



## **BEYOND PESTICIDES**

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September 26, 2006

Public Information and Records Integrity Branch (PIRIB)  
Office of Pesticide Programs (OPP)  
Environmental Protection Agency  
Rm. 119, Crystal Mall #2  
1801 S. Bell St., Arlington, VA  
Attention: Docket ID Number OPP-2004-0385

Re: Permethrin; Notice of Availability of Reregistration Eligibility Decision

Dear Madam/Sir:

Thank you for the opportunity to comment on the Reregistration Eligibility Decision (RED) for the synthetic pyrethroid permethrin. These comments are submitted on behalf of Beyond Pesticides/National Coalition Against the Misuse of Pesticides (Beyond Pesticides). Beyond Pesticides seeks to educate the public on the potential hazards of pesticides, restrict pesticides uses in a manner that protects public health and the environment, and advance alternatives that eliminate dependency on toxic chemicals. To that end, we would like to use this opportunity to comment and make recommendations to the RED for permethrin.

### **1. EPA does not have adequate data to eliminate the 10X FQPA safety factor**

EPA has reduced the 10X safety factor to 1X for permethrin. However, EPA does not have adequate data to abandon the 10X safety factor assigned by the Food Quality Protection Act (FQPA) to protect infants and children. Congress overwhelmingly passed FQPA to address, among other concerns, the particular hazards faced by children from exposure to pesticides. Children are not little adults, and their bodies are unlikely to respond in the same manner as adults. In the case of permethrin, many levels of concern are already exceeded or close to being exceeded for various exposure scenarios for both adults and children. If EPA would retain the 10X safety factor, most uses would have to be cancelled or severely restricted. Beyond Pesticides disagrees with EPA's decision to abandon the 10X safety factor. We believe the decision was political, and not based on sound science. If a chemical fails the test, we cannot simply change the rules.

Permethrin is registered for use on apples, pears, nuts, lettuce, potatoes, peaches, corn watermelon, spinach, tomatoes, soybeans, celery and more. Many of these crops are the favorite foods or fruit juices of children. EPA's methods for calculating exposure through food do not account for the unique diets of children. A child's diet is far less varied than an adult's. In particular children consume large quantities of milk, fruit, and fruit juices. The average one-year-old drinks twenty-one times more apple juice, per unit of body weight than the average American. This is reason alone is enough to preclude EPA from lowering the 10x safety factor for permethrin provided for by FQPA.

EPA also underestimates the exposure to children due to mosquito spraying and in impregnated clothing. As discussed below, clothing labels do not adequately warn consumers of the dangers posed by the pesticides in the clothing, which is often marketed to children. Because permethrin washes off clothing in the laundry, it must be considered that exposure could exceed EPA models in the rain or when damp from sweat. Because this model does not account for real world exposure patterns, and exposure due to public health spraying is not fully considered, the 10X Safety factor must be retained.

With the phasing out of certain organophosphate pesticides between 2002 and 2005, the use of permethrin and other synthetic pyrethroids has increased and is expected to continue to increase. Clearly, permethrin represents a significant source of exposure to pesticides for young children given its common use in and around homes in insect sprays and on lawns and gardens; flea and tick shampoos, powders, and sprays for dogs and cats; as a mosquito repellent, including use in pesticide-impregnated clothing marketed to children; as a community pesticide fog; as a pediculicide; and, in various food uses. With the increase in use, we must carefully monitor its impacts. Unfortunately, EPA abandoned its Pesticide Incident Monitoring System (PIMS) in 1981, so there is no official record of poisoning incidents involving permethrin. However, since the 1980's, Beyond Pesticides has continued to receive reports of possible permethrin poisonings. One can only assume that if EPA had not terminated PIMS, poisoning incidents would increase with the increase in permethrin use. The ubiquitous nature of this pesticide in the everyday lives of children, combined with the impossibility of tracking poisoning events is yet another reason to retain the 10X safety factor.

