RESEARCH

Environmental Health

Open Access

Human acute poisoning incidents associated with neonicotinoid pesticides in the U.S. Incident Data System (IDS) database from 2018– 2022 – frequency and severity show public health risks, regulatory failures

Jennifer B. Sass^{1*} and Daniel Raichel²

Abstract

Background Neonicotinoid pesticides ('neonics') – imidacloprid, thiamethoxam, clothianidin, acetamiprid, dinote-furan—are the most widely used class of insecticides in the world. They have a neurotoxic mechanism of action, similar to nicotine. They are detected in food, waterways, tap water, and breast milk.

Methods We make use of the non-occupational human pesticide poisoning reports in the U.S. Environmental Protection Agency (EPA) online Incident Data System (IDS). The data set contains individual incidents, and incidents aggregated and submitted in bulk to EPA. IDS reports are predominantly self-reported information of varying and often low level of detail and are not routinely validated or verified by EPA.

Results We reviewed 842 non-occupational human poisoning incidents associated with neonics in the IDS from 2018 through 2022. There are four human fatality reports, two associated with clothianidin and two with acetamiprid. Major illnesses such as seizures were reported in several cases, including with dinotefuran cockroach bait product, and an imidacloprid lawn product. Moderate poisonings make up 88% of the total poisonings (740 of 842), with most of those associated with imidacloprid (547 incidents) or dinotefuran (102 incidents). Common reported symptoms classified as moderate often included two or more of the following: headaches; dizziness; lethargy; eye or throat irritation; skin itching and rash; chemical burns and skin peeling; face swelling; muscle weakness or tremors; vomiting; diarrhea; pain and tightness in chest; open sores; and general pain. These incidents stem mainly from residential uses, such as lawn and garden insect repellents, home pest treatments for bed bugs or roaches, and products used to treat pets for fleas and ticks.

Conclusion Given the evidence of neurotoxicity, EPA should use its legal authority to cancel unsafe products and unnecessary uses – including from seed treatments, and residential pet and lawncare products – to prevent further human suffering.

Keywords Neonicotinoid, Neurotoxic, Pesticide, Poisoning, Human, Seizure, Death

*Correspondence: Jennifer B. Sass jsass@nrdc.org Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

Background

Neonicotinoid pesticides, or "neonics," are the most widely used insecticides in the world, making up roughly one-quarter of global insecticide use [1, 2]. Their popularity is in large part because they are often characterized as posing little to no risk to vertebrates, including humans, due to their much lower affinity for the target receptor in vertebrates, compared with insects [3, 4]. The first neonic manufacturer, Bayer, stated in a 2016 report that, "[t]he toxicity of neonicotinoids to mammals and humans is very low" [5]. The chemicals are similar to nicotine and are toxic by a similar mechanism, acting as an agonist on the nicotinic acetylcholine receptor (nAChR), to overstimulate affective nerve cells and systems [3]. The concerns with neonics have focused on their devastating effects on bees, aquatic invertebrates, and beneficial insects, with good reason, as neonics are thought to be responsible for making agriculture almost fifty times more harmful to insects [6]. In fact, the U.S. Environmental Protection Agency (EPA) predicts that the neonics jeopardize the continued existence of over 200 threatened and endangered species - about 11% of the entire endangered species list - including many bees, butterflies, and other beneficial pollinating insects [7-9].

The class of neonics includes: imidacloprid; thiamethoxam; clothianidin; acetamiprid; dinotefuran. They are registered in over 120 countries, on more than 140 fruit, vegetable, and field crops to target sucking and chewing insects such as aphids or emerald ash borers [10]. The EPA has approved over 1,000 products containing neonics, including for agricultural crops, urban landscaping, and indoor bed bug and flea and tick treatments for pets.

Since neonics persist in soil and are highly water soluble, both the agricultural and consumer uses of neonic products contaminate soil and water. A national stream sample report by the U.S. Geological Survey found that clothianidin and thiamethoxam detections in surface water were related to uses on crops, whereas imidacloprid was the most frequently detected neonic in urban stream samples (37% of samples), with concentrations related to use on lawns, gardens, parks, and playgrounds [11]. A study in Minnesota reported a similar pattern, with the highest neonic detections associated with agricultural use, mainly clothianidin, followed by neonics use in urban areas, mainly imidacloprid, suggesting that both agriculture and urban uses contribute to chronic exposure [12]. Neonics have also been reported in tap water and foods including fruits, vegetables and baby foods, and human breast milk [13–17].

Here we provide a summary and discussion of the publicly available neonicotinoid human poisoning reports in EPA's IDS over five years, from 2018–2022.

Methods

As of July 2023, EPA made 10 years of pesticide incident data available on its online IDS database [18]. The IDS is a national database, populated with human health information from several sources, largely from pesticide manufacturers (called "registrants"), which are required to notify EPA of "information regarding unreasonable adverse effects on the environment of the pesticides" they register, including occupational, residential and ecological incidents [19]. Additional submissions come from State agencies, National Poison Centers, and the National Pesticide Information Center (NPIC), as well as individual reports to the database from pesticide applicators, agriculture workers, homeowners or tenants, health care professionals, and the general public [20]. IDS reports are predominantly self-reported information of varying and often low level of detail around exposure circumstances, symptoms, and/or medical outcome. The information is not routinely validated or verified by EPA, though reports from poison control centers and some states may be confirmed [21]. See EPA's website for details including data limitations [22].

While ecological incidents are also included in IDS, we did not analyze these data. Our data analysis excludes any other databases or data sources, so as to avoid potential for double counting the same cases reported to multiple entities. For example, the NPIC shares some incident reports with IDS, roughly five-to-ten reports each month.

While IDS contains some occupational incidents, most occupational poisonings are reported to two other databases. The California Pesticide Illness Surveillance Program (PISP) includes physician-reported pesticide worker poisonings for the state of California. The Sentinel Event Notification System for Occupational Risk (SENSOR) is a national database that aggregates reports from states, physicians, emergency room records, workers' compensation claims, and Poison Control Centers. Neither PISP nor SENSOR are incorporated into the IDS. Since most of the occupational incidents that EPA uses come from PISP or SENSOR, with many fewer coming through IDS, by limiting the source of poisoning incidents to just the EPA's IDS, occupational incidents are largely excluded from this analysis. For those readers interested in occupational exposures, we direct them to the National Institute for Occupational Safety and Health (NIOSH) which compiles data from the SENSOR-Pesticides Program and the National Poison Data System and reports the findings in its Pesticide Illness and Injury Surveillance Program [23].

To avoid double-counting within the IDS data, we scrutinized each line-entry individually, excluding duplicate poisoning cases reported on multiple line-entries. We also excluded any reports not reasonably attributable to pesticide exposure, such as one report of an injury from a 'plane crash,' presumably during crop dusting activities. Intentional pesticide ingestion cases were also excluded since they do not represent the intended use of the product. However, we included poisoning reports where the product was used as intended, but possibly not as per label directions, for example: poisonings from a splash or spill while using the product; exposure due to improper ventilation; or premature re-entry into a pesticide-treated area in conflict with label instructions. We included these reports because they represent the real-world use and injury patterns associated with these products.

Results

Over a five-year period from 2018 through 2022, U.S. EPA received reports of just over 840 people poisoned with neonics; these values should be considered estimates given the lack of individual details in the data reports [24]. Incidents included symptoms ranging from human fatalities (H-A) to major (H-B), moderate (H-C), or minor (H–D) injuries [25]. Imidacloprid was implicated in roughly 70% of the total individual poisonings, most with moderate symptoms of poisoning. See Table 1 for the tabulations of the number of human poisoning incidents by severity and by individual neonic pesticide.

See Table 2 for the list of 56 human incidents between 2018 and 2022 that include reports classified as H-A or H-B. On July 11, 2023, we submitted a request to EPA under the Freedom of Information Act for the full

incident reports for each of the 56 cases, along with any records such as correspondence, meeting minutes, memoranda, and emails associated with the 56 cases. On October 28, 2024 we received redacted reports responsive to our request. Below we provide additional details for the four human fatality cases from the full reports.

The EPA incident reports include four human fatality reports, two associated with clothianidin and two with acetamiprid. For the two clothianidin associated fatalities, EPA states only that in 2019, "2 people died involving Crossfire Bed Bug treatment [25]" (See Table 2). The two acetamiprid fatalities were from 2018: an entry for "Ortho Flower, Fruit and Vegetable Insect Killer Ready-To-Use" with a hand wand applicator reported that "[s] ymptoms include sudden death;" another for "transport termicide [sic] insecticide" reported that, "a man in poor health died after a pesticide application in Sect. 8 apartments [25]" (See Table 2).

