United States Environmental Protection Agency | Prevention, Pesticides and Toxic Substances (7508P) | EPA 738-F-09-001 August 2009

Permethrin Facts

Pesticide Registration

All pesticides sold or distributed in the Unites States must be registered by the Environmental Protection Agency (EPA), based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides, which were first registered before November 1, 1984, be reregistered to ensure that they meet today's more stringent standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. To implement provisions of the Food Quality Protection Act (FQPA) of 1996, EPA considered the special sensitivity of infants and children to pesticides, as well as aggregate exposure of the public to pesticide residues from all sources, and the cumulative effects of pesticides and other compounds with common mechanisms of toxicity. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then registers pesticides that meet the safety standard of the FQPA and can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the revised RED document (May 2009) for the pesticide permethrin, case 2510.

Regulatory History

Permethrin was first registered and tolerances established in the United States in 1979 for use on cotton (April 29, 1979 44FR 24287). The registration was made conditional due to the need for additional toxicology and ecological effects data to fully evaluate carcinogenicity and aquatic risk, respectively. After additional toxicity data were reviewed, EPA concluded that permethrin was a weak carcinogen. Further, laboratory studies indicated that permethrin was highly toxic to fish and aquatic invertebrates; therefore, it was classified as Restricted Use pesticide (RUP) for the cotton use. From 1982 to 1989, an additional 55 + crop tolerances were approved for a wide variety of crops, including various fruits and vegetables, meat, milk and eggs.

In 1985 a Data Call-In (DCI) for ecological effects data for permethrin was issued. After evaluation of this data EPA concluded that the current RUP classification be maintained for all products for wide area agricultural uses (except livestock and premises uses) and outdoor wide area non-crop uses because of the possible adverse effects on aquatic organisms from spray drift and runoff. In 1988 a comprehensive DCI was issued requiring additional residue chemistry, environmental fate and toxicological data. In 1994 the producers of products containing permethrin for use on cotton requested voluntary cancellation of this use. From 1994 thru 2000 permethrin was subject to specific DCIs requesting data to assess agricultural and residential exposure, agricultural re-entry, and mosquito ULV products.

The Reregistration Eligibility Decision (RED) document for Permethrin was signed on April 5, 2006, and was revised (December 2007) based on public comments and post-RED activities. The 2006 RED and 2007 Revised RED, as well as the accompanying risk assessments, benefit assessments, and public comments can be found on the Federal Docket Management System (FDMS), available at http://www.regulations.gov (docket # EPA-HQ-OPP-2004-0385). The permethrin RED was further revised (2009) based on a submitted Estimated Dermal Penetration in Humans Based on In Vitro and In Vivo Data, which decreased the dermal absorption factor relied upon in the cancer portion of the occupational and residential exposure (ORE) risk assessment from 15% to 5.7%. The Agency has also revised the RED document to reflect the current status of Office of Pesticide Program initiatives, such as the cumulative risk assessment and the Endangered Species Program, and updated the label table to reflect updates in labeling on permethrin residential, agricultural, and wide area public health use products.

Uses

- Permethrin is registered for use on/in numerous food/feed crops, livestock and livestock housing, modes of transportation, structures, buildings (including food handling establishments), Public Health Mosquito abatement programs, and numerous residential use sites including use in outdoor and indoor spaces, pets, and clothing (impregnated and ready to use formulations).

- According to Agency data, approximately 2 million pounds of permethrin are applied annually to agricultural, residential and public health uses sites. The majority of permethrin, over 70%, is used in non-agricultural settings; 55% is applied by professionals, 41% is applied by homeowners on residential areas, and 4% is applied on mosquito abatement areas.

- Permethrin is a restricted use pesticide for crop and wide area applications (i.e., nurseries, sod farms) due to high toxicity to aquatic organisms, except for wide area mosquito adulticide use. It is a general use pesticide for residential and industrial applications.

- Permethrin also has non-FIFRA pharmaceutical uses as a pediculicide for the treatment of head lice and scabies. The Food and Drug Administration (FDA) approves use of the pesticide-containing pharmaceutical under FFDCA.

