-Chloro-1,3-thiazol-5-yl)methyl]-5-methyl-N-nitro-1,3,5-oxadiazinan-4-imine, was developed by Syngenta and was registered conditionally in the U.S. in 1999. Thiamethoxam is approved for use in the US as an antimicrobial pesticide, wood preservative, and as an insecticide on more than 115 crops nationwide including corn, soybean, alfalfa, and oilseed rape. Thiamethoxam was an active ingredient in 54 registered products in Minnesota in 2015. Based on USEPA's LD_{50} value for honey bees (<2 µg a.i./bee), thiamethoxam is considered highly toxic to pollinators.

2.1.7 Neonicotinoid metabolites

Most pesticides break down or degrade over time as a result of several chemical and microbiological reactions in soils, water, and/or sunlight. These processes result in the final degradation of the compound into metabolites or mineral compounds. Many metabolites may have no or very little known insecticidal, environmental, or human health importance based on their quantity, their toxicity, or both. In contrast, some metabolites may have toxicity equal to or greater than their parent compound. Neonicotinoids are subjected to intense metabolism in soil and plants leading to the appearance of different metabolites during the degradation process. Some of the known neonicotinoid metabolites of toxicological significance in USEPA risk assessments are presented in table 2.

Table 2. Toxicologically-significant metabolites of neonicotinoids in various plant, soil, water or sediment considered in USEPA risk assessments.

Parent compound	Metabolites
Acetamiprid	IM-1-4
Clothianidin	MNG,N-methyl-N'-nitroguanidine; NTG nitroguanidine; TZNG, CLO-dm; N-(2-chlorothiazol-5-ylmethyl)-N'-nitroguanidine; CLO-NNO; CLO-dm-NNO; CLO-NH, TMG, N-(2-chlorothiazol-5- ylmethyl)-N'-methylguanidine; CLO-Urea, TZMU,N-(2-chlorothiazol- 5-ylmethyl)-N-methylurea; CLO-dm-Urea, TZU, 2-chloro-1, 3-thiazole-5-ylmethylurea.
Dinotefuran	DIN-dm-NNH2; DIN-NH, DN, 1-Methyl-3-(tetrahydro-3- furylmethyl)guanidine; DIN-dm-NH, 3-(tetrahydro-3-furylmethyl) guanidine; DIN-Urea, UF, 1-Methyl-3-(tetrahydro-3- furylmethyl)urea; DIN-dm-Urea, 3-(tetrahydro-3- furylmethyl)urea; DIN-2-OH; DIN-3-OH; DIN-5-OH; IN-a, PHP, 1,3-diazinane aminocarbinol (derivative of DIN-2OH); DIN-g (derivative of DIN-5-OH), MNG (1-Methyl-2-nitroguidine).
Imidacloprid	IMI-olefins, 4,5-dihydroxy-imidacloprid; 5-hydroxy imidacloprid; 6-CNA, 6-chloronicotinic acid; IMI-NH, desnitro-imidacloprid, Imidacloprid guanidine.
Thiacloprid	Thiacloprid amide, thiacloprid sulfonic acid.
Thiamethoxam	Clothianidin, CLO; Thiamethoxam-dm, TMX-dm, N-desmethyl thiamethoxam TMX-NNO; TMX-NNH2; TMX-NH.

3 Federal, state, and other neonicotinoid registration policies and initiatives

Both federal and state laws govern the registration and use of neonicotinoid insecticides in Minnesota. Most neonicotinoid insecticide regulatory or risk-related outreach activities in Minnesota rely on risk assessments, labeling, and health and environmental mitigation developed at the federal level by USEPA. The USEPA registers a pesticide unconditionally after determining that the pesticide meets the statutory standard and there are no outstanding data requirements. However, under certain circumstances, the USEPA may register the pesticide conditionally under FIFRA section 3(c) (7) if the pesticide meets the standard for registration, but there are outstanding data requirements. Before granting a conditional registration, the USEPA must determine that, although an application lacks some of the necessary data, use of the pesticide would not significantly increase the risk of unreasonable adverse effects on the environment during the time needed to generate the necessary data. In the United States, six neonicotinoid insecticides with potential pollinator impacts are registered for controlling agricultural and urban insect pests. Acetamiprid, clothianidin, dinotefuran, and thiacloprid were registered conditionally in the US because of some data gaps.

3.1 USEPA registration review

The Federal Insecticide, Fungicide, and Rodenticide Act of 1972, amended by the Food Quality Protection Act of 1996, and the Pesticide Registration Improvement Act of 2003 require USEPA to periodically review every registered pesticide. Currently, all pesticides are reviewed on a 15-year cycle (USEPA, 2000). Carrying out registration reviews allows USEPA to require new toxicity testing, and incorporate new science, public policy, or pesticide uses that have occurred since the initial registration of the pesticide. Using this up-to-date information, the USEPA is able to re-evaluate human and environmental risks to make sure no unreasonable adverse effects will occur with the continued use of a pesticide. The registration reviews for the neonicotinoid nitroguanidine insecticides (imidacloprid, clothianidin, thiamethoxam, dinotefuran, acetamiprid, and thiacloprid) were initiated between 2008 and 2012 and are expected to be completed between 2016 and 2019 (Table 3).

Table 3. The USEPA registration review schedule for neonicotinoid insecticides

Neonicotinoid	Initiation	Data Generation	Completion
Imidacloprid	Dec. 2008	2010-2015	2016-2017
Clothianidin	Dec. 2011	2013-2016	2016-2017
Thiamethoxam	Dec. 2011	2013-2016	2016-2017
Dinotefuran	Dec. 2011	2013-2016	2016-2017
Acetamiprid	Dec. 2012	2014-2017	2018-2019
Thiacloprid	Dec. 2012	Voluntary cancellation by registrant, review closed	

The USEPA registration review process consists of three phases:

1. Opening a docket;
2. Case development; and
3. Registration review decision.

Opening a docket on www.regulations.gov is USEPA's way of communicating to the public regulatory changes to a pesticide's registration or the initiation of new projects like a registration review. Opening a docket also provides the public with a chance to comment on the action being conducted. After the public comment period, the case development phase begins with USEPA creating a work plan, which summarizes the reasons this action is taking place, the additional information needed to complete the review, and a timeline for the proposed actions to take place. Registrants of the pesticide under review are then notified of additional information needed to support the continued use of the pesticide. Once the requested information is received, the USEPA proceeds with the preliminary risk assessment followed by a public comment period. During phase three, the USEPA revises the preliminary risk assessment to include feedback received by the public. This revised risk assessment then undergoes a final public comment period before a final decision is made by USEPA (USEPA, 2012a).

In order to complete the registration review of neonicotinoid nitroguanidine insecticides, the USEPA's work plans identified information gaps in ecological and human health risk assessments. For ecological risk assessments, the work plans identified information gaps that included: the determination of insecticide toxicity to endangered species; refined assessments for insecticide effects on beneficial insects, birds, and plants; their metabolism and movement in soil and aquatic systems; and evaluation of indirect ecological effects.

There were fewer studies requested to fill information gaps for the human health risk assessments. Some of USEPA's registration reviews will cover aggregate exposure, immunotoxicity, inhalation, and dislodgable or transferable residue studies (see appendix 2). Although the focus of MDA's review is neonicotinoid impacts to insect pollinators, the information in appendix 2 includes a general overview of all USEPA activities related to its registration review of neonicotinoids. For more information on neonicotinoid registration reviews schedule visit http://www2.epa.gov/pollinator-protection/schedule-review-neonicotinoid-pesticides.

Ecological information gaps for neonicotinoids and the studies requested to refine USEPA registration risk assessments – including toxicity studies related to honey bees and other insect pollinators – are discussed below.

3.2 USEPA refined assessment for terrestrial insects (including honey bees and other insect pollinators)

To fill information gaps related to all beneficial insects in terrestrial ecosystems USEPA uses the results of toxicity studies conducted on honey bees as a surrogate species. Many of the neonicotinoid insecticides undergoing registration review are classified as "highly toxic" to honey bees based on acute contact and oral toxicity testing. Because of their classification as "highly toxic", the registration reviews will include a refined assessment for the toxicity and exposure to other life stages and/or full colonies.

Depending on the neonicotinoid under review, different information gaps exist. The USEPA may request a variety of tests from registrants to fill these information gaps and more accurately characterize the effects an insecticide is having on honey bees and by proxy, other terrestrial beneficial insects. While the acute toxicity of neonicotinoids and many other non-neonicotinoid insecticides to adult honey bees is relatively well-documented, uncertainty still exists regarding the acute and chronic exposure concerns associated with different life stages, and colony effects under actual field use and conditions.

Special field studies assessing neonicotinoid residue in pollinator-attractive plants will provide realistic residue concentrations for pollen, nectar, and leaf tissues, and help in assessing pollinator exposure. In addition, other field and laboratory feeding studies will help refine regulators' understanding of the impacts chronic neonicotinoid exposure can have on adult and larval pollinators. During the registration review process, the USEPA may consider potential indirect effects posed to non-target organisms by the parent and degradate compounds. Examples of some indirect effects that may be considered are effects to plant reproduction associated with a decline in pollinating insects. Additional information about USEPA's new risk assessment framework for pollinators, which is being incorporated in this registration review of neonicotinoids, is provided below.

3.3 USEPA new risk assessment framework for pollinators

Historically, the USEPA's testing paradigm for pollinators relied on qualitative evaluations rather than precise quantitative measurements. The process relied primarily on developing an understanding of the types of effects that might be caused by the pesticide (hazard characterization), based on toxicity studies using honey bees as surrogate species.

For example, pollinator toxicity has typically been established by USEPA using the results of standardized toxicity tests on honey bees (a Tier I screen conducted under laboratory conditions). Pesticides with terrestrial, forestry, and residential outdoor uses require an acute contact toxicity test, while it may be conditionally required for pesticides with aquatic uses. Acute contact and oral LD_{50} is assessed after 24, 48, or 72 hours of pesticide exposure. Depending on the outcome of the toxicity tests, pesticides are classified as practically non-toxic (LD_{50} ≥11 µg a.i./bee), moderately toxic (LD_{50} is 2- 10.9 µg a.i./bee), or highly toxic to bees (LD_{50} <2 µg a.i./bee) on an acute exposure basis.

The honey bee acute contact toxicity test uses technical grade active ingredients (TGAI), with median acute LD_{50} values < 11 µg a.i./bee triggering the honey bee toxicity of residues on foliage test using the technical end-use product (TEP). Use of the TEP for these tests ensures some understanding of the potential combined effects of the TGAI and other product ingredients that may result in synergistic, antagonistic or other toxicological interactions. Additional field testing for pollinators is required if data from other sources indicated potential non-acute mortality harm to honey bee colonies or other terrestrial arthropods, or residual toxicity studies indicates a concern. Such field studies have been required as part of refined toxicity tests.

In 2012, the USEPA in collaboration with Health Canada's Pest Management Regulatory Agency (PMRA) and the California Department of Pesticide Regulation (CalDPR) developed a new risk assessment framework for bees. The framework was refined in concert with FIFRA Scientific Advisory Panel review and comment and published as joint USEPA, PMRA, and CalDPR guidance in June 2014. The new framework takes into account multiple lines of evidence including registrant-submitted data, open literature, and ecological incident data. The new testing paradigm relies on a three-tiered assessment and uses honey bees as a surrogate organism for all pollinators. However, if available, acceptable data from other bee species such as bumble bee (*Bombus terrestris*), blue orchard bee (*Osmia lignaria*), and alfalfa leafcutting bee (*Megachile rotundata*) are also considered in the risk assessment.

Use of honey bees as a surrogate for other insect pollinators and beneficial insects has both limitations and benefits. When surrogates are used, there is of course no data generated for the thousands of other terrestrial arthropods and the unique toxicological responses they might exhibit when challenged with a pesticide exposure. With the use of the honey bee as a surrogate for terrestrial beneficial insects, the USEPA assumes that data on individual organisms as well as colony-level data will provide some relevant information on the potential effects of a pesticide on both solitary and social bees. In addition, protection of honey bees may contribute to pollinator diversity indirectly by preserving the pollination and propagation of the many plants species pollinated by honey bees, which also serve as food sources for other pollinating insects.

The results of the new three-tiered assessment may be used to establish a dose-response or cause-and-effect relationship between the amount of pesticide to which the organism was exposed and the effects on the organism. Any signs of abnormal behavior are also considered. In most cases, toxicity tests are conducted on an active ingredient basis. If data from a formulated product or degradates of potential toxicological concern are available, they are also considered in the risk assessment. In addition, data from use patterns is incorporated into the risk assessment.

- In Tier I assessments, honey bee adults and larvae are exposed to varying concentrations of pesticide *in vivo* for a specified time through contact or oral exposures to determine acute and chronic LD_{50} values (doses that kills 50% of the test population). The toxicity of residues on foliage is also evaluated to determine the amount of time during which contact exposure to weathered residues of the test compound remains toxic to >25% of the adult bees. Tier I is considered to be sufficiently conservative and is required for all pesticides intended for outdoor uses. The process serves as a screening tool to determine which pesticides are expected to pose minimal risk and whether higher tier studies are required.

- A Tier II assessment is initiated when the Tier I LD_{50} value is <11 µg a.i./bee and the use pattern indicates that honey bees may be exposed. If a Tier II assessment is started, the agency may require studies designed to more closely reflect real world exposures and the effects on the whole colony. In Tier II, honey bees are exposed to known concentrations of a pesticide in a food source fed to whole bee colonies contained within enclosed structures (semi-field studies) to evaluate effects of pesticides on the colonies and to quantify pesticide concentrations in pollen and nectar of crop plants.

- A Tier III assessment is triggered when the Tier II assessment or any other evidence, such as open literature or a bee kill incident, indicates unacceptable or substantial uncertainties for risks to pollinators. Tier III test conditions resemble those encountered in the field under actual use conditions, such as compounds applied to plant leaves, seed, and soil. Tier III studies take into account the broad dynamics of a whole colony in a free-foraging scenario and evaluate possible long term effects of a pesticide on growth, survival, reproduction, brood survival and development, disease incidence, over-wintering success, behavior, and type of sublethal effects. See, Figure 1 and Figure 2 for an illustration of the decision-making process for assessing risks to honey bees from foliar spray and from soil or seed treatment applications of pesticides. See table 4 for a description of toxicity studies required by USEPA on honey bees as surrogate species for neonicotinoids and other Group 4A systemic insecticides. For additional details visit: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. In addition to developing new risk assessment framework for bees, the USEPA is working with global partners from several federal and international agencies such as United States Department of Agriculture, the Organization for Economic Cooperation and Development's Pesticide Effects on Insect Pollinators Working Group, the International Commission on Plant Pollinator Relationships, the European Food Safety Authority, and Health Canada's Pest Management Regulatory Agency to develop and implement appropriate tests for evaluating both exposure to and effects of pesticides on honey bees. To see details visit: www2.epa.gov/pollinator-protection/epa-actions-protect-pollinators

The MDA is closely monitoring USEPA's Registration Review of neonicotinoid pesticides and the emerging toxicity studies and draft risk assessments. The MDA is in communication with USEPA directly or through the federal docket. Using registration information generated by USEPA, the MDA is reviewing human health and ecological risks with Minnesota-specific concerns in mind. The MDA is also working with the Minnesota Department of Health to establish Minnesota-specific human health risk guidance, and with the Minnesota Pollution Control Agency to explore the appropriateness of USEPA aquatic life benchmarks or other screening values. These Minnesota-specific efforts can result in exposure thresholds of concern that are more conservative than those used by USEPA.

Any USEPA risk assessment updates and label changes are considered during MDA's review of the active ingredient and are generally applicable to all of the registered products containing the active ingredient. The MDA may determine that due to a Minnesota-specific concern a pesticide product may not be initially approved or it may be approved with certain restrictions designed to mitigate scientifically defensible concerns. In such cases, the MDA may work with USEPA, the registrant, and possibly others to develop Minnesota-specific label revisions, management practices, or product stewardship and outreach materials.

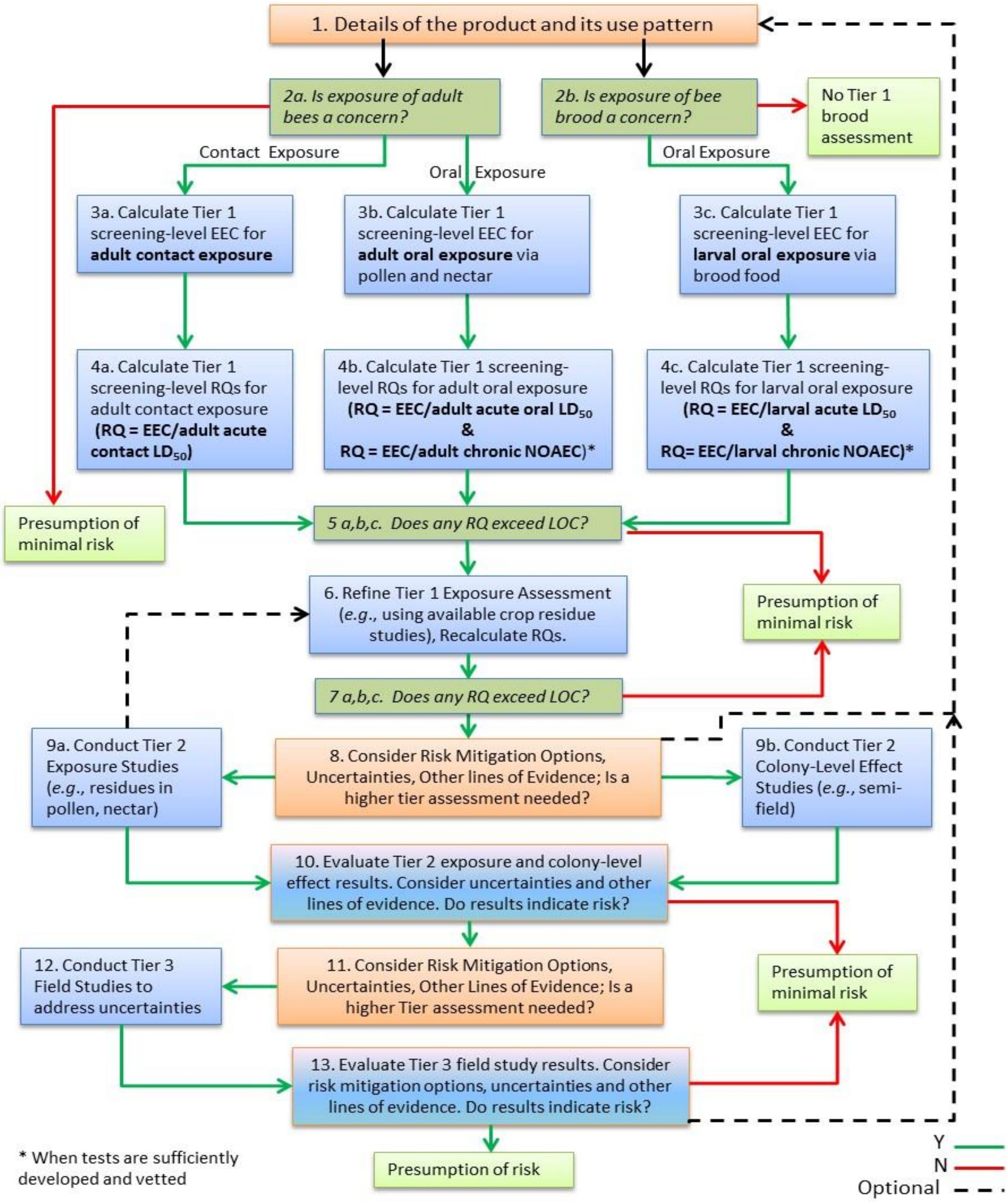

Figure 1. Tiered Approach for Assessing Risk to Honey Bees from Foliar Spray Applications: EEC=Estimated Environmental Concentration; RQ=Risk Quotient; LOC=Level of Concern; and NOAEC=No Observable Adverse Effect Concentration (USEPA, 2014b).

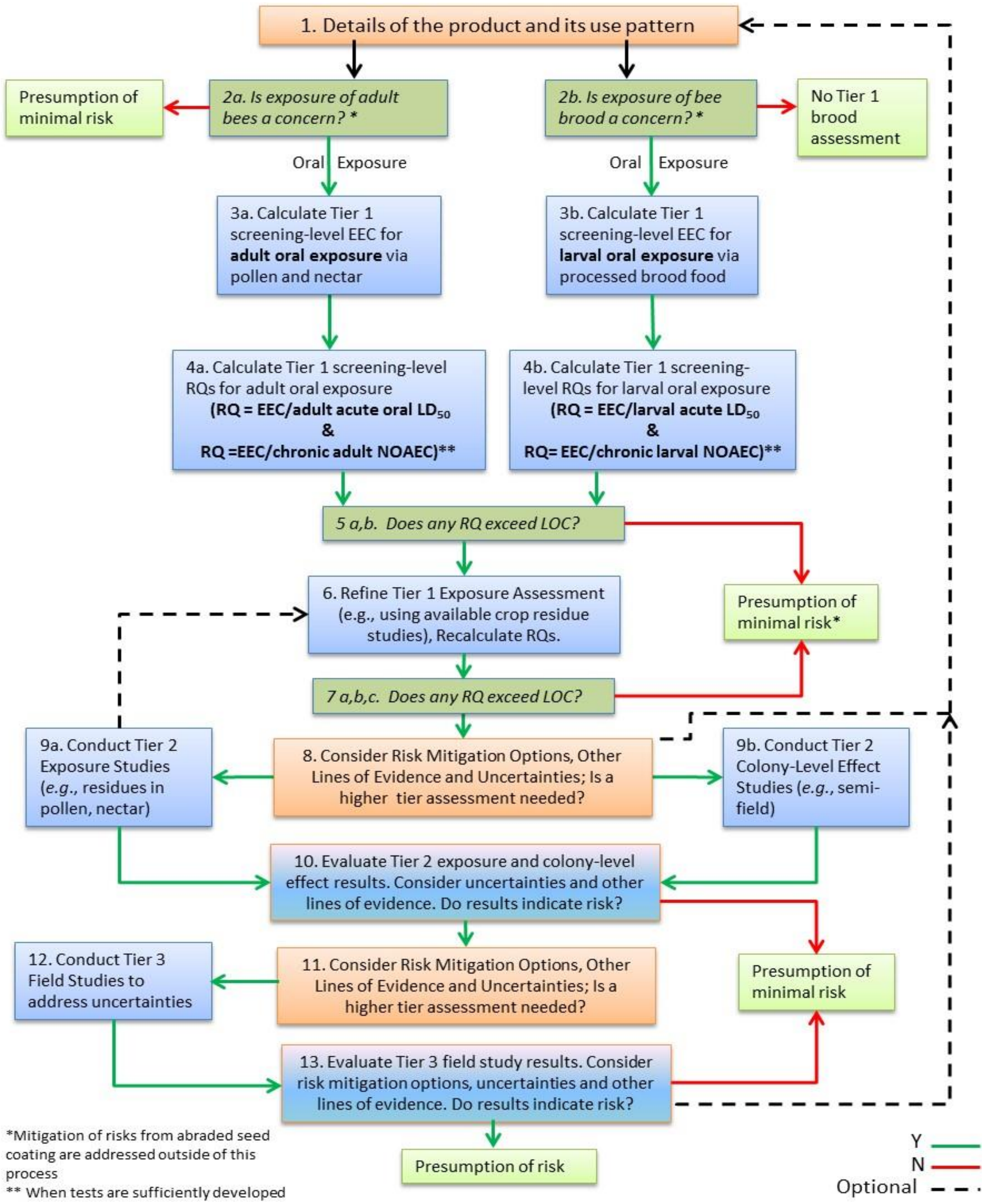

Figure 2. Tiered Approach for Assessing Risk to Honey Bees from Soil/Seed Treatments: EEC=Estimated Environmental Concentration; RQ=Risk Quotient; LOC=Level of Concern; and NOAEC=No Observable Adverse Effect Concentration (USEPA, 2014b).

Table 4. Summary of toxicity studies required by USEPA on honey bees as surrogate species for neonicotinoids and other Group 4A systemic insecticides based on Environmental Fate and Effects Division (EFED) documents submitted at the time of registration and registration review plan.

Insecticide	**Year of registration**	**Tier 1- Toxicity test results based on**					**Tier II- Semi-field test results based on whole colony level effects (also include new guidelines)** [a,d]	**Tier III- Field test results based on whole colony level effects (also include new guidelines)** [a,e]	**Conclusions**
		Adult contact toxicity[a]	**Adult oral toxicity**[a]	**Larval contact toxicity (New guidelines)** [b]	**Larval oral toxicity (New guidelines)** [b]	**Residual contact toxicity effects**[a,c]			
Acetamiprid	2002	Moderate	Low	Not yet submitted (requested for review)	Not yet submitted (requested for review)	Under review (not conducted in 2002)	Registrant may be requested to submit studies	Registrant may be requested to submit studies	Uncertainties identified
Clothianidin	2003	High	High	Not yet submitted	Not yet submitted	Under review (not conducted in 2003)	Under review (Not conducted or considered supplemental)	Under review (Not conducted or considered supplemental)	Uncertainties identified
Dinotefuran	2004	High	High	Not yet submitted	Not yet submitted	48 hr	Registrant may be requested to submit studies	Registrant may be requested to submit studies	Uncertainties identified
Imidacloprid	1992	High	High	Not yet submitted	Not yet submitted	Under review (not conducted in 1992)	Registrant requested to submit studies	Registrant requested to submit studies	Uncertainties identified
Thiacloprid	2003	Low	Low	Not yet submitted	Not yet submitted	< 2hr	Not conducted or considered supplemental	Not conducted or considered supplemental	Active ingredient cancelled
Thiamethoxam	1999	High	High	(Requested for review)	(Requested for review)	(Requested for review)	Registrant may be requested to submit studies	Registrant may be requested to submit studies	Uncertainties identified
Sulfoxaflor (Neonicotinoid-like)	2014	High	High	High	High	< 24hr	Potential risks identified	Likely no long-term effects	Likely no long-term effects
Flupyradifurone (Neonicotinoid-like)	2015	Non toxic	High	Non-toxic	High	<3 hr	Potential risks identified	Likely no long-term effects	Likely no long-term effects

[a] Currently required toxicity tests, under 40 e-C.F.R. pt 158 (July 28, 2015)

[b] Tests suggested in new 2012 guidelines [(USEPA, 2014b)].

[c] Residual time to cause 25% mortality for residues aged for specific periods (RT_{25}).

[d] Triggered when the Tier I assessment, 48-hr LD_{50} oral value, is <11 µg a.i./bee or other data indicates that bees may be at risk.

[e] Triggered when the Tier II assessment or any other evidence, such as open literature or a bee kill incidence, indicates unacceptable risks or substantial uncertainties to pollinators. Honey bees are exposed to known concentrations of a pesticide in a food source, fed to whole bee colonies contained within enclosed structures, to evaluate seasonal effects of pesticides on the colonies and to quantify pesticide concentrations in pollen and nectar of crop plants.

3.4 US registrant product stewardship

As part of MDA's special review, letters were sent to technical registrants of imidacloprid, clothianidin, thiamethoxam, dinotefuran, acetamiprid, and thiacloprid to ask for neonicotinoid and pollinator information related to: toxicity tests conducted but not yet submitted to USEPA; anticipated label modifications; international company initiatives/issues; and company stewardship programs. The following registrants responded: Bayer CropScience (imidacloprid, clothianidin, and thiacloprid), Syngenta CropProtection (thiamethoxam), and Mitsui Chemical Inc. (dinotefuran). Submitted information related to toxicity tests, anticipated label modifications, and international initiatives/issues were reviewed and incorporated into the broader review as appropriate. Stewardship programs conducted by registrants are further described below.

3.4.1 Bayer CropScience (stewardship):

- Sentinel Hive Program: Trains "Bee Care Ambassadors" on bee health awareness, works with beekeepers involved in agricultural production to monitor honey bee colony health, and has been involved with *Varroa* mite control product development.
- North American Bee Care Center: Developed for research (focused on creating solutions to treat *Varroa* mite and other honey bee disorders), education, and training.
- Seed Treatment Stewardship Guide: Designed to communicate proper practices related to seed treatment application and use to applicators, growers, and beekeepers.
- Commitment to Quality (C2Q): Provides a means of technical support to those engaged with the use of any aspect of Bayer CropScience's seed treatment products.
- Other Stewardship Materials: Best practices or tools compiled for use with: turf and ornamentals, horticultural crops, integrated pest management (IPM), growers, bee investigations, pollinators and pesticides (reference guide), etc.