## **2. The Reregistration Eligibility Decision fails to take into account the possible endocrine-disrupting effects of permethrin.**

The RED states, "In the available toxicity studies on permethrin, there was no toxicologically significant evidence endocrine disruptor effects." However, permethrin was classified as a suspected endocrine disruptor at the 1997 Illinois EPA Endocrine Disruptors Strategy Meeting.<sup>1</sup> Permethrin binds to receptors for androgen (a male sex

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<sup>1</sup> Illinois Environmental Protection Agency. 1997. *Endocrine Disruptors Strategy*. Springfield, IL: EPA.

hormone) in cells from human males.<sup>2</sup> It also binds to the peripheral benzodiazepine receptor, which stimulates production of testosterone.<sup>3</sup> In a long-term feeding study of mice, permethrin was shown to cause reduced testes weights.<sup>4</sup> In another study, researchers found that permethrin had significant estrogenic potency as it inhibited the binding of estradiol to the estrogen receptor.<sup>5</sup>

FQPA requires EPA to screen pesticide ingredients and determine their ability to disrupt endocrine systems. EPA is also required to take action to protect public health from those chemicals found to have endocrine effects. Permethrin has shown endocrine disrupting potential and as a precautionary measure these suspected risks must be included in the RED. The current system of testing suspected endocrine disruptors is flawed. Because effects from endocrine disrupting chemicals do not follow the standard dose-response pattern and can affect the body at extremely low doses, often so low that they cannot be avoided, EPA must test at these levels.

For example, Frederick vom Saal, a professor at the University of Missouri, shows that exposure to endocrine-disrupting chemicals can have significant negative effects at a dose 100,000 times smaller than commonly tested in standard methods. The study looked at the effects of Bisphenol-A (BPA) at levels pronounced safe by government regulations and are said to be the equivalent of the exposure people receive in the course of everyday life. Following exposure, the mice began to show reproductive abnormalities. In some of Dr. vom Saal's experiments, low doses of the chemical actually produced the opposite result of a large dose. For example, a very small dose led to an abnormally large prostate, while a large dose led to an abnormally small prostate. Because other endocrine disruptors could cause similar effects, EPA must test for these impacts from exposure to permethrin and all suspected endocrine disruptors.

According to the RED, when the appropriate screening and/or testing protocols being considered under the Endocrine Disruptor Screening Program (EDSP) have been developed, permethrin may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption. When the EDSP is fully developed, this RED must be reevaluated and rewritten to reflect the risks of permethrin's endocrine disrupting potential. It must also include appropriate risk mitigation measures that will immediately change usage patterns to ensure safety.

### **3. EPA underestimates the risks posed by permethrin-impregnated clothing**

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<sup>2</sup> Eil, C. and B. C. Nisula. 1990. The binding properties of pyrethroids to human skin fibroblast androgen receptors and to sex hormone binding globulin. *Journal of Steroid Biochemistry* 35: 409-414.

<sup>3</sup> Ramadan, A. A. et al. 1988. Actions of pyrethroids on the peripheral benzodiazepine receptor. *Pesticide Biochemistry and Physiology* 32: 106-113.

<sup>4</sup> Ref. #6, p. 16.

<sup>5</sup> Chen, H., J. Xiao, G. Hu, J. Zhou, H. Xiao, and X. Wang. 2002. *Journal of Toxicology and Environmental Health, Part A* 65(19): 1419-1435.

Based on comments sent to the agency about permethrin-impregnated clothing losing efficacy after washing, EPA “is requiring product specific efficacy data for all permethrin impregnated fabric products, and wash-off data to support the efficacy claims.” However, EPA ignores numerous comments about the underestimated risks of permethrin-impregnated clothing. In the RED, the Agency uses a generic model that considers the clothing residue concentration, surface area of the skin that is in contact with the fabric, the transfer factor, and body weight to assess exposure risk. Actual exposure may be much greater, however, because real world conditions, such as rainy weather, sweating and other factors, could increase the transfer factor.