Health Effects

Permethrin is a member of the pyrethroid class of pesticides. Pyrethroids are undergoing an extensive collaborative research effort with EPA's Office of Research and Development's National Health and Environmental Effects Laboratory (NHEERL), the National Exposure Research Laboratory, and the National Center for Computational Toxicology (NCCT). This research effort has focused on evaluating whether or not pyrethroids share a common mechanism of toxicity and on developing physiologically-based pharmacokinetic models (PBPK) and exposure models for key pyrethroids. Because of ongoing research, OPP has not made a determination of a common mechanism group for the pyrethroids. However, significant research is now available, and a FIFRA SAP was held June 16-19, 2009 to discuss the state of the science on pyrethroids that may serve as a basis for determining a common mechanism of toxicity. All materials from the FIFRA SAP are available on the Federal Docket Management System (www.regualtions.gov); docket number EPA-HQ-OPP-2008-0489.

If there is scientific consensus by the FIFRA SAP that there is sufficient data to support a common mechanism grouping for pyrethroids, the Agency will make revisions to the draft document, as appropriate, and subsequently will announce the pyrethroids as a common mechanism group in late 2009 or early 2010. After such an announcement, the Agency will begin work on the cumulative risk assessment for this group.

Additionally, the Agency classified permethrin as "Likely to be Carcinogenic to Humans" by the oral route. This classification was based on two reproducible benign tumor types (lung and liver) in the mouse, equivocal evidence of carcinogenicity in Long-Evans rats, and supporting structural activity relationship information.

Risks

<u>Dietary</u>

- Acute, chronic non-cancer, and cancer dietary (food and drinking water) risks from permethrin were below the Agency's level of concern (LOC).

<u>Residential</u>

- All handler scenarios (cancer and non-cancer) assessed were below the Agency's LOC.

- The non-cancer post-application risk estimates for adults, youth aged children, and toddlers exposed to an environment treated with permethrin were below the Agency's LOC. All post-application scenarios for adults, youth aged children,

and toddlers were below the Agency's cancer LOC. However, the combined oral and dermal exposure for toddlers to indoor broadcast surface spray is below the Agency's cancer LOC.

- The Agency considered post-application exposure to both outdoor residential misting systems and permethrin treated clothing. All scenarios were below the Agency's non-cancer and cancer LOCs.

Aggregate Risks

- The acute aggregate risk non-cancer and cancer estimate from food and drinking water does not exceed the Agency's LOC.

- Aggregate short-term (1-30 days) non-cancer risk estimates, which include the contribution of risk from chronic dietary sources (food + drinking water) and short-term residential sources, exceeded the Agency's LOC for toddlers exposed to permethrin through food and drinking water, and through post-application exposure during high contact activities on lawns and indoor surfaces. The risk driver for the aggregate non-cancer risk estimate was post-application exposure to permethrin on treated indoor surfaces (carpets).

- The aggregate cancer risk estimates exceeded the Agency's LOC for adults exposed to permethrin through food and drinking water, and through post-application exposure during high contact activity on lawns and indoor surfaces. Similar to the non-cancer aggregate risk assessment, post-application exposure to treated indoor carpets was the risk driver.

- All residential/recreational exposures are expected to be short-term in duration. Therefore, no intermediate-term (1-6 months) or long-term (>6 months) aggregate risk was assessed.

- EPA believes that the appropriate way to consider the pharmaceutical use of permethrin in its risk assessment is to examine the impact that the additional non-occupational pesticide exposures would have to a pharmaceutical patient exposed to a related (or, in some cases, the same) compound. Based on a worse case scenario assessment, EPA estimates that the permethrin exposure a patient is expected to receive from a typical single application of a 1% and 5% permethrin pharmaceutical cream, respectively, is 450 to 2300 times greater than the combined exposure from the dietary and other non-occupational sources of permethrin. FDA has reviewed these estimates and determined that pesticide exposure in patients receiving treatment with a pharmaceutical permethrin drug product would fall within the expected range of exposure following treatment with permethrin drug product alone, and would not present an increased safety risk.

Occupational

- The majority of occupational handler risk estimates were below the Agency's non-cancer LOC at baseline personal protective equipment (PPE) (long-sleeve shirt, long pants, no gloves, and no respirator). For all other scenarios where the LOC was exceeded considering just baseline PPE, all occupational risk estimates were below the Agency's non-cancer LOC with additional PPE or engineering controls.

