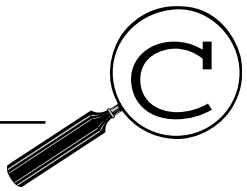

ChemicalWATCH Factsheet

A BEYOND PESTICIDES/NCAMP FACTSHEET

Piperonyl Butoxide (PBO)

Piperonyl Butoxide (PBO), a highly toxic substance that causes a range of short- and long-term effects, including cancer and adverse impacts on liver function and the nervous system, is one of the most commonly used synergists in pesticide products. Synergists are chemicals added to pesticide formulations to enhance the toxicity of the active ingredients. PBO is frequently used, especially in aerosol products and mosquito sprays, to increase the potency of pyrethrin and synthetic pyrethroids, as well as other types of insecticides.[1] Products generally contain between five to ten times as much PBO as pesticide.[2]

Many different formulations of insecticide products contain PBO. These include dusts, sprays, foggers, repellents and pediculicides (lice killers); garden, lawn, ornamental plant, and, agricultural pesticides; mosquito abatement products, termite treatments, veterinary pesticides; and insecticides for human clothing, bedding, and mattresses.[3] According to surveys by the Environmental Protection Agency (EPA), PBO is one of the most commonly used ingredients in insecticides. It is currently found in approximately 1600 to 1700 registered pest control products.[4] On labels, PBO is sometimes listed as an active ingredient, but may also be considered an inert ingredient and not listed. PBO may also be listed as Butacide, Pybuthrin, ENT – 14250, and CAS Reg. No. 51-03-6.[5]

Because of its widespread use, PBO is prevalent in the residential environment. A recent study of pregnant women from northern Manhattan and the Bronx found PBO in air samples from over 80% of the women's residences.[6] The pesticides that are most commonly mixed with PBO, synthetic pyrethroids, are among the most frequently found in the human toxic body burden by the Centers for Disease Control (CDC).[7] Residues are also regularly found on food, especially lettuce, lemons, spinach and tomatoes,[8] as well as basil, chive, cilantro, herbs, mint, pears, bell peppers, oranges, squash, and other fruits and vegetables.[9] While EPA claims that acute dietary food risk is very low, and that chronic dietary exposure is below the acceptable intake limit, others site deficiencies in EPA reviews.[10]

PBO functions as a synergist by slowing the breakdown of toxic chemicals in insects. The first step in the breakdown of many types of chemicals in insects is oxidization by a group of microsomal enzymes called P450 mono-oxygenases, located in the liver. PBO inhibits the activity of these enzymes, and thus prevents the metabolism of many types of molecules, including insecticides. This keeps the pesticide in its toxic form for longer periods of time, increasing the amount of damage it can do to the insect. A heavy dose of PBO makes an organism temporarily vulnerable to a variety of toxic chemicals that would be easily tolerated otherwise.[11,12]

Acute Toxicity

Studies suggest that by interfering with the metabolism of hormones, PBO may damage humeral organs such as the thyroid, adrenal, and pituitary glands.[13] PBO has a low to moderate toxicity based on short-term laboratory animal studies. The acute oral LD50, or dose that kills half the test population, was determined to be 6.15 g/kg for rats.[7] The LD 50 for inhalation of PBO by rats is greater than 5.9 g/kg.[14] It is predicted that the oral lethal dose for a human is 5.15 g/kg, or between 1 pint and 1 quart for a 150 lb person.[15]

Symptoms caused by ingestion of PBO in large doses include nausea, cramps, vomiting, and diarrhea.[16] Inhalation of large amounts of PBO may cause tearing, salivation, labored breathing,[17] accumulation of fluids in the lungs,[18] and may be linked to respiratory problems, including asthma. Acute and repeated dermal (skin) and eye contact has been shown to be slightly irritating, but is not linked to long-term damage.[19]

Overdoses of PBO have been shown to cause hyperexcitibility, unsteadiness, coma, seizures, and brain damage in animals.[20] Most rat deaths in studies are attributed to hemorrhages in the digestive tract, particularly the large intestine. Acute exposure in animals has also triggered hepatic (liver) changes and injury, anemia and loss of appetite, as well as changes in the kidneys, nasal bleeding, loss of muscle coordination, and abdominal swelling.[21]

Long-Term Toxicity

The primary effect of long-term exposure to PBO in animals is an increase in liver and thyroid weight, liver and kidney damage, and a decrease in body weight. These symptoms were observed in a diet of 52.8 mg/kg or more a day in a chronic study with dogs.[22]

