



BEYOND PESTICIDES

701 E Street, SE ■ Washington DC 20003
202-543-5450 phone ■ 202-543-4791 fax
info@beyondpesticides.org ■ www.beyondpesticides.org

February 21, 2012

Office of Pesticide Programs (OPP)
Regulatory Public Docket (7502P),
Environmental Protection Agency,
1200 Pennsylvania Ave. NW.,
Washington, DC 20460-0001

**Re: Pesticide Registration Review; New Dockets Opened for Review :
Clothianidin (Case # 7620) Docket Id. No.: EPA-HQ-OPP-2011- 0865; and
Thiamethoxam (Case # 7614) Docket Id. No.: EPA-HQ-OPP-2011-0581.**

Dear Sir/Madam:

We would like to take this opportunity to submit comments regarding the pesticide clothianidin. The agency has opened the docket to public comment for the insecticide clothianidin as part of its registration review. As the agency is aware, Beyond Pesticides and many other organizations are gravely concerned about the threat clothianidin poses to the environment, especially to essential pollinators like the honey bee. Similarly, we find it appropriate to also comment on the registration review for thiamethoxam, as this chemical is a precursor for clothianidin in the environment. At this time, Beyond Pesticides would like to reiterate concerns and highlight data similar to those in previous communications with the agency regarding clothianidin.

Clothianidin is a broad-spectrum, systemic neonicotinoid insecticide registered for use to control chewing and sucking pests on various vegetables (root, tuber, bulb, leafy: brassica and non-brassica), legumes (soybean), various fruits, tree nuts, cereal grains, oilseed crops (canola, corn, cotton), and other crops. It is also registered for use in poultry houses, and recreational and residential settings.¹ Approximately 800,000 lbs of clothianidin has been used in the U.S.

¹USEPA. 2011. Clothianidin Summary Document Registration Review. Office of Pesticide Programs. Federal Register Docket Id. No.: EPA-HQ-OPP-2011- 0865.

since its conditional registration in 2003. Corn accounts for the overwhelming majority (99%) of uses for clothianidin.²

Clothianidin Poses a Risk To Honey Bees and Other Pollinators, And Its Registration Should Be Cancelled

Clothianidin belongs to the nitroguanidine subgroup of neonicotinoids, a neurotoxic class of insecticides. Neonicotinoids affect the nervous system of insects, causing irreversible blockage of the postsynaptic nicotinic acetylcholine receptors (via a selective agonistic mechanism).³ Clothianidin is a potential risk to non-target organisms including terrestrial and aquatic invertebrates, birds, and mammals. For the honey bee, toxicity has been observed at LD₅₀ 22 ng/bee for clothianidin (30 ng/bee for thiamethoxam),⁴ levels lower than those noted in EPA's clothianidin registration factsheet (LD₅₀> 43.9 ng/bee). In fact, clothianidin and thiamethoxam are only second in toxicity to imidacloprid (LD₅₀ 17.9 ng/bee) for this class of chemicals. Clothianidin has also been observed to be highly toxic to other wild bee species like the common eastern bumble bees (*Bombus impatiens* (Cresson)), alfalfa leafcutting bees (*Megachile rotundata* (F.)) and the blue orchard bee (*Osmia lignaria* Cresson).⁵

Corn cultivation, which accounts for 80 million acres of land planted in the U.S.,⁶ threatens bee colonies. The application rates for clothianidin and thiamethoxam on corn range from 0.25 to 1.25 mg/kernel. A single kernel contains several orders of magnitude of active ingredient more than the published LD₅₀ values for honey bees.⁷ Clothianidin and thiamethoxam residues were found in dead bees and pollen from hives in Indiana apiaries that reported colony losses in the spring of 2010. The compounds however, were not in bees from hives that did not show mortality.⁸ These losses coincided with the peak period of corn planting in the area. Neonicotinoid insecticides like imidacloprid and clothianidin have sublethal effects in honeybees, which include disruptions in mobility, navigation, and feeding behavior.⁹ Lethal and sublethal exposures have been shown to decrease foraging activity, along with olfactory

² USEPA. 2011. BEAD Chemical Profile for Registration Review: Clothianidin (044309). Federal Register Docket Id. No.: EPA-HQ-OPP-2011-0865

³ USEPA. 2011. BEAD Chemical Profile for Registration Review: Clothianidin (044309). Federal Register Docket Id. No.: EPA-HQ-OPP-2011-0865

⁴ Iwasa, T et al. 2004. Mechanism for the differential toxicity of neonicotinoid insecticides in the honey bee, *Apis mellifera*. *Crop Protection*. 23(5): 371-378.