- The estimated cancer risks for the majority of grower scenarios were also within the negligible risk range ($\leq 3 \times 10^{-6}$) or less with baseline PPE and gloves. However, a number of scenarios result in risk in the 10^{-5} to 10^{-6} range at this level of PPE, and either require additional PPE before the cancer risk estimates were below the negligible risk range, have no data available to estimate risk, or further mitigation measures were not feasible.

- For all agricultural post-application scenarios assessed, the non-cancer risks do not exceed the LOC (MOEs > 100) on the day of application, approximately 12 hours following application. Most of the post-application cancer risk estimated for both hired hands and commercial/migratory farm workers were in the 10^{-5} to 10^{-7} range. The highest risk estimates, in the 10^{-4} range, were for conifer seed cone harvesting and thinning of certain fruit trees.

- All non-cancer post-application exposure scenarios for military personnel and garment workers exposed to permethrin-impregnated battle dress or fabric, respectively, do not exceed the Agency's LOC. Further, all of the post-application cancer risk estimates for both populations were in the 10^{-6} range.

Ecological Risks

- Permethrin is highly toxic to both freshwater and estuarine aquatic organisms. Most agricultural, public health, and down-the-drain scenarios modeled resulted in exceedances in the acute risk quotient (RQ) for freshwater and estuarine fish, invertebrates, and sediment organisms. The agricultural and public health scenarios also showed the potential for chronic risks to estuarine and/or freshwater organisms. Further, there is a potential concern for direct effects to a variety of aquatic organisms.

- The acute and chronic RQs for terrestrial avian species are below the Agency's levels of concern. The acute RQs for terrestrial mammals were also below the Agency's acute LOCs; however, some chronic RQs exceeded the Agency's LOC. However, the Agency believes the chronic RQs for mammals are based on a conservative estimate of toxicity, and therefore, may represent an overestimation of risk.

- The potential for risk to terrestrial and aquatic plants from exposure to permethrin cannot be assessed because toxicity data are not available. However, any toxicity

to plants would occur for reasons other than permethrin's insecticidal mode of action because permethrin works as a neural toxin, and unlike insects, plants do not have neural networks that could be affected.

- Permethrin toxicity data show that the compound is highly toxic to honeybees, as well as other beneficial insects.

Risk Mitigation

To address assessed risks of concern, the following mitigation measures will be implemented.

Residential Risk

- Discontinue use of all directed broadcast and spot treatment sprays (i.e., low pressure handwand, backpack sprayer, cold fogger) on all residential indoor surfaces. Baseboard and crack and crevice applications are allowable via directed and RTU sprays.
    - Limit concentration of indoor sprays to 0.5% ai of permethrin. The Agency will consider products with higher concentrations if the registrants for these products are able to provide justification or data to the Agency which demonstrate that little to no exposure will occur due to the specialized use of the product.
- Amend all liquid and wettable powder products registered for outdoor residential use to either prohibit use in outdoor residential misting systems, or provide specific use directions.
- Efficacy data for all finished pre-treated permethrin products, and wash-off data to support efficacy claims is required.

To address assessed risks of concern, the following mitigation measures will be implemented.

Occupational Risk

Handler

- Require wettable powder formulations to be packed in water soluble packaging.
- Require all aerial applications to be in closed cab aircraft.
- Discontinue the use of high pressure handwands in mushroom houses.
- Add PPE requirement to labels as follows:
    - Wettable Powders- baseline PPE (long pants, long sleeved shirt, and shoes), and chemical-resistant gloves for mixers, loaders, and applicators.
    - Emulsifiable Concentrations- baseline PPE and chemical-resistant gloves for mixers, loader, and applicators. Additional chemical-resistant apron is required for applicators performing animal dip applications.

- Dry Flowables- baseline PPE and chemical-resistant gloves.
- Dust- Double layer (coveralls over baseline PPE), chemical-resistant gloves, and a PF5 respirator for loaders and applicators.
- RTU Formulations- Baseline PPE and chemical-resistant gloves.
- Applicators of liquids via cold foggers and fog mister/generators.
    - Require applicators to wear double layers, chemical-resistant gloves, and PF10 respirator.

Post-Application

- Amend agricultural labels to include new use patterns (rate reductions, seasonal maximum reductions, and minimum retreatment intervals) identified for the selected crop uses specified Appendix A.

To address assessed risks of concern, the following mitigation measures will be implemented.

