FIPRONIL
TECHNICAL FACT SHEET

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NPIC Technical Fact Sheets provide information that is complex and intended for individuals with a scientific background and/or familiarity with toxicology and risk assessment. This document is intended to promote informed decision-making. Please refer to the General Fact Sheet for less technical information.

Chemical Class and Type:

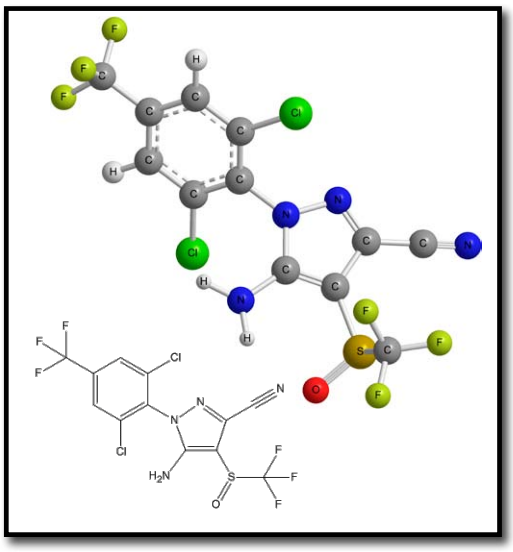
- Fipronil is a broad-spectrum phenylpyrazole insecticide. The International Union of Pure and Applied Chemistry (IUPAC) name for fipronil is (±)-5-amino-1-(2,6-dichloro-α,α,α-trifluoro-*p*-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile. The Chemical Abstracts Service (CAS) registry number is 120068-37-3.[1]
- Fipronil was first registered for use by the United States Environmental Protection Agency (U.S. EPA) in May 1996.[2] See the text box on **Laboratory Testing**.

Laboratory Testing: Before pesticides are registered by the U.S. EPA, they must undergo laboratory testing for short-term (acute) and long-term (chronic) health effects. Laboratory animals are purposely given high enough doses to cause toxic effects. These tests help scientists judge how these chemicals might affect humans, domestic animals, and wildlife in cases of overexposure.

Physical / Chemical Properties:

- Technical grade fipronil is a white powder with a moldy odor.[1,2]
- Vapor pressure[1,2]: 2.8 x 10^{-9} mmHg at 25 °C
- Octanol-Water Partition Coefficient (K_{ow})[1,2]: 1.00 x 10^{4}
- Henry's constant[1]: 3.7 x 10^{-5} atm·m^3/mol
- Molecular weight[1]: 437.2 g/mol
- Solubility (water)[1]: 0.0019 g/L (pH 5); 0.0024 g/L (pH 9) at 20 °C
- Soil Sorption Coefficient (K_{oc})[3]: The average K_{oc} value for fipronil when tested in eight soil types was 825 ± 214, and the K_{oc} values for fipronil-sulfide and fipronil-desulfinyl were 3946 ± 2165 and 2010 ± 1370, respectively.

Molecular Structure - Fipronil



Uses:

- Fipronil is used to control ants, beetles, cockroaches, fleas, ticks, termites, mole crickets, thrips, rootworms, weevils, and other insects.[1,2,4] Uses for individual fipronil products vary widely. Always read and follow the label when applying pesticide products.
- Fipronil is used in granular turf products, seed treatments, topical pet care products, gel baits, liquid termiticides, and in agriculture.[4]
- Signal words for products containing Fipronil may range from Caution to Warning. The signal word reflects the combined toxicity of the active ingredient and other ingredients in the product. See the pesticide label on the product and refer to the NPIC fact sheets on ***Signal Words*** and ***Inert or "Other" Ingredients***.
- To find a list of products containing fipronil which are registered in your state, visit the website http://npic.orst.edu/state1.htm and search by "active ingredient."