3.4.2 Syngenta CropProtection (stewardship):

- Corn Dust Research Consortium (2013 – 2014): A research-based effort to identify honey bee foraging habits at the time of corn planting and evaluating alternatives to graphite- and talc-based seed lubricating agents.
- The Good Growth Plan: A plan to improve 12 million acres of farmland worldwide by increasing pollinator forage and habitat, "a key aspect of improving pollinator health" according to Syngenta.
- Operation Pollinator: A program developed to improve native bee numbers in farmland by establishing wildflower-rich habitat in field margins. This program also develops and tests wildflower mixes suited for regional conditions.
- Biodiversity and Pollinator Forage Improvement Partnerships: A 15-year partnership with Iowa and Illinois to plant trees and shrubs to improve vegetative buffers and preserve biodiversity.
- Seed Care Center, Stanton MN: A research site for application technology seed science and testing, seed treatment quality, crop enhancement, and product support.

3.4.3 Mitsui Chemicals Inc. (stewardship):

- Partnership with CropLife America (CLA) and Pollinator Issue Management Team (PIMT): These groups are involved with product communication, outreach, and stewardship.

3.5 USEPA neonicotinoid product labeling requirements and pollinator protection

The USEPA has acknowledged some uncertainties with initial registration of neonicotinoid insecticides regarding their potential environmental fate and effects, particularly as they relate to pollinators. During the summer of 2013, the USEPA communicated to registrants that they were initiating a project to amend neonicotinoid nitroguanidine insecticide (imidacloprid, clothianidin, thiamethoxam, and dinotefuran) label language to clarify the risk some of these products may have to non-target insect pollinators. This project was undertaken in response to peer-reviewed literature that showed the potential for these insecticides, in conjunction with other stressors, to negatively affect honey bees. This occurred against a backdrop of several unique bee kill incidences that had been linked to neonicotinoid applications to trees in Oregon and the emissions of fugitive dust from seed drills planting neonicotinoid-treated seed in Canada.

One of the major changes USEPA made to neonicotinoid nitroguanidine insecticide products approved for outdoor foliar uses, is the addition of a "Protection of Pollinators" box. This box visually alerts the user of application restrictions when bees are present by displaying a bee icon, near important information, and accenting key phrases in red "Application Restrictions" and "This product can kill bees and other insect pollinators." The "Protection of Pollinators" box further describes how foliar applications of these insecticides can result in pollinator exposure, and provides steps an applicator can take to reduce non-target impacts.

The "Protection of Pollinators" box also states that more information on protecting pollinators can be found under the "Directions for Use" section of the pesticide product label. Depending on the registered uses for the product, the following categories may appear on the label: "For crops under contracted pollination services," "For food crops and commercially grown ornamentals not under contract for pollination services but are attractive to pollinators," and/or "For non-agricultural products." All three categories contain the following statement "Do not apply this product while bees are foraging. Do not apply this product until flowering is complete and all petals have fallen." Depending on the category of use, the label will then provide conditions under which the above statement does not apply. In addition, changes were made to labels referring to bees "actively visiting," "actively foraging," or "visiting" and were replace with "foraging" to add consistency across these pesticide product labels. All label changes were implemented for the 2014 growing season. To view these pollinator specific label additions see appendix 3.

While USEPA has revised labels for foliar neonicotinoid products to clarify pollinator risks and restrict product application during flowering, there remains criticism of the ability of these label amendments to reduce impacts on pollinators. Label revisions requiring that foliar neonicotinoid applications be made to a plant after flower petals have fallen are optional under certain "exception" conditions. There is concern that little has been done to revise label instructions for non-foliar, soil-applied products, and that instructions on such products are either difficult to interpret or may result in differential residue exposures to pollinators in agricultural, orchard, or landscape/residential settings. There is also concern about the balance in responsibility between the beekeeper and the pesticide product applicator to manage bee hives in relation to pesticide applications and to mitigate impacts from applied product. These issues are further discussed below.

3.6 Label instructions and balancing pollinator protection responsibility

Pollinator-protective label amendments adopted in 2015 for neonicotinoids place responsibility on beekeepers for keeping managed bees safe when those bees provide pollination service under contract. The new label amendments also place responsibility on applicators in important ways. Condition statements under which exceptions are made for a foliar application of a neonicotinoid before or during flowering are as follows:

"If an application must be made when managed bees are at the treatment site, the beekeeper providing the pollination services must be notified no less than 48-hours prior to the time of the planned application so that the bees can be removed, covered, or otherwise protected prior to spraying".

The notification scenario is directed at an applicator who has knowledge of a beekeeper engaged in "pollination services," but does not include notification for beekeepers engaged solely or seasonally in honey production or independent pollination activities. So while an applicator must notify the beekeeper 48 hours in advance of spraying and requires the applicator to be able to easily locate nearby beekeepers, the beekeeper has the responsibility of quickly removing or protecting colonies and minimizing the stress such activities can have on bees. Although current labels outline a shared burden for protecting managed honey bees providing pollination services, the risks for beekeepers not providing pollination services or for wild bees and other pollinators, as well as pollinator risks from soil-applied or tree-injected products, appear to be addressed through other, label-related risk mitigation resulting in no "unreasonable adverse effects" within the risk-benefit framework of FIFRA.

3.7 Agricultural vs. orchard vs. landscape/residential application rates

Because of differences in the way agricultural and non-agricultural risks are assessed during pesticide registration, and because the neonicotinoid active ingredient (a.i.) concentration for agricultural and tree-care products can be greater than the concentration of some home and garden products, confusion can arise regarding the approved application rates for neonicotinoids in different settings and the associated potential for environmental impacts.

For example, the USEPA identified that the greatest risk from imidacloprid use that was in need of mitigation through application limits is the potential for residues to reach groundwater and surface water ["MDA-EPA communication on imidacloprid March, 2011"]. By limiting application rates to protect the greatest identified concern at the time of the risk assessment (drinking water and aquatic life protection), the acute contact and oral risk quotients for honey bees and other pollinators would be below their associated level of concern. Although timing of foliar applications in tree-care and landscape settings has been linked to pollinator protection and mitigated through recent label revisions, revising soil-applied application rates in those settings has not yet been identified by USEPA as an important risk-reduction strategy for that purpose.

As such, neonicotinoid exposure risk to pollinators in non-agricultural settings may benefit from further examination, including an evaluation of recommended application rates so that they are reasonably efficacious for pest control but not so large as to result in unnecessary pollinator exposure to residues.

As an example, for some imidacloprid products applied at maximum label rates in landscape/garden settings, a higher application rate per acre can be applied compared to that typically used in agricultural, orchard, or nursery settings. This is especially relevant to invasive species control, such as emerald ash borer, or for control of Japanese beetle on several ornamental bushes or shrubs where maximum annual application rates per tree or ornamental bushes in landscape/garden settings are higher than what is typically used in agricultural, orchard, or nursery settings.

Accordingly, the product labels for most residential treatments are not necessarily clear regarding potential per acre use concerns or do not require homeowners to calculate the area of their property and then pro-rate application dosages for individual tree to avoid exceeding a per acre maximum on areas smaller than an acre. It can be argued that there may be limited instances in which multiple homeowners exceed a cumulative per acre application maximum, since not all homeowners in an area may choose to use neonicotinoid products in a year, and may apply at rates lower than the maximum allowable rate. Nevertheless, educating homeowners and those applying neonicotinoids in landscape settings about proper calculation of application rates and areas can help in reducing the neonicotinoid load in the environment. The MDA has developed guidance for use limits of neonicotinoid products when controlling emerald ash borer in ash trees, with examples of pro-rating application rates based on the size of the treatment area under the applicator's control (www.mda.state.mn.us/~/media/Files/chemicals/pesticides/eablabelguide.ashx). However, similar pro-rated application dosages do not exist for other insect species for which neonicotinoids are approved for use.

Even when adhering to labeled per acre use limits, the maximum amount of imidacloprid approved for application to an individual, backyard tree with a 30-inch circumference, could be up to 16 times more (0.03 pounds imidacloprid per tree)[2] than the amount in an orchard setting for similarly sized trees (0.0025 pounds imidacloprid per tree)[3].

In terms of pest control, it would be helpful to establish if the 0.0025 lb a.i. per tree rate is effective at controlling certain pests (e.g. aphids on apple trees) in orchard settings, or if 0.0025 lb a.i. per tree is effective at controlling similar pests on similar trees in residential settings. If the application rates for the most effective pest control using the least amount of residential product were better indicated on the label, it could result in minimizing unnecessary residue exposure to pollinators and other beneficial insects.

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[2] The Bayer Advanced 12 Month Tree & Shrub Insect Contro II ™

[3] Admire ™

The maximum approved rate of active ingredient per acre for trunk-injected imidacloprid in residential settings can be up to 8 times more than the amount approved for soil drench applications in orchard settings, even for similarly sized trees (i.e., similar trunk circumferences). In yet another scenario, the amount of clothianidin approved for soil drench applications in residential settings for a 30-inch circumference tree could be up to 25 times more than the amount of active ingredient approved for soil drench applications in orchard or nursery settings for similarly-sized trees. Similar differences in maximum approved label rates for soil drenches also exist for thiamethoxam and dinotefuran use in residential vs. orchard settings.

3.8 US state-specific restrictions on neonicotinoid use to protect pollinators

While USEPA is performing registration reviews and has revised label language to clarify the potential non-target effects of these insecticides, some states have decided to restrict neonicotinoids uses in other ways.

3.8.1 Minnesota

During the 2014 and 2015 legislative sessions, new nursery plant labeling restrictions were passed into law. It is prohibited to label or advertise a nursery plant as beneficial to pollinators if it has been treated with a systemic insecticide product bearing a pollinator protection box or other pollinator-related environmental hazards and precautionary statements if the treatment results in a concentration in plant flowers greater than the no observed adverse effect level of the specific systemic insecticide. See MDA Plant Protection Division website for more details
http://www.mda.state.mn.us/en/licensing/licensetypes/nurseryprogram/labelpollstatute.aspx

3.8.2 Oregon

The Oregon Department of Agriculture (ODA) worked with USEPA to adopt permanent restrictions for all clothianidin, dinotefuran, imidacloprid, and thiamethoxam product labels to exclude these products use on *Tilia spp.* (e.g., basswood and linden trees). This action, effective February 27, 2015, was in response to an incident where bumble bees were foraging on linden trees treated with a neonicotinoid, dinotefuran, resulting in at least 25,000 dead bumble bees (ODA, 2013; ODA, 2015). The registrant has since removed the use of all of its neonicotinoid products from use on *Tilia* spp. nationwide (BCS submitted information, 2014a).

3.8.3 Maryland

During the 2016 legislative sessions, the state of Maryland passed a bill to impose restrictions on sale and use of neonicotinoids to consumers. Effective 2018, he bill prohibits a person from selling at retail in the State, a neonicotinoid pesticide unless the person also sells a restricted use pesticide; prohibiting a person from using a neonicotinoid pesticide unless the person is a certified applicator or a person working under the direct supervision of a certified applicator, a farmer or a person working under the direct supervision of a farmer who uses the product for a certain purpose, or a veterinarian (GAM, 2016).

3.8.4 Local level restrictions

Some communities around the United States have decided to minimize any potential impacts of neonicotinoids by making commitments to minimize their use through restricting or banning their use on city, township, or university/school district property. Examples of such communities include: Eden Prairie, Lake Elmo, Maplewood, Mendota Heights, Minneapolis, Saint Paul, Scandia, Stillwater, St. Louis Park, and Shorewood MN; Eugene OR; Spokane and Seattle WA; Melody-Catalpa neighborhood Boulder CO; Emory University, GA; University of Vermont Law School, VT; and the Municipality of Skagway, AK (Beyond Pesticides, 2014; HEWC, 2014; Humming for Bees, 2016). In addition, many Minnesota pesticide and nursery retailers such as Lowes, Bachman's, Gertens, Rose Floral, and other greenhouse and garden centers have voluntarily pledged to not to sell neonicotinoids or greatly reduce neonicotinoid treated-plants sold to the general public.

3.9 Actions in other nations

3.9.1 Australia

The Australian Pesticides and Veterinary Medicines Authority (APVMA) is the national authority for approving pesticide labels in Australia (https://portal.apvma.gov.au/pubcris). Generally, the Australian Government Department of the Environment evaluates environmental data on pesticides and then advises APVMA. Tests for effects of pesticides on non-target species are similar to USEPA testing requirements including studies on short-term acute, sub-acute, reproduction, simulated field, and full field effects. For the results, a hierarchical or tier system is followed. Under this system, the results from the lower-tier laboratory tests are used to determine the need for higher-tier testing, such as full field studies, based on the potential for the chemical to cause harmful effects.

At present, and despite high use of neonicotinoids on the Australian continent, honey bee populations are generally not considered to be in decline and insecticide impacts to pollinators are not considered a highly significant issue (http://archive.apvma.gov.au/news_media/chemicals/bee_and_neonicotinoids.php). The APVMA's efforts on honey bee risk mitigation are in providing appropriate information, warnings, and use instructions on product labels (with a focus on the neonicotinoid insecticides), and in considering the adequacy of current testing methods for examining the effects of crop protection products on bees.

In 2012, the Australian Environment Agency Pty Ltd (AEAPL) investigated the issue of pollinator toxicity testing requirements in Australia and concluded that the detailed testing requirements were not emphasized in the current Australian data requirements. The agency made five recommendations to the APVMA highlighting the need for the improved testing protocols for evaluating the impact of pesticides on the health of honey bees and other insect pollinators. The APVMA is in process of implementing these recommendations. Visit: http://archive.apvma.gov.au/news_media/docs/gw0673.pdf to see details.

In addition, the APVMA released a report in February, 2014 which discussed the current knowledge of neonicotinoids and their effect on honey bees (APVMA, 2014). Because Australia has not seen a decline in their managed pollinators equal to that seen in other international locations, they have not proposed a revision to neonicotinoid labels but have instead listed options the APVMA could take if new information becomes available suggesting neonicotinoids will harm pollinators when used in accordance to labels. The options APVMA have suggested including a formal chemical review of neonicotinoid insecticides and/or a label review of insecticide products.

3.9.2 Canada

Health Canada's Pest Management Regulatory Agency (PMRA) is a federal authority for pesticide regulation in Canada (www.hc-sc.gc.ca/ahc-asc/branch-dirgen/pmra-arla/index-eng.php). PMRA works with provincial, territorial, and federal departments in Canada to help refine and strengthen pesticide regulation across the country. The agency is actively collaborating with USEPA and the California Department of Pesticide Regulation to refine neonicotinoid risk assessment methods and data requirements so that the potential effects on bees are better understood and risks can be mitigated.

In 2012, Canada reported large scale bee deaths during the planting of corn seed treated with neonicotinoids, where 70% of dead bees sampled were confirmed to have residue of neonicotinoids from corn dust (HCPMRA, 2014). As a result of these incidents, PMRA now requires seed treated with imidacloprid, clothianidin, or thiamethoxam products to include label language to inform applicators of the potential impacts these products may have to bees. For the 2013 growing season, treated seed tags/labels include statements under the "Environmental Hazards" and "Use Restrictions" label sections that state this product "may be harmful to bees and other pollinators." The labels also provide a set of Best Management Practices to minimize dust generated from treated seed planting (HCPMRA, 2014; Ontario, 2015), and explained how to address spilled or exposed seeds (HCPMRA, 2014). In addition, Canada is requiring farmers to use a new corn and soybean seed lubricant called Fluency Agent. These changes aim to increase awareness of non-target pollinator exposure and replace high dust forming agents, like talc and graphite, with Fluency Agent. The producers of Fluency Agent claim that the amount of a.i. in dust is reduced by as much as 65 percent (BCS, 2014b). However, one study performed by the Corn Dust Research Consortium showed no significant difference in the amount of a.i. abraded between Fluency Agent and talc or graphite (CDRC, 2015).

In January 2016, Ontario, proposed to discontinue the granting of new conditional registrations under the Pest Control Products Regulations, effective June 01, 2016. The proposal was open for public comment until March 19, 2016. More information about the proposal can be found at: http://www.hc-sc.gc.ca/cps-spc/pest/part/consultations/_noi2016-01/noi2016-01-eng.

At the provincial level, Ontario has sought, through its Ministry of Agriculture, Food and Rural Affairs, to curb future seed treatment impacts to honey bees and other pollinators by using data and reports outside of PMRA's product registration protocols to lay out a three-point initiative it believes will ensure "healthy ecosystems" and a "productive agricultural sector" while reversing the downward trend of pollinator numbers. The strategy includes an 80 percent reduction in acreage planted with neonicotinoid-treated corn and soybean seed by 2017; limiting the number of honey bees that die during winter to 15 percent by 2020; and developing a "comprehensive" action plan for pollinator health. The strategy does not address neonicotinoid uses other than seed treatments. To achieve these goals, PMRA has introduced requirements for farmers to ensure that neonicotinoid-treated corn and soybean seeds are used only when there is a demonstrated pest problem. After August 31, 2016, if farmers want to buy and use any amount of clothianidin, thiamethoxam, or imidacloprid treated seeds, they will be required to: 1. Complete the new integrated pest management (IPM) training, 2. Complete a pest assessment report, and 3. Sign a declaration stating that they have considered IPM principles to the sales representative or seed vendors from whom they purchased the seeds or to the custom seed treater used for treating seeds with neonicotinoids. Starting on August 31, 2017, to buy neonicotinoid treated seed, a soil pest assessment report prepared by a professional pest advisor (Certified Crop Advisor or a person with qualifications equivalent of a CCA) will be required (Ontario, 2015). Other Canadian provinces have reported little to no impacts from treated seed dust-off or from pesticide spray events and Ontario's incidents have been significantly lower since those reported in 2012 and 2013. A report of incidents through July 2015 is available at http://www.honeycouncil.ca/images2/pdfs/2015-07-15_PMRA_Incident_Update.pdf

3.9.3 European Union countries

The information on testing protocols for impact of pesticides on bees and other insect pollinators along with the mitigation options in various European Union (EU) countries are similar to those in the United States and can be viewed at: www.oecd.org/chemicalsafety/risk-mitigation-pollinators/laws-policies-guidance.htm.

Individual EU countries have been restricting uses of neonicotinoid seed treatments on select crops since 1999 (Table 5). Restrictions occurred after honey bee kills were reported from planting of neonicotinoid treated seeds. These non-target exposures occurred due to inconsistencies in seed treatment methodology or from treated seed dust drifting off site either directly onto honey bee colonies or from contamination of bee attractive plants located near fields or in the field's margins.

Table 5. Neonicotinoid restrictions in EU member countries by active ingredient, application method, and crop through 2012 (PANUK, 2012).

Year	**Country**	**Active ingredient**	**Application method**	**Crop**
1999 - 2012	France	imidacloprid	Seed treatment (ex. Gaucho)	Sunflower
2004 - 2012	France	imidacloprid	Seed treatment (ex. Gaucho)	Corn
May 2008 - June 2008	Germany	clothianidin imidacloprid thiamethoxam	Seed treatment (ex. Chinook, Poncho, and Cruiser)	Oilseed rape
2008 - 2012	Germany	clothianidin imidacloprid thiamethoxam	Seed treatment (ex. Chinook, Poncho, and Cruiser)	Corn
2008 - 2012	Italy	clothianidin imidacloprid thiamethoxam	Seed treatment (ex. Gaucho, Poncho, and Cruiser)	Corn
2008	Slovenia	clothianidin thiamethoxam	Seed treatment	Oilseed rape
2011 - 2012	Slovenia	clothianidin thiamethoxam	Seed treatment	Corn

Controversy over the actual impact neonicotinoids were having on pollinator populations prompted the European Commission to have the European Food Safety Authority (EFSA) assess the risk to pollinators of three neonicotinoid insecticides (imidacloprid, clothianidin, thiamethoxam). In January, 2013, EFSA released its findings (EFSA, 2013a,b,c). While EFSA could not fully assess the impacts of all product uses under review due to existing data gaps, the EFSA did note a high acute risk to bees when exposed to abraded seed treatment dust, and residue expressed in pollen, nectar and guttation of some bee-attractive crops (EU, 2013).

The European Commission has not proposed any amendments to neonicotinoid product labels. Instead, on December 1, 2013, the EU suspended for a two year period the use of three neonicotinoids under EFSA's review (ending in 2015). The moratorium applied to seed, soil, and foliar treatments registered for bee-attractive crops and cereal grains. Exceptions exist for products used in greenhouses, products applied to winter cereals, and to foliar products applied after flowering (EU, 2013). In addition, not all restricted uses in the EU have actually ceased during the moratorium: For example, in 2014, Finland was granted a "derogation" (exemption) from the moratorium allowing it to use neonicotinoid-treated seed on 43,000 hectares (106,255 acres) of oilseed rape (canola) for essential protection against pests in early spring plantings (all treated acres were harvestable, compared to a 10-15% harvest from untreated acres). Exemptions were also granted to Romania (for corn), Germany, Latvia and Estonia. By the end of the two-year moratorium, the European Commission will begin reviewing any new scientific information received relating to the safety and non-target effect of these three insecticides.

4 Neonicotinoid use and sales

Currently, insecticides are commonly used and needed to prevent injury and economic loss in a variety of instances, such as prevention of yield and economic loss to a farmers' crops or livestock or to inhibit aesthetic injury or damage to homes, gardens, or managed landscapes. In agricultural situations, for example, farmers frequently use insecticides to prevent damage and economic yield loss from major insect pests, and periodically to thwart damage from minor insect pests.

Neonicotinoid insecticides possess characteristics that make them very effective as insect control compounds. They are water soluble and are readily absorbed by plants via their roots or leaves. Their systemic nature allows them to be transported and expressed throughout all parts of a treated plant including roots, stems, leaves, nectar, and pollen. This provides many advantages in pest control and protection to all parts of treated plants. For example, in addition to controlling sap sucking insects they are effective against boring and root-feeding insects, both of which cannot be easily controlled using foliar sprays of non-systemic compounds.

Additionally, neonicotinoid compounds can be effective at very low concentrations for a prolonged period of time following application. This feature is beneficial for agricultural applications where neonicotinoids (primarily imidacloprid, clothianidin, and thiamethoxam) are predominantly used as seed dressings to protect a broad variety of crop seedlings, such as corn, soybean, oilseed rape, sunflower, cereals, sugar beets, and potatoes. In addition, they can be used as foliar sprays on field, horticultural, vegetable, turf, and ornamental crops. They are also used for the treatment of pastures and grasslands, domestic animal pests, and for domestic use against cockroaches and ants. They can be applied as a soil drench or in irrigation water to treat perennial crops such as vines, and they can be injected into tree roots or stems, or sprayed onto bark to protect trees against invasive pests, emerald ash borer, for example. A single application can provide protection for several months or years.

In Minnesota, neonicotinoids are frequently used to control soil (wireworms, seedcorn maggot, corn rootworm, white grubs, etc.) and foliar insect pests (corn earworm, flea beetles, aphids, armyworms, plant bugs, leaf hoppers, grasshoppers, etc.). With the introduction of soybean aphid in 2004, use of neonicotinoids has increased significantly in soybean in Minnesota through seed treatments or foliar applications. Prior to the introduction of soybean aphid, insecticides (foliar and seed-treated) were not frequently used in soybean production in Minnesota because they were not economically feasible or justifiable because the soybean plant can easily compensate, showing no yield loss from plant damage caused by insects feeding on leaves (USEPA, 2014c). In addition to crop protection, applications of neonicotinoid insecticides in non-agricultural fields such as urban household, lawn, and garden and animal health have also expanded in recent years in Minnesota. For example, ash tree protection from emerald ash borer in Minnesota includes the use of imidacloprid, clothianidin, and dinotefuran as soil-applications, trunk-injections, or basal bark sprays. For homeowners, most seed companies do not treat their vegetable or flower seeds. In the occasional case that seeds are treated with either hot water (to discourage bacterial disease), fungicides (to discourage fungal seeding diseases), or insecticides (to prevent seed damage from soil insects), the seed packages are clearly marked that they are treated.

In the global insecticide market, neonicotinoids accounted for 24% of total insecticide use in 2008. The seed treatment market, initially dominated by insecticides from the carbamate family, was 80% comprised of neonicotinoid insecticides by 2008 (Jeschke and Nauen, 2008). Neonicotinoid insecticides, used primarily as seed treatments, accounted for more than 98% of the annual average 133 million acres of corn, soybean, wheat, cotton, and sorghum acres farmers treated in North America (AgInformatics, 2014a). After planting *Bt* corn, using insecticide seed treatments is the next most frequently used (64.1% of U.S. corn farmers) management practice to control insect pests in corn; and 51.4% of U.S. soybean farmers use insecticide seed treatments (AgInformatics, 2014b). In home lawn and garden applications, homeowners considered neonicotinoid insecticides more valuable than alternatives with potentially lower toxicity to bees. Based on a consumer preference study of 18,885 homeowners, the estimated average value of using neonicotinoid insecticides to control insects in flowers and shrubs, lawns, and trees was $105, $136, and $84 per year more, respectively, than using alternative insecticides (AgInformatics, 2014c).

On a world-wide basis, sales of neonicotinoid pesticides was estimated to exceed $2.6 billion for 2011 with use on approximately 140 crops and in garden and horticultural products (CRS, 2015). The MDA sales and use data shows that there were 510 registered neonicotinoid products in Minnesota in 2015 of which about 240 were registered for crop chemicals. Total sale of neonicotinoid products in Minnesota from 2010 to 2013 was 381.30 thousand pounds (Table 6). Bulk (>99%) of neonicotinoid products sold from 2010 to 2013 in Minnesota comprised of clothianidin, thiamethoxam and imidacloprid. In comparison to all chemicals, neonicotinoids accounted for 0.05, 0.12, 0.06, and 0.09% of pounds of all chemical products (all chemistries including nonagricultural pesticide products) sold in Minnesota in 2010, 2011, 2012, and 2013, respectively. While in comparison to all crop pest control products sold in Minnesota in 2010, 2011, 2012 and 2013 neonicotinoids accounted for 0.13, 0.26, 0.15, and 0.22%, respectively, of all crop chemicals (Table 6). In the garden and lawn category neonicotinoids accounted for 8.24% in 2010 to 38.45% in 2013 while in turf and ornamentals category neonicotinoids accounted for 6.72% in 2010 to 14.35% in 2013.

Table 6. Total pounds and gross sales for neonicotinoid products sold in Minnesota between 2010 to 2013 with corresponding total pounds for all pesticides sold.

Neonicotinoid active ingredient	**Total thousands pounds sold**				
	2010	**2011**	**2012**	**2013**	**Total**
Acetamiprid	0.16	0.25	0.92	0.48	1.81
Clothianidin	20.61	34.23	32.77	44.91	132.52
Dinotefuran	0.53	0.39	0.42	0.91	2.26
Imidacloprid	16.41	25.30	22.84	45.11	109.67
Thiacloprid	0.03	0.01	0.01	0.07	0.12
Thiamethoxam	16.66	67.79	22.27	28.21	134.92
Total: neonicotinoids sold	54.40	127.97	79.24	119.69	381.30
Total: all crop chemicals sold	42,664.38	48,800.18	53,985.46	54,320.89	199,770.91
Garden and Lawn	659.84	446.07	590.65	311.28	2,007.84
Turf and ornamental	809.16	668.71	1,391.67	833.90	2,007.84
Total: all chemical use types sold	112,682.19	110,722.57	124,838.56	128,539.61	467,782.93

A comparison between total pest control products sold in various product type and use categories (crops, garden and lawn, home, industrial, rights-of-way, forestry, turf, and ornamentals) indicated that >99% of clothianidin and thiamethoxam products were sold as crop chemicals (Table 7). Imidacloprid products were primarily sold as crop chemical products (>74%) and turf, ornamental and garden products (10-23%). Dinotefuran was primarily sold as turf and ornamental (42-76%), animal care (9-23%) and garden and lawn (6-16%) products. Although majority of acetamiprid was sold as crop chemical products (13-93%), its sales varied from 2010 to 2013 between crop chemicals, industrial, rights-of-way, forestry (2-32%) and structural products (0-52%). Thiacloprid was only sold as a crop chemical from 2010 to 2013 (Table 7).

Table 7. Total pounds of neonicotinoid products in various use categories in Minnesota from 2010 to 2013.

