NEONICOTINOIDS AND THEIR EFFECTS ON POLLINATORS

A Thesis

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Neonicotinoids and their History

Neonicotinoids are chemical agents used as insecticides in the agricultural sector. The agrochemical industry has developed multiple different neonicotinoids, some of the most prominent include: imidacloprid, acetamiprid, clothianidin, nithiazine, thiacloprid, thiamethoxam, and dinotefuran.[1] Each chemical has been developed from the lead structure of nithiazine and slightly mimics nicotine. Neonicotinoids are a neurotoxin, meaning that they are able to target the neuro transmitters in the brain. Neonicotinoids are unique because they target insect neuronal nicotinic acetylcholine receptors in a way that allows them to be selectively lethal.

Development of present day neonicotinoids began in the 1970's. Shell Development Company was the first to create and commercialize a chemical capable of targeting insect nicotinic acetylcholine receptors. At first, the company utilized the gaseous form of nithiazine to produce the No Pest Strip®, a product used to exterminate houseflies and mosquitos. The success of the product prompted further investigations, and it was later discovered that houseflies were almost immediately affected after consuming nithiazine.[2] However, further investigation revealed that nithiazine has degenerative properties when exposed to hydrolytic and photolytic environments.[3] The chemical was deemed impractical for agricultural use, and as a result development was

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[1] Matsuda, Kazuhiko, Steven D. Buckingham, Daniel Kleier, James J. Rauh, Marta Grauso, and David B. Sattelle. "Neonicotinoids: Insecticides Acting on Insect Nicotinic Acetylcholine Receptors." *Trends in Pharmacological Sciences* 22.11 (2001): 573-80. Web.
[2] Yamamoto, Izuru, and John E. Casida. "Nithiazine Fly Traps." *Nicotinoid Insecticides and the Nicotinic Acetylcholine Receptor*. Tokyo: Springer, 1999. 86-89. Print.
[3] Jeschke, Peter, and Ralf Nauen. "Neonicotinoids-from Zero to Hero in Insecticide Chemistry." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1084-098. Web.

halted. While nithiazine was never commercially produced as an agricultural insecticide, the discovery led to future developments in the insecticide industry.

The expansive use of neonicotinoids did not start until 1991, when Bayer CropScience introduced the especially lethal compound, imidacloprid, to the market. In the early 1980's, Bayer CropScience began experimenting with the chemical structure of nithiazine and its effect on *Neophotettix cincticeps* Uhler (a grasshopper rice pest). After multiple trials, Bayer was able to manipulate the chemical structure of nithiazine to include a chromophore that prevents the absorption of sunlight. With this addition, imidacloprid was no longer photosensitive and the toxicity was increased 125-fold for the rice pest.[4] It was at this time that the term neonicotinoids was coined in order to isolate this new class of pesticides. In the past, the alkaloid, nicotine, was used as a natural pesticide. But, due to its high toxicity to mammal species it was rejected for use as a chemical foundation for modern pesticide inventions.[5] Although, each of the insecticides is chemically similar to nicotine it is important that neonicotinoids are differentiated from nicotinoids, as they are more effective as insecticides and have a lesser impact on vertebrae species.

Imidacloprid quickly became a best seller in the insecticide market. Which prompted Bayer and other chemical companies such as Syngenta, Mitsui Chemicals and Sumitomo Chemical Takeda Agro Company, to continue to modify the chemical structure of imidacloprid and create more variations of insect-targeted pesticides.[6] The

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[4] Jeschke, Peter, and Ralf Nauen. "Neonicotinoids-from Zero to Hero in Insecticide Chemistry." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1084-098. Web.
[5] Yamamoto, Izuru, and John E. Casida. "Nithiazine Fly Traps." *Nicotinoid Insecticides and the Nicotinic Acetylcholine Receptor*. Tokyo: Springer, 1999. 86-89. Print.
[6] Jeschke, Peter, and Ralf Nauen. "Neonicotinoids-from Zero to Hero in Insecticide Chemistry." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1084-098. Web.

chemical structure has since been altered to allow for the creation and patenting of different neonicotinoids. As a result, each of the chemicals has slightly unique levels of photosensitivity, toxicity, and water solubility.

The Nicotinic Acetylcholine Receptor

Neonicotinoids are effective insecticides because they target the nicotinic acetylcholine receptors. As the name implies, the receptors interact with the neurotransmitter, acetylcholine, and can also bind with nicotine. These receptors are essential to synaptic transmission in both vertebrates and insects. In vertebrate species nicotinic acetylcholine receptors can be found at neuromuscular junctions and within the central and peripheral nervous system. In insect species, the muscle-type transmitters are primarily glutamatergic meaning that glutamate acts as the binding neurotransmitter during synaptic transmission at neuromuscular junction. More importantly, nicotinic acetylcholine receptors are the main neuronal receptors in the insect nervous system. As a result, the nicotinic acetylcholine receptors are concentrated in insect brain tissue.[7] The large quantity, as well as, the importance of nicotinic acetylcholine receptors as excitatory neurotransmitter receptors in insect nervous system, helps to explain why these receptors are such an effective target for neonicotinoids.

Neonicotinoids are selectively lethal towards insects rather than vertebrates. The combination of the distinct neurological design of vertebrates and insects, and the specific chemical structure of neonicotinoids allows for this selective biological efficacy.

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[7] Millar, Neil S., and Ian Denholm. "Nicotinic Acetylcholine Receptors: Targets for Commercially Important Insecticides." *Invertebrate Neuroscience Invert Neurosci* 7.1 (2007): 53-66. *Springer*. Web.

During synaptic transmission neurotransmitters are passed from the presynaptic axon and then received by the postsynaptic dendrite via the synapse, the gap between the two cells.

The neurotransmitter receptors, located on the postsynaptic dendrite, act as an ionized channel that allows for the entrance of neurotransmitters through the otherwise impermeable phospholipid bilayer. Although the nicotinic acetylcholine receptors in vertebrates and insects preform similar tasks their physical structure is not identical. Each neurotransmitter receptor is formed by a collection of subunits, which create subtypes. Subtypes act as neuronal receptors with specialized mechanisms. Such subtypes are found in nicotinic acetylcholine receptors.

Scientists have discovered a large set of neuronal subtypes in vertebrates: ten α, four ß, γ, and δ. Nicotinic acetylcholine receptors in vertebrae species are assembled in combinations of α 2-10 and ß 2-4. These combinations can be classified as α and non- α subtypes based on sensitivity to α-bungarotoxin, a type of bungatoxin that can bind to nicotinic acetylcholine receptors in both the brain and body.[8] Certain subunit combinations are more sensitive to acetylcholine and other binding chemicals. The same is true for insect nicotinic acetylcholine receptors. Insect nicotinic acetylcholine receptors are much less understood. Scientists use the subunits discovered in Drosophila, a small fly, Dα 1-4 and ß 1-3 as a proxy for all insects. A conglomeration of studies suggests that

[8] Tomizawa, Motohiro, and John E. Casida. "NEONICOTINOID INSECTICIDE TOXICOLOGY: Mechanisms of Selective Action." *Annu. Rev. Pharmacol. Toxicol. Annual Review of Pharmacology and Toxicology* 45.1 (2005): 247-68. Web.

a single type subunit does not determine the level of sensitivity to neonicotinoids; both the α and ß subunits are prominent factors.[9,10,11,12]

However, subunits are not the only aspect that allows for neonicotinoid insect selectivity. Of the two subcategories of vertebrates, mammals and birds, neonicotinoids were found to have a lethal effect towards some avian species. The avian subunit α7 has been discovered to have a point mutation in which the amino acid glutamine has been exchanged for either arginine or lysine.[13] The mutation allows for an electrophysiological response to the neonicotinoid, imidacloprid. The lethal phenomenon that occurs with certain members of the avian species could parallel what occurs at the nicotinic acetylcholine receptor in insect species.

Differences in the chemical structure of neonicotinoids and nicotinoids also play an imperative role in determining why insect selectivity occurs. There are four nicotinoids: nicotine, epibatidine, ABT-594 and desnitroimidaloprid.[14] The chemical structure of each nicotinoid includes a nitrogen atom with four chemical bonds rather

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[9] Millar, Neil S., and Ian Denholm. "Nicotinic Acetylcholine Receptors: Targets for Commercially Important Insecticides." *Invertebrate Neuroscience Invert Neurosci* 7.1 (2007): 53-66. *Springer*. Web.

[10] Matsuda, Kazuhiko, Steven D. Buckingham, Daniel Kleier, James J. Rauh, Marta Grauso, and David B. Sattelle. "Neonicotinoids: Insecticides Acting on Insect Nicotinic Acetylcholine Receptors." *Trends in Pharmacological Sciences* 22.11 (2001): 573-80. Web.

[11] Tomizawa, Motohiro, and John E. Casida. "NEONICOTINOID INSECTICIDE TOXICOLOGY: Mechanisms of Selective Action." *Annu. Rev. Pharmacol. Toxicol. Annual Review of Pharmacology and Toxicology* 45.1 (2005): 247-68. Web.

[12] Lansdell, Stuart J., and Neil S. Millar. "The Influence of Nicotinic Receptor Subunit Composition upon Agonist, α–bungarotoxin and Insecticide (imidacloprid) Binding Affinity." *Neuropharmacology* 39.4 (2000): 671-79. Web.

[13] Tomizawa, Motohiro, and John E. Casida. "NEONICOTINOID INSECTICIDE TOXICOLOGY: Mechanisms of Selective Action." *Annu. Rev. Pharmacol. Toxicol. Annual Review of Pharmacology and Toxicology* 45.1 (2005): 247-68. Web.

[14] Tomizawa, Motohiro, and John E. Casida. "NEONICOTINOID INSECTICIDE TOXICOLOGY: Mechanisms of Selective Action." *Annu. Rev. Pharmacol. Toxicol. Annual Review of Pharmacology and Toxicology* 45.1 (2005): 247-68. Web.

than three. Nicotionids are protonated and have a slightly positive charge. Neonicotinoids do not have any extra nitrogen bonds. As result, the -nitro and -cyno functional groups create an electronegative tip.[15]

Theoretically, the point mutation of the amino acid, which presumably occurs in the insect nicotinic acetylcholine receptor, creates a cationic subunit. The anionic tip of the neonicotinoids would be drawn to the positive subunit. In contrast, the electronegative tip of the neonicotinoids prevents the chemical from binding to the vertebrate nicotinic acetylcholine receptors.[16] The desire to neutralize the respective positive and negative charge of the receptor and neonicotinoids imparts the selectivity of the insecticide.

Neonicotinoid Use

The introduction of neonicotinoids radically changed the agrochemical industry. Before the commercialization of neonicotinoids, the farming industry relied heavily on organophosphates, pyrethroids, and carbamates. These chemicals, although sufficiently effective, were lethal to many non-target organisms.[17] Organophosphates are acutely toxic to humans in addition to wildlife and insects. Accidental exposure to organophosphates can result in poisoning and other life threatening symptoms.[18] Also, the excessive use of carbamate pesticides eventually resulted in insect resistance and

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[15] Matsuda, Kazuhiko, Steven D. Buckingham, Daniel Kleier, James J. Rauh, Marta Grauso, and David B. Sattelle. "Neonicotinoids: Insecticides Acting on Insect Nicotinic Acetylcholine Receptors." *Trends in Pharmacological Sciences* 22.11 (2001): 573-80. Web.
[16] Tomizawa, Motohiro, and John E. Casida. "NEONICOTINOID INSECTICIDE TOXICOLOGY: Mechanisms of Selective Action." *Annu. Rev. Pharmacol. Toxicol. Annual Review of Pharmacology and Toxicology* 45.1 (2005): 247-68. Web.
[17] Elbert, Alfred, Matthias Haas, Bernd Springer, Wolfgang Thielert, and Ralf Nauen. "Applied Aspects of Neonicotinoid Uses in Crop Protection." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1099-105. Web.
[18] Heel, Willemijn Van, and Said Hachimi-Idrissi. "Accidental Organophosphate Insecticide Intoxication in Children: A Reminder."*International Journal of Emergency Medicine*. Springer, 2011. Web. 15 Mar. 2016. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3131249/>.

weakened the efficacy of the chemical.[19] Lastly, pyrethroid insecticides are photosensitive and normally degenerate one to two days after application.[20]

The popularity of the neonicotinoids released from 1991 to 2002 can be attributed to multiple factors.[21] The first is selective lethality. Neonicotinoids target the nicotinic acetylcholine receptors found in the insect nervous system. This allows the agricultural industry to use the chemical with a relatively low risk of harming non-target creatures like humans or other wildlife. Neonicotinoids are a systemic insecticide. This means that the chemicals are water-soluble and can be absorbed by the plant and stored in the plant tissue. The water solubility allows the compounds to have a multitude of application methods. They can be applied via seed soaking, direct application, or soil exposure and still be effective.[22] The ease of use as well as selective lethality are factors that assisted in allowing neonicotinoids to replace the traditional pesticides used in the agriculture industry. Additionally, neonicotinoids were designed to be resilient in sunny and hydraulic environments. Other pesticides, including pyrethroids, are incapacitated if exposed to sun or water. This characteristic allowed neonicotinoids to be used almost exclusively in a variety of climates and conditions. Neonicotinoids were also able to control the pests that had become resistant to the traditional pesticides. Neonicotinoids

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[19] "Resistance: The Facts - History & Overview of Resistance." (n.d.): n. pag.*IRAC Online*. Insecticide Resistance Action Committee. Web. 15 Mar. 2016. <http://www.irac-online.org/content/uploads/Resistance-The-Facts.pdf>.