Ecological Risks

- Include standard pyrethroid specific spray drift language, including a 25 foot aquatic buffer zone for ground applications, 100-foot for aerial application, and 450 foot for ULV applications.
- Amend agricultural labels to include new use pattern (rate reductions, seasonal maximum reductions, and minimum retreatment interval) identified for the selected crop uses specified in Appendix A.
- Include the following statement in the environmental hazard section of the end use products:
    - This pesticide is highly toxic to bees exposed to direct treatment on blooming crops or weeds. Do not apply this product or allow it to drift to blooming crops or weeds while bees are actively visiting the treatment area.
- For all wide area mosquito abatement products:
    - Remove 100 foot buffer zone restriction;
    - Specify a maximum application rate of 0.007 lb ai/A per day or 0.18 lb ai/A per year.
    - Specify minimum release height of 100 feet for fixed wing aircraft, and 75 feet for helicopter applications.
    - Require droplet size <60 microns for aerial application, and <30 microns for ground application.
- Incorporate Pesticide Registration Notice 2008-1, "Environmental Hazard General Labeling Statements on Outdoor Residential Use Products."
- Include the best management and good stewardship language in the directions for use section of all products registered for outdoor use to reduce the amount of spray drift and runoff that can occur from these applications.

Risk/Benefit Balance Analysis

The Agency also assessed the significance of permethrin use, and conducted a risk/benefit balancing analysis. Given the significance of the use of permethrin and the mitigated nature of the risks of permethrin, the Agency believes, on balance, that the benefits of permethrin outweigh the risks. With respect to the ecological risks, the Agency has reduced those risks by imposing various conditions that should reduce exposure of aquatic species to permethrin. With respect to the benefits, permethrin offers substantial benefits to users. In the agricultural area, permethrin provides a high benefit to the agricultural industry because of its broad label and 1 day PHI. According to comments received from various growers, the broad spectrum of pests that permethrin targets makes its use highly beneficial since the agricultural industry has been losing a number of insecticides, and the newer insecticides replacing them have chemistries that target specific insects and are narrow in their spectrum. Further, permethrin has a 1 day pre-harvest interval, which allows for effective pest control near harvest of registered crops. Also alternatives to permethrin, such as the fourth generation pyrethroids, may pose a greater risk to aquatic organisms because of their persistence in the environment.

For the public health use, permethrin is the most widely used mosquito adulticide in the United States because of its low cost, high efficacy, and low incidence of pest resistance. Although permethrin alternatives are comparably priced and are likely to be as effective as permethrin in many situations, they are not likely to universally substitute for all permethrin uses because of labeling constraints or resistance concerns. The Agency believes that the loss of permethrin would adversely affect the ability of mosquito abatement professionals to control mosquitoes in some situation, such as agricultural-urban interface and areas with known resistance to alternatives. With regard to the treatment of fabrics, permethrin is the only pesticide registered to pre-treat fabrics, which the AFPMB strongly supports as a method of preventing many diseases that might afflict military personnel in the field. On other uses, such as residential uses, where there may be a potential for ecological effects due to urban runoff, the Agency intends to identify steps which can be taken to allow a greater understanding of potential ecological risk from urban uses of pyrethroid as a whole during Registration Review.

Data Requirements

The Agency has identified data necessary to confirm the reregistration eligibility decision for permethrin. These studies are listed below and will be included in the generic DCI for this RED, which the Agency intends to issue at a future date.

Toxicology:
870.1300 Acute Inhalation Toxicity Study

Residue Chemistry:
860.1200 Directions for Use
860.1340 Enforcement Analytical Method-Animals
860.1380 Storage Stability
860.1500 Magnitude of the Residue in Crop Plants (leaf lettuce, collards, and cabbage)

Occupational Exposure
875.1200 Dermal Exposure Indoors (ULV Cold Fogger)
875.1400 Inhalation Exposure Indoors (ULV Cold Fogger)

Environmental Toxicology
850.1735 Whole sediment acute toxicity for estuarine/marine invertebrates
850.1740 Whole sediment acute toxicity for estuarine/marine invertebrates
850.1000 Chronic Freshwater Sediment Testing
850.1000 Chronic Estuarine/Marine Sediment Testing

Regulatory Conclusion

The Agency has determined that permethrin containing products are eligible for reregistration provided that the risk mitigation measures are adopted and labels are amended to reflect these measures.