Active ingredient Year	**Category**									**Total**
	Crop chemicals	**Garden and lawn**	**Industrial, rights-of-way, and forestry**	**Structural**	**Turf and ornamental**	**Animal care**	**Home**	**Miscell aneous**	**Vertebrate control**	
Acetamiprid										
2010	146.36	0.72	3.89	NA	6.22	NA	NA	NA	NA	157.19
2011	160.16	22.97	24.86	31.07	10.41	NA	NA	NA	NA	249.47
2012	126.80	7.36	296.42	479.69	8.64	NA	NA	NA	NA	918.91
2013	185.25	3.00	46.64	237.47	3.76	NA	NA	NA	NA	476.12
Clothianidin										
2010	20,502.04	13.72	NA	NA	98.25	NA	NA	NA	NA	20,614.01
2011	34,011.16	76.70	NA	NA	143.33	NA	NA	NA	NA	34,231.19
2012	32,564.38	84.78	NA	NA	124.77	NA	NA	NA	NA	32,773.93
2013	44,734.89	22.51	NA	NA	154.10	NA	NA	NA	NA	44,911.50
Dinotefuran										
2010	9.53	170.24	NA	0.81	235.00	112.61	21.02	NA	NA	549.21
2011	20.45	60.48	NA	1.42	214.95	95.00	0.07	NA	NA	392.37
2012	2.80	32.15	NA	1.20	329.25	66.48	0.54	NA	NA	432.42
2013	6.30	39.90	NA	0.65	694.21	90.06	10.63	69.93	NA	911.68
Imidacloprid										
2010	12,148.40	1,052.99	22.06	269.62	2,757.74	107.82	5.26	43.30	0.01	16,407.20
2011	20,558.65	1,462.73	6.64	559.31	2,632.77	82.79	1.51	-	NA	25,304.40
2012	17,122.12	1,794.31	2.94	447.69	3,526.36	99.62	3.73	43.91	NA	23,040.68
2013	39,149.73	1,332.62	12.54	1,441.72	3,018.20	129.51	21.50	-	NA	45,105.82
Thiacloprid										
2010	28.00	NA	NA	NA	NA	NA	NA	NA	NA	28.00
2011	6.00	NA	NA	NA	NA	NA	NA	NA	NA	6.00
2012	13.00	NA	NA	NA	NA	NA	NA	NA	NA	13.00
2013	68.45	NA	NA	NA	NA	NA	NA	NA	NA	68.45
Thiamethoxam										
2010	16,562.12	1.78	NA	NA	94.50	NA	NA	NA	NA	16,658.40
2011	66,231.92	-	NA	NA	144.01	NA	NA	NA	NA	66,375.93
2012	22,114.64	-	NA	NA	155.36	NA	0.02	NA	NA	22,270.02
2013	29,983.23	0.72	NA	NA	106.22	NA	0.00	NA	NA	30,090.17

The totals in table 6 represent pounds of neonicotinoids sold for crop, home, garden and lawn, animal care, and other uses, and represent foliar, soil applied, injection, structural sprays or other application methods, including custom seed treatments conducted at Minnesota farm dealerships, distributorships and co-operatives. Because current MDA pesticide sales data does not track pesticide use associated with seeds treated outside of Minnesota's borders and shipped into the state for planting, the values are not comprehensive for all seed treatments. Almost all corn seed and about 20% of soybean seed are treated outside Minnesota and hence is not tracked by MDA. About 40% of soybean (2,908,000 acres) and almost the entire corn crop in the mid-west is considered to be grown from treated seed (personal communication, Robert Koch-University of Minnesota), therefore, the total mass of neonicotinoids that may be potentially applied to Minnesota crops may be many times higher than presented in table 6. As an example, assuming that 100% of corn acres (8,300,000 acres) grown in Minnesota in 2014 were treated outside Minnesota with maximum permitted thiamethoxam labeled rate, 0.21 lb per acre/season and was not reported to MDA, the total load of thiamethoxam released in Minnesota environment from corn planting would be an additional 1,743,000 pounds. Likewise, assuming that about 20% (588,000 acres) of soybean acres grown in Minnesota in 2014 were treated outside Minnesota (Personal communication, DuPont Pioneer, USA) with maximum permitted thiamethoxam labeled rate, 0.083 lb per acre, the total load of thiamethoxam released in Minnesota's environment from soybean planting would be an additional 48,804 pounds. Similar hypothetical maximum possible thiamethoxam load for 100% of canola (15,000 acre) and sunflower (63,000 acre) crops treated with maximum permitted thiamethoxam (Cruiser 5S) label rate, 0.014 lb/acre, would be an additional 210 pounds and 882 pounds, respectively. All neonicotinoid insecticides have per acre maximum limits, therefore, maximum load of any neonicotinoid product may not exceed specific levels depending upon the active ingredient and use site. For example, maximum permitted thiamethoxam application rate per year, regardless of type of application (seed treatment and/or foliar) in corn is 0.21 lb per acre, therefore, total amount of thiamethoxam by all application methods will not exceed 1,743,000 pounds for 8,300,000 acres of corn. While, maximum permitted thiamethoxam application rate per year, regardless of type of application (seed treatment and/or foliar) is 0.125 lb per acre, therefore total amount of thiamethoxam in soybean by all application methods will not exceed 918,750 pounds for 7,350,000 soybean acres. It should be noted that not all seeds are treated with the maximum permitted active ingredient per acre and not all planted seed are treated with neonicotinoid insecticides. Therefore, the above listed hypothetical maximum loads may not represent an actual situation but a worst case scenario for any particular neonicotinoid active ingredient. On the other hand, overall total loads for all neonicotinoids may be more than the one presented above because if maximum limits for one specific neonicotinoid active ingredient are met other neonicotinoid active ingredients may still be used.

According to USEPA, a pesticide is (1) any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, (2) any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccant, and (3) any nitrogen stabilizer. The description includes both agricultural as well as nonagricultural pesticides. The fee to register a pesticide in Minnesota is a minimum, standard registration fee of $350 for each product. Additionally, a Waste Pesticide Program surcharge of $50 is paid by the registrant for each pesticide product registered, for a total per product fee of $400 (minimum registration fee of $350 plus waste pesticide program fee of $50). Fees for other types of registrations (Special Local Need, Experimental Use Permits, and Emergency Exemptions) are separate. In addition, the department also collects sales fees for agricultural and non-agricultural pesticides. According to Minnesota statute, sales fees for non-agricultural and agricultural pesticides are paid separately and have different sales reporting requirements. Sales fees for agricultural pesticides is 0.55 percent of annual gross sales and is paid by the pesticide dealer selling in or into the state to an end-user. Sales fees for non-agricultural pesticides is 0.5 percent of annual gross sales and is paid by the registrant. An "agricultural pesticide" is a pesticide product with a label that includes the "Agricultural Use Requirements" box and a "non-agricultural pesticide" is a pesticide product with a label that does not include the "Agricultural Use Requirements" box. These pesticide registration fees are used to fund several program areas including: inspections and investigations, applicator training, BMP development and outreach, water monitoring, pesticide product review, and emergency response. In addition, the, Minnesota Statutes Chapter 18E.03 allows the department to collect agricultural chemical response and reimbursement account (ACRRA) fee. Currently, the ACRRA fee is 0.1 percent of pesticide sales and is an addition fee paid by both registrants and dealers when reporting sales. The funds in the ACRRA account are used to clean up spills of agricultural chemicals.

Revenues for all pesticide registrations fees in 2013 totaled $9,033.80 thousand (pesticide fee+ AACRA fee + registration fee) of which neonicotinoids ($332.48 thousand) accounted for 3.68% (Table 8). Revenue from neonicotinoids in 2013 ($332.48 thousand) increased from the revenue in 2010 ($244.71 thousand) by 35.86%. Total registration fee revenues from 518 neonicotinoid products ($207.2 thousand) registered in Minnesota in November 2013 accounted for 4.05% of total registration fee ($5,118 thousand) of all 12,795 pesticide products (all chemistries including agricultural and nonagricultural pesticide products) registered in Minnesota in 2013.

Gross sales and revenues from neonicotinoids and all pesticides showed wide variation from 2010 to 2013 and may not be related to pounds sold each year because price of the same pesticide can vary from year to year and also from seller to seller (manufacturers/retailer). For example, the manufacturer can sell the product at the wholesale price while the retailer may sell at the shelf price. In addition, product could be shipped and reported in one year while sales may spread through several years. Sale price of products may vary with the quantity and/or ratio of specific active ingredient used in the product.

Table 8. Total pounds and gross sale dollars for all pest control products by market type- markets that would include products containing neonicotinoid insecticides.

Chemical Use Type	**Thousand dollars**			
	2010	**2011**	**2012**	**2013**
Gross sales of all neonicotinoids	11,669.92	14,647.14	15,042.47	20,802.45
Registration fee from all neonicotinoids	181.60	192.00	200.80	211.20
Pesticide fee from all neonicotinoids	51.69	68.16	69.18	100.76
ACCRA fee from all neonicotinoids	11.42	14.34	14.79	20.52
Total revenue from all neonicotinoids	244.71	274.50	284.77	332.48
Gross sale of all chemicals (all use types)	560,333.67	598,232.48	707,256.23	727,582.30
Registration fee from all chemicals	4,908.00	4,928.40	5,007.20	5,029.20
Pesticide fee from all chemicals	2,412.86	2,712.92	3,206.55	3,355.44
ACCRA fee all chemicals	469.38	530.32	622.17	649.16
Total revenue from all chemicals	7,790.24	8,171.64	8,835.92	9,033.80
Percent total revenue from all neonicotinoids to all chemicals	3.14	3.36	3.22	3.68

5 Neonicotinoid applications and movement in the environment

The potential for adverse environmental impacts from neonicotinoid insecticides is under constant evaluation and research by USEPA, industry, academic researchers, the MDA, and other organizations. More than 60% of neonicotinoids are applied systemically as soil or seed treatment applications (Jeschke et al., 2011). Movement and distribution processes of neonicotinoids insecticides within the environment are often poorly understood. Movement and distribution of pesticides in the environment depend upon the properties of the active ingredient such as water solubility, octanol/water-partition coefficient (log_{POW}), dissociation constant (pK_a), plant species, vapor pressure, and application methods (Sur and Stork, 2003).

5.1 Movement and environmental fate of neonicotinoids in plants

Neonicotinoid insecticides (imidacloprid, thiamethoxam, and clothianidin) are widely used for seed treatment on various crops. Seed treatments are believed to prophylactically protect young plants against the early-season pest complex (soil and foliage pests), reduce potential risks to workers, minimize potential runoff to waterways, and lower the overall amount of insecticide usage. Despite lower overall usage, studies of the uptake of all neonicotinoid seed dressing chemistries into the target crop suggest that between 1.6 and 20% of the active ingredient is absorbed by the plant, depending on the chemistry, while the remainder enters the soil where it may be held by soil mineral or organic matter fractions, is absorbed by neighboring non-target plants, may be degraded by abiotic and biotic mechanisms, or leached into groundwater resources (Sur and Stork, 2003). A proportion (<2%) can be lost in planter dust during sowing. Imidacloprid is held to varying degrees by different soil mineral components. Organic matter was found to be the most important soil component impacting how the soil holds (through adsorption) imidacloprid (Cox et al., 1998; Liu et al., 2006).

Applications of neonicotinoids to soil, seed, or injected into tree trunks will move into a plant via the root system and plant vascular system, moving from older to younger tissue through tissue called xylem, whose cells move water and nutrients in one direction, upward through the plant. Systemic compounds move from the soil and into and around a plant based on water solubility, how they mix with other solvents, and their ability to breakup into smaller components (dissociate). Neonicotinoids possess high water solubility and when applied systemically, they disperse into all plant tissues during growth and degrade slowly (Reetz et al., 2011). Some translaminar movement toward the leaf tips and margins following foliar application has also been observed for neonicotinoids (Bonmatin et al., 2014). Consequently, they can be present in detectable concentrations in plant tissues such as leaves, growing points, vascular fluids, pollen, and nectar and have a potential to be a source of exposure to non-target organisms feeding on contaminated plant parts. For example, experimentation and modeling using a variety of constants and coefficients suggest that imidacloprid is highly mobile in plant xylem. Studies evaluating imidacloprid's uptake, translocation, and metabolism after foliar, soil, or seed treatments showed that, on average, about 5% of the imidacloprid active ingredient is taken up into plants from a soil or seed treatment with good upward mobility in the xylem but poor downward movement in the phloem vascular tissue (Sur and Stork, 2003).

Similar research on thiamethoxam has shown that once in the plant, thiamethoxam is quickly metabolized within the plant to clothianidin (Nauen et al., 2003). However, the precise nature of translocation and distribution of neonicotinoid insecticides within the plant vascular system processes is often poorly understood (Blacquiere et al., 2012; Bonmatin et al., 2014). Data from potato showed that only half of the imidacloprid reached/stayed on/in the foliage of the potato plants (40-49% of the applied radioactivity), the other half reached the soil and only 0.2% reached tubers (Olson et al., 2004; USEPA, 2016). In contrast, no apparent transport of imidacloprid occurred from plant leaves into fruits in apples and tomatoes (USEPA, 2016).

Presence of high concentrations of imidacloprid in the soil lead to high root up-take in corn, eggplant, potato, and cotton. Total root uptake for soil-applied imidacloprid reached equilibrium in early growth stage of cotton, eggplant, and potatoes. However, imidacloprid uptake increased towards maturity in corn. Imidacloprid uptake ranged from 2-5% of the applied in cotton, eggplant, and potato and from 4 to 20% of the applied in corn (USEPA, 2016).

Translocation and residue concentrations in plant tissues depend upon the plant species, active ingredient properties such as water solubility, octanol/water-partition coefficient (log P_{OW}), dissociation constant (pKa), plant species, and application method (Sur and Stork, 2003). In general, concentrations were found to be higher in crops treated through foliar spray, soil drench, or drip irrigation as compared to the seed-treated crops. For example, total imidacloprid residues were up to five times higher in plants treated by foliar spray application than by soil irrigation (Dively and Kamel, 2012; Juraske et al., 2009; USEPA, 2016).

The example concentrations of imidacloprid or its metabolites in nectar and pollen of seed-treated sunflower crops have been reported to be 1.9 and 6.1 ppb, respectively (Blacquiere et al., 2012; Godfray et al., 2014; Godfray et al., 2015; Sur and Stork, 2003). However, from other studies, maximum imidacloprid concentrations up to 36 ppb have also been reported from sunflower pollen samples (Laurent and Rathahao, 2003). In nearly all crops, the metabolic pathway of imidacloprid occurs via three routes (hydroxylation of the imidazolidine ring and elimination of water to form guanidine followed by the formation of 6-chloronictinic acid through nitro-group reduction and oxidative cleavage of a methylene bridge) and results in qualitative and quantitative similar composition of the metabolic spectrum (Sur and Stork, 2003). Krupke et al. (2012) detected 3.9 ppb clothianidin from the seed treated corn anthers up to 1.1 to 9.4 ppb clothianidin and 1.1 to 2.9 ppb thiamethoxam from dandelion pollens. In the same study; however, no thiamethoxam was detected in corn anthers. Clothianidin residues were detected from pollen (6.6 to 23 ppb) and nectar (6.7 to 16 ppb) samples obtained from honey bees foraging on a clothianidin or thiamethoxam seed treated oilseed rape crop (Rundlöf et al., 2015).

A few studies have measured residue levels of neonicotinoids and the major metabolites in pollen and nectar collected from crop plants with different rates, times and methods of application. Foliar-applied neonicotinoid treatments and insecticides applied through chemigation (drip irrigation) during flowering resulted in the highest neonicotinoid residues in cucurbits as compared to the residues resulting from applications at planting (as a seed dressing, bedding tray drench, or transplant water treatment) (Dively and Kamel, 2012). Krischik et al. (2007) found that a soil application using the maximum labeled rate of imidacloprid (5-10g/1 gallon pot) resulted in residue concentrations of 16-29 ppb in buckwheat flowers. Foliar applications of clothianidin to clover resulted in residue concentrations of 171 ppb clothianidin in clover nectar (Larson et al., 2013).

Some plants secrete pesticides through guttation drops (xylem sap secreted through leaf tip or margins). Excretion of guttation drops depends upon several variables such as humidity, temperature, growth stage, water stress, root depth, and soil water potential (Girolami et al., 2009; Tapparo et al., 2011; Thompson, 2010). Guttation drop concentrations of neonicotinoids have been reported to be very high during the first three weeks of plant growth. Mean residues of clothianidin (23.3 ppm from corn plants treated with 1.25 mg per seed) and thiamethoxam (11.9 ppm from corn plants treated with 1 mg per seed) were found in the guttation fluid (Girolami et al., 2009). The imidacloprid concentrations in the guttation fluid of corn plants grown from imidacloprid treated seeds (0.5 mg/seed) ranged from 47 to 83.8 ppm under laboratory conditions (Girolami et al., 2009) and 77 to 222 ppm in field conditions (first day after emergence) (Tapparo et al., 2011). For impact of neonicotinoid concentrations from various plant parts on pollinators see pollinators and neonicotinoid exposure points in plants, page 45.

5.2 Movement and environmental fate of neonicotinoids in soil

Pesticides enter the soil primarily via formulations applied directly into the soil, and from spray drift during foliage treatment, wash-off from treated foliage. Plant uptake processes together with natural degradation of pesticides help in decreasing concentrations in soil over time (Horwood, 2007). However, repeated applications of pesticides in successive years and breakdown of plant material containing pesticide residues may result in accumulating concentrations in soils. The method and timing of insecticide applications, proximity to sensitive aquatic resources (streams, rivers, etc.) and terrestrial habitat (e.g. plants that are attractive to pollinators), and soil type at the site of application are a few of the variables that have the potential to influence the environmental fate and potential ecological effects from neonicotinoid use.

As with any other pesticide, the behavior of neonicotinoids in soils, and hence their bioavailability and transfer to other environmental compartments (i.e. atmosphere, water bodies, etc.), is governed by a variety of complex dynamic physical, chemical, and biological processes, including adsorption–desorption, volatilization, chemical, photo and biological degradation, uptake by plants, run-off, and leaching. The rate and magnitude of transport of pesticides to environmental compartments is also influenced by factors like properties of the pesticide (water solubility, adsorption, chemical structure, acid dissociation constant, etc.) and soil (bulk density, organic matter, texture, pH, etc.), the soil hydrologic cycle, how the pesticide was applied, proximity to sensitive aquatic resources (streams, rivers, etc.), and environmental conditions surrounding the application. These processes directly control the transport of pesticides within the soil and their transfer from the soil to water, air or food. The relative importance of these processes varies with the chemical nature of the pesticides and the properties of the soil (Arias-Estévez et al., 2008). A summary of the most critical neonicotinoid properties that can influence their movement and fate in the environment are presented in table 9.

The high water solubility and low K_{oc} for neonicotinoids indicate low tendency for adsorption to soil particles. Laboratory and field studies reviewed by Goulson (2013) have produced a wide range of values for soil dissipation half-lives (7 to 6,931 days) of neonicotinoid compounds. In general, half-lives have been reported to be longer for N-nitroguanidines (imidacloprid, thiamethoxam, clothianidin and dinotefuran) than N-cyanoamidines (acetamiprid and thiacloprid) (Goulson, 2013; Goulson et al., 2008). The longest calculated half-life in soil for a neonicotinoid compound was reported for clothianidin at 6,931 days under the Fuquay soil series (a fine-loamy sand underlain by clay loams located in the southern coastal plain of North Carolina), while the shortest half-life reported for thiamethoxam was at 7 days. A study summary submitted by the registrant (Bayer CropScience) reported that the clothianidin residues do not increase significantly in soil with repeated years of application. The dissipation half-lives of acetamiprid, dinotefuran, and imidacloprid range between 28 to 1,136 days, 75 to 82 days, and 388-450 days, respectively (Table 9). It should be noted that the highest and lowest values may not represent typical half-life values under the US or Minnesota-specific conditions. For example, dissipation time for clothianidin in sand to silt loam soils ranges from 495 to 1,155 days. The dissipation time of 6,931 days for clothianidin represents estimated half-life under Fugay soil series only (USEPA, 2005a).

Table 9. Physical and chemical properties of six commercially available neonicotinoid insecticides that influence environmental fate of pesticides.

Active ingredient	Dissipation half-life in soil (days) in lab or field		Solubility (ppm)	Adsorption (K_{oc})	Mobility	Leaching Potential	Water contamination potential	
	From USEPA, *EFED documents	From other published literature					Ground water	Surface water
Acetamiprid	<1-8.2	<1-450	4,250	132-267	High	High	No**	Yes
Clothianidin	148-1,155	148-6,931	300	160	High	High	Yes	Yes
Dinotefuran	81.5-138.4	75-138.4	39,830	6-45	High	Very high	Yes, label carries statements about potential groundwater contamination	Yes
Imidacloprid	>120-660	28->2,000	580	300-400	Moderate	High, in areas with low organic matter	Yes	Yes
Thiacloprid	1.5-13.5	1.5->1,000	185	261-870	Low	Low	Yes, label carries statements about potential groundwater contamination	No
Thiamethoxam	13-353	7-3,001	4,100	33-177	High	Moderate	Yes	Yes

*EFED= Environmental Fate and Effects Division; Dissipation half-life can be very dependent on soil texture, moisture, organic matter, fertility and other factors. Source: USEPA

** Although acetamiprid has high mobility, it is not a concern for groundwater because of rapid degradation rate.

Neonicotinoid half-life in soils will vary with soil type, climate, soil pH, moisture, temperature, light intensity, use of organic fertilizers, presence or absence of ground cover, etc. (CDPR, 2006; Goulson, 2013; Goulson et al., 2008). For example, the half-life for imidacloprid is estimated to be longer in temperate regions than in the mid and higher latitudes, because of fewer sun hours, lower sun light intensity, and lower average seasonal temperatures (Bonmatin et al., 2014). Similarly, imidacloprid degradation was found to be more rapid in soils with cover crops (half-life of 48 days) than in bare soils (190 days) and tended to increase with soil pH (Sarkar et al., 2001; Scholz and Spiteller, 1992). Half-life of imidacloprid was found to be 1,000 days in soil and bedding material (Baskaran et al., 1999), while it was 229 days in field studies and 997 days in laboratory studies in the absence of light (CDPR, 2006). The half-life for imidacloprid was found to be 107 days in the humid subtropical climate of Georgia as compared to more than a year in continental climate of Minnesota (Cox, 2001). The half-life for thiamethoxam increased from 46.3 days under submerged conditions to 301 days under dry conditions (Gupta et al., 2008). While acetamiprid half-life was 10 times longer under dry conditions (150.5 days) than under submerged conditions (19.2 days) (Gupta et al., 2002). Imidacloprid undergoes photolytic degradation rapidly (Bonmatin et al., 2015). However, a slower rate of clothianidin and thiacloprid dissipation in field conditions indicated that photolysis in natural systems did not play a large role in the degradation process of these insecticides (Paine et al., 2011). Schaafsma et al. (2015a,b) found that if clothianidin and thiamethoxam were used annually as a seed treatment in a typical crop rotation of corn, soybean, and winter wheat over several years in southwestern Ontario, residues would plateau rather than continue to accumulate in soil. Thiamethoxam and clothianidin residues were found to be more in soil dust than the parent soil in fields with history of seed treatments in Ontario (Limay-Rios et al., 2015). Therefore, depending on site-specific conditions, neonicotinoids in soil can either significantly degrade or dissipate, or they may persist and potentially accumulate over time (Goulson, 2013; Goulson et al., 2008). However, a complete understanding of the mechanisms governing persistence of neonicotinoids in soil is still unclear, specifically with regards to concentrations and dynamics of neonicotinoid metabolites in different soil types and conditions (Goulson, 2013; Goulson et al., 2008).

5.3 Movement and environmental fate of neonicotinoids in water and sediment

Presence of pesticides in water poses a concern for humans relying on groundwater as a source of drinking water, and for aquatic communities of invertebrates, fish and plant life. Except for pesticide impacts to the environment from drift and spills, most pesticide residues found in groundwater, and those present in surface water enter via normal applications to the landscape. Residues in surface water can also result from approved applications to water bodies (to control aquatic pests) or from wastewater treatment facilities. Chemicals applied to the soil or plant surfaces may be transported to groundwater or surface water through leaching, erosion, runoff, and drift. As noted above, the rate and magnitude of transport of neonicotinoids is influenced by complex dynamic physical, chemical, and biological processes and properties of the pesticide and soil the soil hydrologic cycle, method of application, and environmental conditions surrounding the application (Main et al., 2015).

Additional important factors that influence the impact neonicotinoids have on our water resources are its toxicity, degradation rate (photolytic, hydrolytic, anaerobic, and aerobic), and metabolite characteristics, as well as the length of time and level of exposure. Owing to high water solubility, some neonicotinoid insecticide compounds may be more prone to leaching into groundwater or running off into surface water. Both thiamethoxam and imidacloprid have been shown to be highly mobile in soils with a high potential to leach downward through the soil profile or laterally through soil flow paths to contaminate surface and groundwater (Bonmatin et al., 2014; Gupta et al., 2002; Gupta et al., 2008). The persistence of neonicotinoids in aqueous environments depends upon its exposure to sunlight, the soil or water's pH and temperature, the composition of microorganisms and other biotic communities, the concentration of the pesticide in a given water resource, and the pesticide's product formulation (Bonmatin et al., 2014). For example, imidacloprid and thiamethoxam degraded more rapidly in alkaline media, while their concentrations stayed relatively stable at pH 7 and 4 (Guzsvány et al., 2006). However, imidacloprid leaching in the soil column varied with formulation; wettable powder formulations leached the most, followed by soluble concentrates and suspension concentrates (Gupta et al., 2002). Thiamethoxam concentrations in irrigation water, sourced from groundwater, in a potato-growing region of Wisconsin ranged from 0.31 to 0.58 ppb. State-wide sampling in Wisconsin revealed significant groundwater concentrations for clothianidin (0.21–3.43 ppb), imidacloprid (0.26–3.34 ppb), and thiamethoxam (0.20–3.34 ppb) (Huseth and Groves, 2014). Imidacloprid has been detected in numerous groundwater samples in California (CDPR, 2006), New York's Long Island (NYSDEC, 2014a), as well as in Minnesota (MDA, 2014). A study from 13 waste water treatments plants in the US showed that imidacloprid, acetamiprid, and clothianidin persist through wastewater treatment and may enter water bodies at significant loadings potentially harmful to sensitive aquatic invertebrates (Sadaria et al. 2016).

In New York State, Nassau and Suffolk counties located on Long Island rely on a sole-source aquifer for drinking water. Due to these counties' unique hydrogeological characteristics, the state has created a separate source water assessment program for these counties to look at groundwater contamination from various sources including pesticides, microbials, nitrates, and volatile organic compounds. This has resulted in a registration change for several pesticides, including neonicotinoids, to restricted use status (NYSDEC, 2014b; NYSDOH, 2004). While neonicotinoids are highly mobile and have been detected in groundwater, streams, storm-water ponds, and tidal creeks, the relative importance of individual neonicotinoid dissipation routes into water resources have not been clearly established (Goulson, 2013).

In 1985, the MDA and Minnesota Department of Health (MDH) undertook a cooperative survey of groundwater for pesticides. Over the years, this program expanded and MDA established a network of ten water quality pesticide monitoring regions (PMRs) throughout Minnesota for the purposes of collecting, assessing, and reporting monitoring data from both surface and groundwater samples. The MDA Laboratory Services uses well-established laboratory methods to analyze water samples, for the presence of approximately 130 pesticides, including neonicotinoids, and select breakdown products (degradates). The Minnesota Pesticide Management Plan was designed to guide MDA in its efforts to coordinate activities necessary to protect Minnesota's surface water and groundwater resources from pesticide contamination and aid in decision-making related to MDA Water Quality Monitoring results.

Currently, the MDA regularly monitors groundwater and surface water for the presence of neonicotinoids in Minnesota. To date, the detected neonicotinoid insecticide concentrations in groundwater samples have been below the MDH's drinking water guidance values of concern (Table 10).

In 2014, the MDA's water quality monitoring program detected three neonicotinoid insecticides (clothianidin, imidacloprid, thiamethoxam) in 4.3% of water samples collected statewide. However, concentrations found were below guidance values (Table 10). The highest concentration for clothianidin, imidacloprid, and thiamethoxam in groundwater was 391, 59, and 14.8 times below the drinking water level of concern concentrations, respectively (Table 10).

