Clinical Toxicology (2010) **48**, 737–744

ISSN: 1556-3650 print / 1556-9519 online
DOI: 10.3109/15563650.2010.507548

informa
healthcare

ARTICLE

Acute illnesses associated with exposure to fipronil—surveillance data from 11 states in the United States, 2001–2007

SOO-JEONG LEE[1], PRAKASH MULAY[2], BRIENNE DIEBOLT-BROWN[3], MICHELLE J. LACKOVIC[4], LOUISE N. MEHLER[5], JOHN BECKMAN[6], JUSTIN WALTZ[7], JOANNE B. PRADO[8], YVETTE A. MITCHELL[9], SHEILA A. HIGGINS[10], ABBY SCHWARTZ[11], and GEOFFREY M. CALVERT[1]

[1]*Division of Surveillance, Hazard Evaluations, and Field Studies, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Cincinnati, OH, USA*
[2]*Bureau of Environmental Public Health Medicine, Florida Department of Health, Tallahassee, FL, USA*
[3]*Environmental and Injury Epidemiology and Toxicology Branch, Texas Department of State Health Services, Austin, TX, USA*
[4]*Office of Public Health, Louisiana Department of Health and Hospitals, New Orleans, LA, USA*
[5]*Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA, USA*
[6]*Public Health Institute, Oakland, CA, USA*
[7]*Office of Environmental Public Health, Oregon Public Health Division, Oregon Department of Human Services, Portland, OR, USA*
[8]*Office of Environmental Assessments, Washington State Department of Health, Olympia, WA, USA*
[9]*Bureau of Occupational Health, New York State Department of Health, Troy, NY, USA*
[10]*North Carolina Department of Health and Human Services, Raleigh, NC, USA*
[11]*Division of Environmental Health, Michigan Department of Community Health, Lansing, MI, USA*

Introduction. Fipronil is a broad-spectrum phenylpyrazole insecticide widely used to control residential pests and is also commonly used for flea and tick treatment on pets. It is a relatively new insecticide and few human toxicity data exist on fipronil. *Objective.* This paper describes the magnitude and characteristics of acute illnesses associated with fipronil exposure. *Methods.* Illness cases associated with exposure to fipronil-containing products from 2001 to 2007 were identified from the Sentinel Event Notification System for Occupational Risks (SENSOR)-Pesticides Program and the California Department of Pesticide Regulation. *Results.* A total of 103 cases were identified in 11 states. Annual case counts increased from 5 in 2001 to 30 in 2007. Of the cases, 55% were female, the median age was 37 years, and 11% were <15 years old. The majority (76%) had exposure in a private residence, 37% involved the use of pet-care products, and 26% had work-related exposures. Most cases (89%) had mild, temporary health effects. Neurological symptoms (50%) such as headache, dizziness, and paresthesia were the most common, followed by ocular (44%), gastrointestinal (28%), respiratory (27%), and dermal (21%) symptoms/signs. Exposures usually occurred from inadvertent spray/splash/spill of products or inadequate ventilation of the treated area before re-entry. *Conclusions.* Our findings indicate that exposure to fipronil can pose a risk for mild, temporary health effects in various body systems. Precautionary actions should be reinforced to prevent fipronil exposure to product users.

Keywords Fipronil; Pesticides; Poisoning; Surveillance; Phenylpyrazole

Introduction

Every year, several new pesticide active ingredients are introduced into the market in the United States.[1] To ensure that new pesticide products, particularly those containing new active ingredients, do not pose unreasonable risks to human health, post-marketing surveillance efforts are needed to identify any adverse health effects associated with these products.

Received 26 April 2010; accepted 6 July 2010.