[20] Elbert, Alfred, Matthias Haas, Bernd Springer, Wolfgang Thielert, and Ralf Nauen. "Applied Aspects of Neonicotinoid Uses in Crop Protection." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1099-105. Web.

[21] Elbert, Alfred, Matthias Haas, Bernd Springer, Wolfgang Thielert, and Ralf Nauen. "Applied Aspects of Neonicotinoid Uses in Crop Protection." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1099-105. Web.

[22] Elbert, Alfred, Matthias Haas, Bernd Springer, Wolfgang Thielert, and Ralf Nauen. "Applied Aspects of Neonicotinoid Uses in Crop Protection." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1099-105. Web.

became available to the market at the peak of insect resistance, this made the new pesticide especially valuable.[23] The new insecticide was able to replace pesticides that were no longer effective.[24] Currently, some species of insect have developed a slight resistance to neonicotinoids, but dominant chemical companies have implemented resistance management strategies that have been successful in combating resistance in specific crops. Lastly, neonicotinoids have benefitted from a lack of regulations. Many other insecticides and pesticides have fallen under stricter regulations regarding application, concentration of chemicals and overall use. At this point in time, there is an overwhelming lack of federal directive towards regulating the widespread use of neonicotinoids. This topic will be further discussed in the chapter titled Regulating Neonicotinoids. As more restrictions are placed on other chemicals, the use of neonicotinoids will continue to augment, as it is the easiest pesticide to use.

The expansive use of neonicotinoids can be easily demonstrated by the dramatic change in the agrochemical market. Prior to 1991 the agrochemical market was dominated by three main pesticides organophosphates, pyrethroids, and carbamates.[25] The majority of the modern neonicotinoids were released to the market in an eleven-year time span. By 2005, neonicotinoids had gained a market share of about 16% and the use of organophosphates was reduced significantly. In a span of 15 years neonicotinoids also

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[23] Forgash, Andrew J. "History, Evolution, and Consequences of Insecticide Resistance." *Pesticide Biochemistry and Physiology* 22.2 (1984): 178-86. Web. 14 Feb. 2016.
[24] Jeschke, Peter, and Ralf Nauen. "Neonicotinoids-from Zero to Hero in Insecticide Chemistry." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1084-098. Web.

[25] Jeschke, Peter, and Ralf Nauen. "Neonicotinoids-from Zero to Hero in Insecticide Chemistry." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1084-098. Web.

began to dominate the market from a financial perspective.[26] Neonicotinoids accounted for 41% of the global pesticide sales in 2009.[27] Since then, neonicotinoids and more specifically the Imidacloprid insecticide have become the most widely used insecticide worldwide.

Objective

Under the Federal Insecticide, Fungicide and Rodenticide Act, the Environmental Protection Agency must register all pesticides that are sold and distributed in the United States. In order for pesticide to be registered, the EPA must first complete extensive research on the environmental and human health effects of the pesticide.[28] Neonicotinoids, although extremely potent, have been given a conditional registration status. The majority of products containing neonicotinoids were given temporary approval by the EPA, and can therefore be legally sold and distributed through the market. Currently, neonicotinoids dominate the global pesticide market. They are used almost exclusively through out the United States despite the lack of EPA research and understanding of the effects.

Although neonicotinoids are selectively lethal, their lethality extends to non-target insects as well. Insect pollinators are one of the largest categories of non-target insects affected by widespread use of neonicotinoids. The chemicals are not able to differentiate between pests and beneficial organisms. As a result, pollinators have suffered

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[26] Jeschke, Peter, and Ralf Nauen. "Neonicotinoids-from Zero to Hero in Insecticide Chemistry." *Pest. Manag. Sci. Pest Management Science* 64.11 (2008): 1084-098. Web.
[27] United States of America. Department of Legislative Services. Office of Policy Analysis. Pollinator Health and the Use of Neonicotinoids in Maryland. Annapolis: General Assembly, 2015. Oct. 2015. Web. 8 Apr. 2016.
[28] "About Pesticide Registration." *About Pesticide Registration*. Environmental Protection Agency, n.d. Web. 23 Nov. 2015.

tremendously from neonicotinoid exposure. This class of insecticides is systemic; neonicotinoids can be found in nectar and pollen of crops despite the method of application is used. Pollinators, such as bees and butterflies, provide a priceless ecosystem service that cannot be replicated by technology.[29] On the most basic level, pollinator survival is fundamental to maintaining our food supply. However, pollinators are also essential to the survival of wild plants and flowers.

The Environmental Projection Agency has failed to properly regulate neonicotinoids on the basis of sufficient harm to pollinator species, which are essential to the sustainability of both a healthy environment and food supply.

Pollinators

Pollination is the process in which the pollen grain containing genetic information is transferred from the male anther to the female reproductive organ of a plant. The female organ includes a stigma, style, and ovary. Once the pollen grain is deposited on the stigma, it is transported through the style to the ovary. The movement of pollen can occur through different media. There are a variety of plants that self-pollinate, but the majority of plants participate in cross-pollination. Anemophilous plants have fine pollen grains that allow the pollination process to take place via wind. Entumophilous plants have larger pollen grains that rely on insects and other animals to carry their pollen to the stigma of conspecific species. If the pollination process is successful either seeds or fruit can develop. It is the goal of every organism to reproduce. Pollination and therefore

[29] Gallai, Nicola, Jean-Michel Salles, Josef Settele, and Bernard E. Vaissière. "Economic Valuation of the Vulnerability of World Agriculture Confronted with Pollinator Decline." *Ecological Economics* 68.3 (2009): 810-21. Web.

reproduction are required to sustain current ecological mechanisms as well as the human food supply.

Countless species of animals participate in the pollination process. Pollen grains are able to cling on to the majority of fibers, allowing many animals and insects to be accidental pollinators. However, the most efficient pollination in completed by insects categorized as pollinators. Hymenoptera and Diptera are orders of insects that include some of the most effective pollinators.

Hymenoptera is a large order of animals that includes bees. Bees are considered to be the most significant pollinator because they rely on both pollen and nectar for survival. Nectar is a carbohydrate and acts as a simple energy source. While, pollen is a vital source of protein and fats. It is essential to the queen during the reproduction and larval development process. Not all species of bee are capable to collect pollen, yet it is crucial to all species.[30] There are over 3000 species of bees in North America. Out of the many bee species, the European Honey Bee (*Apis mellifera*) and the Buff-Tailed Bumble Bee (*Bombus terrestris*) are among the most referenced. These two types of social bees form colonies and are often managed in artificial hives maintained by beekeepers. While honeybees and bumblebees are considered the ultimate pollinators, certain species of bees specialize in the pollination of specific plants. For example, blue orchard bees (*Osmia lignaria*), are very important apple pollinators because they land directly on the anther and stigma of the orchard blossoms. [31]

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[30] "Entomology: UGA Honey Bee Program: Bees, Beekeeping, and Pollination." *Pollination: Background*. N.p., n.d. Web. 23 Nov. 2015.
[31] "Entomology: UGA Honey Bee Program: Bees, Beekeeping, and Pollination." *Pollination: Background*. N.p., n.d. Web. 23 Nov. 2015.

Out of the all of the species in the Hymenoptera order the honeybee (*Aphis mellifera*) is considered to be the fundamental pollinator. The honeybee originated in Europe, but was transported to the United States by settlers. Presently, *Aphis mellifera* is the most commonly managed species of bee. The practice of beekeeping began in Ancient Egypt and was passed on to the Greek and later Roman empires.[32] In general, the honeybee is most popular type of bee for management and scientific study because of its predominate role in pollination, larger colonies, and easy accessibility due to domestication. They are often used as key subjects in pollination studies because of their generalist nature, meaning that the honeybee is compatible with almost any flowering plant. While honeybees are not the most efficient pollinators, they are the most important pollinator of monoculture agriculture. Their large workforce and extended active season make the honeybee essential to the production of 52 out of the 115 leading global food commodities.[33] The extensive and borderline exclusive use of the *Aphis mellifera* has resulted in a lack of biodiversity among domesticated bees and leaves the agricultural industry very vulnerable to outbreaks of bee diseases and viruses. Bees, and more specifically the honeybee, are the focus of most scientific studies as they are seen as representative pollinators. However, this does not undermine the ecological importance of other pollinators.

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[32] Vanengelsdorp, Dennis, and Marina Doris Meixner. "A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors That May Affect Them." *Journal of Invertebrate Pathology* 103 (2010): n. pag. Web.

[33] Vanengelsdorp, Dennis, and Marina Doris Meixner. "A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors That May Affect Them." *Journal of Invertebrate Pathology* 103 (2010): n. pag. Web.

Flies from the Diptera order are often overlooked as essential pollinators. Yet, more than 71 families in the Diptera order include flower-visiting flies. In the wild they visit at least 555 flowering plant species. Various species of flies are bred and commercially used to pollinate an expansive list of common crops.[34] Flower-visiting flies play an important role because they are abundant in population and can survive in almost all environments.[35] In the past, Diptera pollination services have been underestimated. As they are becoming better understood, scientists are discovering more plants that are completely dependent on the flies for pollination.[36] In fact, the flower-visiting flies seem to fill in the areas when and where bees are less active. Diptera flies visit flowers that bees usually ignore, such as flat flowers. Also, bees tend to be more active in the late morning and noon. While in general, the flies complete the most flower visits in the early morning and late afternoon. [37] The difference in bee and flower-visiting fly activities highlight their respective importance. From an agricultural standpoint, the Diptera flies are even more significant. Flower fly larva prey on aphids and other pests. This makes them an important aspect of natural pest control. When the larva develops into adults, the flies help to pollinate the crops they protected in their earlier stages of life. [38]

[34] Kearns, Carol Ann. "North American Dipteran Pollinators: Assessing Their Value and Conservation Status." *Ecology and Society*. Conservation Ecology, n.d. Web. Nov. 2015.
[35] Bischoff, Mascha, Diane R. Campbell, Janice M. Lord, and Alastair W. Robertson. "The Relative Importance of Solitary Bees and Syrphid Flies as Pollinators of Two Outcrossing Plant Species in the New Zealand Alpine." *Austral Ecology* 38.2 (2012): 169-76. Web. Oct. 2015.
[36] Ssymank, Axel, C. A. Kearns, Thomas Pape, and F. Christian Thompson. "Pollinating Flies (Diptera): A Major Contribution to Plant Diversity and Agricultural Production." *Biodiversity* 9.1-2 (2008): 86-89. Web.
[37] Kearns, C. A. 2001. North American dipteran pollinators: assessing their value and conservation status. Conservation Ecology **5**(1): 5. [online] URL: http://www.consecol.org/vol5/iss1/art5/
[38] Ssymank, Axel, C. A. Kearns, Thomas Pape, and F. Christian Thompson. "Pollinating Flies (Diptera): A Major Contribution to Plant Diversity and Agricultural Production." *Biodiversity* 9.1-2 (2008): 86-89. Web.