Table 10. Neonicotinoid concentrations detected in Minnesota groundwater in 2014.

Insecticide	Samples analyzed	Number of detections	Percent detections statewide (%)	Maximum concentration (ppb)	PMRs with detections[2]	MDH drinking water guidance and screening values (ppb)[3]
Acetamiprid	274	ND[1]	ND	ND	ND	100
Clothianidin	274	31	11	0.511	4,5,7,9	200
Dinotefuran	274	ND	ND	ND	ND	5
Imidacloprid	274	26	9	1.520	1,4	90
Thiacloprid	274	ND	ND	ND	ND	28 (HHBP)[4]
Thiamethoxam	274	14	5	1.350	4	20

[1] ND = Not Detected.
[2] Percent detections in individual PMR can be higher or lower than the statewide detections.
[3] MDH Rapid Assessment values established in 2015.
[4] HHBP = USEPA Human Health Benchmark for Pesticide.

The majority of surface water contamination from neonicotinoids is expected to be through runoff after major precipitation events (Morrissey et al., 2015). Under certain conditions, such as in the absence of light, neonicotinoids do not break down easily and can persist for long periods of time at the site of their application. Under such conditions, they may run off during irrigation or rain events leading to contamination of surface waters. In addition, dust emitted from neonicotinoid-treated seeds during the planting and planter equipment cleaning process has the potential to drift and contaminate adjacent areas and vegetation, surface waters, or temporary puddles near the fields (Main et al., 2014). In addition, when applied as a tree trunk injection, autumn leaf litter could be a source of potential contamination to water bodies (Bonmatin et al., 2014; Kreutzweiser et al., 2007). Neonicotinoids are typically broken down in water by photolysis, although they do not volatilize from water (Liu et al., 2006; Bonmatin et al., 2015).

A summary of 29 studies by Morrissey et al. (2015), which included water monitoring indicated that neonicotinoids were detected in most surface waters sampled, including puddled water, irrigation channels, streams, rivers, and wetlands in proximity to, or receiving runoff from, agricultural cropland. The concentrations of individual neonicotinoids from this dataset indicated an average surface water concentration of 0.13 ppb (n = 19 studies) and a peak concentration of 0.63 ppb (n = 27 studies). Detections were found to be more frequent in wetlands and rivers directly draining or receiving runoff from agricultural crops. However, the survey pointed out that these studies had a major limitation interpreting the actual peak and average concentrations relevant to estimating exposure duration to aquatic species resulting from the different timings of water sampling, particularly in relation to rainfall events (Morrissey et al., 2015). Neonicotinoid presence and concentration in prairie wetlands was found to be a function of plant composition and wetland depth (Main et al., 2015). Clothianidin and thiamethoxam were detected from 100 and 98.7% of 76 water samples collected from the standing water in the puddles of the 18 corn fields in Ontario, Canada. The maximum clothianidin and thiamethoxam concentrations were 43.60 and 16.50 ppb, respectively. The average clothianidin and thiamethoxam concentrations were 2.28 and 1.12 ppb, respectively. The concentrations peaked during the first five weeks after planting and reverted to pre-plant levels after seven weeks (Schaafsma et al., 2015a).

The results of 79 water samples near agricultural fields in Iowa showed that clothianidin, imidacloprid, and thiamethoxam were detected at 0.257, 0.042, and 0.185 ppb, respectively, with temporal patterns in concentrations associated with rainfall events during crop planting (Hladik et al., 2014). In a study from streams across the United States, at least one neonicotinoid was detected in 63% of the 48 streams sampled. In these studies imidacloprid was the most frequently detected (37%) neonicotinoid followed by clothianidin (24%), thiamethoxam (21%), dinotefuran (13%), acetamiprid (3%), and thiacloprid (0%). Clothianidin and thiamethoxam concentrations were found to be positively related to the percentage of the land use in cultivated crop production while imidacloprid concentrations were found to be positively related to the percentage of urban area within the basin (Hladik and Kolpin, 2015). Similarly, imidacloprid detection in the water draining from potato fields after rainfall events in Eastern Canada ranged from below the detection limit (0.5 ppb) to 11.9 ppb (Denning et al., 2004). In California, 89% of surface water samples collected from agricultural regions contained maximum concentrations of imidacloprid up to 3.29 ppb (Starner and Goh, 2012). In addition to surface waters near agricultural fields, neonicotinoids have been detected, in concentrations up to 131 ppb, in water draining from urban environments (Johnson and Pettis, 2014; Sánchez-Bayo and Hyne, 2014).

The MDA's 2014 Water Quality Monitoring Report indicates that neonicotinoids were detected in up to 4.5% of surface water samples (Table 11). In surface water, no neonicotinoids have been found in any lake samples; however, they are being detected in rural and some urban river and stream sites, and in wetland water and sediment samples. The surface water detections at one urban location is currently under investigation due to the fact that they are linked to a unique, point source use pattern rather than to the normal use of a product or practice that leads to non-point source impacts to the environment. The highest concentration for any neonicotinoid compound in surface water was at least 48 times below USEPA acute aquatic life benchmarks for aquatic organisms (Table 11) which are evaluated against a one-day exposure duration. The maximum values for clothianidin (22.23% of chronic benchmark) and imidacloprid (44.5% of chronic benchmark) detections are numerically approaching the chronic aquatic life benchmarks for invertebrates (Table 11), although the chronic benchmarks are evaluated against a smaller (4 day) exposure duration.

Table 11. Maximum neonicotinoid concentrations and number of detections in Minnesota surface waters, in 2014, compared to USEPA aquatic life benchmarks.

Active ingredient	Maximum detection (ppb)	Number of detections	Samples analyzed	% detected	USEPA, aquatic life benchmarks (ppb)				
					Acute			Chronic	
					Fish	Invertebrates	Plant*	Fish	Invertebrates
Acetamiprid	ND**	0	214	0	>50,000	10.5	>1,000	19,200	2.1
Clothianidin	0.260	25	214	12	>50,750	11	64,000	9,700	1.1
Dinotefuran	ND	0	214	0	>49,550	>484,150	>97,600	>6,360	> 95,300
Imidacloprid	0.467	7	214	3	>41,500	34.5	>10,000	1,200	1.05
Thiacloprid	ND	0	214	0	12,600	18.9	45,000	918	0.97
Thiamethoxam	0.223	26	214	12	>50,000	17.5	>90,000	20,000	-

* Values represent the most conservative endpoint for either nonvascular or vascular freshwater plants.
**ND-Not detected.

Neonicotinoids and their environmental degradates have also been reported to bind to particles in sediments (Kurwadkar et al., 2013) that form on the floor of freshwater and marine water bodies. In a water-sediment system, one-half of the imidacloprid residues degraded to guanidine compounds within 30-162 days (Roberts and Hutson, 1999). Sediment samples collected from the Canadian Prairie Pothole Region rarely (6% of the time) contained neonicotinoid concentrations (>0.002 ppb) even though water samples from this region contained high neonicotinoid concentrations (Main et al., 2014), which is not surprising since these pothole regions are ephemeral and farmed (i.e. planted with treated seed) when dry.

Owing to the presence of large wetland bodies in Minnesota, a small MDA study was designed in August 2014 to collect a limited number of samples in order to examine pesticides, including neonicotinoids in Minnesota wetland water and sediment samples. Samples were collected from agricultural, urban (residential, golf course, park, county open space), rural areas and analyzed for acetamiprid, clothianidin, dinotefuran, dinotefuran degradates (dinotefuran DN and dinotefuran UF), imidacloprid, imidacloprid degradates (5-hydroxy imidacloprid, imidacloprid desnitro olefin, imidacloprid HCL desnitro olefin, imidacloprid olefin and imidacloprid urea), nithiazine, thiacloprid, and thiamethoxam. The preliminary results revealed that samples collected from the agricultural areas, clothianidin (1.49 ppb) and thiamethoxam (0.25 ppb) were detected in one sample each. Of the 11 samples collected from urban areas, imidacloprid HCL desnitro olefin (imidacloprid degradate) was detected in one sample each from the residential (2.09 ppb) and golf course (0.69 ppb) areas. No other neonicotinoid or their degradates were detected. This study was possible because of the development of MDA laboratory analytical methodologies for neonicotinoids in sediment.

5.4 Movement and environmental fate of neonicotinoids in air

Vapor pressure values for neonicotinoids range between 2.8×10^{-8} and 0.002 mPa at 25 °C indicating low potential for volatilization from soil and water (Bonmatin et al., 2014; Roberts and Hutson, 1999).

6 Risks of neonicotinoid use

Although neonicotinoids were introduced as reduced-risk alternatives to older insecticides based on lower mammalian toxicity, as with all insecticides, they inherently pose certain risks to terrestrial and aquatic non-target organisms, as well as humans, especially if not used according to label instructions. Similar to all insecticides, they are best used in the context of an Integrated Pest Management (IPM) program, wherein pest pressure and histories are well-understood, and use is limited to occasions when other pest control alternatives are not economical, feasible, or practical. For landscape, arborist, and crop production scenarios, this means understanding when neonicotinoid use is necessary before making foliar or soil applications and before selecting or treating seed. When properly applied, the risks associated with neonicotinoid use in general – and seed treatments in particular – can be offset by their benefits, when used as components of an IPM program for managing major and some minor insect pests (For more information on IPM see Neonicotinoids and IPM, section 7.4).

In addition to the direct risks neonicotinoids potentially present to non-target organisms and humans, the use of systemic neonicotinoids for prophylactic (or preventive) insect control carries several indirect risks, one of which is insect pests evolving resistance to their mode of action, resulting in ineffective pest control and the loss of a pest management tool. It has been argued that such use contributes to a paradigm shift away from traditional IPM (Gray, 2010). IPM is predicated on minimizing use and increasing efficacy of appropriately-timed chemical pesticides via monitoring of pest populations, making maximum use of biological, mechanical, and cultural controls, and only applying chemical pesticides when needed. If used properly, seed treatments can, indeed, be a part of a traditional IPM program, and reduce non-target exposure and risk compared to soil or foliar insecticide applications. However, using neonicotinoid seed treatments in the absence of specific identified pest problems may lead to resurgence of the target pest, replacement by secondary pests, adverse impacts on natural enemies and pollinators, development of pest resistance, soil contamination from abraded seed dust, and increased costs. For example, a recent study (Douglas et al., 2014) illustrated the potential for neonicotinoid insecticides to transfer to different organism trophic levels, resulting in non-target harm. In the study, slugs (a sporadic pest in Minnesota and the Midwest) present in a soybean crop were unharmed by the use of neonicotinoids, but predatory beetles feeding on the slugs were harmed by insecticide concentrations in slugs' bodies; the result being a decline in biological predation of the slugs, leading to increased soybean damage and reduced yield. This observed trophic disruption may occur with neonicotinoids in Mid-Atlantic states where slug damage to soybean crops are a more typical concern due to environment and farming practices in that area. The degree to which similar predator-prey disruptions occur in Minnesota-specific crop scenarios is not entirely known.

6.1 Risk to insect pollinators

Managed and wild pollinators are needed in Minnesota to contribute to ecosystem services, one of which is pollinating a variety of crops including alfalfa, sunflower, canola, and many of our fruits and vegetables (Delaplane and Mayer, 2000). Pollinator-dependent commodities makes up less than 6% of the total agricultural acres planted in Minnesota (Figure 3). However, despite this relatively small portion of Minnesota's crops dependent on insect pollination, greater than 85% of Minnesota crops are visited by and/or may benefit from pollinators. Soybeans, for instance, are mainly self-fertile but yield has been shown to be positively affected in some soybean varieties if visited by bees (Delaplane and Mayer, 2000; USDA, 2009). While potatoes receive no yield benefit from pollinator visits, some wild bee species visit potato flowers to collect pollen (USDA, 2009). This tendency for pollinators to visit a large portion of Minnesota's agricultural landscape highlights the importance of a Minnesota-specific review to cover the range of neonicotinoid uses in agricultural and urban landscapes, including uses for seed treatments, soil drenches, foliar applications, and direct injections of landscape plants.

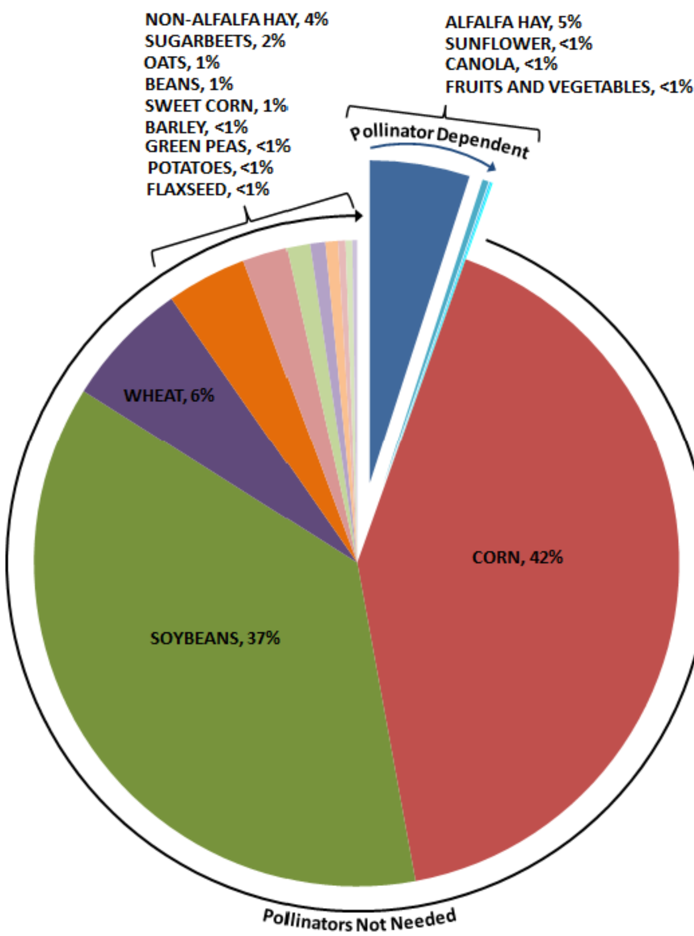

Figure 3. Percent Crop Acres Reported in Minnesota: census and survey data from 2012 – 2014 (USDA NASS 2015).

One of the main advantages of neonicotinoid products is their systemic action. However, this systemic action may expose honey bees and other insect pollinators to contaminated nectar and pollen in treated flowers, or in flowers that take up neonicotinoids applied for purposes other than floral insect control. Such exposure can also occur with systemic pesticides other than neonicotinoids, and with pesticides that are not systemic but to which pollinators are exposed in the form of residues deposited during foliar spray applications to flowering plants. These exposures are anticipated as part of all pesticide registrations and can be incorporated into registration risk assessments.

There are more than 16,000 bee species in the superfamily *Apoidea*, composed of 7 families each with different physiological, behavioral, and morphological characteristics. The honey bee is one of the model organisms used by USEPA in its risk assessments for registration of new active ingredients and is meant to represent the effects an active ingredient may have on insect pollinators and other non-target terrestrial invertebrate species. In addition to easy and abundant availability of test individuals, *Apis mellifera* is considered to be extremely sensitive to pesticides, probably because of a lower number of xenobiotic detoxifying enzymes in their genome compared with other insect species (Claudianos et al., 2006). A meta-analysis by Arena and Sgolastra (2014), showed that *A. mellifera* was often more sensitive to pesticides than other non-*Apis* bee species (*Bombus* spp., *Megachile rotundata*, and *Osmia lignaria*) generally used in ecotoxicological studies. However, even within a species it is understood that toxicological endpoints generated during a chemical's risk assessment, like an organism's LD_{50} values, vary due to the age and subspecies of bee used, the season from which a population was collected, an individual's nutrition and physiological condition, the amount of human handling during assessments, and experimental procedures used to generate LD_{50} values (Cresswell, 2011). These factors have led to a variety of LD_{50} values published by researchers. Table 12 below shows honey bee LD_{50} values used by USEPA for acute contact and oral exposure routes and their corresponding No Observable Adverse Effect Level (NOAEL).

Table 12. Lethal and no observable adverse effect values of neonicotinoid insecticides to honey bee (*A. mellifera*)

Active ingredient	**Lethal Dose to 50% of a population (LD_{50}) (ppb)**				**Reference**
	Honey bee acute		**NOAEL***		
	Contact	**Oral**	**Contact**	**Oral**	
Acetamiprid	81,000	151,000	-	-	(USEPA, 2002)
Clothianidin	439	37	95	9	(USEPA, 2011a) (USEPA, 2003a,b)
Dinotefuran	470	230	32	13	(USEPA, 2011b)
Imidacloprid**	430	39	500	25	(USEPA, 1992; USEPA, 2016)
Thiacloprid	378,000	173,200	-	-	(USEPA, 2012b)
Thiamethoxam	240	50	50	20	(USEPA, 2011c)

*No Observable Adverse Effect Level (NOAEL) is determined using standardized tests. Research from the greater scientific community has shown sublethal effects occurring at lower concentrations in some instances.

** Imidacloprid's contact LD_{50} value was lowered from 780 ppb to 430 ppb while the imidacloprid's oral NOAEL was raised from 15 ppb to 25 ppb in the preliminary pollinator assessment to support the registration review of imidacloprid.

While information regarding neonicotinoid toxicity to many wild insect species is limited, toxicity values are known to differ greatly between beneficial insects and other invertebrate species (Table 13).

Table 13. Neonicotinoid lethal effect values for some wild bees and other insects

Insect scientific name (Common name, and role)	Lethal dose to 50% of a population (LD_{50}) (ppb)			LD_{50} (contact or oral)	Reference
	Clothianidin	Imidacloprid	Thiamethoxam		
Bombus terrestris (Bumble bee, Pollinator)	-	59	63.1	oral	(Mommaerts et al., 2010)
Bombus impatiens (Bumble bee, Pollinator)	3,900	32,200	-	contact	(Scott-Dupree et al.,2009)
Osmia lignaria (Mason bee, Pollinator)	1,000	700	-	contact	(Scott-Dupree et al.,2009)
Megachille rotundata (Leaf cutter bee, Pollinator)	800	1,700	-	contact	(Scott-Dupree et al.,2009)
Eretmocerus eremicus (Wasp, Parasitic)	-	1.9	1.0	contact	(Pisa et al., 2014)
Sasajiscymnus tsugae (Beetle, Predator)	-	1,821	-	contact	(Eisenback et al., 2010)
Coleomegilla maculata (Beetle, Predator)	-	98.7	-	contact	(Eisenback et al., 2010; Lucas et al., 2004)
Hyaliodes vitripennis (True bug, Predator)	-	-	500	contact	(Pisa et al., 2014)
Orius laevigatus (True bug, Predator)	-	-	300	contact	(Pisa et al., 2014)
Danaus plexippus *[3rd instar larvae]* (Monarch butterfly, Pollinator)	15.6	-	-	contact	(Pecenka and Lundgren, 2015)

6.2 Pollinators and neonicotinoid exposure points in plants

For an insecticide to become toxic to an organism, the organism must be exposed to a sufficient amount of active ingredient for a sufficient period of time. The median acute toxicity value for an organism is said to be the lethal dose to 50 percent of a population (the LD_{50}). Exposure points are objects or materials that contain an active ingredient such as a neonicotinoid insecticide. Insecticide residues can vary greatly in their concentration at an exposure point and are also a function of the amount of active ingredient applied. In the case of neonicotinoids, the pathway responsible for neonicotinoid exposure to pollinators in plants is systemic movement. Systemic movement occurs when neonicotinoids dissolve in water and are taken up with water through a plants roots and xylem, water transport system. This translocation process causes neonicotinoid exposure to pollinators when they accumulate in plant tissues collected by a pollinator. For bees, exposure points of concern include pollen, nectar, guttation fluid (plant excreted water droplets) from hydathodes (openings in leaf margins) that can be used by pollinators as a water source, and nesting material or resins collected by pollinators. In addition to pollinators being exposed to neonicotinoids through systemic transportation, pollinators may be exposed to neonicotinoids through additional, unintended, exposure pathways. Exposure pathways like insecticide drift (movement of pesticide particles through the air at the time of application or soon after, to any site other than the area intended) or from pesticide volatilization and may cause exposure to pollinators by direct or indirect contact. Direct contact may occur if a pollinator encounters treated surfaces or airborne neonicotinoid residues from either drift or volatilization. Indirect contact may occur if the airborne neonicotinoid settles into puddles or other bodies of water a pollinator is using to collect water. These pathways make both air and water additional exposure points under specific conditions or events.

Wide variation has been reported in neonicotinoid residue concentrations in various exposure points (Mullin et al., 2010; Samson-Robert et al., 2014; Sanchez-Bayo and Goka, 2014). There are many factors that can influence the rate and amount of active ingredient taken up by the plant including: temperature, moisture, soil type, amount of organic matter, plant age, amount of active ingredient applied, active ingredient's chemical properties, active ingredient's persistence, type of inert material used (adjuvants, surfactants, plant growth regulators, biostimulants, etc.), application methods, and plant species and variety. In addition to factors that influence an active ingredients uptake, there are also factors that influence an active ingredient's rate of degradation and movement in the soil thus impacting the amount of residues available to the plant for uptake at a given time. The complexity of these factors makes it difficult to anticipate the environmental exposure to pollinators over a period of time. Other factors that should be considered for non-Apis species include:

- The daily amount of pollen and nectar consumed by an insect differs between species and can directly influence the amount of neonicotinoid residue to which an insect is exposed (EFSA, 2013a,b,c);
- Wild bees (bumble bees and solitary bees) may be exposed to higher amounts of neonicotinoids in pollen as they eat unprocessed pollen, unlike honey bees that eat processed bee bread or glandular secretions from nurse bees (Averill, 2011); and
- Wild bees may also be exposed to additional neonicotinoid residues by procuring contaminated nesting materials (EFSA, 2013a,b,c).

6.3 Honey bee colony level exposure

Where tables 13 and 14 illustrate the relative toxicity of neonicotinoids on non-target beneficial insects, specifically bee pollinators, other work by Mullin et al. (2010), Sanchez-Bayo and Goka (2014) and Samson-Robert et al. (2014) highlighted some of the larger complexities involved with interpreting effects of neonicotinoids within realistic environments. Field experiments studying pesticide residue accumulation in wax, pollen, water, and individual honey bees, showed colonies located near high intensity agricultural areas accumulated many pesticides in a single sample. For example, residues of up to 39 different pesticides (mean=8) could be detected from one sample of the wax of brood comb, while pollen had up to 31 (mean=7) different pesticides per sample (Sanchez-Bayo and Goka, 2014). Analysis of water in puddles have found residues of up to 30 different pesticides and their metabolites (mean≈4), while analysis of bees revealed residues of up to 25 different pesticides (mean=2.5) on or within their bodies (Samson-Robert et al., 2014). Another analysis of various ecotoxicity studies looked at pesticide residue accumulation from a variety of exposure points and found that out of 161 pesticides identified in honey bee colonies, 77% can be found in pollen, 59% in wax, and 48% in nectar. Of these, 52% were insecticides, 25% fungicides, 17% herbicides, and 6% acaricides (Sanchez-Bayo and Goka, 2014). Despite the influence that experimental design can have on non-target exposure to unwanted active ingredients, it is important to note that many pesticides, not just neonicotinoids, can make their way into honey bee colonies and possibly result in adverse effects on honey bee colony health and behavior.

Within a honey bee colony, individuals may be exposed to neonicotinoids through contact or ingestion of bee bread, honey, resin, or wax. A survey conducted by (Genersch et al., 2010) found residues from bee bread resulting in 3 ppb imidacloprid (7.7% of a honey bees oral $LD_{50,}$ table 12) and up to 199 ppb thiacloprid (0.1% of a honey bees oral LD_{50}). Residues from the most toxic neonicotinoid, clothianidin, were found in honey up to 3.4 ppb (9.2% of a honey bees oral LD_{50}). Other neonicotinoids like thiamethoxam and thiacloprid were found up to 7.7 ppb (15.4% of a honey bees oral LD_{50}) and 11.6 ppb (<0.001% of a honey bees oral LD_{50}), respectively (Paradis et al., 2014; Pohorecka et al., 2012). Residue information from bee collected resin is limited, however (Pareja et al., 2011) collected resin from a colony located near a field planted to sunflower and found residues up to 100 ppb imidacloprid (2.5 times a honey bees oral LD_{50}). Wax can also accumulate pesticide residues; a study by (Mullin et al., 2010) found up to 13.6 ppb imidacloprid (34.9% a honey bees oral LD_{50}). Other neonicotinoids like thiacloprid were reported up to 7.8 ppb (0.004% a honey bees oral LD_{50}) while others were below the limit of detection (Cutler and Scott-Dupree, 2007; Mullin et al., 2010). These manipulated or processed resources may result in changes to residue concentrations due to exposure from light, heat, or microbial activity; however, the extent of these changes is not well understood.

6.4 Exposure routes

Bees may also be exposed to pesticides via many routes of exposure such as through plants, surface water, soil, and seed coating dust. Given that the extent to which bees may be exposed via direct contact with soil or surface water is considered uncertain, focus of this section will be primarily on exposure via treated seed planting dust and plants.

6.4.1 Treated seed planting dust exposure

Treated seeds, for some crops, require lubricant (talc/graphite) in planter to ensure uniform planting. Planting dust emitted during the sowing of treated seeds is another route through which pollinators can be exposed to neonicotinoids. Abraded dust when released into the air during planting, can contain insecticide concentrations toxic to bees. Bees could be directly 'powdered' by insecticides if their flight path went through airborne planter dust or bees may be exposed to the vegetation on which planting dust has settled during planting (Krupke et al., 2012). Many studies around the world have associated incidents of honey bee deaths to planting dust (Bonmatin et al., 2014; Girolami et al., 2012; Krupke et al., 2012; Marzaro et al., 2011; Nikolakis et al., 2015; Pisa et al., 2014; Pistorius et al., 2009; Pistorius et al., 2015; Tapparo et al., 2012). Greatti et al. (2003) and Greatti et al. (2006) showed that the outflow air fans in modern pneumatic planters resulted in the release of imidacloprid into the environment as dust, resulting in honey bee exposure to residues. However, others have shown that neonicotinoid levels found on vegetation near field edges did not contain concentrations high enough to harm foraging bees

(Marzaro et al., 2011; Yang et al., 2008) or reach levels of acute toxicity. Girolami et al. (2012) and Marzaro et al. (2011) reported that bee death seemed to only be associated with bees exposed during conditions of high humidity following exposure.

Research is underway to reduce dust emission from treated seeds. The USEPA facilitated a pollinator summit focusing on dust and seed treatment (USEPA, 2013a). A new seed lubricant, “fluency agent”, has been developed and can be used in place of traditional seed lubricants (BCS, 2014b). This product is currently required by law in Canada, where bee deaths from planter dust have been documented. Another effort to address concern for seed treatment dust is the development of fully automated seed treatment application systems (On Demand™) that reduces human error and uniformly coats the seed with pesticides, thereby improving seed integrity in an effort to control dust abrasion during the seed application and field planting process (BCS, 2014a).

6.4.2 Plant exposure

In assessing a neonicotinoid insecticide’s risk to a pollinator one must look at the exposure point’s residue concentration (the concentration in the pollinator collected resource), frequency of contamination (what proportion of the total resources are contaminated), and the active ingredient’s relative toxicity to the organism (how toxic is the contaminant to the pollinator, often calculated as an LD_{50} value). Bees may be exposed to neonicotinoids outside of the colony when collecting a variety of resources including pollen, nectar, guttation, and water. The amount of residue contained within these resources also depends on the amount of active ingredient applied and the application method used (seed treatment, soil drench, foliar application, or tree injection). A study by Bonmatin et al. (2005) looked at residue concentrations in pollen from a lower application rate, i.e. treated seed typically with ≤ 1 mg active ingredient / seed; collected plant pollen resulted in an average of 2.1 ppb imidacloprid in corn (5.4% of a honey bees oral LD_{50}, table 12) and 3.0 ppb imidacloprid in sunflower (7.7% of a honey bees oral LD_{50}). Higher application rates used in foliar treatments have been shown to result in thiamethoxam concentrations up to 127 ppb in the pollen of pumpkin (2.5 times a honey bees oral LD_{50}) when applied at a rate of 96 g active ingredient / ha (Dively and Kamel, 2012); while other studies have documented up to 206 ppb imidacloprid in pollen (5.3 times a honey bees oral LD_{50}) (Mullin et al., 2010). Pollen of *Heracleum sphondylium* wildflowers growing on field margins of an oilseed crop were found to have up to 85 ppb of thiamethoxam residues (1.7 times a honey bees oral LD_{50}) (Botías et al., 2015).