The full reports we received from EPA in response to our follow-up FOIA request including the following additional information about the above reported fatalities:

EPA Report #0322022-00001 - On 07/28/2017 Certified completed a Heat treatment and used crossfire (clothianidin). Product used: Crossfire Bed Bug Concentrate; Reg. No. 1021-2776. A tenant's daughter was told repeatedly they could not enter the unit. When the tech was finishd and loading equipment he allowed her to enter for meds. She exited and he told

Table 1Tabulation of Entries in the U.S. EPA Incident Data System of human pesticide poisoning incidents associated with
neonicotinoid insecticides over a 60-month period from 2018 through 2022

IDS Data 2018-2022 (60 months)	Human fatality (HA)	Human major (HB)	Human moderate (HC)	Human minor (HD)	TOTAL by chemical	General Observations
Clothianidin	2	7	46	0	55	HA involving Crossfire Bed Bug treatment. HB/C mainly crop uses, some from dust from treated seeds, feed store worker spilled bag of treated seeds
Dinotefuran	0	13	102	5	120	HB mainly roach and ant gel bait. HC mainly during application of dog products
Thiamethoxam	0	1	39	2	42	HC mainly agriculture products
Acetamiprid	2	1	6	10	19	HA sudden deaths reported with home garden product. HB, seizure, tinnitus, 2 miscarriages reported with home garden product
Imidacloprid	0	51	547	8	606	HB/C mainly pet products, some soil and turf products. HB seizures, intracranial bleeding, premature birth. HC vomiting, chemical burns. HD mainly diarrhea (excluded HA plane crash and intentional suicide
TOTAL by severity	4	73	740	25	842	

Each incident represents an individual person; these values should be considered rough estimates given the lack of individual details in the data reports. The severity of the injury is reported as it was reported in the EPA database except in 3 cases for which a seizure was reported, but the incident was classified as H-C (moderate) and which here is classified as H-B (major) consistent with EPA ratings

 Table 2
 IDS entries that include H-A and/or H-B incidents associated with neonicotinoid pesticides, 2018-2022