⁵ Scott-Dupree CD, Conroy L, Harris CR. 2009. Impact of currently used or potentially useful insecticides for canola agroecosystems on *Bombus impatiens* (Hymenoptera: Apidae), *Megachile rotundata* (Hymenoptera: Megachilidae), and *Osmia lignaria* (Hymenoptera: Megachilidae). *J Econ Entomol*. 102(1):177-82.

⁶ Economic Research Service. 2010. Corn. USDA <http://www.ers.usda.gov/Briefing/Corn/>

⁷ Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. 2012. Multiple Routes of Pesticide Exposure for Honey Bees Living Near Agricultural Fields. *PLoS ONE* 7(1): e29268. doi:10.1371/journal.pone.0029268

⁸ Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. 2012. Multiple Routes of Pesticide Exposure for Honey Bees Living Near Agricultural Fields. *PLoS ONE* 7(1): e29268. doi:10.1371/journal.pone.0029268

⁹ Desneaux, N. et al., 2007. Sublethal Effects of Pesticides on Beneficial Anthropods. *Annual Review of Entomology*, 52:81-106

learning performance and decrease hive activity.¹⁰ In a study looking at the acute effects of sublethal doses of clothianidin under field-like conditions at 0.05 -2 ng/bee, a significant reduction of foraging activity and longer foraging flights at doses of ≥ 0.5 ng/bee during the first three hours after treatment were recorded.¹¹ Bees are exposed to these pesticides via foliar and systemic treatments when they pollinate flowering crops, or pesticide drift from surrounding areas. Bees living and foraging near agricultural fields are exposed through multiple mechanisms throughout the spring and summer. One of the greatest source for exposure is from the exhaust of the tractor-drawn planters that spew small residues (dust) of treated seeds into the air while sowing. One Italian study found that bee mortality increased right after seed sowing and confirmed these findings with post mortem chemical analysis that found high concentrations of neonicotinoid insecticides (imidacloprid and clothianidin) as high as 500 ng/bee of active ingredient.¹² A similar study involving the seed sower found comparable results of increased bee mortality on the day of sowing and decreased foraging bees days after the sowing, this time with thiamethoxam.¹³

Researchers are beginning to discover that in addition to residues found in pollen and nectar,^{14,15} neonicotinoid pesticides can be detected in other areas. Guttated water of seed-treated plants, which provides a source of water for bees, can also be a source of contamination and exposure.¹⁶ Reetz et al. found that corn seeds treated with clothianidin resulted in neonicotinoid concentrations up to 8,000 ng/ mL in the guttated fluid.¹⁷ This concentration, while decreasing rapidly, remained detectable over several weeks. In a 2011 study guttation drops from corn plants obtained from commercial seeds coated with thiamethoxam, clothianidin, imidacloprid and fipronil taken from young plants contained high levels of the neonicotinoid insecticides: up to 346 mg/L for imidacloprid, 102 mg/L for clothianidin, and 146 mg/L for thiamethoxam.¹⁸

¹⁰ Decourtye, A. et al., 2004. Effects of imidacloprid and deltamethrin on associative learning in honeybees under semi-field and laboratory conditions. *Ecotoxicology and Environmental Safety*.57: 410-419

¹¹ Schneider CW, Tautz J, Grünwald B, and Fuchs S. 2012. RFID Tracking of Sublethal Effects of Two Neonicotinoid Insecticides on the Foraging Behavior of *Apis mellifera*. *PLoS One*:7(1):e30023.

¹² Girolami, V. et al. 2011. Fatal powdering of bees in flight with particulates of neonicotinoids seed coating and humidity implication. *J. Appl. Entomol.* 136:17–26.

¹³ Tremolada P, et al. 2010. Field trial for evaluating the effects on honeybees of corn sown using Cruiser and Celest xl treated seeds. *Bull Environ Contam Toxicol*.85(3):229-34.