Cancer

PBO is labeled as a group C carcinogen, a possible human carcinogen. [23] Currently there is no data from accidental exposure available regarding its carcinogenicity in humans; the only information is from animal studies. Several studies have shown that PBO treatment in rats causes an increase in liver cancer at high doses.[24] Some studies have shown that PBO treatment in rats corresponds with a very slight increase in thyroid cancer.[25]

Mutagenic Effects

It is generally accepted that PBO does not demonstrate any significant potential for mutagenicity (genetic damage).[26,27]

However, this conclusion is not accepted by everyone, and some studies have shown evidence of genetic damage,[28] including a study that demonstrated gene mutation in mouse lymphoma cells.[29]

Immune System Effects
PBO weakens the immune system by inhibiting lymphocyte response.[30] Lymphocytes are a class of white blood cells that consume potentially dangerous pathogens and release antibodies. Inhibiting lymphocyte response weakens the body's ability to defend against foreign invaders. Furthermore, by preventing the breakdown of toxic chemicals, PBO increases the damage they can do to the body.

Reproductive Effects
PBO has been shown to adversely affect a variety of reproductive functions. Two-generational laboratory studies on rats show that litter weight and size are less for mothers exposed to high concentrations of PBO, and there is an increase in birth defects and fetal death.[31] In one study the difference in the average weight of PBO-exposed offspring immediately after birth is negligible, but 7-14 days post-natal is significantly greater for those mothers that are exposed to PBO than for those that are not.[32] EPA maintains that results for teratogenicity (the ability to produce birth defects) in animals have been mixed,[33] and while some studies suggest some teratogenicity, most do not. PBO may also interfere with sexual development because the enzymes it inhibits are responsible not only for the breakdown of toxic chemicals but also for the metabolism of other compounds such as steroids, which include the sex hormones. Rats exposed to PBO over the course of two years experience an atrophy of the testes a decrease in weight of the seminal vesicles (sperm producing structures), and an increase in ovarian weights. [34] There is no evidence that PBO affects fertility.[35]

Neurotoxicity
Data has shown that PBO alone interferes with enzymes that maintain homeostasis of sodium and calcium in the brain and nervous system, possibly affecting neural response.[36,37] Additionally, it increases the neurotoxicity of other compounds.[38] Despite this data, EPA believes that these neurotoxic effects are slight and maintains that PBO poses no neurological risk.[39]

Behavioral changes have been noted with PBO as well. In a laboratory experiment, exposed rats experience more trouble navigating a maze than unexposed rats. The exposed rats travel longer distances and turned more frequently in the maze.[40] PBO also induces changes in olfactory behavior of the offspring of exposed mothers. Offspring of exposed mothers are less likely to enter a compartment that smells like home than unexposed mothers.[41] Exploratory behavior in mice increases as the dose of PBO they were treated with increased.[42] This data shows that PBO has the ability to affect behaviors in mammals.

Other Chronic Effects
Research on rats has found that PBO can cause intestinal ulcers and bleeding.[43] Liver damage is common in studies,[44] and kidney damage has been found as well.[45] Long-term ingestion of PBO causes anemia, a decrease in the amount of hemoglobin (oxygen-transporting molecules) in blood,[46] and increases the blood cholesterol level in rats.[47] PBO can also damage the larynx, and there have been reports that it can cause labored breathing, an accumulation of fluid in the lungs,[48] nasal bleeding, abdominal swelling, and loss of the ability to coordinate muscle movement.[49] There has been a fair amount of investigation into the effects of dermal contact with PBO since it is used as a topical agent for lice, but there has been no evidence of it causing any local or systemic toxicity, and the amount of PBO absorbed from skin contact is characterized by some researchers as low.[50]

What are synergists?

A synergist is a chemical formulated in pesticide products, in addition to the active and inert ingredients, that increases the potency of the active ingredient. While the increased potency makes the pesticide more deadly to their targets, synergists may also compromise the detoxifying mechanisms of non-target species, including humans. Exposure to an insecticidal synergist like PBO may make a person temporarily vulnerable to a variety of toxic insults that could otherwise be tolerated.

Although PBO is rarely, if ever, used alone, most studies examine it individually. When combined with pyrethrins or other insecticides, the toxic effects of the chemicals cannot simply be added together. The effects are multiplicative. Since PBO amplifies the effects of other pesticides, evaluating its danger alone is of limited value. Most resources, including the published EPA docket and most of the references used in this factsheet, fail to address the health effects of common PBO combinations.