For More Information

Electronic copies of the Permethrin RED and all supporting documents are available in the public docket EPA-HQ-OPP-2004-0385 located on-line in the Federal Docket management System (FDMC) at http://www.regulations.gov.

For more information about EPA's pesticide reregistration program, the Permethrin RED, or reregistration of individual products containing permethrin, please contact the Special Review and Reregistration Division (7508P), Office of Pesticide Programs, U.S. EPA, Washington, D.C. 20460, telephone 703-308-8000.

For information about the health affects of pesticides, of for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticide Information Center (NPIC). Call toll-free 1-800-858-7378, from 6:30 am to 4:30 am Pacific Time, or 9:30 am to 7:30 pm Easter Standard Time, seven days a week. The NPIC internet address is http://npic.orst.edu.

Appendix A:
Amended Agricultural Use Patterns

	Current Labels			Mitigation Per the RED		
Crop	**Max. Rate per application (lb ai/A)**	**Minimum retreatment interval (days)**	**Seasonal Maximum Application Rate (lb ai/A)**	**New Maximum rate per application (lb ai/A)**	**New Minimum retreatment interval (days)**	**New Seasonal Maximum Application Rate (lb ai/A)**
Alfalfa	0.2	14	0.2 per cutting	0.2	30	0.2 per cutting
Almonds	0.4	3	2	0.25	10	0.75
Hazelnuts	0.4	As needed	1.6	0.25	10	0.75
Pistachios	0.4	As needed	1.6	0.3	10	0.9
Walnuts	0.4	As needed	1.6	0.25	10	0.75
Apples	0.4	As needed	0.6	0.25	10	0.5
Pears	0.4	As needed	0.8	0.25 (0.4 dormant only)	10	0.65
Cherries	0.2	As needed	1.2	0.2	10	0.6
Peaches/Nectarines	0.3	7	1.5	0.25	10	0.75
Artichokes	0.3	As needed	1.5	0.3	10	0.9
Asparagus	0.1	As needed	0.4	0.1	7	0.4
Avocados	0.2	7	1.2	0.2	7	0.8
Broccoli	0.2	As needed	0.8	0.2	5	0.8
Brussels Sprouts	0.2	As needed	0.8	0.1	5	0.4
Cabbage	0.2	5	1	0.2	5	0.4 (0.8 in HI)
Cauliflower	0.2	As needed	0.8	0.1	5	0.4 (0.6 in HI)
Cantaloupes	0.2	7	1.6	0.2	7	0.8 (1.2 in HI)
Cucumbers	0.2	As needed	1.6	0.2	7	1.2
Pumpkins	0.2	As needed	1.6	0.2	7	1.2
Squash (summer, winter)	0.2	As needed	1.6	0.2	7	1.2
Watermelon	0.2	As needed	1.6	0.2	7	1.2
Eggplant	0.21	3	2	0.15	7	0.6 (1.0 in HI)
Peppers, bell	0.2	As needed	1.6	0.2	5	0.8
Tomatoes	0.2	5	1.2	0.2	7	0.6 (0.8 in HI)
Celery	0.2	As needed	2	0.2	7	1.0 (1.2 in HI)
Lettuce	0.2	3	2	0.2	7	0.8 (1.2 in HI)
Spinach	0.2	As needed	2	0.2	3	0.6
Collards	0.2	As needed	0.8 (0.4 in SC, GA, FL, WA)	0.15	3	0.45
Greens, Turnip	0.2	As needed	0.8 (0.4 in SC, GA,	0.15	3	0.45

	Current Labels			Mitigation Per the RED		
Crop	**Max. Rate per application (lb ai/A)**	**Minimum retreatment interval (days)**	**Seasonal Maximum Application Rate (lb ai/A)**	**New Maximum rate per application (lb ai/A)**	**New Minimum retreatment interval (days)**	**New Seasonal Maximum Application Rate (lb ai/A)**
			FL, WA)			
Corn, Field	0.2	6	0.6	0.15	7	0.45
Sweet Corn	0.25	3	1.2	0.2	3	0.8
Garlic	0.3	As needed	2	0.2	10	0.8
Onions	0.3	As needed	2	0.3	7	1.0
Horseradish	0.21	As needed	0.6	0.15	10	0.45
Papaya	0.4	7	1.2	0.15	10	0.75
Potatoes	0.2	As needed	1.6	0.2	10	0.8
Soybeans	0.2	As needed	0.4	0.2	10	0.4