Address correspondence to Geoffrey M. Calvert, National Institute for Occupational Safety and Health, 4676 Columbia Parkway, R-17, Cincinnati, OH 45226, USA. E-mail: jac6@cdc.gov

Fipronil is a relatively new insecticide that belongs to the phenylpyrazole family and was first registered by the US Environmental Protection Agency (EPA) in 1996.[2] As a broad-spectrum insecticide, fipronil is widely used to control various residential, veterinary, and agricultural pests such as ants, beetles, cockroaches, fleas, ticks, termites, and weevils.[2] Fipronil disrupts γ-aminobutyric acid (GABA) receptors in the central nervous system thereby blocking GABA-gated chloride channels, resulting in excessive neuronal stimulation and death of the target insect.[2] Fipronil has higher affinity for GABA receptors in insects than in mammals and thus produces greater toxicity in insects.[2] Additional selective toxicity of fipronil to insects is produced by blockage of neuronal glutamate-gated chloride channels, which are found only in invertebrates.[3]

Over the last decade, the usage of fipronil has increased considerably and fipronil residues can now be found in 40% of American homes.[4] Meanwhile, information on human health effects from fipronil poisoning is very limited and only a few reports are available in the literature.[5–8] Reported symptoms include conjunctivitis, headache, dizziness, nausea, vomiting, abdominal pain, oropharyngeal pain, cough, sweating, sensory impairment, weakness, drowsiness, agitation, and seizure.

Recently, the US EPA intensified scrutiny of the spot-on insecticides due to an apparent increase in the number of adverse reaction reports among treated pets.[9] This prompted the present evaluation of the human toxicity associated with fipronil exposure, including spot-on fipronil-containing insecticides for pets. Multi-state surveillance data on pesticide illness in the United States were used. This paper describes the magnitude and characteristics of acute illnesses associated with fipronil exposure among humans identified from 2001 to 2007. This paper also presents three case reports from 2008 and 2009 to illustrate different patterns of fipronil exposure and to provide evidence that problems with fipronil persist.

Methods

Cases that reported acute illness or injury associated with exposure to fipronil were identified from two data sources: the Sentinel Event Notification System for Occupational Risks (SENSOR)-Pesticides program and the California Department of Pesticide Regulation (CDPR). The SENSOR-Pesticides program is run by the National Institute for Occupational Safety and Health (NIOSH) and collects pesticide illness surveillance data annually from state programs residing in state health departments. Currently, 12 states participate in the SENSOR-Pesticides program: Arizona, California, Florida, Iowa, Louisiana, Michigan, New Mexico, New York, North Carolina, Oregon, Texas, and Washington. Cases exposed between January 1, 2001 and December 31, 2007 were included. Few cases were identified before 2001. The year 2007 is the most recent year for which complete surveillance data were available. Most SENSOR-Pesticides states provided data for the entire study period. However, three states joined the SENSOR-Pesticides program after 2001 and contributed data for fewer years (Iowa, 2006–2007; New Mexico, 2005–2007; and North Carolina, 2007). Arizona identifies very few cases of acute pesticide poisoning overall, and data from this state were excluded from analyses. CDPR is an agency under the California EPA and operates its own pesticide illness surveillance program. The state surveillance programs collect information on pesticide poisoning cases identified from various sources (e.g., poison control centers, workers' compensation systems, state agencies responsible for pesticide regulation, and physician reports) and classify cases based on the strength of evidence for pesticide exposure, health effects, and toxicological evidence supporting the association between exposure and health effects.[10] Table 1 provides case definitions used by the SENSOR-Pesticides program and CDPR. The SENSOR-Pesticides program and CDPR use slightly different case definitions and categories. *Definite*, *probable*, *possible*, and *suspicious* cases from SENSOR-Pesticides and *definite*, *probable*, and *possible* cases from CDPR were included in this study. Fipronil cases included persons who were exposed to a single fipronil-containing product only or to at least one fipronil-containing product when exposure involved multiple pesticide products.

Table 1. Case classification matrix for fipronil-related illnesses by the SENSOR-Pesticides program

	Classification category				
Classification criteria[a]	Definite	Probable		Possible	Suspicious
Exposure	1	1	2	2	1 or 2
Health effects	1	2	1	2	1 or 2
Causal relationship	1	1	1	1	4

Source: CDC. Case definition for acute pesticide-related illness and injury cases reportable to the national public health surveillance system. Available at http://www.cdc.gov/niosh/topics/pesticides/pdfs/casedef2003_revAPR2005.pdf.