Environmental Effects

PBO is considered moderately toxic to fish, moderately to highly toxic to invertebrates (including crustaceans and insects), and highly toxic to amphibians.[51] In one study, concentrations of less than one part per million (ppm) killed water fleas, shrimp, and oysters.[52] It is also very toxic to a common type of earthworm.[53] Ingested PBO has a low to very low toxicity in birds.[54]

Not only does PBO kill organisms, it is known to interfere with the reproduction of many types of wildlife at much lower concentrations than those required for mortality. The bio-concentration potential for PBO is low,[55] but can be moderate in some aquatic organisms.[56] PBO also inhibits the breakdown of toxic chemicals in wildlife and the soil, increasing the concentrations of other, more acutely potent, pesticides.

Environmental Fate

PBO is relatively short-lived in the environment and has a low to moderate potential to contaminate groundwater. One study

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found PBO in river water at a concentration of 9.7µg/L.[57] It is rapidly degraded when exposed to sunlight, with a degradation half life of about one day in soil exposed to sunlight, and 14 days in soil without sunlight. The rate of degradation is also affected by how much oxygen is in the environment (particularly in aquatic systems), moisture levels, and application methods.[58] There is less information available about PBO's persistence indoors, but one study found that PBO persisted for at least two weeks after a cockroach treatment on toys and in dust in a kindergarten.[59]

Regulatory Status and History

In the late 1930's U.S. manufacturers of pesticides began looking for a way to increase the potency of pyrethrum, which was being imported from Japan, out of concern that its import could be disrupted. PBO was first synthesized in 1947 by Herman Wachs, who worked for Dodge & Olcutt, Inc. It was made from the naturally occurring raw material safrole. From 1952 onwards the U.S. has been manufacturing large amounts of PBO.[60]

In April 2005, EPA released human health and environmental fate and effects risk assessments and related documents for PBO. This docket is available at www.regulations.gov, docket ID EPA-HQ-OPP-2005-0042. A public comment period was open through June 27, 2005, and the EPA review is projected to be completed by August 3, 2006.

The main concern expressed by the public commentary regarding this docket is that EPA should not evaluate PBO alone, but also should evaluate its synergistic effects, as this is the context in which it is used, and the evaluations of pyrethrins do not take this increased toxicity into account. Furthermore, the review lacks urban environmental data, despite the fact that this is the primary use of PBO.

Common Products Containing PBO

Although EPA maintains that the risk from chronic dietary and water exposure to PBO is very low,[i] it is in dozens of products widely used in the home and community and not fully evaluated for synergistic effects. It is commonly sprayed in insecticide formulations by municipalities as part of mosquito abatement. Children's exposure to PBO is of concern because of their special vulnerability. The following list is a sampling of commonly used products on the market containing PBO. As an ingredient, PBO adds to the overall toxicity of otherwise hazardous pesticide products.

707 Jackpot Formula V – Crawling Insect Spray
Adams Flea & Tick Mist
Bayer – Advanced Garden Mosquito Killer Plus
Bonide Wasp & Hornet Killer, Aerosol
Bonide Ant, Roach & Spider Killer
Champion Sprayon Multi Purpose Insect and Lice Killer
Cutter Bug Free Backyard Outdoor Fogger
Deep 6 Wasp and Hornet Killer
Garden Safe – Garden Dust Insecticide
Garden Safe Brand Flying & Crawling Insect Killer
Miracle Gro Bug Spray
Ortho Plant Care
Ortho Tomato & Vegetable Insect Killer Ready to Use
Raid Flea Killer Plus
Raid Ant & Roach Killer
Raid Commercial Insect Killer
Raid House & Garden Bug Killer
Repel Outdoor Fogger, Camp Fogger
RID Lice Killing Shampoo & Mousse
Schultz Houseplant & Garden Insect Spray
Shoofly Screen and Surface Insect Spray
Shoofly Hornet Wasp Jet bomb II
Spectracide Tomato & Vegetable Insect Spray
Spectracide Flea and Tick Spray 2
Spectracide Pro Wasp & Hornet Killer
Spectracide Bug Stop Insect Killer, Aerosol
Tegrin-LT Lice Treatment Kit
Terro Ant Killer Spray
Zodiac FleaTrol Flea & Tick Shampoo and Flea and Tick Spray

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