Beetles are also a category of pollinators that is overlooked. The abundant population of beetles by default makes them a significant pollinator. They are often the first visitors of flowering plants. Beetles take shelter in heavily planted areas and have been known to feast on the nectar of plants. On global scale, they help to pollinate approximately 88% of the 240,000 species of flowering plants and therefore should not be dismissed from the list of important pollinators.[39]

Pollinator Role in the Environment

Although self-pollinated and anemophilous plants are able to complete the pollination process without animal assistance, for cross-pollinating plants insect pollinators are essential. Only a small percentage of flowering plants complete abiotic pollination. As a result, animal pollinators facilitate the reproduction of a large majority of flowering plants. Pollinators have crucial roles in ecosystem sustainability and the agricultural industry.

Pollinators provide an extensive ecosystem service that has yet to be replicated on such a large scale. Pollinators allow for the survival and reproduction of wild plants that sustain the various ecosystems. They are fundamental species as they provide food and shelter for other animals. In addition, wild plants have a large influence on how ecosystem nutrients are retained and recycled. [40]

Pollinators also enable the reproduction process for agricultural crops. In fact, the human population relies on animal pollination, either directly or indirectly, for

[39] "NCF-Envirothon." *NCF-Envirothon*. N.p., n.d. Web. 23 Oct. 2015.
[40] Iii, F. Stuart Chapin, Erika S. Zavaleta, Valerie T. Eviner, Rosamond L. Naylor, Peter M. Vitousek, Heather L. Reynolds, David U. Hooper, Sandra Lavorel, Osvaldo E. Sala, Sarah E. Hobbie, Michelle C. Mack, and Sandra Díaz. "Consequences of Changing Biodiversity." *Nature* 405.6783 (2000): 234-42. Web.

approximately 35% of the food we consume annually.[41] The economic estimate for the monetary value of global pollinator services in the agriculture industry is $153 billion.[42] To further illustrate pollinator importance, if insect pollinators were obliterated the continent of North America would lose almost 12% of economically important crops.[43] The high monetary value of pollination services relates its importance to food production and food security on a global scale. The United States is becoming increasingly dependent on pollinators. In the last decade, the proportion of pollinator-dependent crops grown in United States farms has become significantly larger. As the global population continues to climb past seven billion, the demand for pollination services will only augment making it imperative that pollinator population is protected.

Pollinator Risks

Yet despite their importance, pollinators are subject to many threats. For many pollinators, aspects of their habitat may pose a threat to their survival. It is likely that each pollinator is the prey of another animal or insect. In addition, the sheer size of most pollinators can make slight changes in the environment a significant danger. Human activity has also created complications for pollinators. Changes in land use have had a large impact on the pollinator populations. Rapid habitat degradation and fragmentation has made it difficult for insects to adapt to new environments. Human manipulation of the land effects most animals, pollinator or not.

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[41] Ghazoul, J. "Buzziness as Usual? Questioning the Global Pollination Crisis." *Trends in Ecology & Evolution* 20.7 (2005): 367-73. Web.
[42] Gallai, Nicola, Jean-Michel Salles, Josef Settele, and Bernard E. Vaissière. "Economic Valuation of the Vulnerability of World Agriculture Confronted with Pollinator Decline." *Ecological Economics* 68.3 (2009): 810-21. Web.
[43] Ghazoul, J. "Buzziness as Usual? Questioning the Global Pollination Crisis." *Trends in Ecology & Evolution* 20.7 (2005): 367-73. Web.

However, each species of pollinator is plagued by its own dangers. A prominent danger for honeybees is the *Varroa destructor*. The *Varroa destructor* is a parasitic mite that is considered the most detrimental parasite to the bee. Originally *Aphis cerana*, the Asian bee, was the sole victim of the Varroa mite. Unfortunately, the mite was introduced to the honeybee population through international trade. Currently it has spread to virtually all continents and can be found in almost every colony. Female mites are capable of feeding off of both adult and juvenile bees. They are most damaging because the female mite and her offspring feed on the hemolymph of developing bee pupae. The parasites cause nutritional deficits, which can weaken the community in the long run.[44] Effects of the Varroa mite are obvious; the symptoms include malnourished and crippled bees that are unable to fly. In addition, the parasitic mites are known to harbor over 18 viruses like Deformed Wing Virus and Acute Bee Paralysis Virus, both of which can have detrimental effects on the individual and the colony. The bees subjected to parasitic activity may be more susceptible to the incoming viruses. Between 1987 and 2002 there was a 40% decline in the number of smaller bee farms. It is likely that the decrease in modest bee farms is a result of beekeeper inability to control the mites. Varroa mites are still a large problem in the United States. A recent survey found that beekeepers felt that the presence of Varroa mites is the third most determining factor of colony mortality.[45] Bee colonies are tremendously sensitive to the Varroa mite. An infestation of even 10% of bee individuals can condemn a winter death for the bee colony.

[44] Vanengelsdorp, Dennis, and Marina Doris Meixner. "A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors That May Affect Them." *Journal of Invertebrate Pathology* 103 (2010): n. pag. Web.

[45] Vanengelsdorp, Dennis, Jerry Hayes, Robyn M. Underwood, and Jeffery Pettis. "A Survey of Honey Bee Colony Losses in the U.S., Fall 2007 to Spring 2008." *PLoS ONE* 3.12 (2008): n. pag. Web.

A microsporidia infection from the Nosema can also have a huge impact on the short-term and long-term health of colony. The infection is spread through the digestion of the microspore, either *Nosema apis* or *Noesma caranae*. Overall performance in an infected bee's designated role is reduced. Some bees have also been found to have a shorter lifespan.[46]

The American and European foulbrood is a bacterial disease. The disease targets the bee brood and is highly contagious. The bacterium, Paenibacillus larvae, absorbs nutrients from the bee larvae before killing it. The spores eventually spread and weaken the adult bees of the colony. Historically, beehives with confirmed cases of American or European foulbrood were burned to prevent the spread of the bacteria. Modern practices are less dramatic. Hives are strictly monitored so that preventative measures can be taken. Sanitation methods and antibiotics have been effective in preventing the bacteria from infecting an entire colony. [47]

Colony Collapse Disorder is a fairly modern epidemic. The disorder became a prevalent concern in 2006. Colony Collapse Disorder is characterized by the permanent disappearance of adult bees from the hive, evidence of rapid bee death, and an abundant food supply. The epidemic affected a startling number of colonies in the winters of 2006 to 2007. So far, scientists have been unable to pinpoint a single cause of Colony Collapse

[46] Vanengelsdorp, Dennis, and Marina Doris Meixner. "A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors That May Affect Them." *Journal of Invertebrate Pathology* 103 (2010): 80-95. Web.

[47] Vanengelsdorp, Dennis, and Marina Doris Meixner. "A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors That May Affect Them." *Journal of Invertebrate Pathology* 103 (2010): 80-95. Web.

Disorder. However, it is hypothesized that Colony Collapse Disorder occurs due to the combination of the various stressors that modern bees face. [48]

While bees suffer from a variety of hazards, flower-visiting flies are less sensitive. They can survive in cool, moist habitats. Also, they require less energy to support daily activity and reproduction.[49] However, pesticide exposure affects both orders, Hymenoptera and Diptera. Despite the recent movement for organic farming, the use and overuse of chemical pesticides is common practice in modern agriculture. The concept of Integrated Pest Management encourages the simultaneous use of insecticides, pesticides, and fungicides. Of the insecticides, neonicotinoids are the most commonly used.

Neonicotinoid Environmental Impact

The effects of neonicotinoids are not isolated to their intended areas of application. Instead, their methods of application and chemical characteristics allow neonicotinoids to be present in soils, waters sources and surrounding foliage. Chemical leeching and migration often results in the unintentional detriment to non-target organism and ecosystems adjacent to farming acres.

Regardless of the method of application, neonicotinoids can be found in agricultural soils. Soil concentrations of neonicotinoids decrease naturally over time. The decay is most accurately measured in half lives; but, the half life of each neonicotinoids varies greatly. For example, the half life of imidacloprid can vary from 100 to 1,230

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[48] Vanengelsdorp, Dennis, and Marina Doris Meixner. "A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors That May Affect Them." *Journal of Invertebrate Pathology* 103 (2010): 80-95. Web.

[49] Bischoff, Mascha, Diane R. Campbell, Janice M. Lord, and Alastair W. Robertson. "The Relative Importance of Solitary Bees and Syrphid Flies as Pollinators of Two Outcrossing Plant Species in the New Zealand Alpine." *Austral Ecology* 38.2 (2012): 169-76. Web. Oct. 2015.

days.[50,51] The wide ranges are due to climate factors such as moisture and temperature that have the ability to influence decay rates. Water content in the soil is key in determining neonicotinoid half life. Water content is known to be an indicator for soil health. As a result, dry soil has been found to lead to longer half lives in the chemicals.[52] Temperature also effects decay rate. A study completed by Scorza et al found that neonicotinoid decomposition is increased in warmer temperatures.[53] Although, the study was completed in lab conditions the strong negative correlation between temperature and imidacloprid half life indicates that the results are genuine and have potential to be replicated in the field. The most effective conditions for rapid decay is in warm and humid climates. This conclusion is supported by field data which revealed that the lowest recorded half life for imidacloprid of 104 days was found in the state in Georgia.[54]

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[50]Baskaran, Sundaram, Rai S. Kookana, and Ravendra Naidu. "Degradation of Bifenthrin, Chlorpyrifos and Imidacloprid in Soil and Bedding Materials at Termiticidal Application Rates." Pesticide Science Pestic. Sci. 55.12 (1999): 1222-228. Web. 15 Nov. 2015.

[51] Half-life of Common Neonicotinoids

Clothianidin	148-7,000 days
Acetamiprid	31-450 days
Dinotefuran	75-82 days
Nitenpyram	8 days
Thiacloprid	3.4- >1,000 days
Thiamthoxam	7-335 days

Goulson, Dave. "REVIEW: An Overview of the Environmental Risks Posed by Neonicotinoid Insecticides." J Appl Ecol Journal of Applied Ecology 50.4 (2013): 977-87. Web.Chapter: i oidsicoitnds

[52] Bonmatin, J.-M., C. Giorio, V. Girolami, D. Goulson, D. P. Kreutzweiser, C. Krupke, M. Liess, E. Long, M. Marzaro, E. A. D. Mitchell, D. A. Noome, N. Simon-Delso, and A. Tapparo. "Environmental Fate and Exposure; Neonicotinoids and Fipronil." *Environmental Science and Pollution Research Environ Sci Pollut Res* 22.1 (2014): 35-67. Web.

[53] Júnior, Rômulo Penna Scorza, Johan H. Smelt, Jos J. T. I. Boesten, Rob F. A. Hendriks, and Sjoerd E. A. T. M. Van Der Zee. "Preferential Flow of Bromide, Bentazon, and Imidacloprid in a Dutch Clay Soil." *Journal of Environment Quality* 33.4 (2004): 1473. Web.

[54] Bonmatin, J.-M., C. Giorio, V. Girolami, D. Goulson, D. P. Kreutzweiser, C. Krupke, M. Liess, E. Long, M. Marzaro, E. A. D. Mitchell, D. A. Noome, N. Simon-Delso, and A. Tapparo. "Environmental Fate and Exposure; Neonicotinoids and Fipronil." *Environmental Science and Pollution Research Environ Sci Pollut Res* 22.1 (2014): 35-67. Web.

However, in most cases neonicotinoid half lives are much lengthier due to the moisture and temperature fluxes created by seasons. The study exemplifies that reality of neonicotinoid decay. The study analyzed seventy-four soils through out the country of France for levels of imidacloprid. Of the soils tested, 91% tested positive for imidacloprid despite the fact that only 15% of the soils had been seeded with treated seeds within the year. Additionally, imidacloprid was found in 97% of the soils seeded with treated seeds one or two years before the sample was collected. Surprisingly, samples taken from soils treated for two consecutive years had higher concentrations of the neonicotinoid than samples collected from soils that had been more recently treated.[55] The results of Bonmatin's study imply that neonicotinoid levels can accumulate in soil. More often than not, the lengthy half life of a neonicotinoid prevents the pesticide from being completely decayed by the next seeding or exposure. This results in highly concentrated levels of neonicotinoids in the soil. Chemical persistence in the soil can result in unintentional exposure and overexposure to crops and other plants. Additionally, neonicotinoids present in the soil can harm essential soil dwellers such as earthworms, which preform important soil ecosystem services.