Nectar collected from canola treated seed resulted in up to 2.24 ppb clothianidin (6.1% of a honey bees oral LD_{50}, table 12), while higher application rates ranged from 9.2 ppb dinotefuran in pumpkin (4% of a honey bees oral LD_{50}) to 319 ppb clothianidin in clover (8.6 times a honey bees oral LD_{50}) (Cutler and Scott-Dupree, 2007; Dively and Kamel, 2012; Larson et al., 2013).

Bees may also collect guttation droplets (excretions at leaf edges from a plants water transport system), providing another point of exposure through which bees may come in contact with systemically absorbed neonicotinoids. Clothianidin, the most toxic neonicotinoid to honey bees, can result in >100,000 ppb clothianidin (>2,700 times a honey bees oral LD_{50}, table 12) from guttation of corn planted with treated seed (Girolami et al., 2009). Other residues reported for guttation in melon reached 37,350 ppb imidacloprid (958 times a honey bees oral LD_{50}) (Hoffmann and Castle, 2012). However, the frequency at which bees actively collect guttation is not well understood (Reetz et al., 2011). Further concerns surround the contamination of water in or near areas treated with neonicotinoids. Residues from treated corn and canola seed have been shown to reach up to 55.7 ppb clothianidin (1.5 times a honey bees oral LD_{50}) and 67.9 ppb imidacloprid (1.7 times a honey bees oral LD_{50}), respectively (Main, et al., 2014; Samson-Robert et al., 2014). High residues in home-landscapes have also been documented. A study using a soil drench product at the labeled rate resulted in 34 ppb imidacloprid in milkweed flowers (87.2% of a honey bees oral LD_{50}) (Krischik et al., 2015); while another study found Eucalyptus trees with 660 ppb imidacloprid in nectar (16.9 times a honey bees oral LD_{50}) (Botías et al., 2015; Paine et al., 2011).

In January 2016, the USEPA identified preliminary risk findings of imidacloprid to insect pollinators using a crop group based approach. The agency conducted a screening level assessment (Tier I) for the various uses of imidacloprid utilizing the toxicity endpoints, conservative (modeled) exposures, actual residue values from pollen and/or nectar (where data were available) to determine if there are risks to individual bees. The agency concluded that imidacloprid application methods and use patterns associated with cotton and citrus present a risk to individual bees. The agency identified a low potential for on-field risk of imidacloprid on root/tuberous, bulb, leafy greens, and brassica vegetables, globe artichoke, and tobacco (harvested before bloom) with all application methods as well as soil applications to blueberries (berries and small fruits) and seed treatment applications to corn. Additionally low risk was identified for members of the cereal grain group (which is registered for seed treatment uses only) including wheat, barley, oats, rye, and millet are either not attractive to honey bees or primarily wind pollinated. With the exception of okra, risk was identified to be low for members of the fruiting vegetable group. The agency also identified crop groups/use patterns for which more evaluation is needed. The crops in this group include legumes, tree nuts, berries/small fruits, citrus fruits (soil applications), pome fruits, stone fruits, berries/small fruits, members of the nectar producing cereal grains, herbs and spices, cucurbit vegetables and oilseeds (USEPA, 2016).

Neonicotinoid effects discussed below are relevant to honey bees and are grouped by lethal and sublethal effects. In most cases, it is not possible to account for exposure frequency and duration, as data are limited. However, it should be assumed that a direct comparison of an exposure point's residue concentration to an organism's relative toxicological sensitivity in many cases may be an overestimate of actual exposure frequency and duration.

6.5 Pollinators and lethal impacts

Typically, lethal effects to insect pollinators are considered on an acute (single) exposure basis, where an organism is exposed to an insecticide and is unable to detoxify it which results in death; however, chronic (multiple or duration-based) exposures to an insecticide at levels below an organism's acute LD_{50} can also cause mortality in insect pollinators. Chronic, prolonged exposure to neonicotinoid insecticides at certain levels can increase a pollinator's sensitivity by lowering the amount of active ingredient needed to cause a lethal effect. For example, honey bees exposed to imidacloprid over 8 days at 1 and 10 ppb in a laboratory study resulted in at least a 60-fold increase in lethal effect, while Africanized honey bees exposed to 5 ppb thiamethoxam over 5 days resulted in 41.2% loss of lifespan (Oliveira et al., 2013; Suchail et al., 2001).

A very common use of neonicotinoid insecticides are as seed treatments for commodity crops like corn, soybeans, sunflowers, sugar beets, canola, potatoes, and other crops. Imidacloprid, clothianidin, and thiamethoxam are the most common active ingredients applied to dress a wide variety of seeds including the majority of corn and soybeans planted in Minnesota. Residue accumulation in plant parts resulting from seed treatments has been relatively well characterized for certain crops, across the majority of exposure points honey bees are likely to visit.

In addition to understanding insecticide accumulation in flowers and plant parts, several common seed-treated crops have been evaluated by registrants to determine the frequency of honey bee visitation as compared to the crop's relative abundance in the landscape. In 2013, corn accounted for 42% of the row crops planted in Minnesota (Figure 3). In areas where corn consisted of 72% of the surrounding land use, honey bees located in the area collected only 19% of their pollen from corn. This indicates that although the relative abundance of corn was high, bees collected less corn pollen than would be expected if bees foraged randomly (i.e., bees appeared to actively choose non-corn pollen). In contrast, honey bees placed next to large canola fields were found to heavily collect canola pollen with 72% of pollen samples collected from hives having some canola pollen present, and 41% of pollen samples from hives consisting only of canola pollen (BCS, 2014c). This information illustrates the importance of looking at both residue accumulation and visitation frequency in order to properly understand a neonicotinoids exposure potential to insect pollinators. The degree to which wild bees or other pollinating insects visit or prefer a specific crop as a food source is not fully understood at this time.

Concerns also exist for other means of exposure from neonicotinoid treated seed including direct contact exposure or indirect exposure from abraded seed dust produced during the planting of seeds by pneumatic planters. Over the last decade, several spring bee death incidents have been reported to be correlated with sowing of neonicotinoid-treated corn seeds (HCPMRA, 2014). In these incidents, sources of neonicotinoids were found in the field as well as in the adjacent vegetation, but the mechanisms by which the bees come into contact with the pesticides were not fully understood (Krupke et al., 2012). In general, pollinator exposure to contaminated treated seed dust during sowing is dependent on the type of crop, the seed treatment and lubricant used.

Usually, large seeded grains such as corn, produce higher quantities of dust during planting compared to other crops (EFSA, 2012). Pollinators may be exposed during the planting process to this dust through direct contact (as pollinators fly through the dust cloud from the planter) and/or indirectly through dust that lands on nearby plants, soil surfaces or water resources. In one study where honey bees presumably flew through dust abraded from the seed during planting, individuals were exposed to an average of 5,700 ppb and up to 12,400 ppb clothianidin; these levels far exceed clothianidin's honey bee acute contact LD_{50} value (Tapparo et al., 2012).

It is worth noting that while abraded planter dust may elicit severe lethal effects on bees, 8.3 million acres of corn were planted in Minnesota in 2013, it is estimated that most acres were treated with a neonicotinoid insecticide, and yet only three alleged pesticide bee kill incidents were reported to MDA in 2013, all of which were investigated for pesticide misuse. Two of these investigations suggested honey bees had been potential exposed to neonicotinoids applied as a seed treatment.

In 2014, the MDA investigations related to alleged pesticide bee kills showed a similar trend to 2013. There were six investigations. Three confirmed exposures to neonicotinoid residues, and one allegedly was linked to the planting of neonicotinoid-treated seed. None showed evidence of exposure indicative of "acute pesticide poisoning" as used in the context of Minnesota's bee kill compensation program beginning in 2014. Note that it is not possible to quantify any lethal effects to unmanaged, wild pollinators or bee kill incidents not reported to MDA.

Other methods of applying neonicotinoid insecticides (i.e., non-seed treatment applications) allow for higher application rates. Soil drenches are used to treat a variety of field and woody crops, and turf/ornamental plants. Neonicotinoid use as a foliar spray in fruit crops, vegetables, and flowers provides yet another route of exposure for pollinators. However, risks to pollinators from direct contact exposure during application or indirect exposure via foliar residues would presumably be similar to risks from other insecticides considered highly toxic to bees, such as those from other chemical classes including synthetic pyrethroids, organophosphates, and carbamates. Whether applied to soil or foliarly to a plants canopy, neonicotinoid translocation into or deposition onto pollen can result in pollinator exposure to lethal concentrations of the insecticide's active ingredient. For example, pumpkins treated with a soil drench or foliar application, on average, resulted in concentrations of neonicotinoid residue in pollen above a honey bee's acute LD_{50} (Table 12) (Dively and Kamel, 2012). Higher residues were found in pollen and nectar if neonicotinoids (imidacloprid, clothianidin, thiamethoxam) were applied closer to flowering. In contrast, translocation of neonicotinoid residues from a soil drench or foliar application resulted in much lower residue accumulation in nectar as compared to pollen because of differences in translocation route of residues through leaves or roots (Dively and Kamel, 2012).

Pollinator exposure to guttation droplets (excretions at leaf edges from a plants water transport system) is another type of exposure through which pollinators may come in contact with systemically absorbed neonicotinoids. While guttated fluid can be used by bees as a water source, the frequency at which bees actively collect guttation is not well understood (Reetz et al., 2011). Several factors are known to influence the concentration at which neonicotinoid residues accumulate in guttation drops including: decreasing soil moisture (increases residue), plant age (younger plants can accumulate larger amounts of residue), and time after application (less residue present over time) (Girolami et al., 2009; Reetz et al., 2011). Average guttation values for seed treated corn and melon treated with a soil drench, under the experimental conditions showed neonicotinoid residue accumulation in guttation drops exceeded honey bee LD_{50} values by 940 times (Girolami et al., 2009; Hoffmann and Castle, 2012).

Similarly, standing water found in fields planted with neonicotinoid-treated seed also showed neonicotinoid concentrations potentially lethal to pollinators. Maximum water concentrations found ranged between (54.4 – 67.9 ppb) depending on the active ingredient; while average concentrations were significantly lower ranging between (1.1 – 7.7 ppb) (Main et al., 2014; Samson-Robert et al., 2014). Although relatively high neonicotinoid concentrations may be found in pooled water in or near fields, at the time of planting, a study analyzing samples taken one month after planting showed significantly reduced concentrations of clothianidin (89% less) and thiamethoxam (92% less) (Samson-Robert et al., 2014). These results are similar to other findings that reported rapid neonicotinoid breakdown in aqueous environments (CCME, 2007).

6.6 Pollinators and sublethal impacts

Pollinator chronic exposure to neonicotinoids at sublethal concentrations is also a concern. Sublethal effects are those behavioral and physiological factors that affect an organism at concentrations below a level that causes mortality. However, exposure thresholds of sublethal concern need to be generated according to standardized protocols and be reproducible across pesticide assessments (see USEPA new risk assessment framework for pollinators for more information).

At the time of registration, the unique properties of neonicotinoids suggested significant risk reduction for human exposure, and more targeted control of plant pests at application rates lower than other insecticides in common use such as organophosphates. Subsequently, a large amount of research has been conducted by the scientific community on sublethal affects. Criteria once used by regulators to establish appropriate exposure thresholds below which honey bees would not reasonably suffer any acute harm (the acute NOAEL) cannot be used to establish the lower bound threshold of sublethal effects being identified in current research.

Sublethal effects of neonicotinoids on pollinators can result from the same oral and contact exposure points associated with acute effects; the difference being that exposure occurs at sublethal concentrations and may occur over a longer period of time. There are several ways in which sublethal concentrations of neonicotinoid residues might adversely affect honey bees or other pollinators such as by impacting their orientation, learning, memory, feeding, movement, foraging, reproduction, or colony health. It is important to note that there have been relatively few field studies that confirm or invalidate the findings associated with these adverse sublethal effects found in laboratory studies (Blacquiere et al., 2012); although several research efforts have begun to explore the differences between field and laboratory sublethal effects (Dively et al., 2015).

6.6.1 Orientation

The survival of honey bees and wild bees requires their ability to navigate complex landscapes in order to find suitable nesting sites and collect food. This ability for bees to orient themselves and find their way back to their nest may be influenced by exposure to neonicotinoid insecticides (and possibly other pollutants as well). For example, honey bee foragers exposed under controlled conditions to thiamethoxam at 13.4 ppb (27% of a honey bee's acute oral LD_{50}, table 12) and released at familiar and unfamiliar foraging sites showed a significant decrease in their ability to navigate back to their nest from both types of sites (Henry et al., 2012). In a different study, foragers familiar with a feeding site, were orally exposed to imidacloprid at 48 ppb (96% of a honey bee's acute oral LD_{50}), and visitation rates before, during, and after treatment were measured to quantify the impact of imidacloprid exposure. Results showed a significant reduction in the number of bees visiting flowers during and after exposure to imidacloprid; bees did not fully recover from exposure until 7 days later (Ramirez-Romero et al., 2005). In yet another study, honey bees that consumed 100 ppb imidacloprid (a potentially lethal concentration) were 27% less likely to be able to navigate back to their colony, and those that could were significantly less likely to be able to make additional foraging trips within the next 24 hours (Bortolotti et al., 2003). The proportion of foragers able to navigate back to their nest may be associated with the time it takes for a neonicotinoid to cause sublethal effects. Abnormal foraging behavior is expressed faster with increasing dose (at 50 ppb, abnormal behavior starts at 20 minutes, and at 100 ppb, abnormal behavior starts at 10 minutes) (Yang et al., 2008). Note that not returning from foraging sites in these studies could also be attributed to mortality (given the experimental doses administered, especially at high concentrations, relative to the insecticide's acute LD_{50}) or some level of predation.

6.6.2 Learning and Memory

Bees use visual and olfactory (smell) senses to interpret their surroundings and successfully find the best forage (Chittka and Raine, 2006). To effectively be able to perform these tasks, bees must be able to learn and remember what plants have higher rewards in terms of nectar or pollen quality and abundance. One way of testing if a pesticide affects a bee's learning and memory is to conduct laboratory studies known as Proboscis Extension Reflex (PER) tests. PER is typically elicited in bees when their antenna come in contact with an odorant or sugar solution (nectar), thereby inducing extension of the bee's proboscis (their elongated sucking mouthpart). To understand if neonicotinoids may disrupt a bee's ability to identify/respond to a nectar source, unexposed bees are compared to neonicotinoid-exposed bees. Lambin et al. (2001) found that honey bee's dosed via contact application with imidacloprid at a concentration of 50 ppb (63% of a honey bee's acute contact LD_{50}, table 12), showed significantly decreased responsiveness to sucrose. Similarly, honey bee's dosed via acute oral application with acetamiprid at concentrations as low as 1,000 ppb (0.7% of a honey bee's acute oral LD_{50}) showed reduced responsiveness to sucrose when compared to controls (El Hassani et al., 2008).

Another type of PER test can be used for determining a bee's ability to learn and remember an odorant associated with a sugar reward. When testing acetamiprid and thiamethoxam at concentrations between 1,000 – 10,000 and 1 – 10 ppb, respectively, no significant differences were observed in a honey bee's ability to learn. However, when memory was tested 48 hours after exposure, bees exposed to 1,000 ppb acetamiprid experienced a significant reduction in their ability to remember the odorant (El Hassani et al., 2008). Conversely, another study found contact exposure of thiamethoxam at 10 ppb (4% of a honey bee's acute contact LD_{50}, table 12) reduced learning ability, while concentrations at 1 ppb (0.4% of a honey bee's acute contact LD_{50}) significantly reduced memory after 24 hours (Aliouane et al., 2009). Further study on the subject by Wright et al. (2015) found imidacloprid at 0.06 ppb and thiamethoxam at 0.0069 ppb reduced rate of learning of honey bees.

While select sublethal concentrations of three neonicotinoids have been shown to significantly influence a honey bee's responsiveness to sucrose, and their ability to learn and remember odorants associated with a sucrose reward, the applicability and meaning of these results in natural field scenarios has not been well established.

6.6.3 Feeding

Exposure to neonicotinoid insecticides can also change the amount of water and sugar syrup an insect pollinator consumes. Contact exposure to acetamiprid, in PER tests, at concentrations greater than or equal to 1,000 ppb have been shown to significantly increase a honey bee's responsiveness to water. In the same study, thiamethoxam exposure up to 10 ppb did not affect a honey bees PER response to water (El Hassani et al., 2008). Other studies have been conducted using the bumble bee *Bombus impatiens* as the test species. One study using *B. impatiens*, showed that colonies consumed significantly less sugar syrup treated with 14 ppb imidacloprid or 9 ppb clothianidin (Scholer and Krischik, 2014).

In addition to changing the amount of dietary resources consumed, neonicotinoid insecticides may also act as feeding attractants or deterrents depending on the chemical, quantity, and insect pollinator. A two-week pan trap survey aimed at quantifying flower-visiting insects looked at how imidacloprid-spiked traps influenced visitation. At imidacloprid concentrations of 0.01, 0.1, and 1.0 ppb, flower visiting flies were significantly deterred from visiting traps while the beetles, mainly pollen beetles, were deterred only at the 1 ppb concentration (Easton and Goulson, 2013). Conversely, *Apis mellifera* and *Bombus terrestris* of foraging age, during a two-choice feeding assay, showed a preference for imidacloprid and thiamethoxam at 0.25 and 2.5 ppb (Kessler et al., 2015). However, it is not known whether a valid relationship exists between results obtained using artificially-spiked feeders compared to results derived from typical food sources as insects visit flowers in the field (e.g., imidacloprid-contaminated pollen or nectar).

6.6.4 Movement

Research studies illustrate the variable effects of neonicotinoid exposure on bee movement. Observed effects in some studies appeared to be dose dependent and resulted in stimulation, while in other studies there was no measureable effect, or decrease in movement.

Neonicotinoids can disrupt normal neuronal and muscle functions as acetylcholine receptor antagonists. When honey bees consumed guttation droplets from corn planted with a neonicotinoid seed treatment, researchers observed uncoordinated movement and paralysis of muscles used for flight (Girolami et al., 2009). Honey bees exposed to imidacloprid at concentrations of 100 and 500 ppb, via acute oral exposure, were significantly more random in their movements, switching between a stationary position and fast movements, more frequently than bees in the untreated control (Medrzycki et al., 2003).

Adverse effects have also been shown at lower neonicotinoid concentrations. Bumble bees, chronically exposed to 16 ppb imidacloprid or 17 ppb clothianidin via chronic oral exposure, showed 47% or 32% less movement, respectively, than bees in the untreated control groups (Scholer and Krischik, 2014). In another study with imidacloprid contact exposure at 25 ppb and above, honey bee movement was also inhibited; conversely, at 12.5 ppb imidacloprid contact exposure, bees were observed moving significantly more than bees in the control treatment (Lambin et al., 2001). Similar increases in movement were measured one hour after acetamiprid contact exposure to honey bees at 1,000 ppb (1.2% of a honey bee's acute contact LD_{50}, table 12) and 5,000 ppb (6.2% of a honey bee's contact LD_{50}). However, at 10,000 ppb acetamiprid, both contact and oral exposure had no effect on honey bee movement; a similar lack off effects was also observed with thiamethoxam for both contact and oral exposure at concentrations of 1, 5, and 10 ppb (20% of a honey bee's acute oral LD_{50}) (El Hassani et al., 2008).

6.6.5 Foraging Effects

Although orientation, memory and learning, feeding, and movement all influence an insect pollinator's ability to successfully forage, there are broader, cumulative, impacts these factors may have on successful pollinator foraging.

A honey bee colony's foragers exposed to thiamethoxam through direct feeding at 13.4 ppb (27% of the acute oral LD_{50}) had up to a 31.6% likelihood of not returning to the hive, or about twice the rate as non-treated foragers (Henry et al., 2012). Other studies have looked at bumble bee exposure to imidacloprid and measured forager collection efficiency of pollen and nectar. A study which fed bees 0.7 ppb imidacloprid in sucrose and 6 ppb imidacloprid in pollen showed no significant difference in the amount of nectar collected between treatments but a significant 31% difference in the amount of pollen collected per hour by treated bumble bees (Feltham et al., 2014). Another study, showed that in addition to less pollen collection, foraging bees took significantly longer to complete their task when orally dosed with 10 ppb imidacloprid (Gill et al., 2012). In contrast, a review looking at other neonicotinoid foraging studies showed no significant adverse effects (Pisa et al., 2014).

6.6.6 Reproduction/development

In addition to parameters that measure a pollinating insect's ability to fly and successfully collect resources, pollinators must also be able to successfully reproduce. A variety of bumble bee experiments have been conducted to evaluate the effects neonicotinoids may have on successful reproduction in bees. In one study, full bumble bee colonies used in a semi-field experiment where exposed to imidacloprid in pollen at either (6 or 12 ppb) and in nectar at either (0.7 or 1.4 ppb) for two weeks. This experimental design was intended to mimic both the time a crop is in bloom, and residue concentrations, found in pollen and nectar of some seed-treated crops. Colonies exposed to pollen and nectar concentrations had significant effects on daughter queen reproduction, those individuals that will overwinter and establish new colonies the next year; the number of daughter queens produced were reportedly reduced by 85 – 90% compared to controls (Whitehorn et al., 2012). In laboratory experiments, small micro-colonies of bumble bees, typically consisting of 5 worker bees, have been used to look at reproduction effects after neonicotinoid exposure. Worker bees, chronically exposed to 10 and 20 ppb imidacloprid via oral exposure and allowed to forage for two weeks, resulted in a significant halt of reproduction within micro-colonies, 0 eggs laid (Mommaerts et al., 2010). Using a similar experimental design, Laycock et al. (2012) found a 42% reduction in the number of eggs laid by workers when orally exposed to 1.3 ppb imidacloprid. Developmental effects have also been documented from sublethal exposure to neonicotinoid insecticides in wild bees. At 30 ppb imidacloprid, *Osmia lignaria* (a solitary, mason bee) took significantly longer for eggs to reach their last larval stage than when exposed to 3 ppb imidacloprid (Abbott et al., 2008).

6.6.7 Colony health effects

Many bee species are considered social organisms and rely upon each other for the good of the collective unit (the colony) to function properly; therefore, colony-level impacts from neonicotinoid exposure should also be considered. To evaluate the effect of irrigation in imidacloprid treated turf on bumble bee colony health, a semi-field, caged study was conducted by (Gels et al., 2002). The experiment was conducted on athletic field plots planted with 25 - 50% white clover and treated with imidacloprid at 3.1 mg a.i. / ft^2 (75% of the maximum allowable rate). Small bumble bee colonies, representing a colony at an early stage of colony development, were caged on treated plots for 28 days. Results showed that when the application was not followed by watering, bumble bee colonies weighed significantly less, had fewer workers and nectar cells (Gels et al., 2002). This study confirms that following label recommendations, specifically regarding irrigating treated areas after application, reduce non-target impacts to bumble bee colonies.

Other studies have shown that bumble bee exposure to imidacloprid at ≤ 14 ppb and clothianidin at 17 ppb in laboratory and semi-field studies can, over a period of time, reduce colony weight (Scholer and Krischik, 2014; Whitehorn et al., 2012). In addition, exposure to neonicotinoids in syrup for an extended period of time may reduce queen survival. After 6 weeks of chronic exposure to dosed syrup, queens of colonies exposed to 71 ppb imidacloprid or 39 ppb clothianidin died significantly sooner than colonies treated with ≤16 ppb imidacloprid or ≤17 ppb clothianidin; after 11 weeks of exposure, queens died significantly sooner at 16 ppb imidacloprid or 17 ppb clothianidin than colonies treated with ≤14 ppb imidacloprid or ≤9 ppb clothianidin (Scholer and Krischik, 2014). Constant exposure to a single food source, containing neonicotinoid insecticides, for 6 – 11 weeks is not typical; as such, this study illustrates potential worst case exposure scenarios and may be helpful for planning subsequent research.

Currently, there are few studies that have broadly measured honey bee colony health and survival after extended exposure to neonicotinoid insecticides. Honey bee colonies exposed up to 20 ppb imidacloprid over 39 days showed no significant difference from untreated colonies with regards to colony weight or population size (Schmuck et al., 2001). Colonies placed in large blooming canola fields that had been planted with clothianidin treated seed were also not significantly affected when colony weight gain, honey yield, adult mortality, area of sealed brood, and worker longevity were evaluated (Cutler and Scott-Dupree, 2007). Conversely, there have been two field studies that have shown a correlation between honey bee decline and neonicotinoid exposure (Lu et al., 2012; Lu et al., 2014). However, these studies have been criticized by many scientists for reasons including but not limited to: poor experimental design (not having an appropriate number of colonies in each trial); treatment of colonies at levels considered unrealistic of field or real life exposure (imidacloprid levels up to 400 ppb); not properly documenting other stressors of concern (*Varroa* mites and *Nosema* spores); and presenting correlative findings as causation findings.

6.7 Neonicotinoid interactions

Pesticide mixtures, as well as pesticide additives can impact insect pollinators and result in three types of effects: synergism (an effect that is greater than the sum of each individual pesticide alone), additive (an effect that is equal to the sum of each individual pesticide), or antagonism (an effect that is less than the sum of each pesticide alone). There have been 161 pesticides found in honey bee hives and up to 31 pesticides (mean = 7), found in a single sample of pollen indicating that exposure to multiple pesticide residues is common (Mullin et al., 2010; Sanchez-Bayo and Goka, 2014). In order to evaluate all of the possible combinations of effects that these 31 pesticides might have on pollinators, regulators would have to perform 8.2 decillion (8.2 E+33) tests. For this reason, the EPA has stated, "the assessment of honey bee exposure to multiple pesticide mixtures, evaluation of pesticide environmental mixtures to any taxa is considered beyond the scope of the ecological assessments because a myriad factors can affect exposure and effects of environmental mixtures which cannot be quantified based on the available data" (USEPA, 2013b). However, a report by the United States Government Accountability Office, reviewed Federal Agency efforts to mitigate bee decline and made the following comment to EPA, "to help comply with the directive in the White House Pollinator Health Task Force's strategy, we recommend that the Administrator of EPA direct the Office of Pesticide Programs to identify the pesticide tank mixtures that farmers and pesticide applicators most commonly use on agricultural crops to help determine whether those mixtures pose greater risks than the sum of the risks posed by the individual pesticides." (USGAO, 2016).

Currently, limited information is available on the effects a pesticide's formulation or tank mixture may have on insect pollinators. Pesticides often consist of an active ingredient formulated with other additives like adjuvants and surfactants which have historically been considered to be inert (having no toxicity to or pesticidal activity on the pest) and are used to convey some additional benefit (increase product efficacy, provide stability, reduce foaming activity in the spray tank, increase penetration, reduce product drift, etc.). Additives and formulation co-solvents such as N-methyl-2-pyrrolidone (NMP) are used to dissolve a pesticides active ingredient and penetrate a plants waxy cuticle. However, research by (Mullin et al., 2015) showed that NMP has moderate toxicity to adult honey bees and an estimated toxicity 20 times higher for larvae than adults.

In addition, adjuvants such as the class of organosilicones (penetrating agents) applied in a tank mixture at 1% with a pesticide active ingredient (typically a fungicide) and applied during almond pollination events (a crop not found in Minnesota), were found to adversely affect honey bee learning. However, the authors stated that tank mixtures typically consist of lower concentrations of an organosilicon and they hypothesized that bees visiting multiple flowers could reach or exceed this 1% exposure concentration (Ciarlo et al., 2011). Recently a method for detecting organosilicones was developed; analysis of wax, pollen, and honey resulted in trisiloxane (an organosilicon component) detections in 100%, 60%, and 0% of samples, respectively (Mullin et al., 2015).