[a]Cases are classified as definite, probable, possible, or suspicious based on scores for exposure, health effects, and causal relationship. Exposure scores: 1 = laboratory, clinical, or environmental evidence for exposure; 2 = evidence of exposure based solely on written or verbal report from the patient, a witness, or applicator. Health effects scores: 1 = two or more new post-exposure signs or laboratory findings reported by a licensed health professional; 2 = two or more post-exposure symptoms reported by the patient. Causal relationship scores: 1 = the observed health effects are consistent with the known toxicology of the pesticide; 4 = insufficient toxicological information available to determine the causal relationship.

Note: Case classifications are slightly different between the SENSOR-Pesticides program and CDPR's Pesticide Illness Surveillance Program. CDPR classifies cases as definite, probable, and possible based on the relationship between exposure and health effects: definite = both physical and medical evidence document exposure and consequent health effects; probable = limited or circumstantial evidence supports a relationship to pesticide exposure; possible = evidence neither supports nor contradicts a relationship. More information is available at http://www.cdpr.ca.gov/docs/whs/pisp/brochure.pdf.

Variables of interest in the analysis included year of exposure, source of the case report, age, gender, location of exposure, work-relatedness, type of fipronil product (i.e., pet-care product versus other), health effects, illness severity, type of activity at the time of exposure, and factors contributing to the exposure. Work-related exposures referred to exposures that occurred while at work. Illness severity was categorized into *low*, *moderate*, and *high* using standard criteria.[10] *Low severity* refers to mild illnesses that generally resolve without treatment and with minimal lost work time (<3 days). *Moderate severity* refers to illnesses that are generally systemic and require medical treatment. They may require hospitalization (≤3 days) and lost work time (≤5 days). *High severity* refers to life-threatening or serious health effects which can result in permanent impairment or disability and may require hospitalization (>3 days) and substantial lost work time (>5 days). Contributing factors to fipronil exposure were coded by a retrospective review of available information.

This study was exempt from consideration by the federal Human Subjects Review Board because only surveillance data were analyzed and each state removes any personal identifiers from the data prior to submission to NIOSH.

Data analysis

Data analysis was performed with SAS v 9.1. Descriptive statistics were used to characterize cases, and cases were stratified by the type of fipronil product. To eliminate duplicate cases that may have been identified by both the SENSOR-Pesticides and CDPR programs, California cases from each program were compared on date of exposure, age, sex, pesticide active ingredients, and county of exposure (Personal identifiers were not available). Three cases were identified by both programs and these cases were counted only once in the data analyses.

Results

From 2001 through 2007, a total of 103 acute illness cases associated with fipronil exposure were identified in 11 states; 92 cases by SENSOR-Pesticides and 11 cases by CDPR. Florida, Texas, and Louisiana accounted for 58% (n = 60) of all cases. Iowa and New Mexico reported no cases. For the 7-year period, reported cases increased from 5 in 2001 to 30 in 2007 (Fig. 1). Most cases (n = 72; 70%) were identified through poison control centers. A total of 86 (83%) cases were exposed to a single fipronil-containing product, and 17 (17%) cases were exposed to multiple pesticide products, at least one of which was a fipronil-containing product. The fipronil products associated with these illnesses are provided in Table 2. Pet-care products (Frontline®) were responsible for 38 (37%) cases. Of cases exposed to pet-care products, 33 were by spot-on treatment products and 5 were by spray products.

