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Reregistration Eligibility Decision for Piperonyl Butoxide (PBO)

List B

Case No. 2525

Reregistration Eligibility Decision (RED) Document

for

Piperonyl Butoxide (PBO)

Approved by: _____ /S/
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Date: _____ June 14, 2006 _____

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Glossary of Terms and Abbreviations

AGDCI	Agricultural Data Call-In
ai	Active Ingredient
aPAD	Acute Population Adjusted Dose
AR	Anticipated Residue
BCF	Bioconcentration Factor
CFR	Code of Federal Regulations
cPAD	Chronic Population Adjusted Dose
CSF	Confidential Statement of Formula
CSFII	USDA Continuing Surveys for Food Intake by Individuals
DCI	Data Call-In
DEEM	Dietary Exposure Evaluation Model
DFR	Dislodgeable Foliar Residue
DWLOC	Drinking Water Level of Comparison.
EC	Emulsifiable Concentrate Formulation
EDWC	Estimated Drinking Water Concentration
EEC	Estimated Environmental Concentration
EPA	Environmental Protection Agency
EUP	End-Use Product
FDA	Food and Drug Administration
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FFDCA	Federal Food, Drug, and Cosmetic Act
FQPA	Food Quality Protection Act
FOB	Functional Observation Battery
G	Granular Formulation
GENEEC	Tier I Surface Water Computer Model
GLN	Guideline Number
HAFT	Highest Average Field Trial
IR	Index Reservoir
LC ₅₀	Median Lethal Concentration. A statistically derived concentration of a substance that can be expected to cause death in 50% of test animals. It is usually expressed as the weight of substance per weight or volume of water, air or feed, e.g., mg/l, mg/kg or ppm.
LD ₅₀	Median Lethal Dose. A statistically derived single dose that can be expected to cause death in 50% of the test animals when administered by the route indicated (oral, dermal, inhalation). It is expressed as a weight of substance per unit weight of animal, e.g., mg/kg.
LOC	Level of Concern
LOD	Limit of Detection
LOAEL	Lowest Observed Adverse Effect Level
MATC	Maximum Acceptable Toxicant Concentration
µg/g	Micrograms Per Gram
µg/L	Micrograms Per Liter
mg/kg/day	Milligram Per Kilogram Per Day
mg/L	Milligrams Per Liter
MOE	Margin of Exposure
MRID	Master Record Identification (number). EPA's system of recording and tracking studies submitted.
MUP	Manufacturing-Use Product
NA	Not Applicable
NAWQA	USGS National Water Quality Assessment
NPDES	National Pollutant Discharge Elimination System
NR	Not Required
NOAEL	No Observed Adverse Effect Level
OP	Organophosphate

OPP	EPA Office of Pesticide Programs
OPPTS	EPA Office of Prevention, Pesticides and Toxic Substances
PAD	Population Adjusted Dose
PCA	Percent Crop Area
PDP	USDA Pesticide Data Program
PHED	Pesticide Handler's Exposure Data
PHI	Preharvest Interval
ppb	Parts Per Billion
PPE	Personal Protective Equipment
ppm	Parts Per Million
PRZM/EXAMS	Tier II Surface Water Computer Model
Q ₁ *	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
RAC	Raw Agriculture Commodity
RED	Reregistration Eligibility Decision
REI	Restricted Entry Interval
RfD	Reference Dose
RQ	Risk Quotient
SCI-GROW	Tier I Ground Water Computer Model
SAP	Science Advisory Panel
SF	Safety Factor
SLC	Single Layer Clothing
SLN	Special Local Need (Registrations Under Section 24(c) of FIFRA)
TCPSA	2,3,3-trichloroprop-2-ene sulfonic acid (nitrapyrin Metabolite)
TGAI	Technical Grade Active Ingredient
TRR	Total Radioactive Residue
USDA	United States Department of Agriculture
USGS	United States Geological Survey
UF	Uncertainty Factor
UV	Ultraviolet
WPS	Worker Protection Standard

Executive Summary

EPA has completed its review of public comments on the human health and environmental risk assessments and is issuing its reregistration eligibility and tolerance reassessment decisions for piperonyl butoxide (PBO). There are currently 69 tolerances being reassessed for piperonyl butoxide. EPA will accept public comments on these decisions and the supporting documents for 60 days. The revised risk assessments and response documents are based on comments submitted, information from the PBO Task Force II (PBOTFII), and other information provided to EPA. After considering the risks identified in the revised risk assessments, comments and mitigation suggestions, EPA developed its risk management decision for uses of piperonyl butoxide that posed risks of concern. As a result, the Agency has determined piperonyl butoxide-containing products are eligible for reregistration provided that risk mitigation measures are adopted and labels are amended accordingly.