Despite acknowledging that permethrin-impregnated clothing are a source of dermal and oral exposure to permethrin, EPA does not require health warnings to be put on the clothing label, nor does the label caution against improper uses, such as prolonged exposure to the clothes. The label states that the clothing is effective for 25 washings, and that the clothing should be washed separately – meaning that it comes off in water. Therefore, rainy weather, sweating and other factors may increase the rate at which the pesticide transfers from the clothing. Some permethrin from the impregnated clothes will inevitably be absorbed into the body.<sup>6</sup> The label does not caution against prolonged exposure to the clothes, despite the fact that the longer and more frequently one wears the clothes, the more permethrin will be absorbed into the body and the greater the risks.

Additionally, the label of Buzz Off clothing (one brand of permethrin-impregnated clothing) recommends to “use in conjunction with an insect repellent...” One of the most common insect repellents used on skin is DEET, and many stores sell the two together. However, use of permethrin-impregnated clothing in conjunction with DEET creates numerous health problems, as explained in the next section, yet this aggregate risk is not taken into account in the RED.

Another potential problem is the possibility of local water contamination. Because permethrin-impregnated clothing is marketed to outdoor enthusiasts, it is likely that backpackers and campers wear this clothing. If a person wearing a treated clothing cools off in a local stream or washes their clothes in a nearby body of water, as through hikers often do, some permethrin will come off into that body of water. Even small doses of permethrin are highly toxic to fish and aquatic invertebrates.<sup>7</sup> Although the label says that the clothes should not be stored or disposed of into water, it does not warn against washing or wearing the clothes in natural bodies of water.

#### **4. EPA does not adequately mitigate the effect of permethrin on asthmatics.**

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<sup>6</sup> Snodgrass, H. 1992. Permethrin transfer from treated cloth to the skin surface: potential for exposure in humans. *Journal of Toxicology and Environmental Health* 35(2): 91-105.

<sup>7</sup> Extension Toxicology Network (ETN), Oregon State University. 1996. Pyrethroids. *Pesticide Information Profiles*. <<http://extoxnet.orst.edu/pips/permethr.htm>> (October 31, 2005).

In the RED, EPA states, “Although it is a relatively safe product, it can aggravate asthma or lead to asthma like symptoms.” Asthma rates in the US have reached epidemic levels, particular in young children, who are most vulnerable. Nearly 1 in 8 school-aged children have asthma, and the rate is rising. Synthetic pyrethroids have been shown to be respiratory allergens and use of them may result in asthma-like symptoms, especially in children with a history of asthma or allergies. Numerous cases of people exposed to synthetic pyrethroids have reported symptoms of irritation of the throat and respiratory tract, shortness of breath, coughing, and other asthmatic symptoms. Despite acknowledging the potential impact of permethrin on asthmatics and describing incidents involving asthma and permethrin, EPA fails to take into account the special vulnerability of asthmatics in its analysis.

### **5. Synergistic effects between common pesticide exposure combinations must be considered**

EPA does not take into account synergistic effects with other chemicals when registering pesticides. However, as studies have shown, many pesticides have dangerous synergistic effects when exposure is combined with pesticides and pharmaceuticals. A likely combination of pesticides that have been shown in scientific literature to cause adverse synergistic reactions is permethrin and DEET. Because of the threat of West Nile virus and other mosquito-borne illnesses, DEET use is recommended by the Centers for Disease Control and Prevention (CDC), so it is likely that individuals will be wearing DEET while outside during mosquito season. Permethrin is widely used by communities for mosquito control, as well as on lawns and gardens, in clothing and for myriad of other uses. Therefore, it is easy to imagine how exposure to both DEET and permethrin is likely.