Table 3 provides selected characteristics of the cases. Fifty-seven (55%) cases were female. The median age of affected persons was 37 years (range: <1–86 years), and 11 (11%) cases were <15 years old. A total of 78 (76%) cases had exposure in a private residence and work-related exposures accounted for 27 (26%) cases. Neurological symptoms predominated (50%), followed by ocular (44%), gastrointestinal (28%), and respiratory (27%) symptoms. Detailed health effects are presented in Table 4. Ninety-two (89%) cases were classified as having low-severity illness and 9 (9%) had moderate-severity illness. There were two cases (2%) of high-severity illness, both of whom were pest control operators. One case with high-severity illness had a brief episode of seizure, blurred vision, and dizziness (previous medical history is not known) while applying Maxforce® Roach Gel and Termidor® (EPA Registration numbers were unidentified). During the application, this case used only chemical-resistant gloves and no other personal protective equipment (PPE). The other case with high-severity illness developed dyspnea, diaphoresis, tremor, paresthesia, and slurred speech while applying Termidor® 80 WG (EPA Registration No. 264-569), which required hospitalization for 7 days. Information on PPE use was not available for this case.

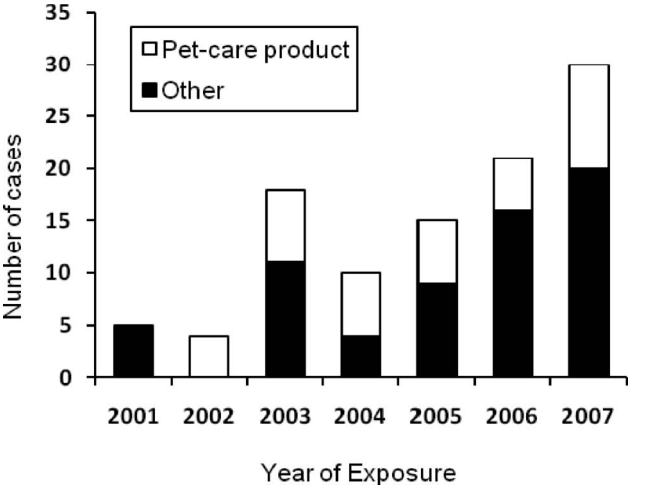

Fig. 1. Acute illnesses related to fipronil exposure by year and the type of product—11 states, 2001–2007 (n = 103).

Factors contributing to fipronil exposures are presented in Table 5. The most common factors included inadvertent splash/spray/spill (e.g., due to human error or unexpected pet movement), inadequate ventilation of the treated area before re-entry, failure to leave the treated area during application, required PPE not worn, pesticide products stored or used within reach of children, and contact with residue (e.g., handling pet before applied product dried).

Case reports

The following three cases illustrate different patterns of exposure to fipronil products.

Table 2. Fipronil products used in fipronil-related illness cases—11 states, 2001–2007 (n = 103)

Product name	Registration No.	Toxicity[c]	Restricted use	No. of cases
Fiprogard SC	432-901[b]	3	(Canceled)	10
Fiprogard 80 WG	432-900[b]	2	(Canceled)	2
Frontline Plus For Dogs	65331-5	3	No	19
Frontline Plus For Cats	65331-4	3	No	6
Frontline Spray Treatment	65331-1	3	No	5
Frontline Top Spot For Dogs	65331-3	3	No	5
Frontline Top Spot For Cats	65331-2	3	No	1
Frontline[a]	Not available	3	No	2
Maxforce ABF4	432-1264, 64248-21[b]	3	No	2
Maxforce Ant Bait F1	64248-10[b]	3	(Canceled)	1
Maxforce IBH10	64248-19[b]	3	(Canceled)	1
Maxforce Roach Gel	Not available	3	No	1
Maxforce[a]	Not available	3	No	1
Product: RBF5	432-1259, 64248-14[b]	3	No	3
Termidor SC Insecticide	7969-210, 264-568[b]	3	Yes	23
Termidor 80 WG Insecticide	7969-209, 264-569[b]	2	Yes	13
Termidor[a]	Not available	—	—	2
Unknown	Not available	—	—	8

[a]Detailed product names are not available.
[b]No longer active. The product was canceled or transferred to a different company.
[c]Toxicity categories of pesticide products are based on established criteria of the Environmental Protection Agency (40 CFR part 156). Category 1 is given for pesticides with the greatest toxicity and category 4 for pesticides with the least toxicity. The signal word for each category is as follows: 1 (danger), 2 (warning), and 3 (caution).

