This fact sheet was created in 2000; some of the information may be out-of-date. NPIC is not planning to update this fact sheet. More pesticide fact sheets are available here. Please call NPIC with any questions you have about pesticides at 800-858-7378, Monday through Friday, 8:00 am to 12:00 pm PST.

NPTN Technical Fact Sheets are designed to provide information that is technical in nature for individuals with a scientific background or familiarity with the regulation of pesticides by the U.S. Environmental Protection Agency (U.S. EPA). This document is intended to be helpful to professionals and to the general public for making decisions about pesticide use.

Piperonyl Butoxide

(Technical Fact Sheet)

Please refer to the **General Fact Sheet** for less technical information.

The Pesticide Label: Labels provide directions for the proper use of a pesticide product. *Be sure to read the entire label before using any product.* A signal word, on each product label, indicates the product's potential hazard.

CAUTION - low toxicity **WARNING - moderate toxicity** **DANGER - high toxicity**

What is piperonyl butoxide?

- Piperonyl butoxide is a synergist used in a wide variety of insecticides (1). Synergists are chemicals that lack pesticidal effects of their own but enhance the pesticidal properties of active ingredients (2). Piperonyl butoxide is used in insecticides containing active ingredients such as pyrethrins, pyrethroids, rotenone, and carbamates (1, 3). See the **Pesticide Label** box above.

- Researchers developed piperonyl butoxide in 1947 using naturally-occurring safrole as a key raw material (1, 3).

- Piperonyl butoxide is a colorless to pale yellow liquid. It is practically insoluble in water and is stable to hydrolysis and ultraviolet irradiation. Researchers consider piperonyl butoxide to be noncorrosive (4).

How does piperonyl butoxide work?

- Piperonyl butoxide inhibits detoxification of pesticides by insects (3, 5). Without piperonyl butoxide, an insect's metabolic enzymes, specifically a class of enzymes known as Cytochrome P450, can detoxify an active ingredient before an insecticidal effect can occur. The addition of piperonyl butoxide to a pesticide reduces the dose of the active ingredient required to generate the desired effect (2).

- Researchers propose that piperonyl butoxide inhibits detoxification by binding a piperonyl butoxide metabolite to Cytochrome P450 enzymes, thus preventing the enzymes from detoxifying pesticides (5).

- Piperonyl butoxide's effect on Cytochrome P450 enzymes is biphasic; it both inhibits and induces enzymatic activity. The inhibition of Cytochrome P450 enzymes occurs rapidly, followed by a slow induction process. The rapid inhibition of Cytochrome P450 enzymes contributes to piperonyl butoxide's effectiveness as a synergist (5).

What types of products contain piperonyl butoxide?

- Indoor household pesticides (dusts, sprays, and foggers)
- Garden, lawn, and ornamental plant pesticides
- Agricultural pesticide products
- Mosquito abatement products
- Termite treatments
- Veterinary pesticide products
- Impregnated materials (animal ear tags and pest strips)
- Repellents or insecticides for human clothing, bedding, and mattresses

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

How toxic is piperonyl butoxide?

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 fed 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. When pesticide products are used according to the label directions, toxic effects are not likely to occur because the amount of pesticide that people and pets may be exposed to is low compared to the doses fed to laboratory animals.

Animals

- Piperonyl butoxide is low to very low in toxicity when ingested by mammals. The acute oral LD50 for rats is 4,570 to 12,800 mg/kg and 2,700 to 5,300 mg/kg for rabbits (6). See boxes on **Laboratory Testing, LD50/LC50,** and **Toxicity Category**.

- Piperonyl butoxide is very low in toxicity when inhaled by rats. The acute inhalation LC50 is >5900 mg/L (6, 7).

- Piperonyl butoxide is low to very low in toxicity to mammals when absorbed by the skin. The acute dermal LD50 is 7950 mg/kg for rats and >2000 mg/kg for rabbits (3, 6, 7). Researchers did not observe dermal sensitization with guinea-pigs exposed to piperonyl butoxide (7).