According to the literature, the use of DEET in combination with permethrin likely facilitates enhanced dermal absorption of permethrin.<sup>8</sup> Studies done by Duke University researcher Mohammed Abou-Donia suggest that DEET in conjunction with permethrin may be linked to Gulf War Syndrome, which affects thousands of veterans. Symptoms include headaches, loss of memory, fatigue, and muscle and joint pain. The authors found that exposure to both DEET and permethrin experienced by service personnel in the Persian Gulf War (PGW) may have played an important role in causing these illnesses. The animals in these study received the same routes of exposure and doses of DEET and permethrin as the PGW veterans – who were wearing permethrin impregnated clothing. Abou-Donia and his colleagues found that a single dermal dose of a combination of DEET and permethrin significantly increased the release of brain mitochondrial cytochrome c, although alone neither chemical affected the amount released. This release of cytochrome c can induce apoptosis, or cell death, which can

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<sup>8</sup> Commission of Life Sciences. “Health Effects of Permethrin-Impregnated Army Battle-Dress Uniforms.” (1994) <http://books.nap.edu/books/NI000104/html/31.html>.

cause neurological damage.<sup>9</sup> Other studies found that the combination of even small doses of DEET and permethrin significantly decreased the permeability of the blood-brain barrier in the cortex and caused impaired sensorimotor performance.<sup>10</sup> These studies all showed that permethrin, and especially permethrin in conjunction with DEET, can have serious neurological health effects.

## **6. EPA must consider the health and ecological impacts of permethrin formulated with piperonyl butoxide (PBO)**

Permethrin is also commonly formulated with the synergist piperonyl butoxide (PBO). EPA did not consider the possible effects of these chemicals in combination. Because of the frequency with which these chemicals are formulated together, EPA should evaluate the combined impact for all health and ecological endpoints.

PBO is added to increase the potency of permethrin product. Many permethrin formulations contain synergists, most commonly PBO. PBO inhibits important liver enzymes responsible for breakdown of some toxins, including the active ingredients of pesticides. Specifically, it has been shown to inhibit hepatic microsomal oxidase enzymes in laboratory rodents and interfere in humans. Because these enzymes act to detoxify many drugs and other chemicals, a heavy exposure to an insecticidal synergist may make a person temporarily vulnerable to a variety of toxic insults that would normally be easily tolerated.

Furthermore, the impact of permethrin combined with PBO to aquatic organisms must be considered. We applaud the agency's acknowledgement that this data is required for an accurate evaluation of its ecological impacts. We encourage EPA to always consider synergists in all applicable exposure scenarios for both health and ecological impacts.

## **7. The cancer risk for permethrin is underestimated and outweighs its benefits to society**

The Agency classifies permethrin as "Likely to be Carcinogenic to Humans" by the oral route. Given the availability of alternative products and practices, we should not be exposing ourselves to this "likely human carcinogen" and uses should be mitigated immediately.

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<sup>9</sup> Abu-Qare, AW, and M. B. Abou-Donia. 2001. Combined exposure to DEET (N,N-diethyl-m-toluamide) and permethrin induced release of rat brain mitochondrial cytochrome *c*. *Journal of Toxicology and Environmental Health*, part A. 63: 243-252.

<sup>10</sup> Abou-Donia, M. B., et al. 2001. "Effects of daily dermal application of DEET and permethrin, alone and in combination, on sensorimotor performance, blood-brain barrier, and blood-testis barrier in rats." *Journal of Toxicology and Environmental health*, Part A, 62:523-541 and Abdel-Rahman, A, et al., "Neurological deficits induced by malathion, DEET, and permethrin, alone or in combination in adult rats," *Journal of Toxicology and Environmental Health*, 2004 Feb 27; 67(4):331-56.

## **8. Permethrin is highly toxic to bees and other beneficial insects**

The RED states that permethrin is highly toxic to bees and other beneficial insects. Permethrin is likely to reduce and eliminate important insect populations. Pollinators provide an essential ecological function in both agricultural and wild land ecosystems. Protection of pollinators should be the highest priority of the EPA, as without them crops would not produce harvests and wild plant communities would decline.

## **9. Permethrin is highly toxic to fish and other aquatic organisms, including endangered species**

Permethrin is highly toxic to fish, due to the sensitivity of their nervous systems. It is also highly toxic to many aquatic invertebrate animals; its effects on insects and crustaceans are particularly severe. According to the RED, risk quotients (RQs) were above the level of concern for endangered species for all freshwater and marine fish and invertebrates for all crop uses and exposure scenarios considered. When used for mosquito control, the RQs often exceed the level of concern for aquatic endangered species in bodies of water. In late June, an estimated 100,000 to 300,000 black crappie fish (*Pomoxis nigromaculatus*) died suddenly in Clear Lake in Waseca County, Minnesota. After the fishkill, water samples showed the presence of permethrin. Some endangered toads and salamanders may also be at risk from permethrin.