Case 1. In September 2009, a 38-year-old pest control technician in Texas, who had worked in termite control for over a year and had never worn PPE, developed dizziness, a shaky feeling, hand stiffness and tingling, abdominal pain, diarrhea, and tachycardia after spraying Termidor® SC (EPA Registration No. 7969-210). He was taken to the Emergency Department by ambulance and underwent decontamination. He was discharged about 6 h later when symptoms resolved. He continued to feel slightly irritable and weak, and was not able to work for 2 days. His illness was classified as moderate severity and was placed in the case definition classification category of "definite".

Case 2. In April 2008, a 33-year-old woman in Washington State developed sore throat, headache, and difficulty in breathing after returning to her apartment after it had been sprayed with Termidor® SC (EPA Registration No. 7969-210) for ants. The pest control company had sprayed her living room, kitchen, and bathroom, and told her to stay out for 1.5 h. She returned home 3.5 h later and became symptomatic. Her symptoms resolved after ventilating the apartment. Her illness was classified as low severity and was placed in the case definition classification category of "possible".

Case 3. In March 2009, a 65-year-old woman in New York State developed a pruritic rash on her neck, scalp, arms, face, ears, and chest after playing with a dog treated with Frontline® Top Spot® for Dogs (EPA Registration No. 65331-3). Unaware that her husband had treated their dog, she played with the dog within hours of treatment. She sought medical treatment 4 days after symptom onset. The illness was classified as low severity and was placed in the case definition classification category of "possible".

Discussion

Fipronil is one of the most commonly used insecticides in American homes. However, limited data are available on the toxicity of this pesticide in humans. Analyzing pesticide illness surveillance data from 2001 to 2007, we identified 103 acute illness cases associated with fipronil exposure in 11 states and the annual number of reported cases was shown to increase over time.

The findings showed that reporting of acute illness related to fipronil exposure was relatively uncommon and most cases were related to residential exposures. However, it should be noted that pesticide-related illnesses, especially non-occupational exposure cases, are substantially underreported.[11] The cases identified in this report should serve as sentinels to warn of the need to reinforce the importance of precautionary measures to prevent fipronil exposure and subsequent adverse health effects.

Our findings showed that the vast majority of cases had low-severity illness, indicating that fipronil exposure, in general, poses a low risk of mild, temporary health effects. Similarly, a report by the Paris Poison Center in France documented that most cases presented with no or mild symptoms probably because these cases experienced relatively low exposures.[5] Consistent with the fact that the central nervous

Table 3. Acute illnesses related to fipronil exposure by selected characteristics—11 states, 2001–2007

Characteristics	Total (n = 103)	Pet-care product (n = 38)	Other product (n = 65)
State (years contributing data)			
Florida (2001–2007)	23	6	17
Texas (2001–2007)	19	2	17
Louisiana (2001–2007)	18	9	9
California (2001–2007)	13	0	13
Oregon (2001–2007)	12	10	2
Washington (2001–2007)	8	5	3
New York (2001–2007)	5	3	2
North Carolina (2007)	4	3	1
Michigan (2001–2007)	1	0	1
Iowa (2006–2007)	0	0	0
New Mexico (2005–2007)	0	0	0
Status			
Definite	2	2	0
Probable	15	5	10
Possible	79	29	50
Suspicious	7	2	5
Sex			
Male	46	11	35
Female	57	27	30
Age			
<15	11	7	4
15–24	8	2	6
25–34	20	9	11
35–44	17	9	8
45–54	14	0	14
55–64	13	4	9
65+	6	1	5
Unknown	14	5	6
Location of exposure			
Private residence	78	36	42
Commercial facility	8	1	7
Institution (e.g., hospital)	4	0	4
Unknown	13	1	12
Work-relatedness			
Yes	27	1	26
No	71	37	34
Unknown	5	0	5
Type of activity at the time of exposure			
Routine indoor living activity	39	12	27
Applying/Handling pesticide	38	20	18
Routine work activity	7	0	7
Routine outdoor living activity	5	1	4
Unknown	14	5	9
Severity of illness			
High	2	0	2
Moderate	9	3	6
Low	92	35	57