Unfortunately, neonicotinoids do not always remain in the original soils. The distance that the chemicals are able to leech outside of the immediate area is dependent on the extent in which the neonicotinoids bind to the soil. Neonicotinoid sorption rates are contingent on soil composition. A study completed by Selim et al. determined that soils composed of high levels of organic matter resulted in increased bonding between

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[55] Bonmatin, J. M., I. Moineau, R. Charvet, M. E. Colin, C. Fleche, and E. R. Bengsch. "Behaviour of Imidacloprid in Fields. Toxicity for Honey Bees." *Environmental Chemistry* (n.d.): 483-94. Web.

the chemical and soil therefore reducing the mobility of the chemical. In contrast, soils lacking organic matter allow for higher rates of neonicotinoid mobility.[56]

Neonicotinoid leeching puts both surface and ground water sources at risk. Runoff is a large source of water contamination in both urban and agricultural settings. Neonicotinoid spraying and seed coating provide opportunities for runoff to occur. Foliage spraying, although intended to be direct, can result in the contamination of water through chemical drifting. Foliage spraying can also leave a chemical residue on plants which is easily rinsed off during rain events and subsequent watering.[57] Seed coating also produces the risk of water pollution. In general, treated seeds are planted by a machine that creates a large neonicotinoid dust cloud. The cloud allows for the neonicotinoid dust to drift away from the planting site and be deposited either on nearby soil or water sources. [58]

Drainage systems also create potential for water contamination. Neonicotinoids are used in urban areas to protect green fields, golf courses, and gardens. Any runoff created in urban settings is deposited into the drainage system and treated as waste water. However, the environment created by waste water treatment plants is not conducive to the rapid decay of neonicotinoids.[59] As a result, the neonicotinoids are filtered back into

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[56] Selim, H. M., Chang Yoo Jeong, and Tamer A. Elbana. "Transport of Imidacloprid in Soils." *Soil Science* 175.8 (2010): 375-81. Web.
[57] Bonmatin, J.-M., C. Giorio, V. Girolami, D. Goulson, D. P. Kreutzweiser, C. Krupke, M. Liess, E. Long, M. Marzaro, E. A. D. Mitchell, D. A. Noome, N. Simon-Delso, and A. Tapparo. "Environmental Fate and Exposure; Neonicotinoids and Fipronil." *Environmental Science and Pollution Research Environ Sci Pollut Res* 22.1 (2014): 35-67. Web.
[58] Bonmatin, J.-M., C. Giorio, V. Girolami, D. Goulson, D. P. Kreutzweiser, C. Krupke, M. Liess, E. Long, M. Marzaro, E. A. D. Mitchell, D. A. Noome, N. Simon-Delso, and A. Tapparo. "Environmental Fate and Exposure; Neonicotinoids and Fipronil." *Environmental Science and Pollution Research Environ Sci Pollut Res* 22.1 (2014): 35-67. Web.
[59] Bonmatin, J.-M., C. Giorio, V. Girolami, D. Goulson, D. P. Kreutzweiser, C. Krupke, M. Liess, E. Long, M. Marzaro, E. A. D. Mitchell, D. A. Noome, N. Simon-Delso, and A. Tapparo.

the surrounding surface waters. Studies completed across the United States of America have detected significant levels of neonicotinoids in streams, storm-water ponds, and ground waters.[60,61,62]

The abundance of neonicotinoids in surface waters creates a large concern for ground water contamination as well. Leeching can occur both horizontally and vertically through the soil, so ground water contamination is likely. The contamination of water sources puts many organisms at risk, as water is biologically essential and is a common habitat. Water contamination provides a secondary outlet of exposure for other non-target invertebrates.

Neonicotinoid Pathways of Exposure

Pollinators are adversely effected by neonicotinoids. Domesticated pollinators are often purposefully exposed to crops treated by the pesticide. While wild pollinators, which include some species of bees, beetles and flies, are unable to detect the harmful chemicals and unknowingly subject themselves to neonicotinoids. Pollinators are exposed to neonicotinoids through a variety of different pathways. The most prevalent pathways of exposure include consumption of treated plant products, physical contact with

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"Environmental Fate and Exposure; Neonicotinoids and Fipronil." *Environmental Science and Pollution Research Environ Sci Pollut Res* 22.1 (2014): 35-67. Web.

[60] Canada. Canadian Council of Ministers of the Environment. *Canadian Water Quality Guidelines : Imidacloprid Scientific Supporting Document*. N.p.: n.p., n.d. Canadian Council of Ministers of the Environment. Web.

[61] Lamers, Marc, Maria Anyusheva, Nguyen La, Van Vien Nguyen, and Thilo Streck. "Pesticide Pollution in Surface- and Groundwater by Paddy Rice Cultivation: A Case Study from Northern Vietnam." *Clean Soil Air Water CLEAN - Soil, Air, Water* 39.4 (2011): 356-61. Web.

[62] DeLorenzo, Marie E. "A Long-term Monitoring Study of Chlorophyll, Microbial Contaminants, a." *Nd Pesticides in a Coastal Residential Stormwater Pond and Its Adjacent Tidal Creek*. N.p., 2011. Web. 16 Jan. 2016.

pesticide or its residue, and inhalation.[63] While exposure can occur through a number of different means, the exposure has potential to be harmful regardless of the pathway.

Consumption is the primary method of exposure. Pollinators often rely on plant pollen and nectar as an essential source of food. The mutualistic relationship between plants and pollinators allows for pollen and nectar to be commonly ingested by the insects that participate in the pollination process. As stated previously, neonicotinoids are systemic, meaning that both the nectar and pollen of plants can be contaminated with neonicotinoids. The concentrations of neonicotinoids found in pollen and nectar is dependent on the application method as well as other variable environmental factors.[64] Plants treated via seed soaking have been found to have concentrations from 1 to 8.6 ppb in nectar and 1 to 51 ppb in pollen.[65] While the neonicotinoid concentration appears to be relatively low, consumption is still a dangerous pathway because pollinators are exposed multiple times per day and, in the case of social species, the contaminated food source is transported and fed to the entire community. Even minimal concentrations of neonicotinoids have the potential to be lethal over the course of multiple day or weeks due to the ability of the pesticide to accumulate in both habitats and the physical bodies of insects.

Many pollinators are in close physical contact with the environment treated with neonicotinoids. The pesticide and their respective residues can be found on plant leaves

[63] Sluijs, Jeroen P Van Der, Noa Simon-Delso, Dave Goulson, Laura Maxim, Jean-Marc Bonmatin, and Luc P. Belzunces. "Neonicotinoids, Bee Disorders and the Sustainability of Pollinator Services." *Current Opinion in Environmental Sustainability* 5.3-4 (2013): 293-305. Web.
[64] Goulson, Dave. "REVIEW: An Overview of the Environmental Risks Posed by Neonicotinoid Insecticides." *J Appl Ecol Journal of Applied Ecology* 50.4 (2013): 977-87. Web.
[65] Goulson, Dave. "REVIEW: An Overview of the Environmental Risks Posed by Neonicotinoid Insecticides." *J Appl Ecol Journal of Applied Ecology* 50.4 (2013): 977-87. Web.

and petals, guttation droplets, and in the soil.[66] Constant interaction between pollinators and treated environments make contact an significant pathway of exposure. Habitat contamination dramatically increases both the duration and concentration of pollinator exposure to neonicotinoids. In wild and domestic environments pollinators use or rely on materials from the environment for shelter. For example, flies and beetles take cover under vegetation and sometimes burrow in the soil. Additionally, social bees that create hives use plant material to structures that act as the foundation.[67] The implementation of all treated plant products into the hives and resting habitats of pollinators results in constant exposure neonicotinoids. In addition, the pesticide products easily accumulation so that as more plant products are used the levels of concentration in the habitats has potential to increase.

The application of neonicotinoid products through foliar and soil treatments can be detrimental to pollinators that reside on agricultural land. It is impossible to evacuate all animals and insects during pesticide spraying and seeding, which creates the possibility of exposure through contact and inhalation. All pollinators are at risk of exposure while plants are being treated with pesticide and planted. However, crawling pollinators such as beetles are especially vulnerable to such application methods. Beetles are limited to a specific range due to their lack of mobility and are often found either on the ground or in leaves of a plant. Beetles and other crawling insects must remain in close

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[66] Sluijs, Jeroen P Van Der, Noa Simon-Delso, Dave Goulson, Laura Maxim, Jean-Marc Bonmatin, and Luc P. Belzunces. "Neonicotinoids, Bee Disorders and the Sustainability of Pollinator Services." *Current Opinion in Environmental Sustainability* 5.3-4 (2013): 293-305. Web.

[67] Sluijs, Jeroen P Van Der, Noa Simon-Delso, Dave Goulson, Laura Maxim, Jean-Marc Bonmatin, and Luc P. Belzunces. "Neonicotinoids, Bee Disorders and the Sustainability of Pollinator Services." *Current Opinion in Environmental Sustainability* 5.3-4 (2013): 293-305. Web.

to their food supply. As a result, the topical applications of pesticides can be extremely lethal when direct contact exposure occurs.

Soil treatments and foliar applications are not the only dangerous application method. Seed dressings can also produce pathways of exposure. Farmers no longer personally plant their individual seeds each season. Instead, many farmers invest in seeding machines that move throughout the fields and plant seeds with minimal efforts from the farmer. The machine is especially useful on large scale farms. Unfortunately, when the machines plant neonicotinoid treated seeds the hard coating is fractured and forms a cloud of neonicotinoid dust. The dust produced during mechanical seeding process is extremely lethal to bees.[68] Bees that are exposed to the dust cloud often succumb to the lethal effects in less than twenty-four hours.[69] Mechanical seeding is also problematic because the particles are not constrained to one spot. Windy conditions can spread the dust far past agricultural boarders.

The overall chance of repeated pollinator exposure to neonicotinoids is very high due to the mobility of both neonicotinoids and the pollinators themselves as well as the variety exposure pathways. For pollinators, neonicotinoid exposure can result in a number of different outcomes. The effects of exposure can be categorized into either sub lethal or lethal, which can be further differentiated into acute and chronic depending on the duration of exposure. The nervous system targeting nature of neonicotinoids allows for sublethal and lethal effects to occur during acute and chronic exposure.

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[68] Girolami, V., M. Marzaro, L. Vivan, L. Mazzon, C. Giorio, D. Marton, and A. Tapparo. "Aerial Powdering of Bees inside Mobile Cages and the Extent of Neonicotinoid Cloud Surrounding Corn Drillers." *Journal of Applied Entomology* 137.1-2 (2012): 35-44. Web.

[69] Girolami, V., M. Marzaro, L. Vivan, L. Mazzon, M. Greatti, C. Giorio, D. Marton, and A. Tapparo. "Fatal Powdering of Bees in Flight with Particulates of Neonicotinoids Seed Coating and Humidity Implication." *Journal of Applied Entomology* 136.1-2 (2011): 17-26. Web.

Regulating Neonicotinoids

Currently, the Federal Insecticide Fungicide and Rodenticide Act (FIFRA) is the main body of law used to register and regulate pesticides in the United States. The modern day FIFRA is the result of a series of mainly reactionary amendments to the original document, the Federal Insecticide Act. The gradual progression of the Federal Insecticide Act (FIA) has resulted in the increased protection of both environment and human health. The development of the FIA into current form of FIFRA truly illustrates how chemicals products are regulated in the United States. The amendment process is not complete, as the following discussion demonstrates, FIFRA still does not provide adequate protection to the environment and it's inhabitants.