Although it is commonly thought that the potential for leaching into water is low because permethrin adsorbs strongly to soil particles and has a short half-life in water, the U.S. Geological Survey has found permethrin in ground and surface water in numerous locations. Furthermore, a very recent study of pesticides in bodies of water in the agriculture-dominated Central Valley in California found high levels of synthetic pyrethroids in stream sediments – levels high enough that they were toxic to freshwater bottom dwellers in almost 50% of the sampled locations. Permethrin was the most commonly detected pesticide in the study. A follow-up study found toxic levels of pyrethroids in sediment of streams in residential communities, proving that even common household use of pyrethroids is negatively affecting the environment. Again, permethrin was one of the most commonly detected pesticides, and in some of the highest concentrations in the study.

Unfortunately, the actual concentrations in water may actually be even greater than the levels included in the RED, which already exceeded the level of concern for endangered aquatic species. A significant problem in the study of pyrethroid toxicity is their extreme hydrophobicity. UC Davis researchers<sup>11</sup> and scientists with the U.S. Geological Survey<sup>12</sup> have conducted studies in this area. Because permethrin is likely to adhere to

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<sup>11</sup> Wheelock, C.E., et al. 2005. "Influence of container adsorption upon observed pyrethroid toxicity to *Ceriodaphnia dubia* and *Hyalella azteca*." *Aquatic Toxicology*, 74, 47–52.

<sup>12</sup> Kuivila, K.M., et al. 2001. "Pyrethroid Insecticides in the San Francisco Estuary: II. Sampling and Analytical Challenges." 5th Biennial State of the Estuary Conference, October 2001.

the walls of test vials, concentrations may be greater than many studies suggest. EPA must consider these likely increased levels.

#### **10. EPA must incorporate expected increases in market share into residential exposures for all groups and scenarios**

The entire market for non-agricultural insecticide use is changing as a result of the phase out of most urban uses of diazinon and chlorpyrifos (Dursban), as well as possible restrictions to other organophosphate and carbamate insecticides. A study funded by the San Francisco Bay Regional Water Quality Control Board looked at the pesticides that are most likely to replace these once widely used pesticides. Of the 45 insecticides that are possible replacements for urban uses of diazinon and chlorpyrifos, permethrin made the list of the top ten pesticides that appeared to be most likely to gain significant market share in the coming years, according to the study. According to the report, permethrin use increased by 52% between 1999 and 2000, even before the organophosphates phase-outs. The increase in permethrin use leads to increased exposure. This market increase must be accounted for in the exposure assessments. Failure to account for the market increases due to the phase out of chlorpyrifos and diazinon uses skews the results of the RED. EPA must include this predicted increase in market share in the RED. This is yet another reason the estimates fall short and EPA should retain the 10X safety factor.

#### **Recommendations**

Our analysis of the Reregistration Eligibility Decision reveals that EPA underestimated the risk that permethrin poses to children and the general public. Additionally, permethrin is an acknowledged hazard to endangered aquatic species, pollinators and other beneficial species. The agency acknowledges many data gaps as well. Until all exposure scenarios, expected increases in market share and adequate endocrine disruption data are included, the report is incomplete and EPA must, at the very least, reinstate the 10X FQPA Safety Standard. In addition, permethrin-impregnated clothing poses serious risks to the public. Pesticide-warning labels, including proper uses of the clothing, should be mandatory. Many of the most common uses of permethrin have unacceptable exposure risks to many of the exposed groups, including the most vulnerable, and pose serious risks to endangered species. These uses should be cancelled immediately. Regulatory actions must be swift and not include a potentially harmful phase-out period.

Sincerely,

Aviva Glaser  
Research Associate  
Beyond Pesticides



John Kepner  
Project Director  
Beyond Pesticides