- Laboratory workers exposed the eyes of rabbits to piperonyl butoxide, and the resulting eye irritations fully recovered within 72 hours post-application (7).

- In a 90-day oral study, investigators exposed male and female mice to piperonyl butoxide at doses of 0, 10, 30, 100, 300, or 1000 mg/kg/day. At the highest dose (1000 mg/kg/day), statistically significant decreases in body weight and body weight gain were evident in males but not females. Researchers identified the liver as the target organ for piperonyl butoxide. Increased liver weights appeared to be dose dependent (6).

- In a 21-day dermal study, laboratory workers exposed male and female rabbits to piperonyl butoxide once a day, 5 days a week for 3 weeks at doses of 100, 300, or 1000 mg/kg. Workers noted dermal irritation in all treatment groups characterized by redness and swelling that increased in severity in a dose-dependent manner. Treatment-related effects were limited to skin changes at the application site (6).

LD50/LC50: A common measure of acute toxicity is the lethal dose (LD50) or lethal concentration (LC50) that causes death (resulting from a single or limited exposure) in 50 percent of the treated animals. LD50 is generally expressed as the dose in milligrams (mg) of chemical per kilogram (kg) of body weight. LC50 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 LD50/LC50 is small and practically non-toxic when the value is large. However, the LD50/LC50 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.

- Researchers fed dogs piperonyl butoxide 6 days a week for 1 year at doses of 0, 3, 32, 106, or 320 mg/kg/day. All dogs died at the highest dose level (320 mg/kg/day). Researchers observed increases in liver, kidney, and adrenal weights. The no observable adverse effect level (NOAEL) was 3 mg/kg/day (6, 7, 8).

Humans

- Eight male human volunteers, ranging in age from 22 to 57, ingested a single dose of 50 mg piperonyl butoxide resulting in an average dose of 0.71 mg/kg. Investigators observed no effect on the normal metabolism of the human volunteers 31 hours after treatment (3, 6).

- Researchers applied a commercial pesticide containing piperonyl butoxide to the forearms of human volunteers at a level of 75.8 µg piperonyl butoxide/cm^2 (1000 µg = 1 mg). Approximately 2.1% of the chemical was absorbed through the forearm skin over a 7-day period. The calculated excretion half-life was 32 hours for the absorbed piperonyl butoxide dose. Researchers observed no evidence of local or systemic toxicity with the application of piperonyl butoxide to the human volunteers (10). See box on **Half-life**.

Toxicity Category

	High Toxicity (*Danger*)	Moderate Toxicity (*Warning*)	Low Toxicity (*Caution*)	Very Low Toxicity (*Caution*)
Oral LD50	Less than 50 mg/kg	50 - 500 mg/kg	500 - 5000 mg/kg	Greater than 5000 mg/kg
Dermal LD50	Less than 200 mg/kg	200 - 2000 mg/kg	2000 - 5000 mg/kg	Greater than 5000 mg/kg
Inhalation LC50	Less than 0.05 mg/l	0.05 - 0.5 mg/l	0.5 - 2 mg/l	Greater than 2 mg/l
Eye Effects	Corrosive	Irritation persisting for 7 days	Irritation reversible within 7 days	Minimal effects, gone within 24 hrs
Skin Effects	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation

Does piperonyl butoxide cause reproductive or teratogenic effects?

Half-life is the time required for half of the compound to degrade.

1 half-life=50% degraded
2 half-lives=75% degraded
3 half-lives=88% degraded
4 half-lives=94% degraded
5 half-lives=97% degraded

Remember that the amount of chemical remaining after a half-life will always depend on the amount of the chemical originally applied.

Animals

- Laboratory workers conducted a two-generation reproduction study by feeding rats piperonyl butoxide at doses of 0, 20, 68, or 350 mg/kg/day to males and 0, 29, 94, or 480 mg/kg/day to females. Workers fed rats piperonyl butoxide before the rats mated and continued feeding them the chemical through mating, pregnancy, and nursing. Researchers detected no negative reproductive effects. They did observe that both adult and young rats that were fed the highest doses (350 and 480 mg/kg/day for male and female rats, respectively) had decreased body weights (7).