Mode of Action:

Target and Non-target Organisms

- Fipronil is toxic to insects by contact or ingestion.[1]
- Fipronil blocks $GABA_A$-gated chloride channels in the central nervous system. Disruption of the $GABA_A$ receptors by fipronil prevents the uptake of chloride ions resulting in excess neuronal stimulation and death of the target insect.[5,6,7]
- Fipronil exhibits differential binding affinity for $GABA_A$ receptor subunits, with a higher binding affinity for insect receptor complexes compared to mammalian complexes. The lower binding affinity for mammalian receptors enhances selectivity for insects and increases the margin of safety for people and animals.[5,6,8,9]
- Fipronil-sulfone, the primary biological metabolite of fipronil, is reported to be twenty times more active at mammalian chloride channels than at insect chloride channels.[10] Fipronil-sulfone is reportedly six times more potent in blocking vertebrate GABA-gated chloride channels than fipronil, but demonstrates similar toxicity to the parent compound in mammals.[8]
- Fipronil-desulfinyl, the primary environmental metabolite (photoproduct) of fipronil, is 9-10 times more active at the mammalian chloride channel than the parent compound, reducing the selectivity between insects and humans when exposed to this metabolite.[8,11]

LD_{50}/LC_{50}: A common measure of acute toxicity is the lethal dose (LD_{50}) or lethal concentration (LC_{50}) that causes death (resulting from a single or limited exposure) in 50 percent of the treated animals. LD_{50} is generally expressed as the dose in milligrams (mg) of chemical per kilogram (kg) of body weight. LC_{50} is often expressed as mg of chemical per volume (e.g., liter (L)) of medium (i.e., air or water) the organism is exposed to. Chemicals are considered highly toxic when the LD_{50}/LC_{50} is small and practically non-toxic when the value is large. However, the LD_{50}/LC_{50} does not reflect any effects from long-term exposure (i.e., cancer, birth defects or reproductive toxicity) that may occur at levels below those that cause death.

Acute Toxicity:

Oral

- Technical grade fipronil is considered moderately toxic by ingestion with an oral LD_{50} of 97 mg/kg in rats and an LD_{50} of 95 mg/kg in mice.[1] See the text boxes on **Toxicity Category** and **LD_{50}/LC_{50}**.
- Investigators fed rats a single dose of fipronil by gavage at a dose of 0, 2.5, 7.5, or 25.0 mg/kg. The lowest dose that produced adverse effects (LOAEL) was 7.5 mg/kg. At that dose, male rats displayed decreased hindlimb splay at 7 hours following administration. Researches also observed decreased body weight gain, decreased food consumption and food efficiency, and decreased grooming among female rats at 7 days after the single 7.5 mg/kg dose. All treatment-related effects resolved by 14 days following the single dose, except decreased grooming among female rats. The acute NOAEL for fipronil was 2.5 mg/kg.[12] See the text box on **NOAEL**, **NOEL**, **LOAEL**, and **LOEL** (page 4).
- The acute oral LD_{50} of fipronil-desulfinyl (primary photodegradate) in rats is 15 and 18 mg/kg for females and males, respectively.[13]

Dermal

- Fipronil is low to moderate in toxicity by contact with a dermal LD_{50} of >2,000 mg/kg in rats and 354 mg/kg in rabbits.[2]
- Researchers applied 15 doses of fipronil to the intact skin of rabbits at doses of 0.5, 1.0, 5.0, and 10.0 mg/kg/day for 6-hour periods over 21 days and observed "decreased mean body weight gain and food consumption" at the highest dose tested. The systemic NOAEL for fipronil was 5.0 mg/kg/day.[12]
- Fipronil may cause slight skin irritation (Toxicity Category IV). Fipronil was not found to be a skin sensitizer when tested on Guinea Pigs.[2]
- Fipronil may cause mild eye irritation (Toxicity Category III) that typically clears within 24 hours.[2]

TOXICITY CATEGORY - FIPRONIL

	High Toxicity Category I	Moderate Toxicity Category II	Low Toxicity Category III	Very Low Toxicity Category IV
Acute Oral LD_{50}	Up to and including 50 mg/kg (≤ 50 mg/kg)	**Greater than 50 through 500 mg/kg (> 50 – 500 mg/kg)**	Greater than 500 through 5000 mg/kg (> 500 – 5000 mg/kg)	Greater than 5000 mg/kg (> 5000 mg/kg)
Inhalation LC_{50}	Up to and including 0.05 mg/L (≤ 0.05 mg/L)	Greater than 0.05 through 0.5 mg/L (>0.05 – 0.5 mg/L)	**Greater than 0.5 through 2.0 mg/L (> 0.05 – 2.0 mg/L)**	Greater than 2.0 mg/L (> 2.0 mg/L)
Dermal LD_{50}	Up to and including 200 mg/kg (≤ 200 mg/kg)	Greater than 200 through 2000 mg/kg (> 200 - 2000 mg/kg)	**Greater than 2000 through 5000 mg/kg (>2000 – 5000 mg/kg)**	Greater than 5000 mg/kg (> 5000 mg/kg)
Primary Eye Irritation	Corrosive (irreversible destruction of ocular tissue) or corneal involvement or irritation persisting for more than 21 days	Corneal involvement or other eye irritation clearing in 8 – 21 days	**Corneal involvement or other eye irritation clearing in 7 days or less**	Minimal effects clearing in less than 24 hours
Primary Skin Irritation	Corrosive (tissue destruction into the dermis and/or scarring)	Severe irritation at 72 hours (severe erythema or edema)	Moderate irritation at 72 hours (moderate erythema)	**Mild or slight irritation at 72 hours (no irritation or erythema)**