1		Report # 032022-00001	MGK: Includes 1 H-A. 2 people died Involving CrossFire Bed Bag treatment.	MCLAUGHLIN GORMLEY KING	04/17/2019	HA	Gothianidin	CROSSFIRE BED BUG	MCLAUGHLIN GORMLEY KING COMPANY	2	
		031616-00001	CIK) Scotts: Includes 1 H-A. Symptoms	co. Scotts co. LLC	11/21/2018	на	Acetamiprid	CONCENTRATE ORTHO FLOWER,	NEPPON SODA CO., LTD.		
2			The second design of the secon					VEGETABLE INSECT KILLER READY TO		1	
-		031700-00004	Nisso: Dec. 2018, a man in poor	NESSO AMERICA,	07/01/2018	на	Acetamipeld	TRANSPORT	NIPPON SODA CO., LTD.		
3		034402-00001	In Section 8 apartments. Nisso: Indudes 1 H-B. Symptoms	SODA CO., LTD. NESSO AMERICA,	06/04/2021	HB	Acetamiprid	TERMICIDE INSECTICIDE TRANSPORT (R)	MIPPON SODA CO., LTD.	1	
46		033054-00005	include numbness/tingling and dermal initiation/pain. (IK) MGK: Includes 2 H-B (-0028-005) and	SODA CD., LTD.	12/30/2019	HB	Oothianidin	INSECTICIDE RAID BED BUS	INCLAUGHLIN GORMLEY		1
12		034505-00019	3 H-C. Symptoms include Emesis, Cough, Wheezing, etc. (JK) SC Johnson: 2 H-8E-004,-009) and 19	GORMLEY KING CO. SC JOHNSON	08/27/2021	HC	Oothianidin	FOAMING SPRAY RAID BED BUG	KING COMPANY, DJB/A MGK MCLAUGHLIN GORMLEY		2
15		011675-00004	H-C. Symptoms include edema, proritos, ocular irritation, etc. (JK) MGC Includes 7 H-C and 1 H-B (-008).	NO.AUGHLIN	09/26/2018	HC	Cothavida	FOAMING SPRAY	KING COMPANY, DJILA MGK MCLAUGHLIN GORMLEY	_	2
25		011730 00001	Symptoms include Diarrhea, IBS, Emesis/Vomiting, etc. (JK)	GORMLEY KING	01010010		Claiblaster	BUG	KING COMPANY		1
26		01739-0001	Symptoms include Palpitation, Dyspnea/Shortness of Breath,	GORMLEY KING	otiotizote	n.	Counterious	AEROSOL	KING COMPANY		1
27		032061-00002	MGK: Indude 1 H-C and 1 H-B (-002). Symptoms include Urinary trac	MCLAUGHLIN GORMLEY KING	03/22/2019	HB	Clothlanidin	OROSSFIRE	MCLAUGHLIN GORMLEY KING COMPANY		1
5		033563-00002	United Industries: Includes 4 H+B (- 005,-007,-009,-013) and 13 H-C.	UNITED INDUSTRIES	08/11/2020	HC	Dirotefuran	HOT SHOT ULTRA LIQUID ROACH	OHEMSIKO		4
		032335-00019	Symptoms include praritus, hives, dermal initiation, etc. (IK) United: Includes 3 H 8(-001,-005&-	UNITED	06/20/2019	нс	Dinotefuran	HOT SHOT ULTRA	CHEMSICO		
6			UIS), IS H-C and S E-A. Symptons include Ataxia, Dizzy/Vertigo, Symcope, etc. DKI	CORP.				LIQUD ANT BALL			3
13		033155-00007	United industries: Includes 2 H-8(-001, 004) and 5 H-C. Symptoms include Asthma, Cough, Chock, etc. (JK)	UNITED INDUSTRIES CORP.	03/30/5050	HC	Dinotefuran	HOT SHOT ULTRA LIQUID ROACH BAIT	CHEMSICO		2
		033477-00006	United Industries: Includes 2 H B(- 0048-006), 19 H-C, and 3 E-A.	UNITED INDUSTRIES	07/08/2020	HB	Dinotefuran	HOT SHOT ULTRA LIQUID ANT BAIT	CHEMSICO		2
		031035-00001	Symptoms include laceration, bleed, numbress, etc. (JK) BASF: Includes 1 H-C. Symptoms	CORP. BASE CORP.	03/12/2018	нс	Dinotefuran	PRESCRIPTION	BASE CORPORATION		•
20	incl seizure, should be H-B		include seizure.					TREATMENT BRAND ALPINE COCKROADH GEL			1
-		033110-00001	Ceva: Includes 1 H-B. Symptoms Include Anaphylactic Shock, Throat	CEVA ANIMAL HEALTH, LLC	03/13/2020	HB	Dinotefuran	BAIT RESERVOIR CATEGO FOR CATS	CEVA ANIMAL HEALTH, LLC		
38		011110-00026	initation and Erythema at the exposure site. (30) Baser: Jackades 21 H-C and 5 H-B.	SAVER	05/29/2018	HC	Inidadoorid	SERVICE DOG	RAYER HEALTHCARE		1
4			Symptoms include paraesthesia, oedema, skin change, etc.	HEALTHCARE, ANIMAL HEALTH,				(UNSPECIFIED)	uc		5
		030787-00054	Bayer Animal Health: Includes 1 D-D, 11 H-C and 2 H-B. Symptoms include Monomalization. Darasethesis	BAYER HEALTHCARE, ANIMAL HEALTH	01/19/2018	нс	Imidacloprid	SERESTO SMALL DOG	BAYER HEALTHCARE		
7			Hypersensibility reaction, etc. The updates in this report are nowhere found in the update.	INC.							2
		010480.0100	updates as a source could not be added.		0000000	w.	Included	APROXIMATE OF M			
8		0,0880-00007	Symptoms includes to H-C and 2 H-B. Symptoms include Taste disorder, Headache, Nausea, etc.	HEALTHCARE, ANDMAL HEALTH,	wit23(2016	ett.	white a clope id	(CAT-UNSPECIFIED)			2
p		031131-00005	Bayer: Includes 8 H-C, 2 H-B and 4 P- A. Symptoms Include Light beadness,	BAYER CROPSCIENCE	05/15/2018	HB	Imidacloprid	CORETECT TREE AND SHRUB	BAYER ENVIRONMENTAL		2
	-	032379-00004	proviness of breath, Edema/Swelling, etc. MGR:Includes 2 H 6(-0016-004) and 4	MCLAUGHLIN	06/15/2019	HB	Imidacloprid	BEDLAM PLUS	INCLAUGHLIN GORMLEY		-
10		033023-00005	H-C. Symptoms include Malaise, Cough, Emesis/Vomiting, etc. (3K) Bayer: Includes 2 H-B(-0018-002) and	GORMLEY KING CO. BAYER	01/30/2020	нс	Imidacloprid	TEMPRID FX	KING COMPANY BAYER		2
11	-	034640-00001	4 H-C. Symptoms include Hair loss, Numbriess, Joint pain, etc. (JK) Banco: Includes 2 H-B. Symptoms	CROPSCIENCE LP ELANCO US INC.	10/06/2021	HB	Imidacloprid	SERESTO COLLAR	ENVIRONMENTAL SCIENCE ELANCO US INC.		2
16		034640-00002	Include headache, hypoaesthesia, dyspeiea, etc. (JK) Elanco: Includes 2 H-B. Symptoms	ELANCO US INC.	08/01/2021	HB	Imidacloprid	UNKNOWN SERESTO LARGE	ELANCO US INC.		2
17		030702-00009	Include headache, hypoaesithesia, dyspnea, etc. (3K) Bayer: Includes 9 H-C and 1 H-B.	BAYER	01/06/2018	нс	Imidacloprid	DOG ADVANTAGE II	BAYER HEALTHCARE		2
18			Symptoms include Dermatitis, Eczema, Paraesthesia, etc.	INEALTHCARE, ANIMAL HEALTH, INC.				MEDIUM DOGS	uc		1
19		030942-00011	Bayer: Mar 2018, 11 human incidents due to pet products, 1 H-0.	BAYER HEALTHCARE, ANIMAL HEALTH,	03/05/2018	нс	Imidacloprid	SERESTO LARGE DOG	BAYER HEALTHCARE LLC		1
	excluded 1 H-C	031075-00005	Bayer: Includes 5 H-C, 1 H-B (-008) and 2 P-A. Symptoms include Rash,	INC. BAYER ENVIRONMENTAL	05/07/2018	HS	Imidacloprid	TEMPRID SC INSECTICIDE	BAYER ENVIRONMENTAL		
21	for potential report mistake		Confusion, Dizziness/Vertigo, etc. (JK) (For -006, source 031076-0001 was put by mistake. Please ignore.)	SCIENCE					SCIENCE		1
22		031207-00003	Scoth: Includes 16 H-C, 10 P-A, 1 W- A (-133), 1 H-B (-204) and 186 P-L. Symptoms include Palpitation,	SCOTTS CO. LLC	05/31/2018	нс	Imidacloprid	DUAL-ACTION BED BUG KILLER	INCLAUGHLIN GORMLEY KING COMPANY		1
21		031232-00021	Dizziness, Chest Pain, etc. (JK) Bayer Animal Health: Includes 1 H-8 and 20 H-C. Symptoms include	BAYER HEALTHCARE,	07/01/2018	нс	Imidecloprid	K9 ADVANTIX II (UNSPECIFIED)			
-		031321-00002	Proritos, crythema, Diamhea, etc. Bayer: Includes 1 H-B and 1 H-C.	ANIMAL HEALTH, INC. BAYER	05/28/2018	нс	Imidecloprid	SERESTO CAT	BAYER HEALTHCARE		
24			Symptonis include Hypoaesthesia, Paraesthesia, Peripheral nervous system disorder, etc. (IK)	ANIMAL HEALTH, INC.					uc		1
28		012218-00006	Symptoms include 5 H-C and 1 H-8(-006). Symptoms include Dysphagia, Alopecia, Weight loss, etc. (IK)	HEALTHCARE, ANIMAL HEALTH,	05/01/2018	145	Insecopris	(UNSPECIFIED)	BAYER HEALTHCARE		1
30		032439-00002	Bayer: Includes 2 H-C, 1 H-B(-002) and 25 P-A. Symptoms include Nausea	BAYER CROPSCIENCE LP	07/15/2019	HB	Imidacloprid	TEMPRID SC INSECTICIDE	BAYER ENVIRONMENTAL		1
-		032465-00002	Bayer: Includes 4 H-C, 1 H-B(-002)	BAYER	07/17/2019	HS	Imidacloprid	TEMPRID SC	BAYER	-	
31			initation, throat initation, Diztness/Vertigo, etc. (30)	Contraction of	0.0000000				SCIENCE		1
32			C. Symptoms include Hypoaesthesia, Central nervous system disorder,	HEALTHCARE, ANIMAL HEALTH,	0423/2019			301210 011	uc		1
33		032706-00005	Bayer: Include 4 H-C, 1 H-8(-005), 2 P A and 3 P-8. Symptoms include	BAYER CROPSCIENCE LP	10/09/2019	HB	Imidacloprid	TEMPRID SC INSECTICIDE	BAYER ENVIRONMENTAL		1
		032808-00002	etc. (JK) Bayer: Includes 1 H-B(-001), 2 H-C and 1 D.A. Surrothema Include	BAYER CROPSCEINCE LP	10/01/2019	нс	Imidacloprid	TEMPRID SC	BAYER		
34		011001-00017	Hypotension, Blood clot in right hand, Skin discoloration, etc. (3K)		01/05/2020		Territorium	LOW COMMON	SCIENCE		1
35			October - December, 2019. Includes 1 H-8(-082), 4 H-C and B-L.	20113CO. LLC	010012020			DUAL-ACTION BED BUG KILLER	KING COMPANY, D/B/A		4
			Hives/Welts, Dermal Irritation, etc. (3K)				In the local d		COM LAND COMPANY		
37		053205-00005	Symptoms include Dyspnea, Emesis, Seizure, etc. (IK)	CORP.	041712020	nc -	moscopro	COMPLETE INSECT KILLER FOR SOIL	CORP.		1
-		033386-00221	Scotts: Includes 1 H 8(-001), 6 H C, 1	SCOTTS CO. LLC	06/25/2020	DA	Imidacloprid	HOME DEFENSE	THE SCOTTS COMPANY	_	
38			Symptoms include bronchospane, congestion, diarrhea, etc. (38)					& TICK KILLER			1
39		033567-00008	Bayer: Includes 9 P-A, 1 H-B(-008), 7 H-C, 1 H-D, 1 D-A, 1 D-B and 4 P-L. Symptoms include pruntus, rash,	BAYER CROPSCIENCE LP	05/01/2020	HS	Inidacloprid	INSECTICIDE	BAYER ENVIRONMENTAL SCIENCE		1
40		033624-00005	Enser: Includes 1 H-B (-003), 7 H-C, 4 H-D, 3 P-A, 2 P-B and 2 P-L	BAYER CROPSCIENCE LP	09/25/2020	нс	Imidacloprid	TEMIRID SC INSECTICIDE	BAYER ENVIRONMENTAL		,
		033894-00001	symptoms include dermal imitation, edema, tingling, etc. (JK) Bayer: Includes 1 H-B(-001) and 1 H-	MONSANTO	01/01/2021	нз	Imidacloprid	TEMPRID FX	BAYER		
41		033918-00022	 c. symptoms include tachycardia, ataxia, confusion, etc. (3K) Elanco: May 2020 thru January 2021 	SCIENCE ELANCO ANIMAL	12/06/2020	нс	Imidacloprid	ADVANTAGE II	SCIENCE ELANCO US INC.		1
42			eventional reports. Includes 1 H-0(- 021) and 21 H-C. (2K)	OF ELI LILLY AND				INCLUIUM DOG			1
43			everef: anouae 1 H-B(-005) and 4 H-C. symptoms include Joint pain, cough, nose bleed, etc. (JK)	CO, BAYER CROP	04/01/2020	-10	anticacloprid	INSECTICIDE	ENVIRONMENTAL SCIENCE		1
44	incl seizure, should be H-B	034040-00001	Elanco: Includes 19 H C. Symptoms include convulsion, seizure, hemorrhage, etc. (3K)	ELANCO US INC.	01/01/2021	нс	Imidacloprid	SERESTO DOG (UNSPECIFIED)	ELANCO US INC.		1
45		094220-00001	csence: Includes 1 H-8(-003) and 8 H- C. Symptoms include muscle tremor, dyskinesia, unticaria, etc. (IK)	ELANCO US INC.	03/31/2021	rRC	unidacloprid	ALVANTAGE II EXTRA LARGE DOG	ICLANCO US INC.		1
47		104567-00002	csence: Includes 1 H-C and 1 H-B(- 002). Symptoms include headache, nwight loss, erresis, etc. (3K)	ELANCO US INC.	0//01/2021	18	unidacloprid	DOG	ICLANCO US INC.		1
48		104587-00005	event: Includes 1 H-B(-001), 4 H-C and 4 P-L. Symptoms include edema, coughing up blood, dysprea, etc. (JK)	CO, BAYER CROP SCIENCE	vs/29/2021	rK.	unidadoprid	INSECTICIDE (CANADA PHRA#	ENVIRONMENTAL SCIENCE		1
49		034712-00001	RD: Includes 1 H+B. Seresto incident. (IK)	U.S. EPA, OPP, RD	12/16/2021	08	Imidacloprid	SERESTO	ELANCO US INC.		1
50		034880-00001	Include prurifus and dypnosa. Earco: Includes 1 H-8. Symptoms Earco: Includes 1 H-8 and D-A.	ELANCO US INC.	01/31/2019	H9, DA	Imidacloprid	SERESTO LARGE	ELANCO US INC.		1
51	ind seizure.	034921-00001	Programs or cred include consulsion. (IK) FMC: Includes 1 H-C. Symptoms include blobbs 8	FMC CORECTOR TO COLUMN	02/23/2022	нс	Imidacloprid	TRIPLE CROWN	FMC CORPORATION		1
52	should be H-B	035279-00003	recude blotchy & red fac, seizure, pass out. (IK) Scotts: Includes 1 H-8(-002), 5 H-C, 6	SCOTTS CO. LLC	05/25/2022	нс	Imidacloprid	ORTHO HOME	MCLAUGHLIN GORMLEY		1
53			P-A and 77 P-L. Symptoms include nauseous, dizzy, chest congestion, etc. (JK)	10010 1007	0400400		lands.	DEPENSE BED BUG, FLEA & TICK KOLLER SPRAY	KING COMPANY, D/B/A		1
54		035375-00002	Bayer: Includes 1 H-B(001), 8 H-C, 2 P L and 9 P-A. Symptoms include burning skin, stomach cramps,	MONSANTO CO, MAYER CROP SCIENCE	04/01/2022	HC	unidadoprid	INEMISE FOAM	ISAYER ENVIRONMENTAL SCIENCE		1
		035389-00002	postales on bodies, etc. (IK) S2M: Includes 1 H-B(-003) and 3H-C. Symptoms include builtae, erythema,	SBM LIFE SCIENCE CORP.	08/17/2022	нс	Imidacloprid	BIOADVANCED - 3 IN 1 INSECT,	SBM LIFE SCIENCE CORP.		
55			burn, etc. (IK)					CONTROL READY- TO-SPRAY			1
56		035646-00002	Elanco: Includes 1 H-8(-002), 1 H-C and 1 H-D. Symptoms include arthritis, reoplasia, urticaria, etc. (JK)	ELANCO US INC.	12/01/2022	нв	Imidacloprid	SERESTO COLLAR UNKNOWN	ELANCO US INC.		1
		032424-00001	Region 9: Jul7 2029, Monterey County Apricultural Commissioner's (CAC) office was notified of this incident by	U.S. EPA, REGION 9	0//20/2019	HB, HC	thiamethosa m	ENDIGO 2C			
			DPR's Worker Health and Safety branch's PISP (Pesticide Incident Surveillance Program) unit on								
			Thursday, July 25th. They interviewed the 33 year old male that same day from his hospital room. Menteever 2447								
29			has also interviewed the five (5) other inspators and their foreman, as of July 20th. Four of the other initiators								1
			experienced pesticide related symptoms, three of them during that workday and the fourth one that								
			following Monday. Monterey CAC staff is currently working on interviews, PUR data, wind data, evaluation training								
			records, and medical records. This								