- Researchers exposed pregnant rats to piperonyl butoxide by gavage (stomach tube feeding) on gestation days 6-15 at doses of 0, 200, 500, or 1000 mg/kg/day. The NOAEL for maternal toxicity was 200 mg/kg/day based on reduced body-weight gain and food consumption, increased liver weight, and signs of toxicity at higher doses. Researchers detected no teratogenic effects and set the NOAEL for developmental toxicity at 1000 mg/kg/day (6, 7).
- Investigators fed pregnant rabbits piperonyl butoxide on gestation days 7-19 at doses of 0, 50, 100, or 200 mg/kg/day. The NOAEL for maternal toxicity was 50 mg/kg/day based on a dose-dependent reduction in body-weights at higher doses. The NOAEL for development toxicity was 200 mg/kg/day (6, 7).

Humans

- Data are not available from accidental poisonings, occupational exposures, or epidemiological studies regarding the reproductive and developmental toxicity of piperonyl butoxide.

Is piperonyl butoxide a carcinogen?

Animals

- Laboratory workers fed male and female mice diets containing piperonyl butoxide at doses of 0, 30, 100, or 300 mg/kg/day for 78-79 weeks. Male and female mice at the high dose (300 mg/kg/day) and male mice at the middle dose (100 mg/kg/day) had increased incidences of liver tumors. Researchers established the NOAEL at 30 mg/kg/day based on effects on the liver (6, 7, 11).

- Male and female rats fed diets containing piperonyl butoxide at doses of 0, 30, 100, or 500 mg/kg/day for 104-105 weeks exhibited decreased body weights at the high dose (500 mg/kg/day) and increased liver weights at the middle and high doses (100 and 500 mg/kg/day). Investigators detected no evidence of carcinogenicity for the piperonyl butoxide treatments (6, 7, 11).

- Researchers often use studies designed to test for mutagenicity to screen chemicals for carcinogenicity. Sufficient evidence exists that piperonyl butoxide does not have significant potential for mutagenicity (6, 7, 12).

Humans

- The U.S. EPA has categorized piperonyl butoxide as a group C carcinogen (13). This means that piperonyl butoxide is considered a possible human carcinogen based on limited evidence of cancer in laboratory animals. See box on **Cancer**.

- Data are not available from occupational exposures or epidemiological studies regarding the carcinongenicity of piperonyl butoxide.

Cancer: The U.S. EPA has strict guidelines that require testing of pesticides for their potential to cause cancer. These studies involve feeding laboratory animals large *daily* doses of the pesticide over most of the lifetime of the animal. Based on these tests, and any other available information, EPA gives the pesticide a rating for its potential to cause cancer in humans. For example, if a pesticide does not cause cancer in animal tests at large doses, then the EPA considers it unlikely the pesticide will cause cancer in humans. Testing for cancer is not done on human subjects.

What is the environmental fate and behavior of piperonyl butoxide?

- Researchers evaluated the degradation of piperonyl butoxide in soil at three sites, and the maximum half-life was 4.3 days. They did not detect residues after 30 days. Piperonyl butoxide has a moderate to low leaching potential (14).

- Researchers evaluated the degradation of piperonyl butoxide in aqueous environments at three sites, and the half-lives ranged from 0.55-1.64 days (14).

- Gravitational settling removes piperonyl butoxide released in the atmosphere as an aerosol. Gaseous piperonyl butoxide degrades in the atmosphere with an estimated half-life of 3.4 hours (15).

What effects does piperonyl butoxide have on wildlife?

- Researchers consider piperonyl butoxide moderately acutely toxic to fish (LC50 = 3.94-6.12 mg/L) and highly acutely toxic to aquatic invertebrate species (LC50 = 0.23-0.51 mg/L). Piperonyl butoxide has a low bioconcentration potential (16).

- Ingested piperonyl butoxide is low to very low in toxicity to birds (LD50 = >2250 - >5620 mg/kg) (16).

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