Piperonyl butoxide was first registered in the 1950's and acts as a synergist. Synergists are chemicals that primarily enhance the pesticidal properties of other active ingredients, such as pyrethrins and synthetic pyrethroids. PBO is a registered active ingredient in over 1500 products used to control many different types of flying and crawling insects and arthropods, although there are no products that contain only PBO. It is registered for use in agricultural, residential, commercial, industrial, and public health sites. Approximately 100,000-200,000 pounds are sold every year for non-agricultural uses, with only about 5,000-10,000 pounds used in agriculture.

Overall Risk Summary

Dietary Risk (Food and Drinking Water)

Acute dietary (food only) risk does not exceed the Agency's level of concern for the general US population at 6% of the aPAD. The risk estimate for the most highly exposed subpopulation, children 1-2, is below the Agency's level of concern at 20% of the aPAD. The PBO dietary assessments are highly refined using residue data from the USDA Pesticide Data Program (PDP), actual percent crop treated data where available, and processing factors from processing study data.

The chronic dietary (food only) risk is below the Agency's level of concern; risk estimates are 11% cPAD for the general U.S. population, and 32% of the cPAD for children 1-2 years old, the most exposed subpopulation.

Acute and chronic drinking water levels of concern (DWLOCs) were calculated based on dietary exposure estimates, default body weight and water consumption figures. The estimated drinking water concentrations (EDWCs) for both surface water and ground water are well below both the acute and chronic DWLOCs indicating that combined exposure to PBO in food and water is not a concern.

Residential

In the residential handler exposure assessment, a number of scenarios were assessed to estimate the exposure to homeowners handling products containing piperonyl butoxide. From the results of the residential handler assessment, there are no residential risks of concern when piperonyl butoxide is mixed, loaded, applied, or handled by homeowners.

A number of post-application residential scenarios were assessed for adults and children exposed to piperonyl butoxide indirectly after application. Of these, three were potentially of concern: 1) broadcast dust applications to carpets; 2) applications from indoor metered release devices; and 3) applications from outdoor residential misting systems. To address the potential risks associated with these post-application scenarios, the PBOTFII has agreed to limit dust application to carpets by allowing spot treatments only, and to add additional label language and use restrictions to address potential by-stander risks from products used in both metered release devices and outdoor residential misting systems. The PBOTFII has agreed to prohibit the use of metered release devices in residential indoor areas and remove the following use sites from their metered release device product labels: day care centers, nursing homes, schools, and hospitals. Further, the Agency will require confirmatory exposure and efficacy data for the outdoor misting systems.

FQPA

After evaluating both the hazard and exposure data for PBO, EPA reduced the FQPA safety factor to 1X due to the low degree of concern for the fetal susceptibility effects and no evidence of residual uncertainties for pre- or post-natal toxicity. There were no residual uncertainties for potential exposures to infants and children.

Aggregate Risks

As noted above, acute and chronic aggregate risk assessments were conducted for exposure to PBO in food and drinking water and did not indicate risks of concern. The short-term aggregate exposures from food, water, and residential (incidental oral) routes associated with application of PBO were also estimated since there is a common toxicity endpoint of decreased weight gain identified for these routes of exposure.

The short term aggregate risk for PBO was calculated by adding exposure estimates from dietary, drinking water, and residential incidental oral exposure pathways for children age 1-2 and comparing them with model based EDWCs. The lowest short term DWLOC is 8500 μ g/L for children 1-2 which is substantially higher the surface water EDWC of 60 μ g/L and the ground water EDWC of 0.26 μ g/L. Thus aggregate short term exposure to PBO does not result in a risk of concern. Some short term post application risks, as noted above, alone are potentially of concern. However, because of the conservative exposure assumptions used in the individual assessments, and with the exposure mitigation requirements described herein, the Agency does not expect aggregate exposures to pose risks of concern.

Cumulative

The Food Quality Protection Act (FQPA) requires that the Agency consider available information concerning the cumulative effects of a particular pesticide and other substances that have a common mechanism of toxicity. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism finding as to PBO and any other substances, and PBO does not appear to produce a toxic metabolite produced by other chemicals. Therefore, for the purposes of this tolerance reassessment action, EPA has assumed that PBO does not have a common mechanism of toxicity with other substances.