Complete unedited information as provided to the authors by EPA of the IDS database entries of H-A and/or H-B incidents associated with neonicotinoid insecticides over a 60-month period from 2018 through 2022

her again that they could not enter. 15 minutes after the tech left, she took the tenants into the unit. A neighbor discovered 1 deceased and 1 unconscious. The name of the deceased was[redacted] The name of the unconscious person who dies several months later was [redacted]. age unknown. Applier said the complex settled. The prosecuting lawyer is saying something about crossfire could have caused/contributed to the death.

EPA Report #031616-00001 - Ortho flower fruit and vegetable insect killer ready to use wand (acetamiprid). Consumer asked if it was safe to use this product while an elderly person with kidney failure, heart failure, Parkinson's disease and gray's disease, is in the area. I told her we do not recommend that, and people and pets should remain out of the area until it is dry, but once it's dry it's safe. She asked if any of this information was on the label and I read her the precautionary statement on the label. She then went on to say that her mother, who had all of the above mentioned medical conditions, was dead, and that her sister had ben spraying this with her mother in the area and that she (the consumer, caller) did not know about it. She said her daughter was also hospitalized. She seems to be trying to gather evidence to show her sister, I'm not sure. She is not coplaining to us about our product, the whole conversation is about what you can and can't do with the product and what her sister did do with the product.

EPA Report #031700-00004 - Transport Termicide Insecticide (acetamiprid). Caller states that he management has been spraying Transport Termiticide since may in her senior facility and multiple people have had symptoms Caller states that they have been spraying for a bed bug infestation in her building - Respiratory issues and headache for at least a dozen people Two people have been taken by ambulance and one person has passed away... "The management of this building is trying to threaten and harass me because I am asking questions and trying get vulnerable residents with health issues to understand what the SDS [Safety Data Sheet] sheets are for and to read them. They are using in the Senior Building" This weekend a man dropped dead in the back of the building. (It is not known what he died from) One person taking in away via EMS [emergency medical service] on Tuesday - that person had COPD [Chronic obstructive pulmonary disease] and on [oxygen]. It had gotten so bad that she could not breathe anymore. She does know this person. Someone else she does not know was taken in an ambulance day before yesterday. She does not know what happened to

the two men. She is the only advocate in the building. She was a senior care giver at one point. She does not personally have a medical concern to be evaluated. Caller would like Information: Her call was to ask if they are supposed to be getting notices and times of sprays that happen in enclosed hallways with no ventilation. They have been spraying weekly since May in the common areas/hallways. Weekly. Many of the apartments have been sprayed but do not know which ones as they will not tell them. She was told by management that do not have to tell them the times and the dates. They have been getting notices off an on due to the mayor of the town being involved to push to get notices. The Dept of Hazmat [Hazardous Materials] has pushed for notices. The County Health Dept has pushed for notices. The head of the management has said that these chemicals are "non toxic" and put it in writing. What kinds of notice should people be getting of spraying? They are not giving information about covering food prep areas. Sometimes they say to get out of the building for 4 hours and sometimes they say you can stay in. She watches for the chemical truck to come around. They do not give notice so a lot of people are walking into the spraying. Since this has been going on since May people are having health side effects. There are 50 plus apartments in the building and the residents are seniors, and ... have COPD.

For nonfatal exposures, the overwhelming majority of them are classified as "moderate" severity (H-C). Moderate poisonings make up 88% of the total poisonings (740 of 842), with most of those associated with imidacloprid (547 incidents) or dinotefuran (102 incidents). Common reported symptoms classified as moderate often included two or more of the following: headaches; dizziness; lethargy; eye or throat irritation; skin itching and rash; chemical burns and skin peeling; face swelling; muscle weakness or tremors; vomiting; diarrhea; pain and tightness in chest; open sores; and general pain (See Table 2).

The nonfatal reported incidents stem mainly from residential uses, such as lawn and garden insect repellents, home pest treatments for bed bugs or roaches, and products used to treat pets for fleas and ticks. In many cases, the person who was poisoned was the person applying the pesticide product. In others, the poisoned individuals were exposed after the product was applied by someone else. For example, in 2018 a family of five (two adults and three children) reported symptoms that included skin rashes, vomiting and dizziness (classified as minor symptoms, H–D) upon returning to their apartment after it was treated with a dinotefuran product. The family did not seek medical attention, according to incident reported [25] (See Table 2).

In some cases, agricultural uses resulted in exposures to non-occupational bystanders. For example, in 2019, a school bus with open windows carrying twenty-nine students was "allegedly drifted on by an air blast sprayer making an application" of an acetamiprid product to a citrus orchard [26]. The bus driver and nine students reported having irritated eyes and skin, nausea and headaches (classified as minor symptoms, H–D).

Other reported symptoms included dizziness, irregular heartbeat, chemical burns, diarrhea, nausea and vomiting, and seizures. It is unclear how each of these are classified - whether as major (H-B), moderate (H-C), or minor (H-D) – since a single line report usually consisted of an aggregate of the number of individuals in each category, sometimes followed by a list of symptoms, but without clarifying which symptoms are associated with which category. For example, a report from 2018 simply states, "Bayer: Includes 21 H-C and 5 H-B. Symptoms include paraesthesia, oedema, skin change, etc.," without any indication of how many people and from which category had suffered which symptoms [27]. In another example, a report from 2020 simply says, "United Industries: Includes 2 H-B (-004&-006), 19 H-C.... Symptoms include laceration, bleed, numbness, etc. [28]". For this reason, we provide a summary of the numbers of individuals in each category, but are unable to include their respective symptoms.

We changed the classification in only three cases. In each of these, seizures were reported, which we reclassified from moderate (H-C) to major symptoms (H-B). One, a 2018 entry for a dinotefuran cockroach bait product, reported, "BASF: Includes 1 H-C. Symptoms include seizure [29]". Another 2021 entry from an imidacloprid pet product reported, "Elanco: Includes 19 H-C. Symptoms include convulsion, seizure, hemorrhage, etc." It is unknown what additional symptoms the "etc." may refer to, or how many of the nineteen individuals had which of the symptoms listed. In this case, we re-classified the report as one H-B individual since there was at least one seizure, and eighteen H-C individuals. The third case was in 2022 by FMC Corporation associated with an imidacloprid lawn product that reported, "FMC: Includes 1 H-C. Symptoms include blotchy & red face, seizure, pass out" (See Table 2) [30]. All other reports we reviewed in the database of convulsions or seizures were already classified the symptoms as major (H-B).

Discussion

Over a five-year period from 2018 through 2022, U.S. EPA received reports of roughly 840 people poisoned with neonics, made public in its IDS national database of incident reports from pesticide manufacturers, individuals, poison control centers, states, and various agencies. Most entries are self-reported and vary in detail regarding exposure, symptoms, and outcomes. While the severity and frequency of the acute pesticide poisoning reports associated with the neonic insecticides are surprisingly high, they are likely to be underreported for many reasons, including not knowing how to report an incident, not going to the hospital or health care facility, many treating physicians are not trained to recognize the signs and symptoms of pesticide poisoning, and, that the person poisoned may not know why they are feeling ill or what product they may have been exposed to [31, 32]. An additional reason for potential underreporting, is that we have excluded multiple data sources on neonic poisoning in an effort to avoid potential double-counting of cases, so the data set here will miss incidents that are not included in IDS database.

