

January 8, 2016

Comments by **Eric Chivian M.D.** Supporting the Office of Health Assessment and Translation (OHAT) Review of Neonicotinoid Pesticides. (80 FR 60692; October 7, 2015)

Dear OHAT Staff,

As a physician and former professor at Harvard Medical School, I am writing to strongly support a scientific review by OHAT of the potential threat to human health from neonicotinoid pesticides. In what I have written below I am representing myself, and myself alone, not the non-profit I now direct (The Program for Preserving the Natural World, Inc.), nor anyone connected with it in any way, not the Department of Organismic and Evolutionary Biology at Harvard University where I am an Associate, nor the Center for Health and the Global Environment, which I founded and directed for many years at Harvard Medical School (now based at the Harvard School of Public Health).

I believe it is of critical importance for OHAT to conduct a comprehensive scientific review of neonicotinoids because:

- these nicotinic acetylcholine receptor blockers are the most widely used insecticides in the world today--on more than 160 million acres of genetically-modified corn and soybean fields in the U.S. alone, and on countless dogs and cats (for fleas and ticks), gardens, and lawns,
- the receptors they target play central roles in the activity, regulation, and development of our nervous systems,
- there is strong and growing evidence that we are chronically exposed to these neurotoxins in our drinking water and in our food,
- and there is now emerging evidence demonstrating that neonicotinoids cross the mammalian placenta and blood-brain barrier and affect mammalian neuronal function, and that serious human health impacts may result from chronic neonicotinoid exposure.

Nicotinic Acetylcholine Receptors in our Nervous Systems

Nicotinic acetylcholine receptors, the molecular target of neonicotinoid insecticides, are found throughout the human central and peripheral nervous systems. They are widely distributed in the human brain, and are particularly heavily concentrated in the thalamus. The thalamus acts as a kind of central communications station for the brain, relaying every sensory input signal (except for smell) to our cortex, and every motor signal from the cortex to our spinal cords. The thalamus also helps regulate consciousness and our level of awareness (a thalamic stroke, for example, can result in permanent coma), and plays a central role in both memory and cognition.

Nicotinic acetylcholine receptors are thought to be one of the main gate-keepers for the transmission of neural impulses in the human brain—modulating and regulating the function of a wide range of other receptors **1. 2.** Nicotinic acetylcholine receptors are already present at very early embryonic stages in mammals and have been shown to play central roles in the development of mammalian nervous systems, helping to regulate the growth of nerve cells, both

the amount of growth and the specific pathways that are taken and attachments that are made **3.**, **4.**

Neonicotinoid Contamination of Water and Food

Neonicotinoids are water-soluble and have long half-lives, with some studies showing they can last more than 3 years in soils. Concentrations can therefore build up with repeated annual applications. There is extensive evidence that neonicotinoids leach from soils into surface waters. For example, they were found in multiple samples taken from Iowa streams by the U.S. Geological Survey in 2013 following rainfall events during crop planting. **5.** A recent review points to the widespread global distribution of neonicotinoids in surface waters. **6.**

Not surprisingly, they have also shown up in ground water in some agricultural areas **7.**, and in drinking water wells. See, for example, the 2011 Well Monitoring Project by the Wisconsin Department of Agriculture in the attached pdf file [note that Clothianidin, Imidacloprid, and Thiamethoxam are all neonicotinoids]

When looking at the presence of neonicotinoids in food, it is important to keep in mind that, in contrast to other insecticides, systemic pesticides like the neonicotinoids cannot be washed or peeled off. They are not on the surface of the food; they are inside of it, within the cells and fluids of treated fruits and vegetables, and perhaps also within the cells of domestic livestock fed neonicotinoid-treated corn and soybeans.

The USDA with its Pesticide Data Program

<http://www.usda.gov/wps/portal/usda/usdahome?contentid=2014/12/0276.xml>

and the Food and Drug Administrations with its Total Diet Study

<http://www.fda.gov/Food/FoodScienceResearch/TotalDietStudy/default.htm>

both measure the presence of neonicotinoids in food.

The USDA samples thousands of fruits and vegetables each year. In 2013, they found more than 30% of the cauliflowers sampled contained Imidacloprid, as did 22% of cherry tomatoes and more than 1/3rd of sweet bell peppers. Of critical concern, from 2010 to 2012, the FDA found that 20% of the baby foods they tested contained one or more neonicotinoid residues.