In addition to adjuvants and surfactants interacting with active ingredients, ergolsterol inhibiting fungicides are known to interact with acetamiprid and thiacloprid (Sanchez-Bayo and Goka, 2014). However, acetamiprid accounts for a relatively small amount of neonicotinoid sales in Minnesota (approximately 0.4%, compared to 37.7% imidacloprid, the most widely used neonicotinoid in 2013) and thiacloprid has been cancelled and will be removed from shelves by 2016 (USEPA, 2014a). Ergolsterol inhibiting fungicides (propiconazole and fenbuconazole) act synergistically by increase acetamiprid's toxicity by 100 and 4.5 fold, respectively. However, when realistic fungicide residues in pollen were used to determine the percent probability these synergistic mixtures would kill 50% of a population, results showed a maximum probability of only 0.09 – 0.85%. The ergolsterol inhibiting fungicide (propiconazole) can increase thiacloprid's toxicity to honey bees by 560 fold; while this mixture, when realistic pollen residues were used, resulted in a maximum of 7.43% chance of killing 50% of a population. A probability above 5% is considered a high risk (Sanchez-Bayo and Goka, 2014). No ergolsterol inhibiting fungicide residues were found in nectar. Another fungicide from a different chemical class, trifloxystrobin, combined with clothianidin has also been shown to have synergistic effects; this mixture, used to treat canola seeds, was shown to increase toxicity toward a leaf feeding *Phaedon* (beetle larvae) by 150 fold. Other synergistic or additive interactions have also been shown between thiacloprid and imidacloprid or clothianidin (Wachendorff-Neumann et al., 2012). Examples shown here display a need for additional research looking into the impact tank mixtures may be having on pollinators when used on pollinator visited crops.

Similar concerns exist over variation in testing requirements EPA uses for approval of an active ingredient verses an active ingredient's formulations (end-use products), which typically contain other ingredients such as carriers, stickers, spreaders, stabilizers, and/or dyes to improve an active ingredients efficacy. Historically, EPA has required honey bee testing only on the technical grade (pure) active ingredient when registering a pesticide and its various formulations. However, requiring testing on honey bees using only the technical grade active ingredient does not always result in the most conservative toxicity assessment. For example, dinotefuran as a technical grade active ingredient is less toxic to honey bees than the typical end use product used by consumers (USEPA, 2011b). Guidance issued by EPA in June of 2014 allows agency staff to require registrants to submit bee toxicity data on a specific end-use product if data support the possibility that the end-use product may be more toxic than the active ingredient alone (USGAO, 2016).

A laboratory study looking at two neonicotinoids (imidacloprid and clothianidin) and an organophosphates (chlorpyrifos) effect on NF-kB protein complex (NF-kB regulates specific immune responses, like antiviral defense), found that bees exposed to sublethal oral exposure (between 0.1 and 10 ppb) of imidacloprid or clothianidin, but not chlorpyrifos, reduced NF-kB's signaling; when individuals were monitored for the effects NF-kB down regulation had on the proliferation of Deformed Wing Virus (DWV) under these same conditions, bees in the imidacloprid and clothianidin treatments were found to have significantly higher viral loads than those of the chlorpyrifos or control groups (Di Prisco et al., 2013). These findings highlight imidacloprid and clothianidin's ability to suppress a bee's immune response where other insecticides like chlorpyrifos do not. Other field studies have correlated increased levels of Black Queen Virus (BQV) and varroa mite numbers in hives near fields treated with thiamethoxam (Alburaki et al., 2015) or increased varroa mite numbers in hives exposed to imidacloprid through a pollen substitute (Dively et al., 2015). Laboratory studies have also looked at the effects neonicotinoids can have on nosema, a fungal microsporidian gut parasite, proliferation within insect pollinators. Honey bees chronically exposed to imidacloprid at 0.7 ppb were shown to suppress their immune system (Alaux et al., 2010; Aufauvre et al., 2014), and interact (additively) with *Nosema ceranae* to increase mortality in honey bees (Alaux et al., 2010). While another study showed three neonicotinoids (acetamiprid, imidacloprid and thiacloprid) acted antagonistically, reducing the load of *N. ceranae* infection (Pettis et al., 2013). Non-pollinator insects have also been studied and shown to have immune responses affected by neonicotinoid exposure; fruit flies challenged with clothianidin at 40 ppb, followed by *S. cerevisiae,* a common yeast, infection showed down regulation of the insect's immune response. This indicates that a fruit flies immune response, typically used to fight *S. cerevisiae* infection, is negatively impacted when also challenged with clothianidin (Di Prisco et al., 2013).

Yet further studies have evaluated neonicotinoid interactions on insect organelle and immune response. Bees require mitochondria organelle to produce energy for proper neuron function. A study exposing bumble bees to 2.1 ppb clothianidin and 210 ppb imidacloprid looked at effects to cultured brain neurons collected from treated bees. Results showed mitochondrial depolarization, a process that results in reduced energy transfer to neurons, and can lead to other impacts on colony behavior (Moffat et al., 2015).

6.8 Risks to non-target organisms other than pollinators

Although this review was scoped to evaluate the impacts of neonicotinoids on insect pollinators, neonicotinoid concentrations can persist, and possibly accumulate under certain soil, water, and sediment conditions and may pose a risk to non-target organisms (mammals, birds, fish, arthropods, etc.) living in these environments. The uptake of soil-borne neonicotinoid residues by plants further expands this risk potential resulting in non-target organism exposure from feeding on these plant materials. Neonicotinoids can pose risks to non-target organisms both directly (exposure from application, ingestion of the formulated product) and indirectly (affecting their food supply such as contaminated prey). Among non-target organisms, beneficial insects (predators, parasitoids, and pollinators) are the most sensitive taxa that are exposed to neonicotinoids; however, their potential long-term, population-level effects on non-target organisms are uncertain.

6.8.1 Non-Pollinator terrestrial organisms

Neonicotinoids work by binding to the nicotinic receptors in the central nervous systems. However, the binding affinity of neonicotinoids at the nicotinic receptors in vertebrates (mammals and birds) is much less than that of insect nicotinic receptors and thus neonicotinoids are considered much less toxic to mammals and birds than to insects. Neonicotinoid insecticides were registered by USEPA as "reduced risk" pesticides due to their low mammalian toxicity, thus protecting applicators and farm workers from adverse impacts. Furthermore, the blood-brain barrier in vertebrates blocks access of neonicotinoids to the central nervous system resulting in reduced toxicity (Jeschke et al., 2011; Tomizawa and Casida 2005).

Nevertheless, the relative toxicity of neonicotinoids varies, both among active ingredients and among the terrestrial taxa, age and gender. For example, imidacloprid acute oral LD_{50} values for female rats ranged from 380,000 to 450,000 ppb as compared to 170,000 ppb for female mice. Imidacloprid acute oral LD_{50} for male rats ranged from 450,000 to 500,000 ppb as compared to 130,000 ppb for male mice. Imidacloprid has very low toxicity via dermal exposure, moderate toxicity through ingestion, and a variable toxicity through inhalation (dust is considered slightly toxic, while aerosol is highly toxic) (Thyssen and Machemer, 1999; USEPA, 2014b; WHO, 2004). The acute mammalian toxicity profile of neonicotinoid compounds is presented in table 14.

Table 14. Toxicity of neonicotinoid compounds to mammals.

*Toxicity (LD_{50})	Acetamiprid	Clothianidin	Dinotefuran	Imidacloprid	Thiamethoxam
Acute Oral	Moderate	Moderate	Low	Moderate	Low
Inhalation	Low	Low	Very Low	High (aerosol), Very Low (Dust)	Very Low
Dermal	Low	Low	Very Low	Very low	Low

*Mammalian toxicity categories:
Acute oral (ppb): Low->500,000-5,000,000; moderate-> 50,000-500,000.
Inhalation (ppb): Very low- >2,000; Low- 500-2.0; High- >0.2.
Dermal (ppb): Very low- >5,000,000; Low- >2,000,000-5,000,000.
Modeled after the U.S. Environmental Protection Agency, Office of Pesticide Programs, Label Review Manual, Chapter 7 (USEPA, 2012C).

As with mammals, the relative toxicity of neonicotinoids to birds varies, both among active ingredients and among species (Gibbons et al., 2014). Clothianidin and thiamethoxam were found to be practically non-toxic to birds with LD_{50} values ranging from 430,000 to >2,000,000 ppb. Dinotefuran was slightly toxic to mallard duck (LD_{50} = 5,000,000 ppb) and Japanese quail (LD_{50} = 1,301,000 ppb) on an acute basis (CRS , 2012; USEPA, 2004). However, imidacloprid has been categorized to have moderate to high toxicity to smaller-bodied bird species such as house sparrows, *Passer domesticus*, and canaries, *Serinus canaria*as compared to being very highly toxicity to grey partridge, *Perdix*, with acute LD_{50} values of 41,000, 35,000, 15,000 ppb, respectively (ABC, 2013; Gibbons et al., 2014; Tomlin, 2006; USEPA, 2014b).

The direct mortality risks to mammals and birds from neonicotinoid contaminated leaves and soils are considered to be low. For example, maximum neonicotinoid residues collected from neonicotinoid-treated sugar beet leaves ranged from 1,000-12,400 ppb (Gibbons et al., 2014; Rouchaud et al., 1994). These residues were at least 10 times lower in magnitude than the lowest LD_{50} values for birds or mammals and thus are unlikely to cause direct mortality risks. However, direct consumption of canola, corn, or soybean treated seeds with up to 1 mg of neonicotinoid active ingredient per seed may be lethal to small granivorous bird species (DeCant and Barrett, 2010). According to one estimate by Goulson (2013), a grey partridge, typically weighing approximately 390 g, would need to eat approximately 5 corn seeds, six beet seeds or 32 oilseed rape seeds treated with clothianidin to receive a dose equivalent to the LD_{50}. A grey partridge typically consumes approximately 25 g of seeds per day, equivalent to about 600 corn seeds; and if those seed had been treated with clothianidin, birds would be exposed to a dose equivalent to greater than the clothianidin LD_{50} (Goulson, 2013). However, the likelihood of significant neonicotinoid exposure for most granivorous birds that visit farmland has not been evaluated. Acute toxicity profile of neonicotinoid compounds to birds is presented in table 15.

Table 15. Acute toxicity profile of neonicotinoid compounds to surrogate bird species.

Neonicotinoid insecticide	*Bird acute oral LD_{50} (ppb)		
	Bobwhite	Japanese quail	Mallard duck
Acetamiprid	180,000	-	98,000
Clothianidin	>2,000,000	430,000	>752,000
Dinotefuran	>2,000,000	>2,000,000	>2,000,000
Imidacloprid	152,000	31,000	283,000
Thiamethoxam	1,552,000	-	576,000
Thiacloprid	2,716,000	-	-

*LD_{50} > 2,000,000 ppb = practically nontoxic; 501,000-2,000,000 ppb = slightly toxic; 51,000-500,000 = moderately toxic; 10,000-50,000 = highly toxic; very highly toxic= <10,000.

Although, neonicotinoids pose low risk to mammals and birds, they have been reported to show sub-lethal impacts to growth, development, and reproduction. Many of these, sub-lethal effects occur at lower concentrations than estimated lethal doses. According to a review by Gibbons et al. (2014) the adverse sub-lethal effects of neonicotinoids on mammals included reduced sperm production, reduced rates of pregnancy, higher rates of embryo death, stillbirth and premature birth, reduced weights of offspring, and adverse effects on the fertilization process. Adverse effects such as lesions of the thyroid, retinal atrophy, reduced movement, increased measures of anxiety and fear, neurobehavioral disorders in offspring have also been reported. Among birds, the effects included testicular anomalies and reduced fertilization success, reduced eggshell thickness and embryo size, reduced hatching success and chick survival, and chick developmental abnormalities (Gibbons et al., 2014).

Some examples of sub-lethal impacts were observed when, dosing rats at 24,400 to 36,800 ppb of clothianidin resulted in reduced body weight and sperm production (Bal et al., 2012), while its use on northern bobwhite quail at >52,000 ppb/day resulted in adverse reproductive effects (ABC, 2013). A review by Gibbons et al. (2014) reported multiple adverse impacts of imidacloprid and clothianidin on mammals (rats, mouse, rabbit) and birds (chicken, mallard, partridge, quail, house sparrow). Weight loss, impaired weight gain, or reduction or cessation of feeding has been reported to occur within all taxa (Gibbons et al., 2014). However, little information exists on the relevant neonicotinoid residues on various crops and soils in Minnesota to estimate the exposure potential and associated sub-lethal effects of those residues on terrestrial mammals, birds, amphibians, or other taxa.

Neonicotinoids are potent insecticides meant for killing harmful insects. However, beneficial insects (predators and parasitoids) may be exposed to neonicotinoids through direct contact from foliar sprays, residues on the surface of treated substrates (vegetation/soil), or through exposure from consumption of contaminated plant material (pollen, nectar, and guttation droplets). For example, carabid beetles showed nearly 100% mortality when they were exposed to corn seedlings treated with field relevant dose of imidacloprid, thiamethoxam, or clothianidin (Mullin et al., 2005). *Harmonia axyridis* larvae (multicolored Asian lady beetle) exhibited neurotoxic symptoms such as trembling, paralysis, and loss of coordination, when they were exposed to corn seedlings grown from seeds treated with the label rates of thiamethoxam or clothianidin (Moser et al., 2008). Similarly, a nectar-feeding wasp, *Anagyrus pseudococci*, showed only 38% survival when imidacloprid was used at labeled rates to treat buckwheat (*Fagopyrum esculentum*) as compared to 98% survival of wasps fed on untreated buckwheat flowers (Krischik et al., 2007). Clothianidin toxicity assays on Monarch butterflies (*Danaus plexippus*) revealed sublethal effects at 1 ppb (Pecenka and Lundgren, 2015). However, it should be noted that exposures and responses are not necessarily unique to neonicotinoids, with adverse effects also occurring from direct and indirect exposures from other insecticides used in the production of corn and other agricultural crops.

Predatory insects and mites may be affected indirectly by neonicotinoid (and non-neonicotinoid) insecticides when they consume contaminated prey. A predaceous ground beetle, *Chlaenius tricolor*, showed a 35% reduction in predation activity when fed a non-target slug pest, *Deroceras reticulatum*, that had consumed soybean seeds treated with a field relevant dose of thiamethoxam. The reduced predation of slugs resulted in a 33% increase in slug density and a 5% decrease in soybean grain yield (Douglas et al., 2014). Other potential indirect effects of neonicotinoid insecticides on predatory insects include reduction in prey host populations and reduced host quality for egg laying (Cloyd and Bethke 2011).

Neonicotinoids may also pose risks to soil inhabiting organisms such as earthworms (Pisa et al., 2014). Neonicotinoid compounds, acetamiprid, imidacloprid, and clothianidin were found to be highly toxic to earthworms (*Eisenia fetida*) with LC_{50} values as low as >1,000 ppb in soil bioassays (Pisa et al., 2014; Wang et al., 2012). Acetamiprid, clothianidin, imidacloprid, and thiacloprid reduced *E. fetida* fecundity by 39.5%, 45.7%, 84.0%, and 39.5%, respectively at the sub-lethal concentrations of 1,500, 2,000, 2,000, and 1,500 ppb, respectively (Wang et al., 2015).

6.8.2 Non-Pollinator aquatic organisms

According to USEPA, the relative toxicity of neonicotinoids to fish and amphibians varies from practically nontoxic to moderately toxic (Gibbons et al., 2014). Review of literature by Gibbons et al. (2014) suggests that clothianidin, dinotefuran, and thiamethoxam are slightly to practically nontoxic to fish and amphibians, while, imidacloprid is moderately toxic to rainbow trout on an acute basis. However, gene transcription, erythrocyte damage, disintegration of gonadal tissue, impaired swimming, notochord degeneration, and locomotor defects in embryos and larvae were reported in fish (Gibbons et al., 2014). Potential effects of acetamiprid on amphibians are not clear, although it exhibits potential acute risks to surrogates of amphibians (USEPA, 2005b).

Measured or estimated environmental concentrations of neonicotinoids in the aquatic environment have been reported to be approximately 2 to 7 orders of magnitude lower than LD_{50} measurements for fish and amphibians. Thus, it is unlikely that mortality rates of these taxa would be directly affected by neonicotinoids under normal exposure at field-realistic doses (Gibbons et al., 2014). Although, neonicotinoids pose low risk to fish they have been reported to show sub-lethal impacts on their growth, development, and reproduction at specific concentrations. A review by Gibbons et al. (2014) reported multiple adverse impacts of imidacloprid and clothianidin on carp, zebra fish, minnow, medaka, tilapia, and catfish at concentrations ranging from 30 to 320,000 ppb. The measured maximum concentration of clothianidin and imidacloprid in Minnesota surface waters in 2014 were 0.260 and 0.467 ppb, respectively (Table 11).

The measured maximum concentration of clothianidin, imidacloprid, and thiamethoxam in Minnesota surface waters in 2014 were 37,307, 2,569, and 89,686 times lower, respectively, than USEPA chronic benchmark values for fish (Table 11). Additive concentrations of clothianidin and thiamethoxam were 20,082 and 41,407 times lower than USEPA chronic benchmark values for fish, respectively. There were no detections of acetamiprid, dinotefuran, and thicaloprid in Minnesota surface waters in 2014. However, dinotefuran was detected in surface waters in 2013 at maximum concentration of 0.03 ppb. The measured maximum concentration of dinotefuran in Minnesota surface waters was 212,000 times lower than USEPA chronic benchmark values for fish. The relationship between measured concentrations and acute benchmark concentration values for fish suggest that fish are unlikely to be adversely affected by neonicotinoid concentrations in the Minnesota waters.

Aquatic invertebrates are extremely important components of aquatic ecosystems and serve as decomposers, grazers, sediment feeders, parasites, and predators. They also provide much of the food that vertebrates within these systems feed upon (Pisa et al., 2014). Unlike terrestrial organisms, aquatic organisms are usually unable to avoid exposures easily by moving to uncontaminated areas, particularly when pesticides are water soluble. Uptake of pesticides in aquatic invertebrates occurs through respiration (gills and trachea), feeding, and through the epidermis (Pisa et al., 2014).

Neonicotinoid compounds, acetamiprid, clothianidin, imidacloprid, thiacloprid, and thiamethoxam are highly toxic to aquatic invertebrates while dinotefuran is practically non-toxic to fresh water aquatic invertebrates (Pisa et al., 2014; USEPA, 2004). Estimates of neonicotinoid acute toxicity to aquatic insects range from 3 to 13 ppb on an acute exposure basis to 0.91 ppb on a chronic exposure bases (Pisa et al., 2014). Imidacloprid acted synergistically with chlorpyrifos on *Chironomus dilutus* midge (LeBlanc et al., 2012). Effects of binary mixtures of imidacloprid and thiacloprid on *Daphnia magna* followed patterns of synergism or concentration addition; however, no clear LC_{50} values were established for the mixtures (Pavlaki et al., 2011). LC_{50} estimates for *B. rhodani* and *S. latigonium* exposed to thiacloprid were 4.6 and 3.7 ppb, respectively (Beketov and Liess, 2008). Toxicity of neonicotinoid metabolites to aquatic invertebrates is considered to be lower than that of the parent compounds (Morrissey et al., 2015). However, clothianidin, a break down product of thiamethoxam has a high toxicity to sensitive aquatic taxa. It should be noted that clothianidin is an active ingredient itself and can be found in several formulated products. According to a review by Pisa et al. (2014) adverse effects of imidacloprid on benthic communities included a 5% reduction in the abundance of invertebrates. Nearly all experiments investigating dose-response relationship report effects on aquatic invertebrates at the lowest concentrations evaluated (Pisa et al., 2014). Because of the frequency at which neonicotinoid compounds are detected in Minnesota surface water systems, they have the potential to impact aquatic invertebrates. In California, imidacloprid was frequently detected in surface waters and exceeded USEPA benchmark for aquatic invertebrates (Starner and Goh, 2012).

In Minnesota, all samples had neonicotinoid concentrations at least 42 times below USEPA acute benchmark values for aquatic invertebrates (Table 11) which are evaluated against a one-day exposure duration. The maximum detected concentrations for clothianidin and imidacloprid were 4.2 and 2.2, times lower, respectively, than USEPA chronic benchmark values for aquatic invertebrates and 1.9 times lower than an imidacloprid chronic LC_{50} value of 0.91 ppb reported by Stoughton et al. (2008) for the chironomid midge, *Chironomus tentans*. The maximum values for clothianidin and imidacloprid detections are numerically approaching the chronic aquatic life benchmarks for invertebrates, though the chronic benchmarks are evaluated against a 4-day exposure duration, which has either not occurred or is being further evaluated with ongoing sampling. In addition, the detection frequency for both these compounds was < 15% of all samples collected from 2011 to 2014, indicating low detection frequencies in Minnesota waters. The detected values for thiamethoxam were 78 times lower than USEPA established acute values for aquatic invertebrates, while there are no USEPA established chronic values for thiamethoxam. There were no detections for acetamiprid, dinotefuran, and thicaloprid in 2014. The measured concentrations of imidacloprid, clothianidin, and thiamethoxam (clothianidin is a break down product of thiamethoxam) are not expected to result in unreasonable adverse effects on aquatic invertebrate communities in the Minnesota surface waters. No specific information exists on chronic or sub-lethal effects of clothianidin or imidacloprid residues on aquatic invertebrate communities in Minnesota.

7 Benefits of neonicotinoids

Neonicotinoid insecticides are currently the most widely used class of insecticides in the world and comprise about 25% of the global agrochemical market. Currently they are registered globally for nearly 140 crops in more than 120 countries (Jeschke and Nauen, 2008; Jeschke et al., 2011). Neonicotinoid insecticides have some distinct advantages over other classes of insecticides such as organophosphates, carbamates, pyrethroids, and chlorinated hydrocarbons. They provide very effective control of piercing and sucking insect pests and some difficult-to-control foliage- and root-feeding insects, such as Colorado potato beetles, termites, and white grub, which have developed resistance to other classes of insecticides (Jeschke et al., 2011). Neonicotinoids show distinct advantages in pest control including efficacy against boring insects and root-feeding insects, both of which cannot easily be controlled using foliar sprays of non-systemic compounds. Neonicotinoids are used to control many major insect pests in Minnesota crops (Table 16).

Table 16. Major soil and foliar insect pests in Minnesota crops based on growers preference (AgInformatics 2014, a,b)

Crop	Soil insects: Soil-applied or Seed treatment	Foliar insects: Foliar treatment	
Canola	Aphids (various) Flea beetle Wireworms	Aphids (various) Armyworms Cabbage curculio Cabbage stem flea beetle	Diamondback moth Flea beetle Plant bugs Saw fly
Small grains	Aphids (various) Wireworms	Aphids (various) Blister beetle Colorado potato beetle	Flea beetle Mexican bean beetle
Corn	Corn rootworm Cutworm Grubs Seedcorn maggot Wireworms	Blister beetle Colorado potato beetle Corn earworm Flea beetle	Japanese Beetle Mexican bean beetle, Rootworm beetle adults
Potato	Tuber flea beetle White grubs Wireworms	Aphids Colorado potato beetle Cutworms	European corn borer Leafhoppers Potato psyllid
Soybean	Seedcorn maggot Wireworm White grub	Aphids Bean leaf beetle Blister beetle Caterpillars Colorado potato beetle	Flea beetle Grasshoppers Leafhoppers Mexican bean beetle Mites
Sugarbeets	Springtails Sugar beet root maggot Wireworms	Sugar beet root maggot (adult)	
Sunflower	Flea beetle, Seedcorn maggot Stored grain insects Sunflower beetle Wireworm	Sunflower beetle Sunflower midge Sunflower stem weevil	

Even though they have been in use for a long period of time (the earliest USEPA neonicotinoid registration occurred in 1991), relatively little resistance has been reported in crop pests under field conditions. Therefore, they have become important tools in insecticide resistance management programs (Jeschke et al., 2011). Neonicotinoids are also known to suppress the secondary spread of insect-transmitted plant pathogens in various crops such as barley yellow dwarf virus in cereal crops (barley, oats, wheat, corn, triticale, and rice) (Jeschke and Nauen, 2008) and the bacterial pathogen *Candidatus liberibacter asiaticus* responsible for causing citrus greening disease in citrus trees (Grafton-Cardwell et al., 2013).

In addition to crop protection, applications of neonicotinoid insecticides in non-agricultural settings such as use within households, lawns, and gardens and for animal health have also expanded in recent years. As previously noted, ash tree protection from emerald ash borer in Minnesota and elsewhere includes the use of imidacloprid, clothianidin, and dinotefuran as soil-applications, trunk-injections, or basal bark sprays. The need for pest control in these non-agricultural settings has led to increased application of neonicotinoids as part of various important IPM programs (Jeschke and Nauen, 2008; Jeschke et al., 2011), as well as part of pest control for cosmetic purposes, or as prophylactic or preventive pest control.

Owing to their systemic activity, they can be applied using a wide range of application techniques including foliar application, incorporation of granules, injection, chemigation, soil treatment, furrow application, drenching, seed dressing (or treatment), pelleting, implantation, dipping, trunk injection, and painting on tree trunks at very low doses. Seed and soil applications represent nearly 60% of their uses worldwide (Jeschke and Nauen, 2008; Jeschke et al., 2011).

Seed treatment provides efficient and prolonged control of insect pests at low dosages when plants are small and most vulnerable to pests. Treating the seed provides protection of the seedling from soil-bound insects as well as from some foliar pests such as western corn rootworm, *Diabrotica virgifera*, whose attacks usually start one or more weeks after the sowing (Van Rozen and Ester, 2010). Given that smaller amounts of the active ingredients are used for seed treatments compared to field applications, theoretically less pesticide is released into the environment, though prophylactic use in the absence of pest pressure can potentially offset this benefit, as can the addition of additional acreage to production systems that benefit from neonicotinoid use.

In addition, the wide-scale and frequent use of these insecticides as seed treatments is disputed. Recently, the USEPA's Biological and Economic Analysis Division completed a draft analysis of the use of neonicotinoid treated seeds as an insect control practice in soybean production (USEPA, 2014c) and concluded that "seed treatments provide negligible overall benefit to soybean production in most situations." The USEPA's overview of published data revealed no difference between soybean yields in seed that was treated with neonicotinoids compared to the control (soybean yield when seeds were not treated with insecticides). As a result, the USEPA determined "that much of the existing usage on soybeans is prophylactic in nature." Since bioactivity of the insecticide in the soybean foliage from a seed treatment lasted about 3 to 4 weeks, and this time period in most cases did not overlap with most soybean pests of concern, the USEPA suggested using available foliar insecticides (including neonicotinoids) when pest populations warranted spraying, and stated that these foliar products were as or more effective on the target pests than the neonicotinoid seed treatments. In some cases, the soil pests targeted by neonicotinoids are generally either occasional, sporadic, or secondary pests, so pest control benefits may not always lead to economic remunerations (Goulson, 2013; Krupke et al., 2012; Pisa et al., 2014; USEPA, 2014c). However, shortly thereafter, as part of comments submitted by pesticide registrants, conclusions made by USEPA on benefits of seed treatment were challenged with additional studies and data suggesting that there are, indeed, yield benefits from the use of neonicotinoid-treated seeds (AgInformatics, 2014a,b). Data submitted to MDA by the Pioneer seed company from long-term (10-12 years) seed treatment trials carried out across 15-20 locations in the US suggested that corn and soybean seed treatment with neonicotinoids resulted in significant economic benefit (>0.8 bushels per acre) over untreated crops. However, pest pressure, crop variety, landscape, and climatic conditions in these trials were either not known or have not been provided to MDA.

Neonicotinoids are considered reduced-risk pesticides by USEPA, due to their low mammalian toxicity. When treated seeds are planted in the soil, the application method generally reduces human exposure to neonicotinoids when compared to other methods of field application by reducing direct exposure to the applicator and drift into the environment. Seed treatment applications also generally limit non-target organism direct exposure, or field runoff from foliar, or soil-applied liquid and granular products. Neonicotinoids have a selective mode of action targeting the same acetylcholine receptor on the insect nerve cell as nicotine (the active ingredient of tobacco). However, in contrast to nicotine, neonicotinoids do not bind well to the nerve cells of humans and, as has been previously discussed, therefore pose little toxicity to humans and other mammals. Other favorable environmental characteristics of neonicotinoids include their ready elimination from the vertebrate body, their relatively rapid breakdown upon exposure to sunlight, and their relative safety to certain natural enemies (predators and parasitoids) when compared to conventional classes of insecticides (Jeschke and Nauen, 2008; Jeschke et al., 2011).

7.1 Alternatives to neonicotinoids

While alternatives to using seed treatments may be effective and include foliar applications of neonicotinoids, as well as applications of older insecticide chemistry classes and modes of action (including the organophosphates, carbamates, and synthetic pyrethroids), such alternatives can also be toxic to bees, other pollinators, and beneficial insects either directly (via contact exposure) or indirectly (via exposure to residues).