In 2021, the Midwest Center for Investigative Reporting reported in USA Today on poisonings from pesticides leaching from flea and tick collars, particularly one brand that contains 10% imidacloprid (a neonic) and 4.5% flumethrin (a pyrethroid insecticide). The reports included around 1,700 pet deaths and just under 1,000 people being poisoned. Unfortunately, the EPA re-confirmed its approval of the collars without any formulation changes, though it did require additional label warnings to report potential poisoning incidents [33]. However, an investigation by the EPA's independent Office of Inspector General reported that EPA staff repeatedly raised concerns about the poisonings that were ignored by both EPA management and the pesticide product manufacturer [34].

While acute illness is more likely to be reported because of the rapid onset of symptoms, it may be that low level chronic exposures to neonics during early life neurodevelopment may be even more problematic [35]. A systematic review of epidemiologic studies of neonic exposure in the general population identified a small but statistically significant association with neonic exposure during pregnancy and adverse developmental or neurological impairments including the following (with citations to the original studies): teratology of Fallot [36], anencephaly [37], autism spectrum disorder [38], and a cluster of nervous system problems including memory loss and finger tremors [39]. The same review also reported that occupational exposure studies of adult forestry workers did not report adverse effects, suggesting that early life development is a period of heightened vulnerability at levels lower than those triggering poisoning in healthy adults [40].

Biomonitoring by the Centers for Disease Control and Prevention (CDC) finds that chronic neonic exposure is widespread in the U.S. population [41], with more recent testing of 171 pregnant women from across the country and Puerto Rico finding neonics in the bodies of over 95% of participants, with levels rising over the course of the four-year study (2017-2020) [42]. Because the human brain has only a very limited ability to repair or recover from neurotoxic assault, even transient or low levels of exposure to environmental pollutants such as lead, mercury, air pollution and neurotoxic pesticides like chlorpyrifos can have lasting adverse effects [43, 44]. A study we recently published reviews the evidence of developmental neurotoxicity associated with neonics. We report on rodent laboratory toxicology studies sponsored by the manufacturer (the 'registrant') exposed to neonics during prenatal and early postnatal development that resulted in statistically significant shrinkage of brain tissue in highdose offspring for five neonicotinoids: acetamiprid, clothianidin, imidacloprid, thiacloprid, and thiamethoxam [45].

Given that workers are largely people of reproductive age, and may also include individuals that are pregnant or breastfeeding, occupational exposures to neonics may pose a risk not only for the exposed adult, but also for the next generation. EPA found that most occupational risks for imidacloprid could only meet the regulatory approval standard if workers wear a long-sleeved shirt, long pants, shoes and socks, or with personal protective equipment (PPE) and gloves, and in some cases would need to wear double layer clothing and gloves [46]. For clothianidin and thiamethoxam, EPA's PPE requirements are similar except that some occupational tasks also require use of a respirator [47].

Fundamentally, PPE is an attempt to provide a barrier between the person and the hazard, but the hazard remains. For this reason, PPE should only be used as a last line of defense [48–52]. The workplace Hierarchy of Controls describes the most effective approach being elimination of the hazard, followed by reducing it through substitution, with PPE being the least effective safeguard measure [53]. Similarly, the essential-use approach, in a regulatory setting, aims to reduce hazardous chemicals by eliminating all nonessential uses, based on the foundational value that we should not use chemicals of concern in products or processes where they are not critical for health, safety, or the function of society [54, 55]. For neonics, the most effective prevention strategy - elimination-can be readily employed since the vast majority of neonic uses are applied in the absence of an actual pest problem, and are thus non-essential [56, 57].

While most of the reported acute poisoning incidents discussed in this paper are non-occupational incidents and non-agricultural uses of the pesticides, three neonics-imidacloprid, clothianidin and thiamethoxam-are also approved for over 100 different products used to coat or "treat" crop seeds. Pesticide seed treatments take advantage of the systemic nature of the chemicals. The coatings are designed to be absorbed through a plant's roots as it grows, making all of the plant's tissues including the pollen and nectar poisonous to target pests and beneficial insects such as bees, butterflies, and other pollinators [58-60]. Though the use of seed treatments is not tracked, one can estimate it by examining U.S. Geological Survey (USGS) Pesticide Use annual reports, which beginning in 2015 discontinued reporting on the seed treatment applications [61]. The precipitous drop in reported use from 2014 to 2015 can be presumed to be roughly the amount used as seed treatments that are no longer reported. USGS reports indicate that agricultural uses of thiamethoxam are almost all from seed treatments (1.2 million pounds per year, lbs/year, on corn and soy seeds, and about 0.2 million lbs/year for non-seed uses), and the case is similar for clothianidin (3.5 million lbs/year on corn seed treatments, and about 0.1 million lbs/year for non-seed uses). Imidacloprid agricultural use is split about half and half (with about 1 million lbs/year for soybean and cotton seed treatments, and about 1 million lbs/year on non-seed uses).

In 2024, EPA updated its occupational risks for neonics to include health risks to workers treating seeds with pesticides and handling treated seeds; EPA identified several activities that posed elevated risks to workers, including cleaning seed treatment equipment, even when maximum personal protective equipment (PPE) is used (double-layered clothing and a respirator rated with a protection factor of 10, PF-10) [62]. Of concern, PPE is often uncomfortable, poorly fitted, difficult to wear while doing work tasks, and can be less effective in higher temperatures such as during outdoor farmwork [63, 64]. A small study that conducted biomonitoring (urine samples) and tap water testing of Iowa farm families found that for people that worked directly with pesticides including treated seeds, occupational exposures and house dust was their greatest source of exposure [65].

While regulatory agencies require PPE to be used in occupational settings, that is often impractical or impossible for many of the consumer uses that led to the acute human poisonings reported in this paper. Applying pesticides on lawns, gardens, around homes, and on pets can cause poisonings in people that come into contact with the treated surfaces hours or even days after the initial product application. For example, the Seresto[®] flea and tick collars for pets include a warning on the package against letting children play with the collar, but children are frequently in close extended direct contact with their pets. The collar is made with a mix of imidacloprid and a non-neonic pesticide called flumethrin, which is "released from the collar" over time, according to the product website [66]. Pesticide residues on lawns, parks, and playground equipment can all be a source of nonoccupational exposure to people without PPE.

In its 2020 imidacloprid evaluation and proposed regulatory determination - part of a federally mandated periodic review process known as "registration review" - EPA noted that, "[t]he total number of imidacloprid incidents reported to IDS, from 2013 to 2018, appeared to be increasing over time. The agency will continue to monitor the incident data and if a concern is triggered, additional analysis will be conducted [46]". The U.S. Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Federal Food Drug and Cosmetic Act (FFDCA) require EPA to cancel a pesticide registration when existing risks related to its use are unacceptable and registrants have not made changes to the registration to address the unacceptable risks [67]. EPA is underestimating or ignoring neurodevelopmental and endocrine risks of neonicotinoid pesticides, which we have asserted is a violation of federal law. Even so, EPA's proposed 2020 regulatory determination for imidacloprid still found that cancellation of residential imidacloprid lawn sprays was "necessary" under federal law to "eliminate risks of concern to both children and adults from the residential turf use [46]". However, due to significant delays in the regulatory process, the proposed determinations were never finalized, and new "amended" proposed determinations are expected to be issued in 2025 [68].

Other jurisdictions have imposed significant restrictions on neonicotinoid uses, often for environmental reasons. Between 2013 and 2018, the European Union (EU) prohibited nearly all outdoor uses of the three most-used neonicotinoid active ingredients [69] - clothianidin, imidacloprid, and thiamethoxam - but EU-based agrochemical companies continue to produce and export them, largely to low- and middle-income countries [70]. In Canada, the federal government has imposed a number of restrictions on neonicotinoid use to protect pollinators and aquatic ecosystems in the last several years [71], with the provincial governments of Ontario and Québec requiring the identification and certification of a legitimate pest-control need before using neonicotinoid seed treatments for major field crops [72]. The result, at least in Québec, has been a near elimination of neonicotinoid seed coatings for these crops [73].

In absence of action by the federal government, a number of U.S. states have also enacted restrictions on neonicotinoid use. New York and Vermont recently became the first two states to restrict the use of neonicotinoids on crop seeds, adopting the "verification of need" model pioneered in Ontario and Québec [74]. New Jersey [75], New York [74], Nevada [76], and Maine [36] have also banned most neonicotinoid use on lawns, gardens, and other non-agricultural landscapes, while Minnesota has prohibited neonicotinoid use on state lands [77]. Eleven states have also restricted most or all outdoor neonicotinoid use to certified applicators – which has the effect of removing neonicotinoid lawn and garden products from retail store shelves, but still allows for agricultural use, indoor use, and applications provided by most commercial lawn care or pest control providers [78].