¹⁴ Bernal J, et al. 2010. Overview of pesticide residues in stored pollen and their potential effect on bee colony (*Apis mellifera*) losses in Spain. *J Econ Entomol*;103(6):1964-71.

¹⁵ Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. 2012. Multiple Routes of Pesticide Exposure for Honey Bees Living Near Agricultural Fields. *PLoS ONE* 7(1): e29268. doi:10.1371/journal.pone.0029268.

¹⁶ Hoffmann, E and Castle, S. 2012. *Imidacloprid in Melon Guttation Fluid: A Potential Mode of Exposure for Pest and Beneficial Organisms*. *J Economic Entomology* 105(1):67-71.

¹⁷ Reetz, J. et al. 2011. Neonicotinoid insecticides translocated in guttated droplets of seed-treated maize and wheat: a threat to honeybees? *Apidologie* 42(5): 596-606.

¹⁸ Tapparo, A. et al. 2011. Rapid analysis of neonicotinoid insecticides in guttation drops of corn seedlings obtained from coated seeds. *J Environ Monitoring* 13(6): 1564-1568.

Clothianidin is also persistent in the environment and residues have been detected in soil and other areas not under corn cultivation. Clothianidin residues remain present in the surface soil of agricultural fields long after treated seed had been planted, as long as two growing seasons.¹⁹ This leads to long-term contamination of surrounding vegetation, including wild plants like dandelions that bees also visit for pollen and nectar. According to Krupke et al. clothianidin in/on the dandelions could have resulted from translocation from the soil to the flower, from surface contamination of the flowers from dust, or a combination of these two mechanisms.²⁰

The rapid disappearance of the honey bees, also dubbed “Colony Collapse Disorder” or CCD, has been observed in the U.S. since 2006. Even though researchers have indicated that there may be several variables associated with CCD, clothianidin, and other chemicals in its class, cannot be ruled out as a major contributor and this must be factored into the agency’s assessment. Honey bees intercept, and are contaminated by, particles on crops and suspended in the air, and retain them in their hair and/or accumulate them in their bodies and hives. Mitigation techniques (e.g. product label restrictions) to prevent honeybees from coming into contact with this highly toxic pesticide once it is used in the environment are highly infeasible. The only way to protect important pollinators is to remove these toxic neonicotinoids from the environment.

Clothianidin Conditional Registration is Unlawful

Section 3(c)(7)(A) of the *Federal Insecticide, Fungicide and Rodenticide Act* (FIFRA) states that conditional registration may be given if “(i) the pesticide or proposed use are identical or substantially similar to any currently registered pesticides and use....(ii) approving the registration or amendment in the manner proposed by the applicant would not significantly increase the risk of any unreasonable adverse effects on the environment.” Data is required to be submitted to obtain registration in accordance with Section 3(c)(5). Section 3(c)(7)(A) also states, “If the applicant is unable to submit an item of data because it had not yet been generated, the agency may register or amend the registration of the pesticide under such conditions as will require the submission of such data not later than the time such data are required to be submitted....”

The conditional registration of clothianidin violated the terms set out in Section 3(c)(7)(A). First, we believe that its registration does pose unreasonable adverse effects on the environment.

¹⁹ Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. 2012. Multiple Routes of Pesticide Exposure for Honey Bees Living Near Agricultural Fields. *PLoS ONE* 7(1): e29268. doi:10.1371/journal.pone.0029268

²⁰ Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. 2012. Multiple Routes of Pesticide Exposure for Honey Bees Living Near Agricultural Fields. *PLoS ONE* 7(1): e29268. doi:10.1371/journal.pone.0029268

FIFRA defines the term "unreasonable adverse effects on the environment" as "(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under Section 408 of the *Federal Food, Drug, and Cosmetic Act*."²¹ The risk posed to bees far outweighs any economic, social or environmental benefit of clothianidin's registration. In fact, the risks posed to bees would translate to a \$15 billion impact of the agriculture sector and millions of dollars loss for commercial beekeepers, not to mention the economic and environmental costs to native, wild pollinators.