The effectiveness of any alternative will depend on how well the alternative pesticide or control practice can substitute for the neonicotinoid in terms of the number of pest species killed, application timing, and how long it remains effective (Zalom et al., 2005). In addition, an alternative's efficacy may vary depending on the insect and its biology, the crop and its value, climate conditions, individual field or greenhouse conditions and micro climates, and the number of insects (its population size and whether it is increasing or decreasing) relative to its economic threshold. There is no single solution that fits all pest management situations; therefore, IPM should be used when making pest management decisions. In addition, pest management programs that rely on fewer chemical choices and foliar applications may result in the evolution of resistance in insect populations (AgInformatics, 2014a,b,c; Gray, 2010).

7.2 Neonicotinoids compared to other conventional insecticides

Prior to neonicotinoid insecticides, organophosphate and carbamate insecticides were popular because they were effective against a broad range of pests, which prevented growers from having to make additional pesticide applications with other products. The widespread use of organophosphate and carbamate insecticides lead to the evolution of resistance in many insect populations, which in turn led growers to adopt synthetic pyrethroids. In many cases synthetic pyrethroids were used as a direct replacement for organophosphates because of their comparable cost, effectiveness against pest species, timing of application, and length of effectiveness (Zalom et al., 2005).

Since neonicotinoid insecticides, to date, have shown little resistance within insect populations, they have largely replaced many uses of synthetic pyrethroid, organophosphate, and carbamate insecticides that insects have evolved resistance to. In addition, neonicotinoids have other positive attributes such as a unique mode of action, systemic uptake in plants, high toxicity to insects allowing for use at lower concentrations, and low mammalian toxicity (Zalom et al., 2005). While neonicotinoid insecticides have some unique advantages over other insecticide classes, it is important that they be used in rotation with other insecticides modes of action to prevent future pest resistance.

Research evaluating biological control agents' effectiveness at controlling some major pests has some shown positive results. For example, the most serious pests of dent corn (variety of corn with a high starch content) in the Midwest and Canada are the western (WCR) and northern (NCR) corn rootworm beetles (Levine and Oloumi-Sadeghi, 1991). Research evaluating biological control options for this serious pest, showed adequate protection below the commercially acceptable root rating (root injury rating below 3) and reduced corn rootworm adult emergence at the two highest application rates of the entomopathogenic nematode, *Steinernema carpocapsae* (Journey and Ostlie, 2000). Research using fungal pathogens is usually impacted by environment (temperature and moisture) thus variable results are common. Trials evaluating entomopathogenic fungi *Metarhizium anisopliaea* and *Beauveria bassiana* for southern rootworm control showed positive but variable results year to year (Braga et al., 2001).

Biological control is not intended to work alone. Kuhlmann and van der Burgt (1998) reviewed biological options for controlling the introduced western corn rootworm in Europe as part of an integrated pest management approach that includes monitoring pest populations, releasing biological control agents, cultural practices to enhance beneficial organisms, crop rotation, and orientation disruption of adults. Research by Degenhardt et al. (2009) is a more recent example demonstrating increased effectiveness integrating strategies; i.e. utilizing a biological control agent in combination with modern corn breeding to restore lost volatile genes that attract entomopathogenic nematodes. This combined strategy provides a natural defense to rootworms.

7.3 Neonicotinoids and IPM

There are many working definitions of Integrated Pest Management (IPM). In general, IPM is a crop production system that uses economically, environmentally, and sociologically sound methods to control or manage pests. This sustainable pest management approach integrates biological, cultural, physical, mechanical, and chemical practices after crop scouting and monitoring of pest populations determines that conditions warrant some control in order to prevent significant economic loss. IPM reduces pesticide use and cost by determining whether there is a need to use chemical control. IPM helps build beneficial organism populations that may be negatively impacted by widespread or unnecessary pesticide use. However, sometimes when control is needed, using a pesticide may be more cost-effective and efficacious than alternative non-chemical methods of control. University Extension Services have developed unbiased scouting information, and guidance regarding economic thresholds or other risk factors to assist producers and the public with making pest management decisions including those that require smart use of a pesticide. However, scouting methods and economic thresholds do not exist for all insects and more research is needed to develop effective scouting techniques and thresholds.

The goals of IPM

- Optimizing control of pests (hold pest populations below economic injury levels, nuisance levels, or public health concerns).
- Increasing yield or quality, protecting a structure or investment, or protecting public health must be of sufficient benefit to justify attendance risks or the cost of control.
- Utilizing control methods to minimize adverse environmental effects.
- Utilizing control methods generally acceptable to society.

The use of systemic neonicotinoids in the absence of a supported need for insect control may contribute to a paradigm that moves away from traditional integrated pest management. IPM is predicated on minimizing use and increasing efficacy of appropriately-timed chemical pesticides via monitoring of pest populations, making maximum use of biological, mechanical, and cultural controls, and only applying chemical pesticides when needed (Furlan and Kreutzweiser, 2014). If used properly, seed treatments can lower non-target exposure and risk compared to soil or foliar insecticide applications. Using neonicotinoid seed treatments in the absence of specific identified pest problems may lead to resurgence of the target pest, replacement by secondary pests, adverse impacts on natural enemies and pollinators, development of pest resistance, and increased costs.

8. Proposed action steps regarding use of neonicotinoids

Based on the review, the MDA identified several opportunities for action to minimize the impact of neonicotinoids on pollinators.

1. Action: Create a Treated Seed Program (Requires Legislative Action)

Currently, the State does not have the authority to regulate the sale and use of pesticide treated seeds; they are considered to be "Treated Articles" and not pesticides. Treated articles that meet USEPA's exemption criteria are not subject to USEPA or MDA pesticide regulations. The Treated Seed Program will provide the State with the authority to regulate seeds treated with pesticides. The program will also fund research to develop need based recommendations for the use of seed treatments. The program may also require that untreated seeds and seeds treated at lower pesticide application rates are available in the market. The program would be funded through a new pollinator protection account. Creation of such a program will require legislative action.

Seed treatments protect young plants against early-season soil and foliage pests, reduce potential risks to workers, minimize potential runoff to waterways, and lower the overall amount of pesticide usage. However, broad-scale and prophylactic uses of seed treatments with pesticides such as neonicotinoids may increase the risk to the environment and specifically to pollinators. Therefore, it is important that treated seed use decisions be based on the best available science and Minnesota specific conditions. The treated seed program will provide staff and resources to ensure a sound understanding of efficacy of seed treatment rates, scouting techniques, pest pressures, economic thresholds, planting technology differences, etc. In addition, farmers may not have ready access to untreated seed or seed treated at lower pesticide application rates. The MDA will continue to evaluate national and international research for its applicability to Minnesota specific conditions. The MDA will also work with the University of Minnesota and other interested parties to identify the research needs and projects. Appropriate changes will be introduced on the use of treated seeds based on the outcome of research data.

2. Action: Create a Dedicated "Pollinator Protection Account" (Requires Legislative Action)

Create a dedicated "Pollinator Protection Account" funded through fees on pesticide treated seeds and on pesticides classified by the USEPA as moderately or highly toxic to pollinators on acute exposure basis. The program will carry out activities related to pollinators including evaluating and supporting research on economic thresholds, developing an educational campaign on use of pesticides, development of stewardship materials, etc. Creation of such an account would require legislative action.

3. Action: Require Formal Verification of Need Prior to Use of Neonicotinoid Pesticides, Where Appropriate

Application requirements restricting foliar application of neonicotinoid pesticide products on pollinator attractive food crops and commercially grown ornamentals while bees are foraging and until flowering is complete already exist on product labels. This includes applications to soybeans, the most important crop for neonicotinoid use in Minnesota. Under these requirements farmers would be able to apply neonicotinoids when the application is needed because of an imminent threat of significant crop loss, consistent with an IPM plan, or when a predetermined economic threshold is met. However, what qualifies as an imminent threat or an adequate IPM plan requires further definition for Minnesota specific conditions.

The MDA will work with the U of M and other stakeholders to develop pest thresholds and acceptable IPM criteria that should be used to justify product application before final flowering for those products and crops which currently have these requirements on the label. The MDA will also work with the U of M and other stakeholders to develop need based guidance and acceptable IPM criteria for other significant crop uses of neonicotinoids.

As this criteria is developed there will be an education period where it is widely promoted through multiple channels including pesticide applicator training and in coordination with registrant stewardship and other educational activities. The MDA will ensure that applications of neonicotinoids are made only when a qualified individual verifies that there is a demonstrated pest problem and there is a need for neonicotinoid pesticide use. The MDA will develop a formal process for verification of need by a trained and approved individual prior to the use of neonicotinoid pesticides on crops.

These requirements would be phased in over time as Minnesota specific pest thresholds and similar need based guidance becomes available and would only apply to products and uses which have MDA approved need based guidance for their use.

4. Action: Develop an Educational Campaign for Homeowners and Residential Users of Insecticides

An educational campaign to educate homeowners and other residential users of insecticides would be developed. The campaign will include educational activities to promote appropriate practices for use of all insecticides. Emphasis would be on neonicotinoids. The campaign would be funded through the pollinator protection account.

5. Action: Review Product Labels for Appropriate Use of Neonicotinoids for Homeowners and Residential Users

On an ongoing basis, the MDA will review product labels for appropriate urban and suburban uses and restrictions of neonicotinoids to minimize the impact to pollinators. The MDA in consultation with the U of M and other interested parties would identify products and uses with a high potential for pollinator exposure. The MDA will then work with registrants to make Minnesota specific label changes. For example, registrants may be asked to evaluate and lower neonicotinoid application rates or approved uses for certain pollinator attractive plants. The MDA will also reevaluate appropriate actions following completion of the USEPA neonicotinoid registration review (due for completion in 2017).

6. Action: Develop Minnesota Specific Pollinator Stewardship Materials

MDA would work with pesticide registrants to develop additional stewardship materials and a stewardship program to promote practices targeted at minimizing non-target exposure to pollinators in Minnesota. Separate stewardship material would be developed to address exposure concerns related to:

- Insecticide treated seed
- Agricultural use of soil and foliar applied neonicotinoids
- Home and residential use of neonicotinoids

The MDA will increase use inspections for insecticides that are classified as highly toxic to pollinators on acute exposure basis. EPA has added a pollinator protection box to foliar insecticides that are considered highly toxic to pollinators. Increased inspections will increase the attention on concerns for pollinators and will enforce the label requirements related to pollinators. Targeted inspections by the MDA would increase awareness among applicators that language contained in the pollinator protection box is important and product use provisions are being enforced.

7. Action: Increase Use Inspections for Insecticides that are Highly Toxic to Pollinators

MDA will increase use inspections for insecticides that are classified as highly toxic to pollinators on acute exposure basis. EPA has added a pollinator protection box to foliar insecticides that are considered highly toxic to pollinators. Increased inspections will increase the attention on concerns for pollinators and will enforce the label requirements related to pollinators. Targeted inspections by the MDA would increase awareness among applicators that language contained in the pollinator protection box is important and product use provisions are being enforced.

8. Action: Review Label Requirements for Individual Neonicotinoid Products

The MDA will review product labels for enforceable language and appropriate requirements. After reviewing and identifying the language steps may be taken to clarify and revise the label language. Some insecticide products that are acutely toxic to pollinators have language that is unclear or may be interpreted as advisory rather than enforceable. The MDA will review label language to ensure that label requirements for neonicotinoid products are appropriate for Minnesota specific conditions and are clear, unambiguous and enforceable.

Appendix 1: A brief review of *Apis mellifera* health stressors

Managed honey bees (*Apis mellifera*) are the most important pollinator of agricultural crops worldwide. More than 70% of the food crops including fruits, vegetables, tree nuts, forage crops, some field crops, and other specialty crops are dependent on insect pollinators for pollination (Klein et al., 2007). Honey bees are managed for both honey production and pollination services. In addition to honey production, managed honey bees are ideally suited for pollination because of their body structure and biology, relatively large year round populations (10,000–40,000 individuals), easy transport of colonies over large distances to pollination sites, and ease of colony manipulation for providing pollination services (vanEngelsdorp and Meixner, 2010).

Long-term colony declines and annual colony losses

Surveys of managed honey bees in terms of the number of honey-producing colonies tabulated by the USDA National Agricultural Statistics Service (NASS) shows that the number of managed colonies in the US. has declined over the last half century (Figure 4). Declines in honey bee colonies have been attributed to several factors including biological, political, and socioeconomic factors associated with honey prices, and counting methods (Aizen and Harder, 2009; vanEngelsdorp and Meixner, 2010). For example, a steep reduction of about one million colonies during the 1980s (Figure 4) coincides with NASS discontinuing the inclusion of colonies from operations with five or fewer hives (vanEngelsdorp and Meixner, 2010).

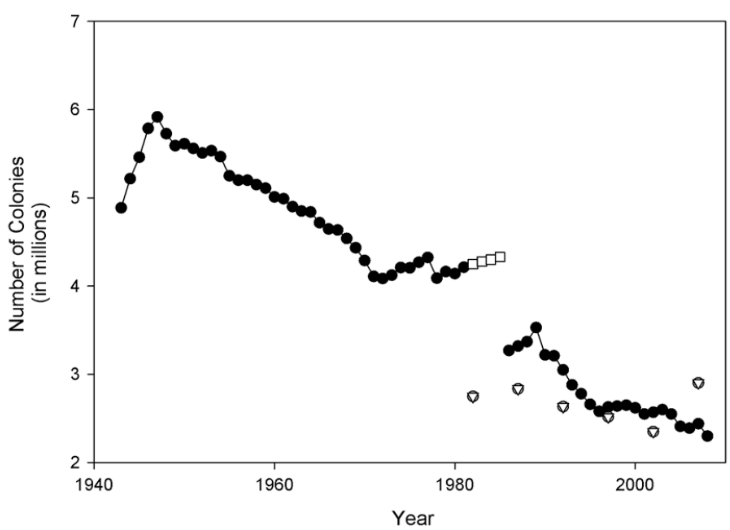

Figure 4. Number of managed honey bee colonies in the United States from 1944-2008 (adapted from vanEngelsdorp and Meixner, 2010).

Number of managed honey bee colonies in the United States of America 1944-2008. Annual estimates of the number of honey-producing colonies (solid circles) were obtained from the annual honey reports with the expectation of the years 1982-1985 when the survey was discontinued. During these years estimates are provided by the USDA Agricultural Stabilization and Conservation Service (hollow squares). Estimates of the total number of colonies as inventoried by AG census are also provided (hollow triangles).

Similarly, suspension of federal support of honey prices in the U.S. in 1996 and the cessation of exports from the US to Canada in 1987 led to a loss of 250,000 colonies a year in California alone (vanEngelsdorp and Meixner, 2010). Standardized periodic surveys that quantify colony numbers provide a measure of total losses and/or gains over a period, but do not necessarily capture actual colony losses over that period (vanEngelsdorp and Meixner, 2010). Annual colony losses are designated as colonies that fail each year. Beekeepers can replace losses (i.e. winter losses) by splitting surviving colonies and/or by purchasing and installing packages of bees (vanEngelsdorp et al., 2008). Therefore, in some cases the number of colonies reported by a given periodic survey can remain stable or even increase when substantial losses have occurred between survey dates (vanEngelsdorp and Meixner, 2010). For example, the total number of colonies recorded by the honey report increased by 5% between 2006 and 2007 even though estimated overwintering loss were 32% and 36% in the winters of 2006–2007 and 2007–2008, respectively (vanEngelsdorp and Meixner, 2010).

According to the annual survey conducted by the Bee Informed Partnership and the USDA, total losses of managed honey bee colonies from all causes in the U.S. were 23.2 percent for the 2013-2014 winter as compared to 30.5 percent loss reported for the winter of 2012-2013, 21.9 percent in 2011-2012, 30 percent in 2010-2011, 33.8 percent in 2009-2010, about 29 percent in 2008-2009, about 36 percent in 2007-2008, and about 32 percent in 2006-2007. Although, precise reasons for fluctuations in honeybee population are not known; queen failure, poor wintering conditions, and damage by *Varroa* mites are among the leading causes of colony losses as self-reported by beekeepers in annual surveys. The average and total winter losses reported from Minnesota beekeepers from 2010 to 2014 surveys ranged from 42.64 to 65.85 and 17.74 to 38.73 percent, respectively (Figure 5, USDA, 2015b).

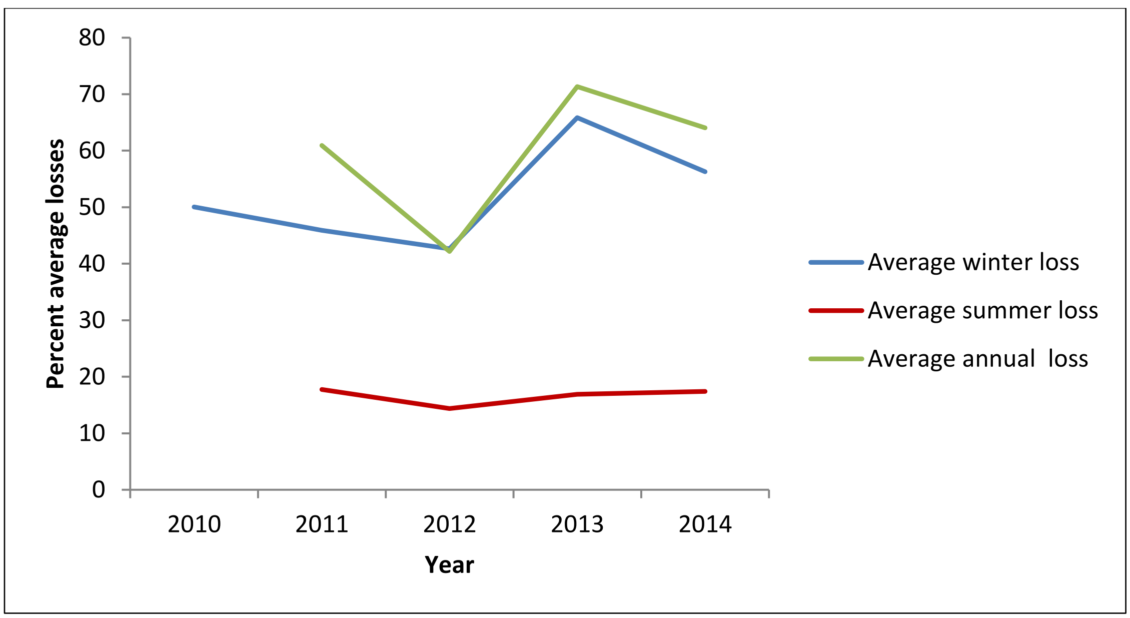

Figure 5. Average bee losses experienced by Minnesota beekeepers from 2010 to 2014.
"Average loss" represents the average level of loss experienced by a beekeeper in its operation.

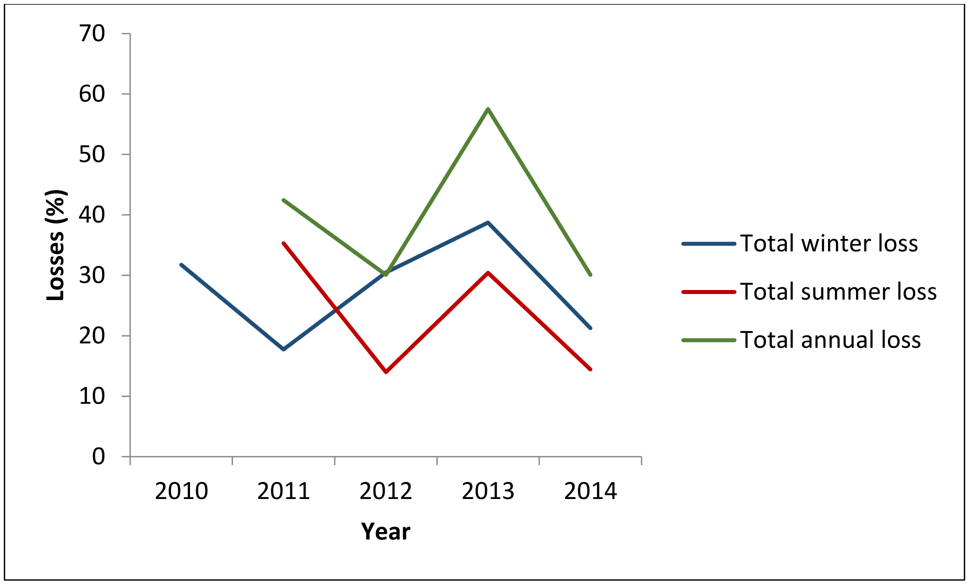

Figure 6. Total honey bee colony losses experienced by Minnesota beekeepers from 2010 to 2014. "Total loss" is the estimate of the number of colonies lost by the whole beekeeping population. Total annual losses differ from the sum of summer and winter losses reported because of differences in responding individuals during each season.

Colony collapse disorder (CCD)

In October 2006, some beekeepers reported 30-90 percent losses of their honey bee hives. While losses of 15 to 30% are not unexpected, especially over the winter, the magnitude of reported losses were unusually high. The term colony collapse disorder (CCD) was introduced to describe these losses because no single factor could explain the reasons for high mortality (Smith et al., 2013). The main symptom of CCD is a low number of adult bees in the hive with few or no dead bees in or around the colony; food stores, the queen, and immature bees (brood) remain present in the hive. Colonies with CCD have no outward signs of disease, pests, or parasites and the bees are reluctant to consume food provided to them by the beekeeper (Oldroyd, 2007; vanEngelsdorp et al., 2009). Numerous causes of CCD have been proposed however, the causes and significance of CCD are still unclear (vanEngelsdorp et al., 2009). The proposed causes of CCD include: bee pests and pathogens, management stresses, poor genetic biodiversity, chemical use in bee colonies to control bee pests/pathogens, chemical toxins present in the environment, bee nutritional fitness, undiscovered/newly discovered pests and pathogens or increasing virulence of existing pathogens, and potential synergistic interactions between two or more of the above possible causes (vanEngelsdorp et al., 2009).

Bee stressors

Effect of stressors on honey bee colony health and population decline are still poorly defined. There are numerous factors such as viral and fungal diseases, parasitic mites, habitat loss, plant and bee protection products, nutritional deficiencies, and hive management practices that can negatively impact honey bee health (Figure 7).

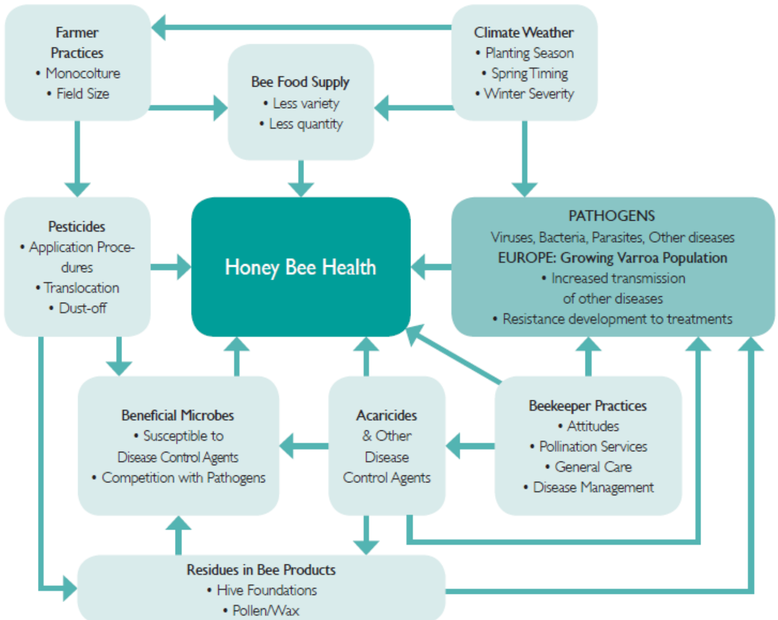

Figure 7. Interrelationship of bee health stressors (adapted from Le Conte et al., 2010).

Bee pests and pathogens

There are numerous pests and pathogens that can negatively impact honey bee health including parasitic mites, viruses, microsporidia, bacteria, fungi, and insects (vanEngelsdrop and Meixner, 2010). Pathogens and pests are known to cause annual colony losses and have been corratively linked to long-term declines in bee populations. The parasitic mite, *Varroa destructor,* is the most serious pest of honey bee colonies and one of the primary causes of honey bee decline. Although the *Varroa* complex includes multiple species, *V. destructor* is the species responsible for the vast majority of the damage attributed to mites from this genus. A honey bee colony infested with *V. destructor* is likely to die within one to three years if left untreated (Fries et al., 2006; Moore et al., 2014). *V. destructor* are ectoparasites that feed on the hemolymph of immature and adult honey bees. The mites injure bees physically, reduce a bee's protein content and body weight, interfere with organ development, and transmit numerous viruses including Deformed Wing Virus (DWV), Black Queen Cell Virus (BQCV), Kashmir Bee Virus (KBV), Cloudy Wing Virus (CWV), and Sacbrood Virus (SBV) and many more. The viruses cause morphological deformities (small body size, shortened abdomen, deformed wings) and weakens the bee's immune system. These viruses also reduce bee longevity, worker survivorship, and colony fitness (Le Conte et al., 2010). Traditionally, *Varroa* mites have been controlled chemically. Some pesticides are available to control mites in the hive; however, mites have developed resistance to some products, thereby reducing the effectiveness of these control methods. Because of the reduced efficacy of chemicals used to control *Varroa*, a number of nonchemicals methods are under investigation by scientists, including evaluation of breeding programs to develop tolerant strains of domestic honey bees. Another common pathogen is the microsporidian *Nosema* spp. which causes bee dysentery. *Nosema* has been cited as the cause of significant colony losses in Spain, though such mortality has not been documented in the United Sates (Smith et al., 2013). In addition to pathogens, a wide range of predators including insects (moths, beetles), spiders, amphibians, reptiles, and mammals can adversely affect managed honey bee productivity and survival. However, healthy colonies can usually manage such pests without significant harm to the colony although a beekeeper may feel their presence unsanitary or unsightly (Gupta et al., 2014; Higes et al., 2009; Morse and Flottum, 1997; vanEngelsdrop and Meixner, 2010).

Table 17. Some of the common managed honeybee diseases and pests.

Disease/Pest	Cause	Symptom/Effect
Chalkbrood	Fungus *Ascophera apis*	Mummified larvae White or black
Nosema	Microsporidia *Nosema apis*	Dysentery, reduced lifespan, reduced ability to feed larvae
American Foulbrood (AFB)	Bacteria *Paenibacillus larvae*	Dead larvae/pupae on back, extended tongues, "ropy" condition, dried brittle scales, sunken cappings
European Foulbrood (EFB)	Bacteria *Melissococcus pluton*	Dead larvae all positions, slight ropiness, rubbery scales, sour smell
Tracheal mites	*Acarapis woodi*	Spring crawling, k-wing, reduced adult longevity, colonies die in early spring, microscopic examination
Varroa mites	*Varroa jacobsoni* *Varroa destructor*	Visible mites, deformed wings, reduced longevity, colony loss, PMS (parasitic mite syndrome)
Wax Moths	*Galleria mellonella* *Achroia grisella*	Visible damage to wax and stored food, cocoons, moths, silk webbing
Stone brood	*Aspergillus sp.*	Larvae and pupae turn into hard stone — like mummies
Mice	—	Mice in hives, comb destruction

Loss of habitat

Habitat loss and fragmentation are considered to be major contributors to the decline of insect pollinator populations. Bees need high quality forage consisting of a variety of plant species to support good nutrition and health. Poor nutrition can result in reduced longevity and increased susceptibility to disease and parasites. Flower-rich habitat has decreased with increased: agricultural land planted in monoculture, resource extraction, and urban and suburban development. Habitat loss can negatively affect the timing and amount of food availability, thereby increasing competition for limited resources. Fragmented habitats also restrict the movement and population size of pollinators. In addition, modern practices of monoculture cropping rely on herbicides for the removal of weeds, which are often used by pollinators as forageand futher limits food availability for pollinators.

Hive management practices

While habitat loss is a major driver of wild bee declines, managed honey bees have been bred for certain triats (reduced aggression, earlier build up, the amount of food provisioned) which can be advantgeous for management but can, in some instences, lead to unintended selection pressure resulting in acompromised immune system. Reduced immune function can leave honey bees susceptible to pests and diseases resulting in increased risk of hereditable diseases, loss of vitality or vigour, and heightened susceptibility to infectious diseases. Poor nutrition due to apiary overcrowding, increased migratory stress brought on by the honey bees being transported to multiple locations across the country, and use of in-hive pesticides to manage honey bee pathogens and pests are other management stressors considered to be related to bee decline.