The Federal Insecticide Act of 1910 is the foundational document of FIFRA. It was first ratified to protection to American citizens from inauthentic or altered pesticides. However the federal government eventually recognized that the chemicals in pesticides posed a greater risk then previously thought.[70] As a result, the Federal Insecticide Fungicide and Rodenticide Act was established in 1947 under the United States Department of Agriculture in order to replace the Federal Insecticide Act. FIFRA furthered the protections outlined by the FIA by requiring that manufactures register their products before opening them to the market. The registration process asked that the product label displayed an accurate ingredient list as well as instructions for proper application. However, if the product did not meet the standard the pesticide could still be registered under protest and with a warning to consumers.[71] In 1947, FIFRA lacked the

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[70] Finegan, Pamela. "FIFRA Lite: A Regulatory Solution or Part of the Pesticide Problem?" *Pace Environmental Law Review* 6.2 (1989): 615-641. Print.

[71] Lolley, Marina M. "Carcinogen Roulette: The Game Played Under FIFRA." *Maryland Law Review* 49.4 (1990): 975-1007.Web.

substantive means to prevent mislabeled chemicals from entering the market. This problem was addressed in the 1964 amendment to the Federal Insecticide Fungicide and Rodenticide Act. The act was amended in order to require that a product be approved by the United States Department of Agriculture prior to sale. Furthermore, the Secretary of Agriculture was given the ability to suspend the registration of a chemical or product if it was considered an “imminent hazard”.[72]

In 1972 FIFRA was amended as a result of public concern about the effects of dichlorodiphenyl trichloroethane (DDT) in the environment. The DDT crisis caught the attention of the nation and illustrated for the first time the holistic consequences of pesticide and insecticide use. DDT had been used extensively to control mosquito populations and combat malaria. Although the pesticide had greatly improved the quality of life for human populations, the environmental consequences could not be ignored. The problem was not truly understood until the publication of *Silent Spring*, which demonstrated how synthetic chemicals and pesticides can endanger ecosystems.[73] In response, the Federal Environmental Pesticide Control Act was passed as an amendment to FIFRA. This amendment changed FIFRA to include protections for environmental health. The dedication of FIFRA to the environment was further solidified when the responsibility for implementing FIFRA was shifted from the United States Department of Agriculture to the newly established Environmental Protection Agency. Additionally, the Federal Environmental Pesticide Control Act demanded that the criteria for product registration became more stringent. The manufacturer became responsible for complete,

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[72] Lolley, Marina M. "Carcinogen Roulette: The Game Played Under FIFRA." *Maryland Law Review* 49.4 (1990): 975-1007. Web.
[73] Carson, Rachel, Lois Darling, and Louis Darling. Silent Spring. Boston: Houghton Mifflin, 1962. Print.

clear, and truthful labeling. In addition, the product must be able to preform the intended or expected function in accordance with common usage practices. Finally, the product cannot have “unreasonable adverse effects on the environment”.[74] The inclusion of this clause requires the EPA to include economic, social, and environmental factors into the cost-benefit analysis before determining if a pesticide is acceptable for the market. Traditionally, the EPA had used its discretionary powers to restrict and deny the use of chemicals that have detrimental effects on humans. However, the amendment allowed FIFRA itself demand that environmental damage be considered as a means to regulate a pesticide.

The addition of the Federal Environmental Pesticide Control Act was the final fundamental amendment to FIFRA. The Federal Environmental Pesticide Control Act mandated that all pesticides and insecticides, including previously registered products, be registered under the new, stricter criteria. New pesticides were not the only pesticides subjected to the new criteria. Pesticides that had already been registered were required to be re-evaluated through a reregistration process in order to confirm the safety of each pesticide being used. FIFRA of 1972, lays the foundation for current regulations of the registration process. The registration process is quite elaborate and requires time for data collection and evaluation as well as a period for open commentary. As a result, the evaluation and re-evaluation of each pesticide required a considerable amount of time. So that in 1978, the registration process was switched to focus on active ingredients rather than products in order to allow for more efficiency. [75]

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[74] Federal Insecticide Fungicide and Rodenticide Act §3 (a)
[75] Lolley, Marina M. "Carcinogen Roulette: The Game Played Under FIFRA." *Maryland Law Review* 49.4 (1990): 975-1007. Web.

In 1988, concerns about pesticides resurfaced when a significant number of child cancer cases were linked to the use of the pesticide, ethylene dibromide, a commonly sprayed in apple orchards across the nation. Young children were exposed to significant doses of the carcinogen due to the often habitual consumption of apples in the form of healthy snacks such as, apple juice, apple sauce, and apple slices. The EPA struggled to quickly remove ethylene dibromide from the agrochemical markets due to industry claims of uncertainty in the link between ethylene dibromide and the cancer cases. [76] The federal government, with the goal of preventing similar situation from occurring in the future, amended FIFRA to include a budgeting provision to provide funding for EPA studies as well as give EPA the jurisdiction to demand for more information about the product in question.[77]

The various additions and amendments to FIFRA have resulted in the laws in place today. The main regulatory mechanisms of FIFRA include the EPA's ability to register, conditionally register, or deny the registration of a pesticide. The registration status is based on an understanding of the environmental and health impacts of the applied active ingredients when the product is used as directed by the label, which also must be approved by the EPA.

Despite all of the amendments made to FIFRA, there are still weaknesses in the law. The limitations include: vague definitions, lack of explicit thresholds to determine danger, untimely research, and inefficient hearings.

[76] Finegan, Pamela. "FIFRA Lite: A Regulatory Solution or Part of the Pesticide Problem?" *Pace Environmental Law Review* 6.2 (1989): 615-641. Print.
[77] Finegan, Pamela. "FIFRA Lite: A Regulatory Solution or Part of the Pesticide Problem?" *Pace Environmental Law Review* 6.2 (1989): 615-641. Print.

The inadequacy is reflected in the lack of regulation surrounding neonicotinoids. Currently, the majority of pesticide products that use neonicotinoids as an active ingredient have been given a conditional registration status.[78] Conditional registration is only given under the special circumstances outlined in Section 3(7) of FIFRA. The registration of many pesticides containing neonicotinoids was given under the condition that more data and research be submitted to the EPA. Once a pesticide is given conditional registration, it can legally be bought and sold making it available to the markets. Neonicotinoids were classified as conditionally acceptable for public use in 1994. Since then, active ingredients have grown to dominate the domestic and agricultural pesticide markets. Despite the sufficient amount of time, neonicotinoids have been virtually ignored until recent concern for pollinators put pressure on the agency. The EPA has released schedule for the review of five neonicotinoids. The first report on imidacloprid was released January 4, 2016. Reviews of clothianidin, thiamethoxam, dinotefuran,and acetamiprid are scheduled to be completed no later than 2019. [79] The results and implications of the EPA neonicotinoid registration review will be discussed in further detail in the chapter titled Proposals.

Evidence of Harm

As pervious sections have related, pollinators play a significant role in both natural and agricultural environments. The key ecosystem service both wild and domestic pollinators provide as pollinators is essential, valuable, and virtually irreplaceable. There are growing concerns about the decreases in both wild and domestic pollinator

[78] Federal Insecticide Fungicide and Rodenticide Act. §3(C)(7)(c)
[79] "Schedule for Review of Neonicotinoid Pesticides." *EPA*. Environmental Protection Agency, n.d. Web. 16 Jan. 2016.

populations across the globe as extreme pollinator declines could have a detrimental effect on the environment, food supply, and the international economy. [80]

The use of neonicotinoids in agricultural and botanical settings may play a role in the disappearance of common pollinators. Neonicotinoids have become increasingly popular since the discovery of imidacloprid in 1991. Their recent increase in use has occurred simultaneously with the decrease in pollinators at a national and global level. In addition, the lethal and sub lethal toxicity of neonicotinoids to pollinators has been illustrated through numerous laboratory and field studies, which will be outlined and discussed further in the upcoming section. Neonicotinoids have also raised significant concerns in other nations. The European Union found neonicotinoids to be an ominous danger and as a result instated a ban on the chemicals. The swift, substantive action of the European Union implies a significant relationship between neonicotinoids and pollinator deaths. [81]

Although there is concern for all pollinators, importance has been placed on insects that have a significant impact on agricultural production. The recognizable decrease in natural bee, beetle, and fly services have forced farmers to rent bee colonies in a newly formed market for pollinator services. Current research on the effects of neonicotinoids on pollinators relies heavily on *Apis mellifera* (honey bee) and *Bombus terrestris* to represent the pollinator population. Although the use of bumble and honey bees as subjects is justified due to their large populations and easy access, the extent to

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[80] Goulson, D., E. Nicholls, C. Botias, and E. L. Rotheray. "Bee Declines Driven by Combined Stress from Parasites, Pesticides, and Lack of Flowers."Science 347.6229 (2015): 1255957. Web. 5 Jan. 2016.
[81] "Commission Implementing Regulation (EU) No 485/2013." The European Commission. Official Journal of the European Union, 25 May 2015. Web. 18 Mar. 2016.

which the studies results can be appropriately extrapolated to other species is limited. The bees in the United States alone have suffered tremendous losses. Between the years of 1974 and 2005 approximately 59% of domesticated honey bee (*Apis mellifera*) colonies were lost.[82] Since 2006 beekeepers have lost 26% to 30% of hives during overwintering.[83] The 2014-2015 statistics found losses of 42.1% while the average loss should be closer to 10%.[84] The well-evidenced loss of pollinators has prompted research in the area of pollinator health.

Sublethal effects of neonicotinoid exposure do not result in direct mortality. Instead, the resulting effects cause indirect deaths by altering the physiology and behavior of the exposed creature. Some of the documented changes include: impaired foraging, complications with orientation and finding home, reduced rates of reproduction, and weakening of upcoming generations.[85] Neonicotinoid exposure at sublethal levels is capable of increasing individual and community susceptibility to other stressors. In general, sublethal effects are measured in terms of No Observable Effect Concentration or Lowest Observable Effect Concentration. Both NOEL and LOEC are standardized

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[82] Potts, S., Biesmeijer, J., Kremen, C., Neumann, P., Schweiger, O., & Kunin, W. (2010). Global Pollinator Declines: Trends, Impacts and Drivers. *25* (6), 345-353.
[83] Lapin, Danny. "Neonicotinoids and Bees Assessing the Debate Surrounding the Impacts of Neonicotinoids on Pollinator Populations." (n.d.): 105-26. Otsego County Conservation Association. Web.
[84] "Colony Loss 2014-2015: Preliminary Results." *Bee Informed Partnership*. Bee Informed, n.d. Web. 16 Jan. 2016.
[85] Sluijs, Jeroen P Van Der, Noa Simon-Delso, Dave Goulson, Laura Maxim, Jean-Marc Bonmatin, and Luc P. Belzunces. "Neonicotinoids, Bee Disorders and the Sustainability of Pollinator Services." *Current Opinion in Environmental Sustainability* 5.3-4 (2013): 293-305. Web.

measurements commonly used during the development and testing of new pharmaceuticals.[86]

Acute sublethal effects are often studied in laboratory settings in order to allow for explicit control over the exposure time and environmental factors. Studies completed in this fashion are able to isolate neonicotinoids as a cause of the changes in behavior. However, the interactions between the pesticide and the subjects are often inauthentic which can create implications for how the results can relate to field situations. In contrast, chronic sublethal effects are more easily observed in the field. Honey and bumble bees alike are chronically exposed to neonicotinoids through agricultural practices. As a result, many of the studies interested in the sub lethal effects of chronic exposure occur in the field. This method allows for a better understanding for the reality of chronic sublethal exposure.

Lethal effects result in direct death due to neonicotinoid exposure. The amount of pesticide required to create a lethal dose or concentration is generally much higher than a sublethal dose. A dose or concentration is considered to be lethal if 50% of the exposed subjects experience death within a range of forty-eight hours to ten days.[87] Such levels are labeled as LD50 or LC50.

Mortality resulting from acute exposure has been observed historically and replicated in studies during the use of pneumatic seeding machines. The most drastic instance of acute lethality from mechanic seeding occurred in Germany during the Spring

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[86] Laskowski, Ryszard. "Some Good Reasons to Ban the Use of NOEC, LOEC and Related Concepts in Ecotoxicology." Oikos 73.1 (1995): 140. Web. 20 Nov. 2015.