Modeled after the U.S. Environmental Protection Agency, Office of Pesticide Programs, Label Review Manual, Chapter 7: Precautionary Labeling.
http://www.epa.gov/oppfead1/labeling/lrm/chap-07.htm

Inhalation

- Fipronil is low to moderate in toxicity by inhalation with the 4-hour LC_{50} ranging from 0.390 to 0.682 mg/L in rats.[1,2]

Signs of Toxicity - Animals

- Mice injected intraperitoneally with fipronil exhibited tonic-clonic seizures, facial clonus, or head twitching.[5,14]
- Signs of acute toxicity in rats and mice given single doses of fipronil via oral or inhalation exposure generally include changes in activity or gait, hunched appearance, tremors, convulsions, and seizures.[7]
- Clinical signs of toxicity in mice fed doses of fipronil (87.4-97.2%) in the diet for 6 weeks included overactivity, irritability, abnormal gait or posture, body tremors, convulsions, and death.[7]
- Signs of toxicity during a 52-week chronic rat feeding study included reduced feeding and food conversion efficiency, reduced body weight gain, seizures and seizure-related death, changes in thyroid hormones, increased mass of the liver and thyroid, and kidney effects.[12]

Signs of Toxicity - Humans

- Clinical signs and symptoms reported after ingestion of fipronil by humans include sweating, nausea, vomiting, headache, abdominal pain, dizziness, agitation, weakness, and tonic-clonic seizures. Clinical signs of exposure to fipronil are generally reversible and resolve spontaneously.[15,16,17]
- In one case report, a 50-year-old man complained of headache, nausea, vertigo, and weakness after spraying his field with a fipronil product for five hours. Symptoms were reported to have developed after two hours and resolved spontaneously. The authors suggested inhalation or dermal contact as the routes of exposure, although there were no signs of conjunctivitis or skin irritation.[18]
- Always follow label instructions and take steps to avoid exposure. If any exposures occur, be sure to follow the First Aid instructions on the product label carefully. For additional treatment advice, contact the Poison Control Center at 1-800-222-1222. If you wish to report an incident, please call 1-800-858-7378.

Chronic Toxicity:

Animals

- Investigators fed rats 0.5 ppm (0.019-0.025 mg/kg/day) fipronil in their diets for 52 weeks and observed no signs of systemic toxicity (NOAEL). The lowest dosage at which effects were observed (LOAEL) was 1.5 ppm (0.059 mg/kg/day males, 0.078 mg/kg/day females), and included increased incidence of seizures and death, protein alterations, and alterations in thyroid hormone levels.[12] See the text box on **NOAEL**, **NOEL**, **LOAEL**, and **LOEL**.

NOAEL: No Observable Adverse Effect Level

NOEL: No Observed Effect Level

LOAEL: Lowest Observable Adverse Effect Level

LOEL: Lowest Observed Effect Level

- Researchers fed dogs 0.2 mg/kg/day fipronil (length unknown) and observed no adverse effects. In the same study, researchers observed clinical signs of neurotoxicity at 2.0 mg/kg/day.[2]
- Scientists fed rats fipronil-desulfinyl (primary photodegradate) at 0, 0.5, 2.0, or 10.0 ppm for two years (0, 0.025, 0.098, and 0.050 mg/kg/day males, and 0, 0.032, 0.130, and 0.550 mg/kg/day females). The 10 ppm dose was reduced to 6 ppm for female rats after week 26 due to increased mortality. Male and female rats displayed increased incidence of aggression and irritability to touch at the highest doses tested. Female rats also developed bloody tears and increased salivation at 10 or 6 ppm, and convulsions at 2 and 10 or 6 ppm. No effects were seen at or below 0.5 ppm (0.025 mg/kg/day).[19]

Humans

- The chronic reference dose (RfD) for fipronil is 0.0002 mg/kg/day based on the NOAEL for chronic toxicity (0.5 ppm or 0.019 mg/kg/day) and an uncertainty factor of 100.[12] See the text boxes on **Reference Dose (RfD)** (page 9).