Additionally, outstanding data have not been submitted to the agency nine years after it was first requested. At the 2003 conditional registration of clothianidin, the submission of the outstanding data (final study) was expected in December 2004, as laid out by the agency in its 2003 risk assessment for clothianidin use. In this document, the Environmental Fate and Effects Division (EFED) in the Office of Pesticide Programs suggested that conditional registration be granted to the registrant "contingent on [the registrants] conducting the chronic honey bee study that evaluated the sublethal effects of clothianidin to the hive over time."²² To date, these pertinent honey bee studies have not been submitted, nine years after EFED's timeline was laid out. As a result, the conditions for the conditional registration of clothianidin according to Section (3)(c)(7) have been breached, and thus conditional registration should be rescinded.

An effort to collect exposure and hazard information is now underway according to the data requirements now being requested in the 2011 registration review documents, years after clothianidin has been contaminating the environment and killing bees. In the 2003 conditional registration fact sheet for clothianidin, the agency acknowledged that clothianidin "has the potential for toxic chronic exposure to honey bees, as well as other non-target pollinators, through the translocation of clothianidin residues in nectar and pollen."²³ Further it states, "...the effects of this toxic chronic exposure may include lethal and/or sub-lethal effects in the larvae and reproductive effects in the queen." At that time, the agency said that certain honey bee studies were required, "In order to fully evaluate the possibility of chronic exposure to honey bees, a complete worker bee life cycle study will be required, as well as an evaluation of exposure and effects to the queen."²⁴

²¹ USEPA. Summary of FIFRA. 7 U.S.C. §136 et seq. (1996). Washington DC Available at <http://www.epa.gov/lawsregs/laws/fifra.html>

²² USEPA. 2003. Addendum Referring to EFED's Risk Assessment on Clothianidin Use as a Seed Treatment on Corn and Canola (PC code 044309). Office of Pesticide Programs. Washington DC.

²³ USEPA. 2003. Pesticide Fact Sheet: Clothianidin. Office of Pesticide Programs. Washington DC

²⁴ USEPA. 2003. Pesticide Fact Sheet: Clothianidin. Office of Pesticide Programs. Washington DC

Beyond Pesticides and others pointed out to the agency in December 2010 that at the time of conditional registration, the agency was aware that clothianidin posed a threat to honey bees and other pollinators, yet went forward with authorizing its use in the wider environment, without the “required” honey bee data to support registration. The agency in response argued that “the uses met the Federal Insecticide, Rodenticide and Fungicide Act (FIFRA) risk/benefit standard for registration.”²⁵ In this letter the agency stated, “the 2003 conditional registration of clothianidin was granted based on.... the submission of a field test for pollinators.” The letter goes on to state that this study was reclassified as a supplemental study, i.e. “a study that provides scientifically sound information, but did not follow all protocols set forth in EPA test guideline.” At the point of this reclassification, the study was no longer acceptable to support registration. The reclassification is troubling given that clothianidin was already granted conditional registration by this time, after the agency acknowledged that clothianidin posed a threat to bees and took no action.

As a result, clothianidin’s 2003 conditional registration is unlawful as it violated the terms set on in Section 3(c)(7)(A) of FIFRA, and thus should be cancelled.

EPA is Playing Catch-Up with Pollinator Data

According to the summary document for clothianidin for its registration review, the agency states that it is seeking ecological effects data for use in conducting “a complete ecological risk assessment,” including an endangered species assessment.²⁶ These include, among others :

- (i) Honey bee toxicity of residues on foliage (GLN 850.3030)
- (ii) Field testing for pollinators (GLN 850.3040)
- (iii) Pollinator larval toxicity (Non-Guideline)
- (iv) Laboratory pollinator feeding study (Non-Guideline)
- (v) Residues in pollen and nectar/field residue analysis study (Non-Guideline)
- (vi) Chronic sediment toxicity test with midge larvae (Non-Guideline)

In order to address data regarding risks to honey bees the agency also states that it will consider recommendations from the Society of Environmental Toxicology and Chemistry (SETAC) Workshop on Pesticide Risk Assessment for Pollinators. This SETAC workshop, which convened in January 2011, recommended the following, and others, for further research and

²⁵ Letter from S. Bradbury, Director, Office of Pesticide Programs (Feb, 18, 2011) to response to Dec 8, 2010 communication from Beyond Pesticides et al.