Conclusion

Here we have presented an analysis of non-occupational human poisoning incidents associated with neonicotinoid pesticides, as reported in EPA's Incident Database System. While the data have recently become available to the public, they are not in a form that can be aggregated for analysis. Here we have done the work of aggregating and then individually evaluating each of the data summary reports (EPA does not make the full reports publicly available). This information is particularly important as local, state, and federal agencies grapple with how to address the impacts to workers, families, communities and ecosystems from the widespread use of this class of neurotoxic and developmentally neurotoxic insecticides. We reviewed 842 non-occupational human poisoning incidents associated with neonics in the IDS from 2018 through 2022. There are four human fatality reports, two associated with clothianidin and two with acetamiprid. People reported headaches, dizziness, nausea and skin irritation from using lawn and garden insect repellents, home pest treatments for bed bugs or roaches, and pet products made with imidacloprid or dinotefuran. In addition to the acute poisoning incidents reported in this paper, there is also evidence from rodent toxicology and human epidemiology linking early-life exposure to neonics with lasting neurodevelopmental harm [45]. And, neonics are regularly detected in waterways including drinking water sources, fresh fruits and vegetables, and human body fluids including breast milk and cerebrospinal fluid.

Regulatory agencies worldwide should use their legal authority to cancel unsafe products and unnecessary uses – including from seed treatments, and residential pet and lawncare products—to prevent further human poisoning, environmental contamination, and wildlife harm. Such actions would be consistent with One Health approach advanced by the World Health Organization (WHO), the World Organization for Animal Health (WOAH), the United Nations Food and Agriculture Organization (FAO) and the United Nations Environment Programme (UNEP). It's goal is to optimize the health of people, animals and the environment by ensuring food and water safety, reducing environmental contamination, and protecting biodiversity including pollinators and other beneficial insects [79].

Abbreviations

COPD Chronic obstructive pulmonary disease	
EMS Emorgoney modical services	
LIVID LITIEIGENCY THEORCAL SELVICES	
EPA U.S. Environmental Protection Agency	
EU European Union	
FAO United Nations Food and Agriculture Organization	
FFDCA Federal Food Drug and Cosmetic Act	
FIFRA U.S. Federal Insecticide, Fungicide and Rodenticide Act	
FOIA U.S. Freedom of Information Act	
FQPA U.S. Food Quality Protection Act	
HazMat Hazardous Materials	
H-A Human fatality	
H-B Human major injuries	
H-C Human moderate injuries	
H–D Human minor injuries	
IDS EPA Incident Data System	
nAChR Nicotinic acetylcholine receptor	
Neonics Neonicotinoid pesticides	
NIOSH U.S. National Institute for Occupational Safety and Healt	٦
NPIC National Pesticide Information Center	
PF-10 Respirator with a protection factor of 10	
PISP California Pesticide Illness Surveillance Program	
PPE Personal Protective Equipment	
SDS Safety Data Sheet	
SENSOR Sentinel Event Notification System for Occupational Risk	
UNEP United Nations Environment Programme	
USGS U.S. Geological Survey	
WHO World Health Organization	
WOAH World Organization for Animal Health	

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12940-024-01139-2.

Supplementary Material 1.	
Supplementary Material 2.	
Supplementary Material 3	

Acknowledgements

We thank the reviewers of this article for suggestions to improve it.

Authors' contributions

J.B.S. conducted all the data analysis and wrote the main manuscript text. D.R. contributed portions of the manuscript including policy and legal analysis. All authors reviewed the manuscript.

Funding

Natural Resources Defense Council (NRDC) general funds.

Data availability

The poisoning reports are now publicly available on EPA's online Incident Data System database. https://www.epa.gov/pesticide-incidents/about-incident-data-system-ids.

Declarations

Ethics approval and consent to participate $\ensuremath{\mathsf{N/A}}\xspace.$

Consent for publication N/A.

Competing interests

The authors declare no competing interests.

Author details

¹Natural Resources Defense Council, 1152 15Th Street NW, Washington, DC 20005, USA. ²Natural Resources Defense Council, 20 N Wacker Dr #1600, Chicago, IL 60606, USA.

Received: 8 September 2024 Accepted: 5 November 2024 Published online: 20 November 2024

References

- Hladik ML, Main AR, Goulson D. Environmental risks and challenges associated with neonicotinoid insecticides. Environ Sci Technol. 2018;52(6):3329–35. Available from: https://pubs.acs.org/doi/10.1021/acs. est.7b06388.
- Klingelhöfer D, Braun M, Brüggmann D, Groneberg DA. Neonicotinoids: a critical assessment of the global research landscape of the most extensively used insecticide. Environ Res. 2022;213:113727. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0013935122010544.
- Tomizawa M, Casida JE. Neonicotinoid insecticide toxicology: mechanisms of selective action. Annu Rev Pharmacol Toxicol. 2005;45(1):247–68. Available from: https://www.annualreviews.org/doi/10.1146/annurev. pharmtox.45.120403.095930.
- Costas-Ferreira C, Faro LRF. Neurotoxic effects of neonicotinoids on mammals: what is there beyond the activation of nicotinic acetylcholine receptors?-a systematic review. Int J Mol Sci. 2021;22(16):8413.
- Bayer CropScience. The bee safety of neonicotinoid insecticides. Bayer Bee Care Center; 2016. (BeeInformed N° 3_2016). Available from: https:// www.bayer.com/sites/default/files/BEEINFOrmed_issue3_The_Bee_ Safety_of_Neonicotinoids-1iusc0izc_0.pdf.
- DiBartolomeis M, Kegley S, Mineau P, Radford R, Klein K. An assessment of acute insecticide toxicity loading (AITL) of chemical pesticides used on agricultural land in the United States. PLoS ONE. 2019;14(8):e0220029.
- U.S. EPA. Imidacloprid, Thiamethoxam and Clothianidin: Draft Predictions of Likelihood of Jeopardy and Adverse Modification for Federally Listed Endangered and Threatened Species and Designated Critical Habitats. Environmental Protection Agency; 2023 May. Available from: https:// www.epa.gov/system/files/documents/2023-05/ESA-JAM-Analysis.pdf.
- U.S. EPA. Acetamiprid: Final Biological Evaluation and Associated Effects Determination for Endangered and Threatened Species and Their Designated Critical Habitats. Environmental Protection Agency; 2024 Oct. Available from: https://www.regulations.gov/document/ EPA-HQ-OPP-2023-0513-0022.
- U.S. EPA. Dinotefuran: Final Biological Evaluation and Effects Determinations for Federally Endangered and Threatened Species and Designated Critical Habitats. Environmental Protection Agency; 2024 Oct. Available at https://www.regulations.gov/document/EPA-HQ-OPP-2023-0506-0025.
- Thompson DA, Lehmler HJ, Kolpin DW, Hladik ML, Vargo JD, Schilling KE, et al. A critical review on the potential impacts of neonicotinoid insecticide use: current knowledge of environmental fate, toxicity, and implications for human health. Environ Sci Process Impacts. 2020;22(6):1315–46.
- Hladik ML, Kolpin DW. First national-scale reconnaissance of neonicotinoid insecticides in streams across the USA. Environ Chem. 2016;13(1):12. Available from: http://www.publish.csiro.au/?paper=EN15061.
- Berens MJ, Capel PD, Arnold WA. Neonicotinoid insecticides in surface water, groundwater, and wastewater across land-use gradients and potential effects. Environ Toxicol Chem. 2021;40(4):1017–33. Available from: https://onlinelibrary.wiley.com/doi/10.1002/etc.4959.