system is the primary target of fipronil, neurological symptoms were the most commonly observed health effects. Ocular symptoms were also commonly reported, which were usually related to inadvertent splash/spray to the eyes. Although it was rare, high-severity illnesses requiring hospitalization or presenting with seizure were also identified in our study. The two cases with high-severity illness were both pest control operators who were exposed on-the-job while applying fipronil products. Although most fipronil-related illnesses identified in this report arose from non-occupational exposures, our findings suggest that occupational exposures to fipronil, which can involve repetitive exposure to products

Table 4. Clinical manifestations of fipronil-related illness—11 states, 2001–2007 (n = 103)

Health effects	No.
Neurological	51
Headache	24
Dizziness	14
Paresthesia	10
Muscle weakness	7
Confusion	7
Ocular	45
Irritation, pain, inflammation, lacrimation	38
Conjunctivitis	11
Gastrointestinal	29
Nausea	22
Vomiting	14
Respiratory	28
Upper respiratory pain/irritation	16
Dyspnea	9
Cough	8
Wheezing or exacerbation of asthma	5
Dermatologic	22
Irritation, pain, rash, erythema	15
Pruritus, swelling, hives	12
Cardiovascular	4
Tachycardia, palpitation	2
Other	11
Fatigue	9

Note: Presented are health effects reported by at least 5 cases, except for cardiovascular effects. The sum of health effects exceeds 103 because some cases had more than one health effect.

with higher concentrations, can pose a risk of more severe health effects. Thus, strict compliance with required PPE including chemical-resistant gloves, long-sleeved shirt, long pants, socks, and shoes, and protective eyewear such as goggles, a faceshield or safety glasses with front, brow, and temple protection should be reinforced among professional users.

This study also found that pet-acare products (Frontline®) were related to more than one-third of cases and accounted for the majority of childhood cases (64%). This finding suggests the need for special attention by parents to prevent exposure among children. In the United States, 39% of households own at least one dog and 33% own at least one cat[12] and many of these pets are treated for fleas and ticks. Pet owners who use fipronil should remember that these pet-care products are pesticides with inherent toxicity. As such, when handling these products, appropriate precautions should be taken to avoid contact with skin, eyes, or clothing during the application and also to prevent exposure to residue on the treated pets by avoiding contact with the treated areas of the pet until dry as instructed by the product label. Additionally, users may need to avoid such contact at least until bathing or shampooing treated pets, which the label recommends not be undertaken until at least 48 h after application. An experimental study showed that for up to four weeks after spot-on treatment of dogs with Frontline®, fipronil residues were detected on gloves worn while petting the dogs for 5 min.[13] The effect of Frontline® is reported to last for a month and monthly reapplications are usually recommended. Thus, repetitive and/or chronic exposure to low doses may occur if precautionary actions are not taken. Fipronil product users should be aware of the potential presence of residue after using the product. Employing good hygiene such as hand-washing after contacting treated pets would help to minimize exposure.