²⁶ USEPA. 2011. Clothianidin Summary Document Registration Review. Office of Pesticide Programs. Federal Register Docket Id. No.: EPA-HQ-OPP-2011- 0865.

data collection:²⁷

- (i) Compile residue data for pollen, nectar, guttation
- (ii) Pesticide fate within the colony
- (iii) Standardized protocol for chronic feeding study
- (iv) Method to assess effects on foraging behavior
- (v) Adoption of a larval (early life stage) test
- (vi) Toxicity testing for non-*Apis* species

Looking at SETAC's recommendations and EPA's data requirements, pesticide risks to honey bees have not been extensively studied and the agency is playing catch-up with bee data. Much remains unknown about the effects of pesticide contaminants and exposure pathways on the honey bee and other bee and pollinator populations. The members of the SETAC workshop agreed that the most significant routes of exposure for both honey bees and other bees (from foliar and systemic seed treatments), are through dermal contact and oral exposure of foraging adults, hive adults, and larvae to contaminated pollen, nectar, and processed food (honey, bee bread, etc).²⁸ Contact with contaminated soil, sprayed leaves and petals were also notable exposure pathways, especially for other bees. In light of this and independent studies demonstrating that these routes of exposures do occur resulting in bee mortality and impaired bee health, serious action is warranted. Thus far the agency has not sufficiently reviewed pertinent honey bee data regarding clothianidin. As a result, the agency has not fulfilled its statutory mandate under FIFRA to pose no unreasonable adverse effect on the environment.

Thiamethoxam, A Source For Clothianidin, Should Also Be Cancelled

Thiamethoxam, like its degradate clothianidin, is a broad spectrum nitroguanidine nicotinoid. It was first registered for antimicrobial uses as a wood preservative. The agency states that pesticide products containing thiamethoxam were first registered in 1999,²⁹ as a Section 18 emergency exemption. New uses for thiamethoxam in agricultural crops have been petitioned and registered since 2006 and thiamethoxam is now registered for use on various fruits and vegetables, cereals, and some non-agricultural sites. Over 500,000 lbs of thiamethoxam have been used annually between 2001 and 2008, with soybeans, corn and cotton being the top crops.³⁰ Ecological risks assessments conducted by the agency have stated "risks to non-target

²⁷ Fischer D, Moriarty T. 2011. Pesticide risk assessment for pollinators: Summary of a SETAC Pellston Workshop. Pensacola FL (USA): Society of Environmental Toxicology and Chemistry (SETAC).

²⁸ Krupke CH, Hunt GJ, Eitzer BD, Andino G, Given K. 2012. Multiple Routes of Pesticide Exposure for Honey Bees Living Near Agricultural Fields. *PLoS ONE* 7(1): e29268. doi:10.1371/journal.pone.0029268

²⁹ USEPA. 2011. Thiamethoxam Summary Document Registration Review. Office of Pesticide Programs. Federal Register Docket No: EPA-HQ-OPP-2011-0581.

³⁰ USEPA. 2011. Registration Review: Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Thiamethoxam. Office of Pesticide Programs. Washington DC.

arthropods, including pollinators, remain a key issue with thiamethoxam registrations.”³¹ In a 2010 ecological risk assessment document for thiamethoxam, Field Test for Pollinators (850.3040) was identified, among others, as an outstanding data gap. Like clothianidin’s assessments, it states “EFED recommends that the registrant conduct field studies at maximum proposed label rates using crops that are attractive to bees (*e.g.*, pears or apples) for seed treatment, foliar, and soil applications. These three studies should be conducted in consultation with EFED and should examine the exposure and effects to adults and larvae. The studies should measure the amount of thiamethoxam translocated to the nectar and pollen of the target crop and rotational crops and potential adverse effects, including sublethal effects.”

These pollinator studies have still not been completed and submitted to the agency for review, years after the agency acknowledged risks to pollinators. In the most recent assessment for thiamethoxam (2011), pollinator studies were again identified as data gaps. Some studies have been submitted but suffered study design limitations, and are therefore still classified as data gaps.³² Also identified were bee incident data involving thiamethoxam.