Exposure: Effects of fipronil on human health and the environment depend on how much fipronil is present and the length and frequency of exposure. Effects also depend on the health of a person and/or certain environmental aspects.

- No human data were found on chronic effects of fipronil. See the text box on **Exposure**.

Endocrine Disruption:

- Data from short-term and long-term toxicity studies with fipronil in rats, rabbits, mice and dogs "do not suggest any endocrine disruption activity".[20] In long term studies fipronil was shown to decrease thyroid hormone levels in rats. However, researchers concluded this effect resulted from "increased clearance, rather than a direct effect on the thyroid."[20]
- In a 2-year dietary study with rats, investigators observed thyroid tumors in rats related to altered thyroid-pituitary status at the highest dose tested (300 ppm). Results were determined to be specific to rats.[20]

Carcinogenicity:

Animals

- Researchers administered fipronil to rats at doses of 0, 0.5, 1.5, 30.0, and 300.0 ppm in the diet for nearly two years and observed increased incidence of benign and malignant follicular cell tumors in the thyroid gland for both sexes at the highest dose tested.[12]
- Investigators fed fipronil-desulfinyl (primary photoproduct) to rats at 0, 0.5, 2.0, and 10.0 ppm for 2 years (0, 0.025, 0.098, and 0.050 mg/kg/day males, and 0, 0.032, 0.13, and 0.55 mg/kg/day females) for 2 years. The 10 ppm dose was reduced to 6 ppm for female rats after week 26 due to increased mortality. Male rats at 10 ppm and female rats at 2, 6, and 10 ppm developed clinical signs of toxicity with no evidence of carcinogenicity.[19]
- Researchers often use studies designed to test for mutagenicity to screen chemicals for carcinogenicity. Fipronil did not cause mutations in human lymphocytes, Chinese hamster V79 cells, *Salmonella* (Ames test), or mouse micronuclei.[2]

Cancer: Government agencies in the United States and abroad have developed programs to evaluate the potential for a chemical to cause cancer. Testing guidelines and classification systems vary. To learn more about the meaning of various cancer classification descriptors listed in this fact sheet, please visit the appropriate reference, or call NPIC.

Humans

- The U.S. EPA classified fipronil as "Group C - possible human carcinogen," based on "increases in thyroid follicular cell tumors in both sexes of the rat."[12] See the text box on **Cancer**.
- No human data were found on carcinogenic effects of fipronil.

Reproductive or Teratogenic Effects:

Animals

- Researchers administered fipronil to rats (route of exposure not included) to determine reproductive effects. No reproductive effects were noted at 30 ppm (2.54 mg/kg/day in males and 2.74 mg/kg/day in females), though systemic toxicity, including increased thyroid and liver weights (males and females), decreased pituitary gland weights (females), and an increased incidence of thyroid hypertrophy (females) were observed. The lowest dosage at which reproductive effects were observed was 300 ppm (26.0 mg/kg/day in males and 28.4 mg/kg/day in females) based on unspecified clinical signs in the offspring, reduced litter size, decreased body weights, decreased mating, reduced fertility, reduced post-implantation and offspring survival, and delay in physical development.[2]
- In a dietary short-term developmental neurotoxicity study, the LOAEL was 0.90 mg/kg/day based on a significant decrease in pup weights during lactation, and signs of delayed of sexual development in males.[12]

Humans

- No human data were found on the teratogenic or reproductive effects of fipronil.