- Craddock HA, Huang D, Turner PC, Quirós-Alcalá L, Payne-Sturges DC. Trends in neonicotinoid pesticide residues in food and water in the United States, 1999–2015. Environ Health. 2019;18(1):7. Available from: https://ehjournal.biomedcentral.com/articles/10.1186/ s12940-018-0441-7.
- Chen D, Liu Z, Barrett H, Han J, Lv B, Li Y, et al. Nationwide biomonitoring of neonicotinoid insecticides in breast milk and health risk assessment to nursing infants in the Chinese Population. J Agric Food Chem. 2020;68(47):13906–15. Available from: https://pubs.acs.org/doi/10.1021/ acs.jafc.0c05769.
- Klarich KL, Pflug NC, DeWald EM, Hladik ML, Kolpin DW, Cwiertny DM, et al. Occurrence of neonicotinoid insecticides in finished drinking water and fate during drinking water treatment. Environ Sci Technol Lett. 2017;4(5):168–73. Available from: https://pubs.acs.org/doi/10.1021/acs. estlett.7b00081.
- Klarich Wong KL, Webb DT, Nagorzanski MR, Kolpin DW, Hladik ML, Cwiertny DM, et al. Chlorinated byproducts of neonicotinoids and their metabolites: an unrecognized human exposure potential? Environ Sci Technol Lett. 2019;6(2):98–105. Available from: https://pubs.acs.org/doi/ 10.1021/acs.estlett.8b00706.
- Zhang D, Lu S. Human exposure to neonicotinoids and the associated health risks: a review. Environ Int. 2022;163:107201. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0160412022001271.
- U.S. EPA. EPA Posts Pesticide Incident Data Publicly. Environmental Protection Agency. 2023. Available from: https://www.epa.gov/pesticides/epaposts-pesticide-incident-data-publicly#:~:text=Released%20on%20July% 2027%2C%202023,incident%20data%20on%20its%20website.
- U.S. EPA. Incident Reporting by Pesticide Manufacturers/ Registrants. Environmental Protection Agency. 2024. Available from: https://www. epa.gov/pesticide-incidents/incident-reporting-pesticide-manufacturersregistrants.
- U.S. EPA. Reporting unintended exposure and harm from pesticides (Incidents). Environmental Protection Agency. 2024. Available from: https:// www.epa.gov/pesticide-incidents.
- 21. U.S. EPA. OPP Report on Incident Information: The Baseline. Document ID EPA-HQ-OPP-2011–0183–0026. Regulations.gov. 2015. Available from: https://www.regulations.gov/document/EPA-HQ-OPP-2011-0183-0026.
- 22. U.S. EPA. About the Incident Data System (IDS). Environmental Protection Agency. 2024. Available from: https://www.epa.gov/pesticide-incidents/ about-incident-data-system-ids.
- 23. NIOSH. pesticide illness and injury surveillance national institute for occupational safety and health. national institute for occupational safety and health. Centers for Disease Control and Prevention. 2024. Available from: https://www.cdc.gov/niosh/surveillance/pesticide/index.html.
- Rhoads, Lucas. U.S. EPA response to LJ Rhoads, Natural Resources Defense Council (NRDC) Freedom of Information Act request EPA-2023–002283. 2023.
- U.S. EPA. Pesticide Poisoning Incident Reports for five pesticide active ingredients for the years 2009 through present, with special priority given to those from 2019 through present, provided in Excel Workbook format. Request Number EPA-2023–002283. U.S. Environmental Protection Agency; 2023 Mar. Available from: https://docs.google.com/spreadshee ts/d/1f0qEXVxZ_V49waD-t54aOKdTS06lfzeh/edit?gid=736068342#gid= 736068342.
- U.S. EPA. Report 032589–00001. U.S. Environmental Protection Agency. Pesticide Poisoning Incident Reports. Environmental Protection Agency; 2023. Available from: https://docs.google.com/spreadsheets/d/1f0qE XVxZ_V49waD-t54aOKdTS06lfzeh/edit#gid=736068342.
- U.S. EPA. Report 031139–00026. U.S. Environmental Protection Agency. Pesticide Poisoning Incident Reports. Environmental Protection Agency; 2023. Available from: https://docs.google.com/spreadsheets/d/1f0qE XVxZ_V49waD-t54aOKdTS06lfzeh/edit#gid=736068342.
- U.S. EPA. Report# 033477–00006. U.S. Environmental Protection Agency. Pesticide Poisoning Incident Reports. Environmental Protection Agency; 2023. Available from: https://docs.google.com/spreadsheets/d/1f0qE XVxZ_V49waD-t54aOKdTS06lfzeh/edit#gid=736068342.
- U.S. EPA. Report# 031035–00001. U.S. Environmental Protection Agency. Pesticide Poisoning Incident Reports. Environmental Protection Agency; 2023. Available from: https://docs.google.com/spreadsheets/d/1f0qE XVxZ_V49waD-t54aOKdTS06lfzeh/edit#gid=736068342.

- U.S. EPA. Report 034921–00001. U.S. Environmental Protection Agency. Pesticide Poisoning Incident Reports. Environmental Protection Agency; 2023. Available from: https://docs.google.com/spreadsheets/d/1f0qE XVxZ_V49waD-t54aOKdTS06lfzeh/edit#gid=736068342.
- Boedeker W, Watts M, Clausing P, Marquez E. The global distribution of acute unintentional pesticide poisoning: estimations based on a systematic review. BMC Public Health. 2020;20(1):1875. Available from: https://bmcpublichealth.biomedcentral.com/articles/10.1186/ s12889-020-09939-0.
- Donley N, Bullard RD, Economos J, Figueroa I, Lee J, Liebman AK, et al. Pesticides and environmental injustice in the USA: root causes, current regulatory reinforcement and a path forward. BMC Public Health. 2022;22(1):708. Available from: https://bmcpublichealth.biomedcentral. com/articles/10.1186/s12889-022-13057-4.
- U.S. EPA. Seresto[®] Pet Collar Review. Environmental Protection Agency; 2023 Jul. Available from: https://www.epa.gov/pets/seres to-pet-collar-review.
- 34. Office of Inspector General, U.S. Environmental Protection Agency. The EPA Needs to Determine Whether Seresto[®] Pet Collars Pose an Unreasonable Risk to Pet Health. 2024 Feb. Report No.: 24-E-0023. Available from: https://www.epaoig.gov/reports/evaluation/epa-needs-determinewhether-seresto-pet-collars-pose-unreasonable-risk-pet.
- Bennett D, Bellinger DC, Birnbaum LS, DABT, A.T.S, Bradman A, et al. Project TENDR: Targeting Environmental Neuro-Developmental Risks The TENDR Consensus Statement. Environ Health Perspect. 2016 Jul;124(7). Available from: https://ehp.niehs.nih.gov/doi/10.1289/EHP358.
- Carmichael SL, Yang W, Roberts E, Kegley SE, Padula AM, English PB, et al. Residential agricultural pesticide exposures and risk of selected congenital heart defects among offspring in the San Joaquin Valley of California. Environ Res. 2014;135:133–8. Available from: https://linkinghub.elsevier. com/retrieve/pii/S0013935114002990.
- 37. Yang W, Carmichael SL, Roberts EM, Kegley SE, Padula AM, English PB, et al. Residential agricultural pesticide exposures and risk of neural tube defects and orofacial clefts among offspring in the San Joaquin valley of California. Am J Epidemiol. 2014;179(6):740–8. Available from: https:// academic.oup.com/aje/article-lookup/doi/10.1093/aje/kwt324.
- Keil AP, Daniels JL, Hertz-Picciotto I. Autism spectrum disorder, flea and tick medication, and adjustments for exposure misclassification: the CHARGE (CHildhood Autism Risks from Genetics and Environment) case– control study. Environ Health. 2014;13(1):3. Available from: https://ehjou rnal.biomedcentral.com/articles/10.1186/1476-069X-13-3.
- Marfo JT, Fujioka K, Ikenaka Y, Nakayama SMM, Mizukawa H, Aoyama Y, et al. Relationship between urinary n-desmethyl-acetamiprid and typical symptoms including neurological findings: a prevalence case-control study. Okamoto S ichi, editor. PLOS ONE. 2015;10(11):e0142172. Available from: https://dx.plos.org/10.1371/journal.pone.0142172.
- Cimino AM, Boyles AL, Thayer KA, Perry MJ. Effects of neonicotinoid pesticide exposure on human health: a systematic review. Environ Health Perspect. 2017;125(2):155–62. Available from: https://ehp.niehs.nih.gov/ doi/10.1289/EHP515.
- 41. Ospina M, Wong LY, Baker SE, Serafim AB, Morales-Agudelo P, Calafat AM. Exposure to neonicotinoid insecticides in the U.S. general population: data from the 2015–2016 national health and nutrition examination survey. Environ Res. 2019;176:108555. Available from: https://linkinghub. elsevier.com/retrieve/pii/S0013935119303524.
- Buckley JP, Kuiper JR, Bennett DH, Barrett ES, Bastain T, Breton CV, et al. Exposure to contemporary and emerging chemicals in commerce among pregnant women in the United States: the Environmental influences on Child Health Outcome (ECHO) program. Environ Sci Technol. 2022;56(10):6560–73. Available from: https://pubs.acs.org/doi/10.1021/ acs.est.1c08942.
- Landrigan P, Grandjean P. Pollution and the developing brain. Lancet. 2021;398(10315):1961. Available from: https://linkinghub.elsevier.com/ retrieve/pii/S014067362102393X.
- Grandjean P, Landrigan PJ. Neurobehavioural effects of developmental toxicity. Lancet Neurol. 2014;13(3):330–8. Available from: https://linki nghub.elsevier.com/retrieve/pii/S1474442213702783.
- Sass JB, Donley N, Freese W. Neonicotinoid pesticides: evidence of developmental neurotoxicity from regulatory rodent studies. Front Toxicol. 2024;2(6):1438890. Available from: https://www.frontiersin.org/articles/ 10.3389/ftox.2024.1438890/full.