Thiamethoxam is also persistent in soils with a half-life ranging between 101-353 days. A major transformation product of thiamethoxam is clothianidin, which is more persistent. Clothianidin is identified as a major transformation product in field dissipation studies after broadcast applications, and as a minor product in various other environmental conditions including aquatic dissipations studies.³³ At a transformation rate of about 13.2%, thiamethoxam applications are not an ignorable source of clothianidin residues in the environment. Even though the agency makes reference to this in its assessment, we do not believe that the agency goes far enough to protect vulnerable pollinators and other non-target organisms from clothianidin and thiamethoxam. Like clothianidin, the agency allowed thiamethoxam into the environment without a full analysis of the data relating to pollinators, even though it is well known that these chemicals pose serious risks to pollinator health.

In addition, the agency has classified thiamethoxam as a ‘likely’ human carcinogen.³⁴ Treatment in mice induces cytotoxicity, leading to regenerative proliferation and the development of tumors.³⁵ Decreased white blood cell count (leukopenia) has been observed in dog studies.³⁶

³¹ USEPA. 2010. Ecological Risk Assessment for the Proposed New Use of Thiamethoxam as a Seed Treatment for Alfalfa. Office of Pesticide Programs. Washington DC.

³² USEPA. 2011. Registration Review: Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Thiamethoxam. Office of Pesticide Programs. Washington DC.

³³ USEPA. 2011. Registration Review: Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments for Thiamethoxam. Office of Pesticide Programs. Washington DC.

³⁴ USEPA. 2000. Report of the Risk Assessment Review Committee. Office of Pesticide Programs. Washington DC

³⁵ Cohen, S. Evaluation of Possible Carcinogenic Risk to Humans Based on Liver Tumors in Rodent Assays The Two-Year Bioassay Is No Longer Necessary. *Toxicol Pathol*, 38: 487-501.

³⁶ USEPA. 2009. Addendum to the HED Risk Assessment for the Use on Citrus and Tree Nuts. Office of Pesticide Programs. Washington DC

Studies with rats have observed that thiamethoxam induces an increase in anxiety behavior and significantly decreases both high-affinity choline uptake and acetylcholinesterase activity, indicating that thiamethoxam also acts on the central nervous system (nicotinic acetylcholine receptors) in mammals.^{37,38} Thiamethoxam therefore not only poses risks to pollinators and other non-target insects, but also poses a risk to mammals and potentially humans.

Conclusion

Honey bees are the most economically valuable pollinator worldwide, and many high-value crops such as almonds and broccoli are entirely reliant upon pollination services by commercial beekeepers and their honey bees. Globally, 9.5% of the total economic value of agricultural production for human consumption comes from insect pollination – in 2005, this amounted to just under \$200 billion.³⁹ However, each year since 2006, commercial beekeepers have reported annual losses of 29% - 36%. Such losses are unprecedented, and approximately double what is considered normal. Like France, Germany and other European countries, EPA must make a proactive decision against the neonicotinoid class of chemicals. Clothianidin and thiamethoxam are not only extremely persistent in the environment, but they are highly toxic to bees and other non-target insects. Clothianidin's use as a systemic pesticide means that every part of the plant is potentially toxic to the honey bee, and can result in widespread contamination of soil and wild plants. We believe the risks posed by clothianidin and other neonicotinoids have been underestimated by the agency, especially given the outstanding honey bee data that have yet to be adequately reviewed. In light of the agency's mandate in Section 3(c)(7)(A) of FIFRA to ensure that pesticides do not pose unreasonable adverse effects on the environment, clothianidin and its parent thiamethoxam should be cancelled. We look forward to working with the agency to ensure that it upholds its statutory duty.

Respectfully,

Beyond Pesticides

³⁷ Rodrigues KJ, et al. 2010. Behavioral and biochemical effects of neonicotinoid thiamethoxam on the cholinergic system in rats. *Ecotoxicol Environ Saf*;73(1):101-7.

³⁸ de Oliveira IM., et al. 2010. Effects of the neonicotinoids thiamethoxam and clothianidin on in vivo dopamine release in rat striatum. *Toxicol Lett*. 192(3):294-7.

³⁹ PANNA and Beyond Pesticides. 2012. Economic Value of Commercial Beekeeping . Available at <http://www.beyondpesticides.org/pollinators/EconomicValueCommercialBeekeeping.pdf>