Moreover, a recent study showed that pet owners had an increased risk for the presence of fipronil residue in their homes.[14] The study measured fipronil and its degradates in 24 Texas residences and found that the median concentration of total fipronil was 15 times greater in indoor dust than in outdoor dust, and the concentration of fipronil sulfide in indoor dust was four times greater in pet-owners' residences than non-pet-owners' residences. Although these residue exposures to fipronil and its metabolites may not produce acute toxicity, the effects of chronic, low-level exposure are

Table 5. Factors that contributed to fipronil exposure—11 states, 2001–2007 (n = 103)

Factors[a]	No. of cases
Inadvertent spray/splash/spill (due to human error, pet behavior, package design, etc.)	23
Inadequate ventilation of treated area before re-entry or early re-entry	16
Required personal protective equipment not worn or inadequate	7
People were in the treated area during application	7
Pesticide stored or used within reach of child	7
Contact with treated pets	6
Inappropriate use (excessive application, outdoor product used indoors)	6
Notification/posting absent or ineffective	4
Off-site movement of pesticides	3
Applicator not properly trained or supervised	3
Other	7
Unknown	25

[a]Cases can have more than one contributing factors.

unknown. Furthermore, some fipronil degradates, such as fipronil desulfinyl (the primary photodegradate), are more potent in blocking mammalian chloride channels than fipronil,[2] which raises additional concern about the chronic health effects from fipronil residue exposure. Animal studies have demonstrated that fipronil can produce chronic neurological, developmental, reproductive, and endocrine toxicity (summarized in Ref. 2).[2] Furthermore, EPA classifies fipronil as a possible human carcinogen based on an increased incidence of thyroid tumors in rats.[15] Because chronic health effects are not typically captured by acute pesticide poisoning surveillance systems and are absent from our report, and because little is known about these as related to fipronil, further research is needed to better evaluate chronic health effects of fipronil products. In addition, because the residues of several pesticides may be found in many homes (e.g., permethrin is found in up to 89% of American homes),[4] consideration should be given to study the chronic health effects that may arise from exposure to these potentially synergistic pesticide mixtures.

We found that exposures often occurred from inadequate ventilation in the treated space before re-entry. This factor contributed to the illness of 16 individuals, and is illustrated in Case 2. Although Case 2 stayed away from her treated apartment even longer than she was told from the pest control operator, she still developed symptoms when she re-entered her home. The label for Termidor® SC, a restricted use pesticide, has the following instruction "DO NOT allow residents, children, other persons or pets into the *immediate* area during application. DO NOT allow residents, children, other persons or pets into treated area *until sprays have dried*."[16] A restricted entry interval (REI), which is the time interval after a pesticide application when re-entry should be avoided to prevent exposure to hazardous residues, is provided for some restricted use and over-the-counter pesticides (e.g., total release foggers). Providing recommended re-entry intervals would be more informative for users of fipronil-containing restricted use products, compared to a recommendation to wait for sprays to dry. Also, given that cases became ill after staying in the treated area during the application, precautionary information can be strengthened by instructing residents to leave the treated home, apartment, or structure during the application and until expiration of the REI.

The findings in this report are subject to several limitations. First, the number of cases identified by passive surveillance systems likely underrepresents the true magnitude of fipronil-associated illnesses. Additionally, the number of cases is not comparable across states and years because the presented data are case counts, not rates, and also because data from three states were available for only a part of the study period. Second, the surveillance data are limited to acute health effects with a short latency. Third, the data may include false-positive cases because clinical findings of fipronil poisoning are nonspecific and diagnostic tests for fipronil overexposure are not routinely available. Fourth, cases exposed to multiple products may have had some symptoms erroneously attributed to fipronil. Likewise, some health symptoms may have been caused by the solvents and adjuvants present in the fipronil products. Lastly, most cases were identified through poison control centers and information for these cases largely rely on self-reports. However, for the vast majority of these cases, the surveillance systems conduct additional follow-up to embellish the amount of information known, which increases data reliability and quality.

Conclusion

In conclusion, exposure to fipronil can pose a risk for mild, temporary health effects in humans. Those using fipronil products should take all necessary precautions to prevent exposure to fipronil. Fipronil users should comply with all label instructions including use of PPE such as eye protection and chemical-resistant gloves. To prevent exposure to post-application surface/air residue, product labels can be improved by adding more detailed precautionary information such as warning about the potential for exposure to humans from contact with treated pets, the length of time the potential for fipronil exposure from treated pets exists, and the duration of REIs before entering treated spaces. Finally, the public, particularly pet-owners, should be aware of the potential presence of residential fipronil residues and employ good hygiene to minimize exposure.