[87] Sluijs, Jeroen P Van Der, Noa Simon-Delso, Dave Goulson, Laura Maxim, Jean-Marc Bonmatin, and Luc P. Belzunces. "Neonicotinoids, Bee Disorders and the Sustainability of Pollinator Services." *Current Opinion in Environmental Sustainability* 5.3-4 (2013): 293-305. Web.

of 2008. Pneumatic seeding machines are used to plant pesticide coated seeds more efficiently. In the specific instance of Germany, the seeds were coated with the neonicotinoid, clothianidin. During the seeding process the hard coating breaks down into fine particles and enters the air as a fine dust. The clothianidin particles were suspended in the air and drifted over unintended tracts of land. More than eleven thousand honey bee colonies were damaged by the toxic dust cloud.[88]

Girolami was able to replicate rapid honey bee deaths as a result of a single exposure during the use of the pneumatic seeding machine in two separate studies. In the first study, Girolami used a seeding machine in an area that worker bees had been trained to forage. The bees were allowed to fly freely through the area of exposure. Girolami found that bees can in fact be powdered by the seeding machine while flying by. The bees exposed to clothianidin and imidacloprid experienced significant levels of mortality. In the second experiment mobile cages were used to replicate the flight paths of bees around a functioning pneumatic machine. Again, the exposure of neonicotinoids resulted in lethality for the majority of subjects. The consistency of Girolami's results illustrate a highly certain example of acute lethality.

Currently, there is a great debate about the lethality of chronic neonicotinoid exposure to pollinators. The controversy is fueled by the clashing interests of agrochemical industry and environmentalists. Each of the parties have been able to point to studies to support their stance on the safety of neonicotinoids. Yet, the conclusions are contrasting. Additionally, there is a large disconnect between laboratory results and in-

[88] Vanengelsdorp, Dennis, and Marina Doris Meixner. "A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors That May Affect Them." *Journal of Invertebrate Pathology* 103 (2010):Web.

field studies. Many labs isolate bees in an attempt to reduce the variables in the experiment. Labs studying chronic exposure like the one completed by Aline Fauser-Missilin found that long term dietary exposure can have fatal effects.[89] In contrast, studies that aim to replicate the natural interaction between bees and treated agricultural fields often come to different conclusions about chronic lethality and neonicotinoids. Multiple studies including the one completed by G. Christopher Cutler have found that neonicotinoid exposure in agricultural settings pose a "low risk to bees" and find little to no decrease in colony performance. Some of the controversy can be attributed to scientific bias respective to the best interests of certain groups. However, the disconnect between in-field and lab studies was legitimate and unexplained until a study was released in Fall of 2015. The study used Radio Frequency Identification technology to track the life movements of 6,847 individual bees. From the findings, the study was able to conclude that field exposure to a combination of thiamethoxam and imidicloprid does result in individual mortality and that the honey bee colonies specifically are able to compensate for the population losses by focusing on the reproduction of worker bees rather then drone bees. [90]

As stated earlier, bees and especially honeybees, are used overwhelmingly to represent pollinators in neonicotinoid studies. The ability to regenerate missing groups of the population is not a survival trait that all pollinator species have. The primary use of

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[89] Fauser-Misslin, Aline, Ben M. Sadd, Peter Neumann, and Christoph Sandrock. "Influence of Combined Pesticide and Parasite Exposure on Bumblebee Colony Traits in the Laboratory." J Appl Ecol Journal of Applied Ecology 51.2 (2013): 450-59. Web. 2015.
[90] Henry, Mickaël, Nicolas Cerrutti, Pierrick Aupinel, Axel Decourtye, Mélanie Gayrard, Jean-François Odoux, Aurélien Pissard, Charlotte Rüger, and Vincent Bretagnolle. "Reconciling Laboratory and Field Assessments of Neonicotinoid Toxicity to Honeybees." *Proceedings of the Royal Society B: Biological Sciences Proc. R. Soc. B* 282.1819 (2015): 20152110. Web.

honey and bumble bees in studies has created a façade of immunity among the individual bees which has been extrapolated to pollinators as a whole. However, the results of Henry's study may provide the "missing link" that could help to explain the difference in conclusions. It may also invalidate some of the studies that dismiss neonicotinoids as a threat.

Data Evaluation

The purpose of this section is to review various sources and studies that provide an understanding of neonicotinoids and their interaction with the agriculture industry as well as pollinator species. In order for a policy to be effective, there must be a comprehensive understanding of the associated risks. In this case, the proposed regulation could have an effect of farming practices and therefore food supply. An understanding of the current shortcomings of neonicotinoid management and its effect on environmental and agricultural health is necessary in order to suggest responsible, sustainable solutions.

The United States is a prominent force among the nations and is able to influence the decisions made by other countries; thus, it is important to have an understanding that includes the global prospective. The article, "Global Pollinator Declines: Trends, Impacts and Drives," recognizes a decrease in pollinators on a global scale. The article argues that without a dramatic change the loss of ecosystems services will have a large effect on crop production, food security, and overall ecosystem stability.[91] Although the described consequences are calculated based on a decline of all pollinators, it is clear that we must protect the bee populations to reduce the severity of the consequences. An analysis of

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[91] Potts, S., Biesmeijer, J., Kremen, C., Neumann, P., Schweiger, O., & Kunin, W. (2010). Global Pollinator Declines: Trends, Impacts and Drivers. *25* (6), 345-353.

the economic valuation of insect pollinator services concluded that the economic value of insect pollination was approximately $171 billion.[92] The estimated value highlights the importance of insect pollinators as a whole, but it also reveals the implicit economic importance of pollinators.

In general, bees are viewed as the most prominent pollinator. However, flies also contribute significantly to the natural process of pollination. Frank Jauker and Volkmar Wolters were interested in determining the effectiveness of the *Episyrphus balteatus* (hover fly) as a pollinator for *Brassica napus* (oilseed rape). In order to test the hypothesis, the pair placed cages over the hover flies and the oilseed rape plant. Three separate conditions were tested. To establish a control group, cages were placed over the four designated areas. The cages prevented biotic pollination from occurring. In the second condition, a low density of hoverfly pupae was placed in the cage. Containing a high density of hoverflies in the cages created the third condition. The pupae were released into the caged environment once flowers began to open. The success of the hoverflies as pollinators was measured by the greatest increase in seed yield and seed set. It was found that the low-density group of hoverflies produced the greatest increase in crop yield. The experiment was completed twice in a two-year time period. The results were replicated during the second year of testing.

It is interesting that the authors choose to use a self-pollinating plant in this experiment. It is true that pollinators can help to increase the crop yield of a self-pollinating plant. However, that use of an already successfully pollinating plant seems to

[92] Gallai, N., Salles, J.-M., Settele, J., & Vaissiere, B. (2009). Economic Valuation of the Vulnerability of World Agriculture Confronted with Pollinator Decline. *Ecological Economics* , *68* (3), 810-821

exaggerate the usefulness of the hoverfly as a pollinator. Self pollinating plants only need their pollen to be shifted to different reproductive organ located on the same plant. The boundaries created by the cage in combination with the number of flies in the cage creates an environment where the effectiveness of hoverfly effectiveness is forced and to some extent artificial.

The primary author, Frank Jauker, has contributed to fourteen published works. His expertise is illustrated in the very thoughtfully controlled details of the experiment including the location, timing, and orientation of the crops. His goal was to highlight hoverflies as pollinators. The simple experiment is effective in illustrating that hoverflies can participate in the pollination process; however, their implied importance is exaggerated. [93]

The article co-authored by Dennis vanEngelsdorp and Marina Doris Meixner confirmed that the easiest way to prevent bee exposure to neonicotinoids is through pesticide control. Their article summarizes the history of managed bee populations as well as considered why the populations are decreasing. In essence bees are most affected by insecticides and diseases.[94] Given that neonicotinoids are immune system suppressants, it seems that a decrease in neonicotinoids would have a two-pronged benefit for bee populations by reducing the effects of exposure and not weakening the immune systems, which would leave the bees less vulnerable to diseases. The article

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[93] Jauker, Frank, and Volkmar Wolters. "Hover Flies Are Efficient Pollinators of Oilseed Rape." *Oecologia* 156.4 (2008): 819-23. Web.

[94] Engelsdorp, D. v., & Meixner, M. D. (2010). A Historical Review of Managed Honey Bee Populations in Europe and the United States and the Factors that may Affect Them. *Journal of Invertebrate Pathology , 103*, S80-S95.

implies that one focus of a policy with the objective to protect bees should specifically include measures to mitigate neonicotinoid exposure.

The article co-authored by Peter Jeschke and Ralf Nauen that provides insight on the history as well as the chemical structure and correlated characteristics of neonicotinoids.[95] The key to understanding how neonicotinoids became the global insecticide of choice is through its favorable characteristics. The chemical structure of the neonicotinoids allows the compounds to have a multitude of application methods and a relatively low risk to non-target creatures in comparison to traditional pesticides. It is these characteristics that make neonicotinoids such a favorable chemical. Recognizing why the chemical is used is important, and is an effective means for the identification of other effective chemicals that could replace the use of neonicotinoids. Additionally, neonicotinoids with an N-cyanoimine moiety have been found to be non-toxic to bees.[96] The information from this article could be used to determine if all neonicotinoids should be regulated or if the use of specific categories of the insecticides could be promoted as bee friendly.

It is also important to recognize that it is very unlikely that global neonicotinoid usage will decrease. A study published in the *Journal of Agricultural and Food Chemistry* found that in the past six years, three neonicotinoids (clothianidin, thiamethoxam and dinotefuran) have been removed from the list of patent protected

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[95] Jeschke, P., Nauen, R., Schindler, M., & Elbert, A. (2011). Overview of the Status and Global Strategy for Neonicotinoids . *Journal of Agricultural and Food Chemistry , 59*, 2897-2908.

[96] Jaschke, P., & Nauen, R. (2008). Review Neonicotinoids- from zero to hero in insecticide chemistry. *Pest Management Science , 64*, 1084-1098.

insecticides.[97]This suggests that more of the different chemical variations will be used in the future and it is often the case that generic formulas allow for the product to be sold at a reduced price. This means that as the generic chemical formulas become available to the market at a lower cost, neonicotinoids will be introduced as products for the domestic use. These insecticides dominate and will continue to dominate the global chemical market. This likely increased use is an important fact to keep in mind when contemplating the content of a policy. If the United States places restriction on neonicotinoids as a whole, there is a large possibility that the agriculture industry will be at disadvantage in the global food markets.

The study by Elbert et al. provided the necessary information about how the insecticides can be applied to crops, however the study did not include a satisfactory amount of information on the effects of neonicotinoids on the environment. Dave Goulson's article in the *Journal of Applied Ecology* delivers a comprehensive review of the environmental risks associated with neonicotinoid insecticides. The article discusses the accumulation of the insecticides in both the soil and water sources. In fact, Goulson argues that seed coating is not as safe as the previous study implied. Only 16-20% of the insecticide is absorbed into the seed after it is planted, so the rest of the chemical is absorbed in to the soil. During sowing, the newly treated dust enters the air, which can be lethal to bees in the vicinity. This article is unique due to the fact that it also considers how water sources could be affected. The build up of neonicotinoids in soil ultimately leads to problems of leaching and eventually the presence of the chemicals in water

[97] Jeschke, P., Nauen, R., Schindler, M., & Elbert, A. (2011). Overview of the Status and Global Strategy for Neonicotinoids . *Journal of Agricultural and Food Chemistry , 59*, 2897-2908.

sources. Neonicotinoids are water-soluble; their presence in the water supply puts non-target plants at risk of absorbing the chemicals.[98] The spread of chemicals to non-target plants will result in more bee exposure than originally estimated. Unfortunately, Goulson's work does not include possible methods to prevent the build up and spread of neonicotinoids in soil and water. Nevertheless, the piece is fundamental in understanding the extent of the risks posed by neonicotinoids, which is essential to ensuring that policies regarding neonicotinoids address all of the potential dangers.