The findings that neonicotinoids are in both surface and ground water and in our food, suggest that it is likely we are ingesting these compounds on a regular basis. Large numbers of people, including pregnant women and children, are also being exposed to these neurotoxins through contact with their pets, their gardens, and their lawns. Should this concern us?

Potential Human Health Impacts of Neonicotinoid Exposures

The USDA, EPA, and FDA all say it should not. They conclude that the concentrations of neonicotinoids that we are being exposed to are so small that they do not constitute a risk to human health. But, in fact, there is little hard evidence to support this conclusion, and much to call it into question.

1. For one, the studies that the EPA relies on to determine safe neonicotinoid exposure levels are largely, and to the best of my knowledge exclusively, performed by the companies that produce the compounds studied. There is no independent testing. See, for example, this study on rats exposed to Imidacloprid during gestation, widely cited by the EPA as proof of there being no developmental neurotoxicity from neonicotinoid exposures, a study performed by the Bayer Corporation (which makes Imidacloprid). **8.**

Neonicotinoids were developed as they were shown to have stronger effects on insect nicotinic acetylcholine receptors than they did on those of mammals, including humans. But while they are less toxic to us, they are still toxic.

2. There are several reported cases in the literature of acute human neonicotinoid poisoning, with respiratory failure, shock, and death after large ingestions. **9.**

But there is also cause for concern about potential human health impacts resulting from neonicotinoid exposures at much lower levels.

3. It is highly likely that neonicotinoids cross both the human placenta and the blood brain barrier, as they have been shown to do in rats. **10. 11.**
4. Neonicotinoids can cause significant neurobehavioral deficits in rats and alter nicotinic acetylcholine receptor activity in the rat midbrain, cortex and brainstem following low dose exposures during pregnancy. **12.**
5. Minute concentrations of neonicotinoids have been demonstrated to affect nicotinic acetylcholine receptors in rat **13.**, and in human **14.** neurons when tested in tissue culture studies.
6. There have been very few studies of human health impacts following chronic exposures to neonicotinoids, but the few that have been done have produced highly disturbing results. They have found:
 - An association between exposure to agricultural neonicotinoids during pregnancy and the risk of anencephaly (a catastrophic failure of brain, skull, and scalp development) in newborns. **15.**
 - An association between exposure during pregnancy to the neonicotinoid Imidacloprid used on pets to control fleas and ticks, and the risk of autism spectrum disorder in the offspring. **16.**
 - And an association between exposure to agricultural neonicotinoids during pregnancy and the risk of “Tetralogy of Fallot,” a congenital heart defect involving three, and sometimes four, anatomical defects of the heart. **17.**

Final Comments

1. Despite the likely widespread distribution of neonicotinoids in the U.S., particularly in agricultural regions, there has been limited monitoring of these neurotoxic insecticides in food by the USDA and FDA, and almost no monitoring of them at all in our drinking water. As a result, we have little to no information about the extent of human exposures.
2. Despite our likely exposures to neonicotinoids, there has been no human urine or serum bio-monitoring of them by the Centers for Disease Control and Prevention, as they do

with other pesticides in their NHANES Program, so we know nothing at all about the presence of these compounds in our bodies.

3. We have no knowledge whether individual neonicotinoids, or combinations of them, will affect the structure, function, and development of the human brain, particularly during critical developmental periods in the embryo, and during childhood and adolescence.
4. The far greater vulnerability of infants and children to pesticides **18**. should have led the EPA to apply a 10-fold child-protective safety factor into its risk assessment calculations for neonicotinoids, which it has failed to do.
5. We have no knowledge whether, and at what concentrations, neonicotinoids will alter the activity of human nicotinic acetylcholine receptors in the central and peripheral nervous systems.
6. Finally, there have been very few studies that have looked at the impacts of chronic human neonicotinoid exposures, so that we know next to nothing about the impact these compounds may have on human health. While they are preliminary and need to be replicated, the studies that have been done found highly disturbing associations between human neonicotinoid exposures during pregnancy and serious birth defects and other health impacts.

Given these facts, it should be beyond question that OHAT must now begin a comprehensive scientific review of the potential human health threats posed by the use of neonicotinoid insecticides in the United States, in order to ensure that every possible precaution is being taken to protect the American people.

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Submitted by:
Eric Chivian M.D.

Affiliations

Associate
Department of Organismic and Evolutionary Biology
Harvard University

Founder and Director Emeritus
Center for Health and the Global Environment
Harvard Medical School

Former Assistant Clinical Professor of Psychiatry
Harvard Medical School

No Sponsoring Organization

Contact Information

REDACTED

Email—eric_chivian@hms.harvard.edu