Fate in the Body:

Absorption

- Researchers applied a 79% solution of ^{14}C-fipronil to the backs of shaved rats. Test samples showed radio-labeled fipronil in blood, carcass, cage wash and wipe, urine, and feces. Researchers found less than 1% of the applied dose was absorbed after 24 hours at all doses tested.[7]
- In an *in vitro* study of ^{14}C-fipronil absorption through human, rabbit, and rat epidermal membranes, researchers recorded penetration rates after eight hours of 0.08% (rat), 0.07% (rabbit), and 0.01% (human) of the applied dose of 200 g/L fipronil solution. Researchers reported greater absorption from a 0.2 g/L solution of fipronil, with 0.9% (rat), 13.9% (rabbit), 0.9% (humans) of the dose being absorbed.[7]
- In another *in vitro* study, researchers measured penetration of fipronil through human epidermal membranes (0.15-3.00%) and rat epidermal membranes (1-35%), after 24 hours. Variation in absorption was dependent on the dilution rate of fipronil, as more diluted mixtures had a lower penetration rate and higher overall mean penetration.[21]
- A spot-on treatment study with ^{14}C-fipronil on dogs and cats found that radio-labeled fipronil was distributed primarily in the superficial skin layers. Radio-labeled fipronil was not detected in the dermis or the hypodermis (adipose tissue).[22]
- Scientists applied doses of 0.08 to 7.20 mg of ^{14}C fipronil-desulfinyl (primary photoproduct) to the skin of rats. Approximately 0.2-7.0% of the applied dose penetrated the skin over a 24-hour period.[7]
- Researchers administered radio-labeled fipronil to goats in feed at doses of 0.05, 2.00, and 10.00 ppm for seven days and found that absorption ranged from 15-33%. A study in rats found absorption rates between 30-50% after oral administration of fipronil.[19]

Distribution

- Fipronil is widely distributed in mammals and is found predominantly in fatty tissues. Rats given a single oral dose had the highest concentrations of fipronil in the stomach, Gastrointestinal (GI) tract, fat, and adrenals. Moderate levels were found in the liver, pancreas, thyroid, and ovaries. Low levels were present in the muscle, brain, heart, and cardiac blood.[2,7]
- A spot-on treatment study in dogs and cats detected ^{14}C-fipronil concentrated in the sebaceous glands, epithelial layers surrounding the hairs, and exposed part of the hair shaft 2 months after treatment, suggesting the passive diffusion of fipronil in the sebum covering hair and skin.[22]
- Researchers applied a spot-on fipronil product to dogs and vigorously petted them for 5 minutes every day with cotton gloves to mimic normal exposures to treated animals. Residues transferred to the gloves peaked at 589 (± 206) ppm fipronil 24 hours after treatment, decreased steadily over time (448 ± 118 ppm after 8 days), and were undetectable after 36 days.[16]

Metabolism

- The whole-blood half-life of fipronil in rats ranged from about 6.2-8.3 days after a single 4 mg/kg oral dose and decreased significantly to 2.1-2.3 days after a single 150 mg/kg oral dose.[2]
- The primary metabolite of fipronil in armyworms, mice, and presumably other insects and vertebrates is the fipronil-sulfone derivative.[8,11] Researchers injected mice with fipronil and detected the sulfone derivative in the brain, liver, kidney, fat, and feces.[11]
- Fipronil-desulfinyl, the primary photodegradate of fipronil, has been measured in the fat, brain, liver, kidney, skin, and feces of mice, rats and lactating goats after oral exposure or injection.[7,11,19]

Excretion

- Rats given an oral dose of fipronil excreted 45-75% in the feces and 5-25% in the urine. The parent compound and the oxidation product, fipronil-sulfone, were present in both media.[2,7]
- Lactating goats ingested fipronil for seven days and excreted 18-64% of the compound in the feces and 1-5% in milk; 8-25% remained in body tissues.[7]
- Goats dosed with fipronil-desulfinyl excreted 20-50% in feces and 3-7% in the urine.[19]

Medical Tests and Monitoring:

- Exposure to fipronil and its metabolites can be measured via a blood sample or in the gastric lavage fluid. Samples should be collected as soon after the exposure as possible.[21] Methods of analysis include an ELISA developed to detect total fipronil (fipronil and its metabolites) and liquid chromatography mass spectrometry which can distinguish fipronil from its sulfone and desulfinyl metabolites.[17]
- Fipronil was not among the pesticides included for biomonitoring assessment in the third National Health and Nutrition Examination Survey (NHANES).[23]

The "half-life" is the time required for half of the compound to break down in the environment.