Abiotic factors

In addition to the botic stresses, the variability and inconsistency of seasonal weather patterns can also impact bee health, especially with regard to overwinter survival rates. Periods of drought or continuous rain can negatively affect colony productivity. Unseasonably cool temperatures can result in increased losses due to temperature related mortality. Changes in climatic factors may also result in new bee pests and predators that were not previously present in the region. Starvation, long-distance transportation, and exposure to pesticides are some of the stressors that have also been reported to contribute to honey bee losses (Ahn et al., 2012; vanEngelsdorp et al., 2008).

Appendix 2: USEPA neonicotinoid registration review activity

Determination of insecticide toxicity to endangered species

To assess the potential risk to an endangered or threatened species (listed species), listed species are screened to determine if there are potential overlapping sites of a pesticides use and the species' habitat. If the listed species habitat overlaps with the potential pesticide use area, a listed species determination will be conducted to determine if the species of interest or its habitat "may be" adversely affected. If the assessment shows there is potential for the pesticide to affect a listed species, a refined assessment will be conducted to see if it is "likely to adversely affect" that species. If USEPA finds the pesticide may affect the listed species but is not likely to adversely affect the species of concern, the U.S. Fish and Wildlife Service (USFWS) and National Marine Fisheries Services (NMFS) will both be consulted for an agreed upon determination. If USEPA finds the pesticide is likely to adversely affect a listed species, the USFWS and NMFS will enter into a formal consultation process ending in a biological opinion document to USEPA. This document may be used to mitigate adverse effects to the species of concern by altering the terms of registration.

Refined fish and aquatic organism assessment

The USEPA has identified aquatic organism data gaps for the neonicotinoid active ingredients, acetamiprid, clothianidin, and thiamethoxam. For acetamiprid, uncertainty exists for how well information submitted on water flea represents other aquatic invertebrate taxa. For this reason, tests using two additional immature aquatic invertebrates has been requested. Data gaps for clothianidin and thiamethoxam are also related to aquatic invertebrates. Because studies originally submitted to fill these data gaps were considered supplementary[4], the USEPA has requested that registrants submit toxicity information for the chronic exposure of these active ingredients on freshwater midges in sediment.

Refined avian assessment

All neonicotinoids, except imidacloprid, undergoing USEPA registration review have gaps in their avian toxicity testing information. Gaps exist for the acute oral toxicity and/or reproduction of passerines. Passerines are perching birds and represent the largest diversity of species and individuals within the US. The USEPA has requested that registrants carryout additional studies so refined assessments can be made for the effects these chemicals may have on birds. The USEPA requires that passerines be tested for acute oral toxicity due to their higher metabolic rate (stemming from their low body weights) and utilization of different metabolic pathways when compared to other bird orders. Available information on acetamiprid showed a very high acute oral toxicity to passerines. Additionally, effects observed in the completed studies for other neonicotinoids included the thinning of egg shells (imidacloprid, and $<3.5\%$ for clothianidin), and fewer normal hatchlings compared to the total number of eggs laid (thiacloprid).

Refined soil and aquatic metabolism assessments

Understanding the degradation rate of an insecticide is used by USEPA for analysis in Pesticide Root Zone Model and Exposure Analysis Modeling System or (PRZM) and (EXAMS) respectively. These models are used to develop estimated environmental concentrations (EECs) which occur in soil and aquatic systems. In addition to any available empirical data on residue impacts on the environment (monitoring, studies, and peer-reviewed research) the EECs can then be used to evaluate the risk posed to different organism groups. The USEPA has requested additional soil and aquatic metabolism studies to understand how neonicotinoids are metabolized in four types of soil and within aquatic environments with two different sediments.

Plant toxicity

For all outdoor uses of pesticides, terrestrial and aquatic plant studies are required to ensure no unreasonable damage occurs to non-target plants due to a pesticide application. Several incidents of phytotoxicity have been reported involving the application of imidacloprid to lawns. In response, the USEPA has requested a variety of plant emergence, vigor, and growth studies for imidacloprid. For other neonicotinoids undergoing review, aquatic and terrestrial plant studies may be requested if studies previously submitted were considered supplemental.[4] Additionally, the USEPA may determine that species tested do not accurately represent the range of effects a pesticide may have to a group of plants and may therefore request additional species to be evaluated.

Indirect effects

During the registration review process, the USEPA may consider potential indirect effects posed to non-target organisms by the parent and degradate compounds. Examples of some indirect effects that may be considered are effects to plant reproduction associated with a decline in pollinating insects, or effects to fish populations dependent on insecticide-vulnerable aquatic organisms for food.

Human health aggregate exposure

To address the potential impact an insecticide may have on humans, the USEPA conducts a human health risk assessment to look at dietary, residential, and occupational exposures. Aggregate assessments are also included to account for combined exposure from dietary and residential handler / post-application exposures. These assessments may be done for short, intermediate, and long-term exposure durations and depend on the registered uses for the insecticide. For imidacloprid, a long-term aggregate risk assessment will be conducted due to its use on domestic pets. For the other neonicotinoids under registration review, aggregate risk assessments may be added or revised to include changes to toxicological endpoints, residential and/or dietary risks.

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[4] A toxicity study is categorized as to its usefulness in a risk assessment. The three general categories used for classifying scientific studies are (1) Core or Acceptable, (2) Supplemental, Upgradable, or Ancillary, and (3) Invalid or Unacceptable. Only studies from (1) or (2) can be used in risk assessment determinations, though more refined studies may be necessary for information considered supplemental. More information available at http://www.ipmcenters.org/Ecotox/DatabaseGuidance.pdf

Immunotoxicity

The human health risk assessment also evaluates studies on immunotoxicity. Immunotoxicity studies are used to help determine if chronic exposure to an insecticide has a potential to suppress the immune system, and make a person more susceptible to bacterial and viral infections. As part of registration review, the USEPA has requested such studies from registrants of imidacloprid and thiacloprid. If the immunotoxicity studies show the potential to suppress human immune systems, above the levels of concern, the risk assessments may be revised to mitigate these effects.

Inhalation

The risk of human inhalation of a neonicotinoid may occur if the chemical drifts, volatilizes, or is re-suspended from an application, use, or during occupational work (e.g. seed treatment, soil drench, or foliar application, treating or using treated wood, application to turf, or use in poultry houses). Insecticides like thiamethoxam are approved for use as a wood preservative and may result in exposures up to 6 months after application. The USEPA registration reviews will use the results from a 21/28 day rat inhalation study to recalculate inhalation values for clothianidin, thiamethoxam, and acetamiprid to ensure no unreasonable exposures occur.

Dislodgeable/transferable residues

Another form of exposure can result from insecticide residue being dislodged or transferred from application sites. Possible application sites include, treated fields, lumber, and pet (flea and tick) products. The USEPA will reevaluate exposure from these sources to account for changes in residential standard operating procedures and occupational uses.

Appendix 3: Label additions for protection of pollinators

Below are two examples of how the Protection of Pollinator information may be formated.

Example 1:

PROTECTION OF POLLINATORS

APPLICATION RESTRICTIONS EXIST FOR THIS PRODUCT BECAUSE OF RISK TO BEES AND OTHER INSECT POLLINATORS. FOLLOW APPLICATION RESTRICTIONS FOUND IN THE DIRECTIONS FOR USE TO PROTECT POLLINATORS.

Look for the bee hazard icon in the Directions for Use for each application site for specific use restrictions and instructions to protect bees and other insect pollinators.

This product can kill bees and other insect pollinators

Bees and other insect pollinators will forage on plants when they flower, shed pollen, or produce nectar.

Bees and other insect pollinators can be exposed to this pesticide from:

- o Direct contact during foliar applications, or contact with residues on plant surfaces after foliar applications
- o Ingestion of residues in nectar and pollen when the pesticide is applied as a seed treatment, soil, tree injection, as well as foliar applications.

When Using This Product Take Steps To:

- o Minimize exposure of this product to bees and other insect pollinators when they are foraging on pollinator attractive plants around the application site.
- o Minimize drift of this product on to beehives or to off-site pollinator attractive habitat. Drift of this product onto beehives or off-site to pollinator attractive habitat can result in bee kills.

Information on protecting bees and other insect pollinators may be found at the Pesticide Environmental Stewardship website at: http://pesticidestewardship.org/PollinatorProtection/Pages/default.aspx.

Pesticide incidents (for example, bee kills) should immediately be reported to the state/tribal lead agency. For contact information for your state, go to: www.aapco.org/officials.html. Pesticide incidents should also be reported to the National Pesticide Information Center at: www.npic.orst.edu or directly to EPA at: beekill@epa.gov

CONDITIONS OF SALE AND LIMITATION OF WARRANTY AND LIABILITY

NOTICE: Read the entire Directions for Use and Conditions of Sale and Limitation of Warranty and Liability before buying or using this product. If the terms are not acceptable, return the product at once, unopened, and the purchase price will be refunded.

The Directions for Use of this product must be followed carefully. It is impossible to eliminate all risks inherently associated with the use of this product. Crop injury, ineffectiveness or other unintended consequences may result because of such factors as manner of use or application, weather or crop conditions, presence of other materials or other influencing factors in the use of the product, which are beyond the control of SYNGENTA CROP PROTECTION, LLC or Seller. To the extent permitted by applicable law, Buyer and User agree to hold SYNGENTA and Seller harmless for any claims relating to such factors.

SYNGENTA warrants that this product conforms to the chemical description on the label and is reasonably fit for the purposes stated in the Directions for Use, subject to the inherent risks referred to above, when used in accordance with directions under normal use conditions. To the extent permitted by applicable law: (1) this warranty does not extend to the use of the product contrary to label instructions, or under conditions not reasonably foreseeable to or beyond the control of Seller or SYNGENTA, and (2) Buyer and User assume the risk of any such use. TO THE EXTENT PERMITTED BY APPLICABLE LAW, SYNGENTA MAKES NO WARRANTIES OF MERCHANTABILITY OR OF FITNESS FOR A PARTICULAR PURPOSE NOR ANY OTHER EXPRESS OR IMPLIED WARRANTY EXCEPT AS WARRANTED BY THIS LABEL.

To the extent permitted by applicable law, in no event shall SYNGENTA be liable for any incidental, consequential or special damages resulting from the use or handling of this product. **TO THE EXTENT PERMITTED BY APPLICABLE LAW, THE EXCLUSIVE REMEDY OF THE USER OR BUYER, AND THE EXCLUSIVE LIABILITY OF SYNGENTA AND SELLER FOR ANY AND ALL CLAIMS, LOSSES, INJURIES OR DAMAGES (INCLUDING CLAIMS BASED ON BREACH OF WARRANTY, CONTRACT, NEGLIGENCE, TORT, STRICT LIABILITY OR OTHERWISE) RESULTING FROM THE USE OR HANDLING OF THIS PRODUCT, SHALL BE THE RETURN OF THE PURCHASE PRICE OF THE PRODUCT OR, AT THE ELECTION OF SYNGENTA OR SELLER, THE REPLACEMENT OF THE PRODUCT.**

SYNGENTA and Seller offer this product, and Buyer and User accept it, subject to the foregoing Conditions of Sale and Limitation of Warranty and Liability, which may not be modified except by written agreement signed by a duly authorized representative of SYNGENTA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

See individual crops for specific pollinator protection application restrictions. If none exist under the specific crop, for foliar applications, follow these application directions for crops that are contracted to have pollinator services or for food/feed crops & commercially grown ornamentals that are attractive to pollinators.

FOR CROPS UNDER CONTRACTED POLLINATION SERVICES

Do not apply this product while bees are foraging. Do not apply this product until flowering is complete and all petals have fallen unless the following condition has been met:

If an application must be made when managed bees are at the treatment site, the beekeeper providing the pollination services must be notified no less than 48-hours prior to the time of the planned application so that the bees can be removed, covered or otherwise protected prior to spraying.

FOR FOOD/FEED CROPS AND COMMERCIALLY GROWN ORNAMENTALS NOT UNDER CONTRACT FOR POLLINATION SERVICES BUT ARE ATTRACTIVE TO POLLINATORS

Do not apply this product while bees are foraging. Do not apply this product until flowering is complete and all petals have fallen unless one of the following conditions is met:

- **The application is made to the target site after sunset**
- **The application is made to the target site when temperatures are below 55°F**
- **The application is made in accordance with a government-initiated public health response**
- **The application is made in accordance with an active state-administered apiary registry program where beekeepers are notified no less than 48-hours prior to the time of the planned application so that the bees can be removed, covered or otherwise protected prior to spraying**
- **The application is made due to an imminent threat of significant crop loss, and a documented determination consistent with an IPM plan or predetermined economic threshold is met. Every effort should be made to notify beekeepers no less than 48-hours prior to the time of the planned application so that the bees can be removed, covered or otherwise protected prior to spraying.**

Example 2:

ENVIRONMENTAL HAZARDS

This pesticide is toxic to aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Do not apply when weather conditions favor drift from treated areas. Drift and runoff from treated areas may be hazardous to aquatic organisms in water adjacent to treated areas. Do not dispose of equipment washwaters or rinsate into a natural drain or water body.

This product is toxic to honey bees. The persistence of residues and potential residual toxicity of dinotefuran in nectar and pollen suggests the possibility of chronic toxic risk to honey bee larvae and the eventual instability of the hive.

- This product is toxic to bees exposed to residues for more than 38 hours following treatment.
- Do not apply this product to blooming, pollen-shedding or nectar-producing parts of plants if bees may forage on the plants during this time period, unless the application is made in response to a public health emergency declared by appropriate state or federal authorities.

Dinotefuran and its degradate, MNG, have the properties and characteristics associated with chemicals detected in groundwater. The high water solubility of dinotefuran, and its degradate, MNG, coupled with its very high mobility, and resistance to biodegradation indicates that this compound has a strong potential to leach to the subsurface under certain conditions as a result of label use. Use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination.

PHYSICAL OR CHEMICAL HAZARDS

Do not use, pour, spill or store near heat or open flame.

SPRAY DRIFT ADVISORY

Do not apply under conditions involving possible drift to food, forage or other plantings that might be damaged or the crop thereof rendered for sale, use or consumption.

PROTECTION OF POLLINATORS

APPLICATION RESTRICTIONS EXIST FOR THIS PRODUCT BECAUSE OF RISK TO BEES AND OTHER INSECT POLLINATORS. FOLLOW APPLICATION RESTRICTIONS FOUND IN THE DIRECTIONS FOR USE TO PROTECT POLLINATORS.

Look for the bee hazard icon in the Directions for Use for each application site for specific use restrictions and instructions to protect bees and other insect pollinators.

This product can kill bees and other insect pollinators.

Bees and other insect pollinators will forage on plants when they flower, shed pollen or produce nectar.

Bees and other insect pollinators can be exposed to this pesticide from:

- Direct contact during foliar applications, or contact with residues on plant surfaces after foliar applications.
- Ingestion of residues in nectar and pollen when the pesticide is applied as a seed treatment, soil, tree injection, as well as foliar applications.

(continued)

PROTECTION OF POLLINATORS (continued)

When Using This Product Take Steps To:

- Minimize exposure of this product to bees and other insect pollinators when they are foraging on pollinator attractive plants around the application site.
- Minimize drift of this product onto beehives or to off-site pollinator attractive habitat. Drift of this product onto beehives or off-site to pollinator attractive habitat can result in bee kills.

Information on protecting bees and other insect pollinators may be found at the Pesticide Environmental Stewardship website at: http://pesticidestewardship.org/PollinatorProtection/Pages/default.aspx.
Pesticide incidents (for example, bee kills) should immediately be reported to the State/Tribal lead agency. For contact information for your State, go to: www.aapco.org/officials.html. Pesticide incidents should also be reported to the National Pesticide Information Center at: www.npic.orst.edu or directly to EPA at: beekill@epa.gov.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

READ ENTIRE LABEL. USE STRICTLY IN ACCORDANCE WITH PRECAUTIONARY STATEMENTS AND DIRECTIONS, AND WITH APPLICABLE STATE AND FEDERAL REGULATIONS.

FOR COMMERCIALLY GROWN ORNAMENTALS NOT UNDER CONTRACT FOR POLLINATION SERVICES BUT ARE ATTRACTIVE TO POLLINATORS

- **Do not apply this product while bees are foraging.**
- **This product is toxic to bees exposed to residue for more than 38 hours following treatment.**
- **Do not apply this product to blooming, pollen-shedding or nectar-producing parts of plants if bees may forage on the plants during this time period, unless the application is made in response to a public health emergency declared by appropriate state or federal authorities.**

Do not apply Safari® 20 SG Insecticide while bees are foraging. Do not apply *Safari* 20 SG Insecticide to plants that are flowering. Only apply after all flower petals have fallen off.

Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

Appendix 4: Additional MDA efforts to protect pollinators and their habitat

Minnesota Department of Agriculture (MDA): efforts toward protecting pollinators and their habitat

The MDA has conducted many efforts to provide unbiased, research-based information about insect pollinators and their habitat in order to train pesticide applicators and county agriculture inspectors and increase public awareness. These efforts and the educational materials produced were completed through partnerships with many stakeholders, government agencies, university experts, growers, and industry representatives. One example is this Special Review of Neonicotinoid insecticides. Others include but are not limited to the following (a short description of each effort is described below):

1. **Pollinator Report**
2. **Best Management Practices (BMPs)**
3. **The MDA Pollinator Website**
4. **Protect Pollinators Campaign**
5. **Pesticide Applicator Training (PAT)**
6. **Pollinator List Server**
7. **Bee Kill Compensation Program**

1. *Insect Pollinator Report: Pollinator Bank, Habitat Protection, and Pesticide Special Review*

In response to 2013 Pollinator Legislation H.F. 976, the MDA collaborated with MnDOT, DNR, Natural Resources Conservation-MN (NRCS-MN), U of M, MPCA, and BWSR, to report on the feasibility of establishing a 'pollinator bank'; historical, current and future efforts to create and enhance pollinator nesting and foraging habitat and refuge areas; best management practices (BMPs) that protect pollinators; existing and new BMP development; and a special review of neonicotinoid insecticides.

Pollinator banks

Research suggests four interpretations of a **'pollinator bank'** as Museum, Database, Genetic, and Ecological 'Pollinator Banks'. The report discusses the feasibility, constraints, and uncertainties of each interpretation:

1. Existing programs at museums, zoos, and U of MN could be adapted as Museum and Database Banks;
2. A repository of honey bee genes exists in Washington State; a genetic 'Bank' in Minnesota is not necessary;
3. Ecological 'Bank' was defined as establishing habitat areas and was the main focus of the report.

The report proposes creation of a new U of M faculty position to direct museum database efforts, coordinate a statewide online database, and lead ecological efforts with partners.

Pollinator habitat

Many state, federal, and non-profit programs support pollinators by encouraging habitat. Challenges exist and resources and research are needed to fill knowledge gaps about pollinator species, and to understand effectiveness and success of existing programs. Habitat requirements for honey bees are not the same as those for native bees and other pollinators.

Improving pollinator habitat relies on updating successful education and training programs and enhancing public awareness of pollinators. Activities outlined in the report that propose to understand and enhance pollinator habitat include:

1. Inventory invertebrate pollinators to determine abundance, diversity, and 'at-risk' populations;

2. Revisit state roadside mowing law, restore roadside program funding, and revise cost-share funding.

BMPs for pollinator habitat

New and existing BMPs were reported by MDA, DNR, BWSR, and NRCS. MDA has partnered with other agencies to establish a Core Advisory Working Group, conducted a stakeholder meeting, and created three Pollinator Workgroups which met in 2014 to write BMPs for habitats associated with:

1. Roadsides – such as rights-of-way and ditches;

2. Managed landscapes – such as home/institutional gardens, parks, and parkways, and;
3. Agricultural landscapes – near, adjacent to, or in agricultural fields, such as grassed waterways and vegetative filter strips.

Special review of neonicotinoid insecticides

MDA has established criteria and a process used to conduct a variety of pesticide reviews. MDA and its collaborators worked to develop the scope for the special neonicotinoid insecticide review.

2. Best Management Practices (BMPs)

A multi-agency workgroup (the Pollinator Advisory Core Workgroup) was convened for the purpose of helping implement 2013 legislation. This Core Workgroup recommended the creation of three Pollinator Best Management Plan Workgroups composed of diverse stakeholders to write BMPs for habitats associated with:

1. Roadsides – such as rights-of-way and ditches;
2. Managed landscapes – such as home/institutional gardens, parks, and parkways, and;

Agricultural landscapes – near, adjacent to, or in agricultural fields, such as grassed waterways and vegetative filter strips. Using enabling statute as a foundation, the Workgroups were given the following goals and objectives for developing their perspective BMPs.

Goals	Objectives
What to do: Increase awareness of the importance of pollinators and pollinator habitat How to do it: Develop best management practices (BMPs) that protect pollinators by providing habitat necessary for their survival and reproduction by approximately June 2014 For whom to do it: • Pesticide applicators and County Agricultural Inspectors that receive training • The general public	Reduce negative impacts of current activities Improve or preserve existing habitat Create new habitat

Workgroups met once per month from February through May 2014.
Final BMPs were completed between July and September 2014. The BMPs are available at: www.mda.state.mn.us/pollinators

Final BMP titles are:

- Promote Pollinators in Agricultural Landscapes
- Insect Pollinator Best Management Practices for Minnesota Yards and Gardens
- Pollinator Best Management Practices for Roadsides and Other Rights-Of-Way

The BMPs have been well received and a second printed and revision was completed in December 2014 for the Agricultural Landscapes and Yards and Gardens BMPs. As of April, 2016, more than 70,000 BMP brochures have been distributed by MDA and its partners.

3. The MDA pollinator website

The MDA has created a Pollinator website at: www.mda.state.mn.us/pollinators

All activities related to MDA's activities and directive towards insect pollinators can be found at or accessed through this site.

4. The MDA protect pollinators campaign

The Minnesota Department of Agriculture launched a new campaign (at the Minnesota State Fair, August 2014) to "Protect Minnesota Pollinators" in yards and gardens, along roadsides and on farms. The MDA's campaign helped increase public awareness of the importance of insect pollinators, not only to our food chain, but also to a healthy environment overall. The campaign provided Minnesotans with easy guidelines on how they could help Minnesota pollinators, and asked each of us to take one small step to help them.

The campaign outlined simple acts everyone could do to help pollinators. The new Best Management Practices were made available at the fair. Everyone was asked to make their own **Minnesota pollinator promise** to help protect insect pollinators. An ongoing opportunity to share your promise on social media is available with the hashtag #MNpollinatorhero. Like the Minnesota Department of Agriculture on Facebook and follow them on Twitter at @mnagriculture.

5. Pesticide Applicator Training (PAT)

The MDA, in collaboration with various partners including the U of M, prepares study manuals and exams used to establish competency of unlicensed applicators and holds recertification workshops designed to maintain competency of licensed Commercial and Noncommercial Pesticide Applicators and Structural Pest Control Applicators. Supplemental pollinator information is being included in new category certifications manuals as deemed appropriate by MDA and Subject Matter Experts. Additional information may also be included in the Minnesota Core Manual when revisions tentatively begin in fiscal year 2018. For example, a new national Core manual was adopted January 1, 2015; within Chapter 7, the section regarding "Preventing Harmful Effects on Sensitive Areas and Nontarget Organisms," contains a sub-section devoted to pollinators, called, "Bees and Other Beneficial Insects." Other initiatives MDA has taken to ensure applicators have appropriate information related to pollinators include:

- Preparing slide presentations regarding the development of their BMPs to train pesticide applicators;
- Participating in and presenting training information about Pollinator BMPs and other pollinator activities at pesticide applicator recertification workshops and with Minnesota Pesticide Information and Education (MN PIE). Presentations share some ways that pesticide applicators can reduce negative impacts to pollinators and their habitat, improve existing habitat, and create new habitat.

6. Pollinator list server

The MDA has created an email list server dedicated to providing you with the latest information on review related topics being researched for the Special Registration Review of Neonicotinoid Use, Registration, and Insect Pollinators Impacts in Minnesota, along with other pollinator related activities MDA is involved with. You can sign up to participate in this list server at: https://public.govdelivery.com/accounts/MNMDA/subscriber/new?topic_id=MNMDA_17

As of January 15, 2016, there were 243 participants signed up for the list server information.

7. Bee kill compensation program

Under Minnesota Statutes, Chapter 18D.201, the Minnesota Department of Agriculture (MDA) is the state agency responsible for the investigation of bee kills alleged to be caused by pesticides. The MDA's Pesticide & Fertilizer Management Division conducts the investigations.

In 2014, the Minnesota Legislature appropriated $150,000 per fiscal year from the pesticide regulatory account to pay compensation claims for bees killed by pesticide. In any fiscal year, a bee owner must not be compensated for a claim that is less than $100 or compensated more than $20,000 for all eligible claims. More information on MDA's bee kill compensation program can be found by visiting: www.mda.state.mn.us/en/protecting/bmps/pollinators/beekillcompensation

Appendix 5: Abbreviations and definitions*

Abbreviations

ACRRA: Agricultural Chemical Response and Reimbursement Account
AEAPL: Australian Environment Agency Pty Ltd
a.i.: Active Ingredient
APVMA: Australian Pesticides and Veterinary Medicines Authority
BWSR: The Board of Water and Soil Resources
CalDPR: California Department of Pesticide Registration
CDRC: Corn Dust Research Consortium
EEC: Estimated Environmental Concentration
EFED: Environmental Fate and Effects Division
EFSA: European Food Safety Authority
EU: European Union
FIFRA: Federal Insecticide, Fungicide, and Rodenticide Act
HHBP: Human Health Benchmark for Pesticide
IPM: Integrated Pest Management
IRAC: Insecticide Resistance Action Committee
LD_{50}: Lethal dose to 50% of a population
LOC: Level of Concern
MDA: The Minnesota Department of Agriculture
MDH: The Minnesota Department of Health
MoA: Mode of Action
MPCA: Minnesota Pollution Control Agency
NASS: National Agricultural Statistics Service
NA: Not Applicable
PER: Proboscis Extension Reflex
PMR: Pesticide Monitoring Region
PMRA: Pest Management Regulatory Agency
PPB: A unit of measure expressed as parts per billion. Equivalent to 1 x 10-9.
PPM: A unit of measure expressed as parts per million. Equivalent to 1 x 10-6.
RQ: Risk Quotient
RT_{25}: Residual time to cause 25% mortality to Honey bees
TEP: Typical End-Use Product
TGAI: Technical Grade Active Ingredient
USEPA: United States Environmental Protection Agency
USDA: United States Department of Agriculture

Definitions**

Acute toxicity: Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours.

Apis mellifera: Honey bee, which includes many subspecies

Bombus spp: Bumble bee species

Chronic toxicity: The capacity of a substance to cause adverse effects as a result of repeated or long term (chronic) exposures.

Half-life: Indicates the time required to reduce the concentration by 50% from any concentration point in time.

K_{OC}: Soil Organic Carbon-Water Partitioning Coefficient – the ratio of the mass of a chemical that is adsorbed in the soil per unit mass of organic carbon in the soil per the equilibrium chemical concentration in solution.

LD_{50}: A calculated dose of a chemical in water to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal: Exposure sufficient to cause death.

log P_{ow}: The log of the octanol/water partition coefficient – the ratio of the equilibrium concentrations of a dissolved substance in a two phase system consisting of two largely immiscible solvents. The partition coefficient being the quotient of two concentrations, is dimensionless and is usually given in the form of its logarithm to base ten.

NOAEC: No Observable Adverse Effect Concentration - The highest exposure concentration at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects.

pH: A value between 0 and 14 used to express the acidity or alkalinity of a solution, where a value of 7 is neutral, lower values are more acidic and higher values are more alkaline.

pKa: Dissociation of a chemical determined by the relative concentrations of ionized and un-ionized forms of the substance and the pH of the solution. The relationship between these terms is given in the following equation, pKa = pH – log [X–]/[HX].

Sublethal: Exposure insufficient to cause death.

***** The list of abbreviations and definitions is not intended to exhaustive but rather assist the reader in understanding some of the more commonly used acronyms and terms.

******Many of the definitions have been adopted from the United States Environmental Protection Agency.

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