The purpose of the study completed by Scott D. Stewart was to determine if pollinators are exposed to neonicotinoid insecticide due to insecticide seed treatments. The study takes place in the Mid-southern region of the United States and includes samples from Arkansas, Mississippi, and Tennessee. In addition, the study focuses on plots in which corn, cotton, and soybean seeds were treated with a neonicotinoid insecticide. Four types of samples were taken and analyzed for neonicotinic content. First, the researchers took samples of the soil where neonicotinoids had been previously used. The sample was taken before the annual planting was completed to test for neonicotinoid accumulation. After the planting occurred, samples of wild flowers adjacent to the recently planted field were taken. Also, bee and bee pollen samples were taken from surrounding hives and apiaries during the planting and flowering periods. Finally, samples were also taken at sites where the effectiveness of neonicotinoid seed treatment was being tested.

[98] Goulson, D. (2013). An Overview of the Environmental Risks Posed by Neonicotinoid Insecticides. *Journal of Applied Ecology , 50* (4), 977-987.

The researchers found that approximately 80% of the pre-planting soil samples were contaminated with at least 1 ng/g of neonicotinoids. The samples also revealed that 43% of the fields tested were contaminated with two or more types of neonicotinoids. The researchers also tested 4 sites where neonicotinoids had not been used. Two out of the four sites tested positive for detectable levels of neonicotinoids. Detectable levels of neonicotinoids were found on 23% of the wild flowers located no further than twenty meters from the planted fields. However, only two out of the seventy-four bees tested carried neonicotinoids. The same apiaries were tested for pollen contamination, but only one of the twenty-four pollen samples collected contained pollen.

The study goes on to conclude that while there is potential risk to of pollinator exposure the information cannot determine if the reported levels of neonicotinoids are a risk to bee health. However, the LD_{50} for imidacloprid is 17.9 ng/bee, and many of the highest found levels of neonicotinoids in post-planting wild flowers and bee samples. In addition, one sample of corn pollen from a test site contained 23 ng/g of clothianidin. The LD_{50} for clothianidin is 21.8 ng/bee.[99] An unrelated study suggested that bee exposure to neonicotinoids exceeding the LD_{50} level might be fatal. The study only discloses that average and maximum levels of insecticide contamination. There is a possibility that multiple samples were contaminated with potentially lethal levels of neonicotinoids.

The researchers received funding to complete the study from the National Cotton Council, Cotton Incorporated, multiple Soybean Promotion Boards, and the Mississippi

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[99] Stewart, Scott D., Gus M. Lorenz, Angus L. Catchot, Jeff Gore, Don Cook, John Skinner, Thomas C. Mueller, Donald R. Johnson, Jon Zawislak, and Jonathan Barber. "Potential Exposure of Pollinators to Neonicotinoid Insecticides from the Use of Insecticide Seed Treatments in the Mid-Southern United States." *Environmental Science & Technology Environ. Sci. Technol.* 48.16 (2014): 9762-769. Web.

Corn Promotion Board. The mission of these organizations is to increase the profitability of their respective industries. Neonicotinoids are a logical choice for inexpensive and effective insecticides. All academic areas are plagued by the possibility of bias; science is not an exception. There is a possibility that the interests of the funding organization may have influenced the results of the study.

The scientific experiment completed by Beketov and Liess confirms that neonicotinoids in freshwater sources are harming non-bee arthropods.[100] The experiment did not include bees, but bees are included in the Arthropod phyla. The researchers focus on one type of neonicotinoid called Thiacloprid where the researchers conclude that even lower concentration of the Thiacloprid insecticide can have lethal and sub lethal effects on fresh water Arthropods.[101] The majority of studies included in the Literature Review focus on Imidacloprid because it is the most widely used insecticide. The experiment illustrates that other neonicotinoids are also effective in achieving sufficient mortality rates. In addition, the study helps to illustrate that neonicotinoids can effect various aspects of the environment including non-pollinator species which may be fundamental in proving that neonicotinoids have "unreasonable and adverse effects on the environment" as required by the Federal Insecticide Fungicide and Rodenticide Act.

Some evidence suggests that the sublethal effects of neonicotinoids can eventually result in the weakening and death of entire colonies. The objective of the study completed

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[100] Beketov, Mikhail, and Matthias Liess. "Acute and Delayed Effects of the Neonicotinoid Insecticide Thiacloprid on Seven Freshwater Arthropods."Environmental Toxicology and Chemistry Environ Toxicology ChemPreprint.2007 (2007): 461-70. Web.

[101] Beketov, M., & Liess, M. (2008). Acute and Delayed Effects of the Neonicotinoid Insecticide Thiacloprid on Seven Freshwater Arthropods. Environmental Toxicology and Chemistry , 27 (2), 461-470.

by Cédric Alaux was to investigate the how the combination of a pathogen infection and neonicotinoid exposure effect the honeybee. A combination of *Apis mellifera* lingustica and *Apis mellifera* mellifera were the subjects of the experiment. The researchers created four experimental groups. The control was not exposed to either imidicloprid or Nosema spores. One group was exposed solely to imidicloprid and the other was exposed only to the Nosema spores. The final group was exposed to both the pesticide and the pathogen. Imidicloprid was administered the bees via a sucrose solution in doses of 0.7 µg/kg, 7 µg/kg, and 70 µg/kg. The spores were distributed through an individual sucrose food source harboring 200,000 spores. The researchers tested four biological indicators of stress: sucrose consumption, haemocyte count, phenoloxidase, and glucose oxidase enzyme. The goal was to identify the respective changes in energetic stress, immunity, immune reaction, and production of antiseptics.

The data illustrated a higher mortality rate in bees exposed to both the Nosema pathogen and the neonicotinoid. Bees infected with the Nosema spores consumed more of the sucrose solution than bees that were not infected. It is possible that the Nosema induced hunger increased the levels of exposure of the neonicotinoids located supply. Greater exposure to the chemical would result in more lethal and sub lethal responses to exposure. Neither the phenoloxidase nor the haemocyte activity was triggered by the presence of the pathogen or Imidicloprid. However, imidacloprid and nosema spores significantly reduced the antiseptic production. Again, the combination of the two factors resulted in the most significant impact.[102]

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[102] Alaux, Cédric, Jean-Luc Brunet, Claudia Dussaubat, Fanny Mondet, Sylvie Tchamitchan, Marianne Cousin, Julien Brillard, Aurelie Baldy, Luc P. Belzunces, and Yves Le Conte. "Interactions between Nosema Microspores and a Neonicotinoid Weaken Honeybees (Apis mellifera)." *Environmental Microbiology* 12.3 (2010): 774-82. Web.

The reviewed literature provides significant insight on the science and economics surrounding neonicotinoids and bees. However, the research question demands for a policy that would enable the bees to continue to pollinate without excessive risk. Kelsey Ott argues that the most effect policy would be in the form of a federal regulation. Currently, disputes about the harmful effects are addressed in state courts. Bee populations have continued to decline despite state jurisdiction. Ott concludes that there is a need for a clear policy that applies at the national level in order to avoid confusion among the farmers. The most significant aspect of the article is how Ott derives her conclusion and evaluation of other potential policy options.

Proposals

The Environmental Protection Agency governs pesticide usage under the Federal Insecticide Fungicide and Rodenticide Act. It is the responsibility of the EPA to monitor and if necessary take action to remove environmental risks created by chemicals. Unfortunately, the language used in the Federal Insecticide Fungicide and Rodenticide Act allowed for EPA inaction in regards to neonicotinoid regulation. The case of neonicotinoids easily demonstrates the consequences of inadequacy in federal policy. It is inevitable that as time passes the human race will continue to develop new technologies with unknown environmental consequences in the agricultural sector. As a result, it is imperative that the Federal Insecticide Fungicide and Rodenticide Act must be amended not only to address the shortcomings of neonicotinoid regulation but to also prevent similar acts of negligence in the future.

Scientific research has indicated a connection between diminishing pollinator populations and neonicotinoids for a significant amount of time, as demonstrated by the

European Union's hasty action to ban three prominent neonicotinoids almost three years ago. Also, in the time since neonicotinoids were first approved in the 1990's, the insecticide has grown to dominate the agrochemical market. It has been estimated that neonicotinoids are actively used on almost 75% of agricultural acres in the United States.[103] The almost exclusive use of neonicotinoids alone should warrant attention from the EPA. Yet, the EPA only recently began reevaluating the status of neonicotinoids as active ingredients. Currently, FIFRA does not specify any timeline for the registration review of approved chemicals. Instead the act only requires that the registrations of pesticides be "periodically reviewed" with the goal of reviewing a pesticide's status every fifteen years.[104] The language of the statute only suggests a timeline of review; the EPA is in no way bound to the fifteen year goal. It is understandable that FIFRA allows for flexibility in the registration review schedule, as strict time limitations would make registration reviews an extremely difficult task to complete given the variability of factors involved in the process. However, the EPA has been given too much discretion in determining the schedule in which pesticides should be reviewed. The registration status of the various neonicotinoids as active ingredients is just now being reviewed despite their approval approximately twenty-five years ago. The lack of a stringent review schedule for pesticides allowed the EPA to overlook the potential dangers of neonicotinoid use in the agricultural industry for too long. In order to prevent similar occurrences in the future, FIFRA should be amended to demand that the registration of any active ingredient used extensively in their respective market be reviewed in seven to

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[103] Grossman, Elizabeth. "Declining Bee Populations Pose A Threat to Global Agriculture." Yale Environment 360. Yale University, 30 Apr. 2013. Web. 23 Mar. 2016.
[104] Federal Insecticide, Fungicide, and Rodenticide Act § (G)(1)(A)

ten year intervals. Such a change to the act ensures that any chemical being introduced to the ecosystem in large quantities is thoroughly monitored and scientifically researched. It is imperative that chemicals with a large potential to impact environmental and human health are closely supervised so that unintended consequences can be recognized and addressed before irreversible harm occurs. It should be noted that the amendment would only apply to heavily used pesticides. Active ingredients that are used minimally in the agricultural markets would be spared such extensive research as to respect the realistic capabilities of the EPA.

The registration review clause should also be amended to include public participation in the monitoring process. Often, members of the community that complete the groundwork or hard labor are able to recognize trends in the changes occurring to human health or the environment. Beekeepers and farmers recognized the loss of pollinators and speculated neonicotinoids as the cause very early; much like how agricultural workers recognized the toxic effects of pesticide exposure during the Delano Grape Strike. Laborers that work directly with pesticides are currently an untapped resource. Hence, an addition should be made to FIFRA to give the public the explicit power to request the initiation of the registration review process for pesticides utilizing a common active ingredient. Early identification of injury is essential to successfully mitigating suspected harm due to the time requirements of completing and collecting representational data. Unfortunately, the initiation of scientific research is often reactionary; a disaster or tragedy must occur to inspire the high level of scientific interest needed to make a regulatory change. The history of FIRA itself, demonstrates this phenomenon.[105] As a result, it is essential that FIFRA be amended to employ a "all hands on deck" mentality. Consumer knowledge, expertise, and intuition are valuable tools in recognizing harm either as soon as possible or before dramatic changes in the environment or human health occur.

The final amendment to FIFRA should address the conditional registration clauses that have allowed for the use of neonicotinoid pesticides to persist despite the overwhelming lack of research and understanding. [106] The current state of the clauses has proven to be an inadequate means of registering pesticides. All pesticides that are deemed conditionally registered by the EPA should continue to be researched and monitored until an educated decision about the registration status can be made. As a result, the circumstances for conditional registration must be revised to include language that demands the use of active adaptive management. Active adaptive management practices requires that decisions are made based on information derived from specifically designed scientific experiments.[107] The inclusion of active adaptive management into the conditional registration clauses would provide the EPA with an opportunity to truly investigate the potential impacts of a pesticide on the environment and human health before registration is confirmed. It may also be beneficial for the EPA to employ the precautionary principle when outlining research limitations for new or historically ambiguous pesticides. Initial experiments designed to study the impacts of conditionally registered pesticides should not include immediate exposure to humans. Rather, until the EPA can demonstrate with reasonable certainty that a pesticide will not harm either

[105] See Chapter: Regulating Neonicotinoids
[106] Federal Insecticide Fungicide and Rodenticide Act. §3(C)(7)(c)
[107] Doremus, Holly. "Precaution, Science, and Learning While Doing in Natural Resource Management." SSRN Electronic Journal SSRN Journal (2007): 12-18. Web. 28 Mar. 2016.

human or environmental health, the scope of experiments should be constrained to a system that would allow for the maximum acquisition of information while reducing the possibility of excessive potential impacts on both humans and the environment. Ultimately the inclusion of the precautionary principle and active adaptive management methods would help to prevent the rampant use of pesticides before they are truly understood.