Disclaimer: The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health or each author's state agency.

Declaration of interest

Funding to support this study was provided by NIOSH, EPA, and the state agencies that contributed data. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

References

1. US Environmental Protection Agency. Fact Sheets on New Active Ingredients, 2010. http://www.epa.gov/opprd001/factsheets. Accessed 1 August 2010.
2. National Pesticide Information Center. Fipronil: Technical Fact Sheet, 2009. http://npic.orst.edu/factsheets/fiptech.pdf. Accessed 1 August 2009.
3. Zhao X, Yeh JZ, Salgado VL, Narahashi T. Fipronil is a potent open channel blocker of glutamate-activated chloride channels in cockroach neurons. J Pharmacol Exp Ther 2004;310:192–201.
4. Stout DM 2nd, Bradham KD, Egeghy PP, Jones PA, Croghan CW, Ashley PA, Pinzer E, Friedman W, Brinkman MC, Nishioka MG, Cox DC. American Healthy Homes Survey: a national study of residential

pesticides measured from floor wipes. Environ Sci Technol 2009;43:4294–4300.
5. Gasmi A, Chataigner D, Garnier R, Lagier G. Toxicity of fipronil-containing insecticides. Report of 81 cases from the Paris Poison Center. Vet Hum Toxicol 2001;43:247.
6. Chodorowski Z, Anand JS. Accidental dermal and inhalation exposure with fipronil—a case report. J Toxicol Clin Toxicol 2004;42:189–190.
7. Fung HT, Chan KK, Ching WM, Kam CW. A case of accidental ingestion of ant bait containing fipronil. J Toxicol Clin Toxicol 2003;41:245–248.
8. Mohamed F, Senarathna L, Percy A, Abeyewardene M, Eaglesham G, Cheng R, Azher S, Hittarage A, Dissanayake W, Sheriff MHR, Davies W, Buckley NA, Eddleston M. Acute human self-poisoning with the *N*-phenylpyrazole insecticide fipronil—a $GABA^A$-gated chloride channel blocker. J Toxicol Clin Toxicol 2004;42:955–963.
9. US Environmental Protection Agency. EPA Evaluation of Pet Spot-On Products: Analysis and Mitigation Plan, 2010. http://www.epa.gov/pesticides/health/petproductseval.html. Accessed 26 July 2010
10. Calvert GM, Mehler LN, Alsop J, De Vries AL, Besbelli N. Surveillance of pesticide-related illness and injury in humans. In: Krieger RI, ed. Hayes' Handbook of Pesticide Toxicology. 3rd ed. New York: Elsevier; 2010:1313–1369.
11. Mehler LN, Schenker MB, Romano PS, Samuels SJ. California surveillance for pesticide-related illness and injury: coverage, bias, and limitations. J Agromedicine 2006;11:67–79.
12. The Humane Society of the United States. U.S. pet ownership statistics, 2009. http://www.humanesociety.org/issues/pet_overpopulation/facts/pet_ownership_statistics.html. Accessed 3 March 2010.
13. Jennings KA, Canerdy TD, Keller RJ, Atieh BH, Doss RB, Gupta RC. Human exposure to fipronil from dogs treated with frontline. Vet Hum Toxicol 2002;44:301–303.
14. Mahler BJ, Van Metre PC, Wilson JT, Musgrove M, Zaugg SD, Burkhardt MR. Fipronil and its degradates in indoor and outdoor dust. Environ Sci Technol 2009;43:5665–5670.
15. US Environmental Protection Agency. Fipronil; Pesticide Tolerance, 1998. http://www.epa.gov/EPA-PEST/1998/July/Day-17/p18987.htm. Accessed 26 July 2010.
16. BASF Corporation. Termidor SC Termiticide/Insecticide, 2008. http://www.americanpest.net/docs/msds/termidor-sc-label.pdf. Accessed 26 July 2010.