- U.S. EPA. Imidacloprid Proposed Interim Registration Review Decision. Environmental Protection Agency; 2020 Jan. Available from: https:// www.epa.gov/sites/default/files/2020-01/documents/imidacloprid_pid_ signed_1.22.2020.pdf.
- U.S. EPA. Clothianidin and Thiamethoxam. Proposed Interim Registration Review Decision Case Numbers 7620 and 7614. Environmental Protection Agency; 2020 Jan.
- Barrón Cuenca J, Dreij K, Tirado N. human pesticide exposure in bolivia: a scoping review of current knowledge, future challenges and research needs. Int J Environ Res Public Health. 2024;21(3):305. Available from: https://www.mdpi.com/1660-4601/21/3/305.
- Liang Y, Tong F, Zhang L, Li W, Huang W, Zhou Y. Fatal poisoning by terbufos following occupational exposure. Clin Toxicol. 2018;56(2):140–2. Available from: https://www.tandfonline.com/doi/full/10.1080/15563650. 2017.1340647.
- 50. Khode D, Hepat A, Mudey A, Joshi A. Health-Related Challenges and Programs Among Agriculture Workers: A Narrative Review. Cureus. 2024 Mar 29; Available from: https://www.cureus.com/articles/237407-healthrelated-challenges-and-programs-among-agriculture-workers-a-narra tive-review.
- Perry MJ, Marbella A, Layde PM. Compliance with required pesticide-specific protective equipment use. Am J Ind Med. 2002;41(1):70–3. Available from: https://onlinelibrary.wiley.com/doi/10.1002/ajim.10026.
- Mandel JH, Carr WP, Hillmer T, Leonard PR, Halberg JU, Sanderson WT, et al. Factors associated with safe use of agricultural pesticides in minnesota. J Rural Health. 1996;12(S4):301–10. Available from: https://onlin elibrary.wiley.com/doi/10.1111/j.1748-0361.1996.tb00819.x.
- 53. NIOSH. Hierarchy of Controls. National Institute for Occupational Safety and Health - National Institute for Occupational Safety and Health. National Institute for Occupational Safety and Health. Centers for Disease Control and Prevention. 2024. Available from: https://www.cdc.gov/ niosh/hierarchy-of-controls/about/?CDC_AAref_Val=https://www.cdc. gov/niosh/topics/hierarchy/default.html.
- 54. Bălan SA, Andrews DQ, Blum A, Diamond ML, Fernández SR, Harriman E, et al. Optimizing Chemicals Management in the United States and Canada through the Essential-Use Approach. Environ Sci Technol. 2023 Jan 19;acs.est.2c05932. Available from: https://pubs.acs.org/doi/10.1021/acs.est.2c05932.
- European Union. Communication from the Commission Guiding criteria and principles for the essential use concept in EU legislation dealing with chemicals. 2024 Apr. Available from: http://data.europa.eu/eli/C/ 2024/2894/oj.
- Grout TA, Koenig PA, Kapuvari JK, McArt SH. Neonicotinoid insecticides in New York state: economic benefits and risk to pollinators. Cornell University; 2020 Jun p. 432. Available from: https://cornell.app.box.com/v/ 2020-neonicotinoid-report.
- 57. CornellCALS. Neonicotinoid Insecticide Alternatives. Cornell College of Agriculture and Life Sciences (CALS). New York State Integrated Pest Management. Cornell College of Agriculture and Life Sciences; 2024. Available from: https://cals.cornell.edu/new-york-state-integrated-pest-management/resea rch-initiatives/current-projects/alternatives-neonic-insecticides.
- Lin C, Sponsler DB, Richardson RT, Watters HD, Glinski DA, Henderson WM, et al. Honey bees and neonicotinoid-treated corn seed: contamination, exposure, and effects. Environ Toxicol Chem. 2021;40(4):1212–21. Available from: https://setac.onlinelibrary.wiley.com/doi/10.1002/etc.4957.
- 59. Van Deynze B, Swinton SM, Hennessy DA, Haddad NM, Ries L. Insecticides, more than herbicides, land use, and climate, are associated with declines in butterfly species richness and abundance in the American Midwest. Longcore T, editor. PLOS ONE. 2024;19(6):e0304319. Available from: https://dx.plos.org/10.1371/journal.pone.0304319.
- Woodcock BA, Bullock JM, Shore RF, Heard MS, Pereira MG, Redhead J, et al. Country-specific effects of neonicotinoid pesticides on honey bees and wild bees. Science. 2017;356(6345):1393–5. Available from: https:// www.science.org/doi/10.1126/science.aaa1190.
- USGS. National Water-Quality Assessment (NAWQA) Project. Pesticide National Synthesis Project - Estimated Annual Agricultural Pesticide Use. U.S. Geological Survey; 2024 Feb. Available from: https://water.usgs.gov/ nawqa/pnsp/usage/maps/compound_listing.php.
- U.S. EPA. EPA Releases Updated Occupational Exposure Assessments for Seed Treatment Uses for Three Neonicotinoids. Environmental Protection Agency. 2024. Available from: https://www.epa.gov/pesticides/

epa-releases-updated-occupational-exposure-assessments-seed-treat ment-uses-three.

- 63. Ismail I, Gaskin S, Pisaniello D, Edwards JW. Organophosphorus pesticide exposure in agriculture: effects of temperature, ultraviolet light and abrasion on PVC gloves. Ind Health. 2018;56(2):166–70. Available from: https:// www.jstage.jst.go.jp/article/indhealth/56/2/56_2017-0157/_article.
- 64. Thredgold L, Gaskin S, Quy C, Pisaniello D. Exposure of agriculture workers to pesticides: the effect of heat on protective glove performance and skin exposure to Dichlorvos. Int J Environ Res Public Health. 2019;16(23):4798. Available from: https://www.mdpi.com/1660-4601/16/23/4798.
- 65. Thompson DA, Kolpin DW, Hladik ML, Lehmler HJ, Meppelink SM, Poch MC, et al. Prevalence of neonicotinoid insecticides in paired private-well tap water and human urine samples in a region of intense agriculture overlying vulnerable aquifers in eastern lowa. Chemosphere. 2023;319:137904. Available from: https://linkinghub.elsevier.com/retri eve/pii/S0045653523001716.
- Elanco. Your Pet's Health Is Our Top Priority: Learn about the efficacy and safety profile of Seresto[®]. PM-US-22–1342. 2024. Available from: https:// www.epa.gov/sites/default/files/2020-01/documents/imidacloprid_pid_ signed_1.22.2020.pdf.
- 67. U.S. EPA. Pesticide Cancellation Under EPA's Own Initiative. Environmental Protection Agency. 2023. Available from: https://www.epa.gov/pesticide-tolerances/pesticide-cancellation-under-epas-own-initiative.
- U.S. EPA. Schedule for Review of Neonicotinoid Pesticides. Environmental Protection Agency. 2024. Available from: https://www.epa.gov/pollinatorprotection/schedule-review-neonicotinoid-pesticides.
- 69. EC-European Commission. Commission Implementing Regulation (EU) No 485/2013 of 24 May 2013 amending Implementing Regulation (EU) No 540/2011, as regards the conditions of approval of the active substances clothianidin, thiamethoxam and imidacloprid, and prohibiting the use and sale of seeds treated with plant protection products containing those active substances Text with EEA relevance. May 2013. Available from: https://eur-lex.europa.eu/eli/reg_impl/2013/485/oj.
- 70. Dowler C, Gaberell L. EU sending huge quantities of banned, bee-killing pesticides to poorer countries, documents reveal New investigation shows for first time the full scale of the EU's trade in neonicotinoid chemicals it has branded a global threat to biodiversity and food security. 2023. Available from: https://www.publiceye.ch/en/topics/pesticides/eu-sending-huge-quantities-of-banned-bee-killing-pesticides-to-poorer-count ries-documents-reveal.
- Health Canada. Neonicotinoid Insecticides Health Canada's Pest Management Regulatory Agency (PMRA). Neonicotinoid insecticides. 2024. Available from: https://www.canada.ca/en/health-canada/services/consu mer-product-safety/pesticides-pest-management/growers-commercialusers/neonicotinoid-insecticides.html.
- 72. Ontario Canada. Neonicotinoid rules for growers What corn and soybean growers need to know about rules for neonicotinoid-treated seed (Class E pesticides). 2024. Available from: https://www.ontario.ca/page/ neonicotinoid-rules-growers#:~:text=The%20requirements%20for%20far mers%20ensure,integrated%20pest%20management%20(%20IPM%20)% 20training.
- Quebec Canada. Report on Pesticide Sales in Québec Canada (French) for 2022. 2024 p. 31. Available from: https://www.quebec.ca/en/businessesand-self-employed-workers/permits-and-certification/pesticide-purch ases-sales-declarations#c109465.
- 74. NY ECL. Birds and Bees Protection Act New York State Environmental Conservation Law Article 33 (ECL 33–1301(13)) Dec 31, 2024. Available from: https://dec.ny.gov/environmental-protection/pesticides#:~:text= Beginning%20December%2031%2C%202024%2C%20Article,pesticide% 20products%20containing%20imidacloprid%2C%20thiamethoxam.
- New Jersey Statutes. An Act concerning the use of neonicotinoid pesticides. Sect. 1–3, 2021 Chapter 386 Jan 18, 2022. Available from: https:// pub.njleg.state.nj.us/Bills/2020/AL21/386_.PDF.
- Nevada Pesticides Act. Neonicotinoid Pesticides: Prohibition on purchase and use for certain purposes; exceptions; application for commercial agricultural use; regulations. Sect. 586.600, 586 2023. Available from: https:// www.leg.state.nv.us/nrs/NRS-586.html#NRS586Sec600.
- 2023 Minnesota Statutes Insecticides on State Lands. Sect. 84.9735. Available from: https://www.revisor.mn.gov/statutes/cite/84.9735.
- Washington Becomes the 11th State Legislature to Restrict Neonicotinoids. National Caucus of Environmental Legislators. 2024. Available from:

https://www.ncelenviro.org/articles/washington-becomes-the-11thstate-legislature-to-restrict-neonicotinoids/.

79. World Health Organization. One Health - Overview. 2024. Available from: https://www.who.int/health-topics/one-health.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.