1 half-life	**=**	**50% remaining**
2 half-lives	**=**	**25% remaining**
3 half-lives	**=**	**12% remaining**
4 half-lives	**=**	**6% remaining**
5 half-lives	**=**	**3% remaining**

Half-lives can vary widely based on environmental factors. The amount of chemical remaining after a half-life will always depend on the amount of the chemical originally applied. It should be noted that some chemicals may degrade into compounds of toxicological significance.

Environmental Fate:

Soil

- The half-life of fipronil is 122-128 days in aerobic soils. Under aerobic conditions, naturally occurring soil organisms break down fipronil to form fipronil-sulfone. Fipronil can also be hydrolyzed to form fipronil-amide.[2] See the text box on **Half-life.**

- Fipronil degrades on soil surfaces by ultraviolet radiation (i.e., sunlight) to form fipronil-desulfinyl, and has a measured half-life of 34 days in loamy soil. However, soil particles may prevent light from penetrating any significant depth of soil under field conditions and thereby increase residence time.[2,24]
- In studies to determine the fate of fipronil in soil, researchers found "no evidence of volatility" of fipronil or fipronil metabolites.[2]
- Fipronil has low mobility in soil and is not expected to leach into groundwater. After soil treatment, fipronil usually does not travel further than the upper six inches of soil, and significant lateral movement is not expected.[1,2,25]
- The K_{oc} values for fipronil range from 427-1248 in sandy loam, but will vary depending on clay and organic carbon content of the soil. The K_{oc} is 3946 (± 2165) for fipronil-sulfide and 2010 (± 1370) for fipronil-desulfinyl.[1,25]

Water

- Fipronil degrades rapidly in water when exposed to UV light to form fipronil-desulfinyl. Under these conditions, fipronil has a half-life of 4 to 12 hours.[24,26]
- Fipronil is stable to hydrolysis at pH 5 and pH 7. However, it degrades in alkaline conditions in direct proportion to increasing pH values. Fipronil-amide is the primary residue formed from hydrolysis.[2,24,26]
- Fipronil was measured in surface water at concentrations of 0.829 to 5.290 µg/L in southwestern Louisiana during March through April, which corresponds to the timing of releases of ricefield tailwater. Results indicate that fipronil degradation products accumulate in riverbed sediment while the parent compound does not.[27]
- Fipronil-desulfinyl photodegrades in aerated and static water with recorded half-lives of 120 (± 18) hours and 149 (± 39) hours, respectively.[26]
- Fipronil and fipronil-desulfinyl are less volatile than water and can concentrate under field conditions.[1,2]

Air

- The vapor pressure for fipronil is 3.7×10^{-4} mPa at 25 °C.[1] Photodegradation studies in soil found no evidence of volatility of fipronil or its metabolites.[2]

Plants

- Fipronil is not well absorbed by plants after soil treatment (about 5%) and partially degrades in plants to the sulfone and amide derivatives. Fipronil applied to foliage partially photodegrades to form fipronil-desulfinyl.[1]

Indoor

- No indoor fate data were found.

Food Residue

- The United States Food and Drug Administration (FDA) Pesticide Residue Monitoring Program conducts regulatory and incidence/level monitoring for pesticide residues in domestic and imported foods (except meat, poultry, dairy, and eggs). In 2003, the FDA analyzed 84 domestic samples (3.6% of domestic samples) for levels of fipronil for tolerance compliance. No samples contained detectable levels of fipronil.[28]
- In 2003, the FDA analyzed more than 150 imported food samples for levels of fipronil. Two samples had residues of fipronil that exceeded the legal limit (tolerance).[28]
- The United States Department of Agriculture (USDA) conducts regulatory monitoring for pesticide residues in meat, poultry, dairy, and eggs. In 2006, the USDA analyzed 655 poultry breast samples and 655 poultry thigh samples for levels of fipronil. One poultry breast (0.2%) and 2 poultry thighs (0.3%) had detectible levels of fipronil. No samples contained residues that exceeded the established U.S. EPA tolerances.[29]

- From 2003-2006 the USDA analyzed other commodities for fipronil residues, including butter (732 samples in 2003), milk (739 samples in 2004 and 746 samples in 2005), heavy cream (369 samples in 2005), and pork (352 samples in 2005), and found that no samples contained residues that exceeded U.S. EPA tolerances.[30]

Ecotoxicity Studies:

Birds

- Fipronil is highly toxic to bobwhite quail and pheasants, with an acute oral LD_{50} of 11.3 mg/kg and 31.0 mg/kg, respectively. Fipronil also has high sub-acute toxicity with a 5-day dietary LC_{50} of 49 mg/kg in bobwhite quail.[1]
- Fipronil is practically non-toxic to mallard ducks with no documented acute, sub-acute, or chronic effects.[1,2]
- The fipronil-sulfone metabolite is highly toxic to upland game birds and moderately toxic to waterfowl by ingestion.[2]

Fish and Aquatic Life

- Fipronil is highly to very highly toxic to marine and freshwater fish. The 96-hour LC_{50} is 0.246 mg/L for rainbow trout, 0.083 mg/L for bluegill sunfish, and 0.130 mg/L for sheepshead minnows.[2]
- Fipronil-sulfone is 6.3 and 3.3 times more toxic to rainbow trout and bluegill sunfish, respectively, than the parent compound.[2]
- Fipronil accumulates in fish with a bioconcentration factor of 321 for whole fish, 164 for edible tissue, and 575 for non-edible tissue. Fish eliminated fipronil completely 14 days after being transferred to clean water. The primary metabolites in fish are fipronil-sulfone and fipronil-sulfide.[2]
- Fipronil is highly toxic to freshwater invertebrates. In daphnids, the NOEL for fipronil was measured at 9.8 µg/L, and the LOEL was 20.0 µg/L. The fipronil-sulfone and fipronil-desulfinyl metabolites are 6.6 and 1.9 times more toxic to freshwater invertebrates, respectively, than the parent compound.[2]
- In one study, male copepods reared in a 0.63 µg/L fipronil solution had a 75-89% decrease in reproductive success. Carry-over effects were significant for males (but not females) moved to clean seawater three days before mating.[31]
- Fipronil is highly toxic to oysters with an EC_{50} of 0.77 mg/L and very highly toxic to mysid shrimp with a 96-hour LC_{50} of 140 ng/L. Exposure to less than 5.0 ng/L fipronil affected mysid growth, reproduction, and survival.[2] See the text box on **EC_{50}**.
- When applied to water, fipronil varies greatly in its toxicity and potential to bioaccumulate in aquatic arthropods, depending on the species.[32]

EC_{50}: The median effective concentration (EC_{50}) may be reported for sublethal or ambiguously lethal effects. This measure is used in tests involving species such as aquatic invertebrates where death may be difficult to determine. This term is also used if sublethal events are being monitored.

Newman, M.C.; Unger, M.A. *Fundamentals of Ecotoxicology*; CRC Press, LLC.: Boca Raton, FL, 2003; p 178.

Terrestrial Invertebrates

- Fipronil is highly toxic to honeybees by contact and ingestion when applied to plant foliage.[1]
- Researchers found that fipronil killed 38.8-94.5% of beneficial predators such as *Orius spp.* (flower bug) and *Geocoris spp.* (big-eyed bug) and significantly reduced reproductive success and prey consumption when applied at labeled rates.[33]
- When applied to fields for locust control, fipronil killed >90% of the resident nontarget insects *Carabidae, Tenebrionidae, Scelionidae,* and *Sphecidae* populations in 2 days. Recolonization was very poor for 2-4 weeks, depending on the application rate.[34]
- Fipronil treated soil is non-toxic to worms, including earthworms of the *Pheretima* group.[1,35]

Regulatory Guidelines:

- The RfD for fipronil is 2.0 x 10^{-4} mg/kg/day based on the NOAEL for chronic toxicity (0.500 ppm or 0.019 mg/kg/day).[12] See the text box on **Reference Dose (RfD)**.
- The U.S. EPA has classified fipronil as "Group C - possible human carcinogen" based on "increases in thyroid follicular cell tumors in both sexes of the rat."[12] See the text box on **Cancer** (page 5).

Reference Dose (RfD): The RfD is an estimate of the quantity of chemical that a person could be exposed to every day for the rest of their life with no appreciable risk of adverse health effects. The reference dose is typically measured in milligrams (mg) of chemical per kilogram (kg) of body weight per day.

U.S. Environmental Protection Agency. Office of Water. 2002 Edition of the Drinking Water Standards and Health Advisories. EPA 822-R-02-038.
http://www.epa.gov/ost/drinking/standards/dwstandards.pdf

- There are no recommended or regulatory occupational exposure limits for fipronil.

Date Reviewed: January 2009

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