Neonicotinoids have been identified to play a significant role in the decline of pollinator populations via a sizable amount of evidence demonstrated by laboratory experiments, field studies, pollinator population statistics, and the developing commercial market for traveling pollinator services. It is imperative that actions are taken to prevent any further significant losses as well as encourage the rebuilding of wild and domesticated pollinator populations. To truly address pollinator declines, policies must be enacted to regulate the significant stressors that impact the lifespan of solitary and social pollinators. However, of the various stressors, neonicotinoid application is one of the most prominent factors that can be explicitly controlled by human action, and will therefore be essential to the human efforts of maintaining and restoring pollinator populations.

Until recently, the United States government has taken little initiative in recognizing or addressing concerns about pollinators. In the summer of 2014, President Barack Obama signed a Presidential Memorandum that demanded the organization of a Pollinator Health Task Force. The Memorandum assembled members of various departments and agencies in an effort to produce a comprehensive strategy to address pollinator losses.[108] The Task Force published the *National Strategy to Promote the Health of Honey Bees and Other* Pollinators in 2015, which outlined plans for research, education, and the the creation of public-private partnerships with the goals of reducing bee overwintering mortality, increasing the butterfly population, and restoring pollinator habitats across the nation.[109] The Pollinator Health Task Force and their resulting National Strategy highlighted the severity of the pollinator situation and was able to suggest a viable strategy to remedying the problem. However, the Task Force is limited by its inability to create enforceable federal regulations, and therefore cannot act as the only means to combat pollinator decline. Instead departments and agencies with the jurisdiction to implement laws must take the lead.

The Environmental Protection Agency has initiated the reregistration review process for five neonicotinoids prominently used in the agricultural industry, imidacloprid, clothianidin, thiamethoxam, dinotefuran, and acetamiprid. Pesticides that include the identified five neonicotinoids as an active ingredient are generally listed as conditionally registered. The conditional status of the various pesticides products allows the EPA to either recall or confirm their registration status once the active ingredients have been properly researched. Reregistration review has already begun and all five neonicotinoids will be addressed no later than 2019.[110] Imidacloprid was the first neonicotinoid to be reviewed and the EPA has already successfully released the

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[108] "Presidential Memorandum -- Creating a Federal Strategy to Promote the Health of Honey Bees and Other Pollinators." The White House. Office of the Press Secretary, 20 June 2014. Web. 16 Mar. 2016.
[109] United States of America. Pollinator Health Task Force. National Strategy to Promote the Health of Honey Bees and Other Pollinators. Comp. Tom Vilsack and Gina McCarthy. The White House, 19 May 2015. Web. 16 Mar. 2016.
[110] "Schedule for Review of Neonicotinoid Pesticides." EPA. Environmental Protection Agency, n.d. Web. 17 Mar. 2016.

Preliminary Pollinator Assessment to Support the Registration Review of Imidacloprid, which recognized on and off field risks to the *Aphis Mellifera.* While more studies are expected to be completed for imidacloprid and the other four neonicotinoids, it is likely that the EPA will find varying degrees of the similar results in regards to pollinator associated risks. At the conclusion of the multiple year review, the EPA will be charged with determining the reregistration status of neonicotinoid pesticides.

It has become clear that neonicotinoids need to be regulated, but it is difficult to determine the extent of regulation required to improve pollinator health and increase pollinator populations. Neonicotinoids have become a highly debated topic; opinions about the pesticide vary on a spectrum from a complete ban to business as usual behavior. In 2013, the European Union determined that three neonicotinoids, imidacloprid, clothianidin, and thiamethoxam, posed too large of a potential risk to pollinators and instituted a union-wide ban.[111] The application of the precautionary principle was rooted in a scientific concern for pollinator health and the resulting a high potential risk of human hunger. Yet, as is the case with many precautionary regulations, the decision was highly praised and highly contested by various stakeholders. European farmers have struggled to maintain crop yields given the very few effective pesticide alternatives. The National Farmers Union lobbied for an emergency lift of the neonicotinoid ban in an effort to protect their remaining crops. This specific request was denied; however, in 2015 the European Union allowed for a temporary lift of the ban which allowed farmers to use two of the three banned neonicotinoids on a small percent of the oil seed rape crop

[111] European Union. The European Commission. 1., 25 May 2013. Web. 21 Mar. 2016. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:139:0012:0026:EN:PDF>.

for a 120 day time-period.[112] The ban on neonicotinoids despite the temporary lift has detrimentally effected the crop yield. Research has found that the ban has cost farmers almost 30 million dollars in alternative pesticides, crop damage, and replanting costs.[113] Farmers have reported completely plowing their pest infested crops with hopes that planting a new crop would be more successful. The neonicotinoid ban has unintentionally encouraged the overuse of toxic chemicals; European Union Farmers unsuccessfully increased their use of older pesticides such as carbamates and organophosphates in an effort to prevent pest damage.[114]

Given the results, a ban on neonicotinoids may not be the best course of action for the United States. It is likely that American farmers will also encounter a large increase in crop damage due to pests and attempt to protect their crops with older and more harmful chemicals in exchange for neonicotinoids. Older chemicals, like the carbamate and organophosphate insecticides, are still toxic to pollinators, as the original intent of neonicotinoids was to replace toxic agro-chemicals with a less harmful alternative.[115] Carbamates and organophosphates are less efficient and often require larger application amounts. If the United States parallels the actions of the European Union, a ban on neonicotinoids will result in the excessive use of older and still toxic pesticides which

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[112] Marshall, Claire. "Ban Lifted on Controversial 'neonic' Pesticide." BBC News. British Broadcasting Corporation, 23 June 2015. Web. 22 Mar. 2016. <http://www.bbc.com/news/science-environment-33641646>.
[113] Scott, Charles, and Paul Bilsborrow. An Interim Impact Assessment of the Neonicotinoid Seed Treatment Ban on Oilseed Rape Production in England A Report for Rural Business Research Charles Scott and Paul Bilsborrow (2015): 6-20. Rural Business Research, 25 Aug. 2015. Web. 22 Mar. 2016.
[114] Randall, Rebecca. "Pests Invade Europe after Neonicotinoids Ban, with No Benefit to Bee Health." Genetic Literacy Project. Genetic Literacy Project, 27 Jan. 2015. Web. 22 Mar. 2016.
[115] "Honey Bee Health and Colony Collapse Disorder." Agricultural Research Service. United States Department of Agriculture, 5 Nov. 2015. Web. 22 Mar. 2016.

will impact pollinators and detrimentally effect nearby ecosystems. As a result, the complete elimination of neonicotinoids from the agriculture industry may not sufficiently resolve the problem of pesticide risk to pollinators. Instead it is essential that the EPA take the necessary steps to properly regulate neonicotinoids with pollinator health and restoration in mind.

The first step in addressing neonicotinoids is to reduce unnecessary use. The recent initiation of the reregistration process gives the EPA the opportunity to withdraw the current conditional status of over 200 pesticide products. While many neonicotinic pesticides are used in the agriculture industry, the EPA has also the allowed the conditional use of pesticides created for domestic lawn and gardening. The main benefit of using neonicotinoids in household gardens is that plants are protected from pest damage without potential harm to humans. However, the presence of neonicotinoids in domestic products create an unnecessary risk to pollinators. Neonicotinoids must be removed from the list of active ingredients that can be used in household pesticides. Personal gardens are not critical agricultural entities and therefore cannot be afforded the same protection as agricultural farms. Additionally, neonicotinoids are the primary insecticides used on a significant number of crops in the United States.[116] Many of these crops are irreplaceable and can justify the need for such extensive protection from pests. However, some crops, such as rape seed, have viable commercial substitutes. Rape seed is more commonly known in its processed form of Canola Oil, which is the main use for rape seed crops. Canola Oil does not provide essential nutrients to the human body and can be easily substituted for a market equivalent such as vegetable or olive oil. Pesticides

[116] Grossman, Elizabeth. "Declining Bee Populations Pose A Threat to Global Agriculture." Yale Environment 360. Yale University, 30 Apr. 2013. Web. 23 Mar. 2016.

that contain neonicotinoids should be reserved for crops that have significant nutritional value and have very few market substitutes. It is these types of crops that need the most protection; rather crops that non-essential by nature. Therefore, the application of neonicotinic pesticides should also be limited to highly nutritional and irreplaceable crops.

In addition to limiting the types of plants that can be treated by neonicotinoids, it is essential that the practice of applying neonicotinoids every season even when not necessary be prohibited. Neonicotinoids are persistent pesticides and are able to accumulate in the soil. Climate is a key factor in determining how long the pesticide will remain in the environment, so variability in levels of persistence can be very high. The continuous reapplication of neonicotinoids each season increases the concentrations of the pesticide in both the nectar and pollen and may ultimately result in an increase in pollinator exposure to lethal doses of neonicotinoids. In order to ensure that crops are treated with least of amount of neonicotinoids possible the EPA must require that all soils are tested before more neonicotinoids applied. If high concentrations of neonicotinoids remain in the soil, the crop will be protected due to the systemic nature of the pesticide. As a result, it would be completely unnecessary for more pesticides to be applied.

If the excessive and unnecessary use of neonicotinoids can be eliminated, the next step would be to heavily regulate the remaining use that occurs. It is imperative to the goal of maintaining and restoring pollinator populations that the agricultural use of neonicotinoids is carefully controlled. The implementation of a nation-wide certification program for applicators may help to reduce careless and unneeded neonicotinoid use. Risk associated with the pesticide application process would significantly decrease if farmers were encouraged to hire commercial applicators rather then attempting to apply the neonicotinoids themselves. While the use of commercial applicators could be considered a best management practice there may be unintentional consequences to completely eliminating private applicators. The financial burden of hiring commercial applicators could result in increase in the illegal and therefore unregulated use of neonicotinoids or a return to the traditional and very toxic pesticides in order to avoid the applicator costs. In order to prevent these undesirable outcomes, the EPA must only require that all parties interested in using neonicotinoids participate in the Certified Applicator program to ensure that all applicators are thoroughly educated about the pesticide they are using. In the current form of FIFRA, the certified applicator program is under state jurisdiction. It is important that the rights of the state be respected. The federal applicator program should be recognized simply as a baseline standard; so that the state may impose more stringent certification protocols if it deems them necessary. Education is a crucial tool in developing an applicator culture that is aware and invested in pollinator safety. The federal certification program should continually be adapted in order to reflect the most modern scientific discoveries as well as keep applicators informed about developing technologies that could reduce environmental risks.

Currently, there are no regulations that encourage farmers and applicators to use neonicotinoid pesticides in a way that minimizes harm to pollinators. Unfortunately, the systemic nature of neonicotinoids only allows the opportunity for regulation through direct exposure. It is essential that direct exposure is reduce because it is one of the only pathways that is easily controlled. One method to prevent direct exposure to pollinators would be to prohibit neonicotinoid application during high pollinator activity time periods. The proposed regulation would help to prevent accidental spraying of pollinators that active in the agricultural fields. In addition, the use of seeding machines on neonicotinoid coated seeds must be prohibited. The large neonicotinoid dust cloud poses to large of a risk to both the immediate area of use and further adjacent lands. The removal of the toxic cloud from the agriculture industry will promote the maintenance and restoration of pollinator populations by eliminating the ambient air as a possible path way of exposure.

Conclusion

Neonicotinoids are not the only stressor contributing to pollinator declines, but they are one of the most damaging stressors easily controlled by human action. The scientific evidence summarized in various chapters of this thesis demonstrate that neonicotinoids are highly likely to cause significant harm in the form of both sublethal and lethal effects to pollinators. Pollinators cannot be replaced, as their ecosystem services extend too far and wide. The language used the Federal Insecticide Fungicide and Rodenticide Act appears to create a demand for the regulation of neonicotinoids. However, the lack of regulation calls for both an amendment to FIFRA and a change in the way neonicotinoids are registered. It is essential that amendments made to FIFRA continue to promote the values of human and environmental safety while preventing similar occurrences in the future.

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