Occupational Risks

Thirty-four occupational exposure scenarios were assessed for agricultural, forestry, professional pest control operator, and mosquito control applications of PBO. The exposure of concern is only inhalation, with target MOEs of 300 for short and intermediate term exposure due to the lack of a NOAEL in the critical study and 1000 for long term exposures due to extrapolation from a sub-chronic study. Of the scenarios assessed, several were potentially of concern assuming baseline clothing. These include: 1) mixing and loading wettable powders for agricultural handlers and PCOs; 2) applying PBO with handheld foggers indoors; 3) applying dusts through power duster equipment; 4) mixer/loaders for aerial forestry applications; 5) PCOs applying indoor crack and crevice treatments with a low pressure handwand; 6) high pressure handwand applications in greenhouses; and 7) PCOs applying indoor space sprays. To address these potential risks, the PBO Task Force II has agreed to repackaging all wettable powder formulations in water soluble packages, develop data, reduce application rates in some instances, prohibit power dusters as an application method, and add additional respiratory protection for some applications.

There were potential post-application risks estimated for products used in metered release devices which are commonly used in dairy barns and other sites. EPA believes that the potential post-application risks are lower for people working in these settings than for residential settings due to the fact that the occupational areas generally have a greater ventilation capacity. While it is possible workers could be exposed to PBO from these metered release devices, it is not likely a worker would be exposed to the full daily amount for 30 or more days, as was assumed in EPA's assessment. Therefore, no occupational mitigation is being required at this time. However, data to better characterize the duration and extent of exposure to workers will be required.

Ecological Risks

Aquatic Organisms

Risk to aquatic organisms can occur through exposure from agriculture, wide area mosquito abatement, and other non-agricultural (urban) use. Risks to aquatic organisms from agricultural applications appear to be reduced if typical application rates, frequency, and numbers of applications are considered. There are possible risks from mosquito abatement

applications to invertebrates and amphibians, which can be addressed by establishing release heights, droplets size, and application rates on all PBO mosquito abatement product labels. There are no risks of concern predicted from down-the-drain use. Non-agricultural (urban) use was not quantified in this assessment, but there is an on-going effort to develop a model and work with a number of stakeholders in order to address this source of pesticide exposure in the near future.

Terrestrial Organisms

There are estimated LOC exceedences for mammals and birds at the maximum agricultural rate of 0.5 lbs/ai/A, which is not routinely used for all crops. All agricultural product labels will be revised to include a maximum of 10 applications per season and a minimum of 1-3 days reapplication interval depending on pest pressure.

Risk Associated with Mixtures

Available evidence indicates that PBO does not effectively act as a pyrethroid synergist in mammals. It is well known to inhibit microsomal enzymes in insects. It also inhibits microsomal enzymes in several other species (e.g., rats, rabbits, and mice). However, this enzyme inhibition in mammals appears to be transient and occurs at high doses. Data for other species indicate that the toxicity of PBO mixed with pyrethrins or synthetic pyrethroids may be higher than the toxicity of the individual active ingredients. To address the uncertainty related to the effects a synergist would have to the environment when mixed with other chemicals, EPA will require product-specific eco-toxicity data.

Summary of Mitigation Measures

EPA has determined that the currently registered uses of piperonyl butoxide are eligible for reregistration provided the mitigation measures outlined in this document are implemented through label amendments. Mitigation measures include:

Residential

- Restrict carpet dust applications to only spot treatments.
- Prohibit use of products in metered release devices in residential areas and remove day-care centers, nursing homes, schools and hospitals from product labels.
- Restrict use of outdoor residential misting systems by establishing a maximum use rate and precautionary label statements.

Occupational

- Require wettable powders to be repackaged in water soluble packages.
- Reduce indoor crack and crevice application rate from 2.2 lbs ai/1000 square feet to 0.56 lbs/ai/1000 square feet
- Require all applicators using hand held foggers indoors to wear a dust-mist (PF10) respirator.
- Require mixer/loaders supporting forestry applications to wear a dust-mist (PF 5) respirator.

- Require mixer/loader/applicators using high pressure handwands in greenhouses and other enclosed areas to wear a dust-mist respirator (PF 5).
- Prohibit power dusters as an application method.

Ecological

- All agricultural product labels must be updated to specify the following application information:
 - No more than 10 applications per season.
 - Do not reapply within 3 days, except under extreme pest pressure.
 - In case of extreme pest pressure, do not reapply within 24 hours.

I. Introduction

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) was amended in 1988 to accelerate the reregistration of products with active ingredients registered prior to November 1, 1984. The amended Act calls for the development and submission of data to support the reregistration of an active ingredient, as well as EPA review of all submitted data. Reregistration involves a thorough review of the scientific database underlying a pesticide's registration. The purpose of the Agency's review is to reassess the potential risks arising from the currently registered uses of the pesticide, to determine the need for additional data on health and environmental effects, and to determine whether or not the pesticide meets the "no unreasonable adverse effects" criteria of FIFRA.

On August 3, 1996, the Food Quality Protection Act of 1996 (FQPA) was signed into law. This Act amends FIFRA to require reassessment of all tolerances in effect on the day before it was enacted. In reassessing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility among infants and children, and the cumulative effects of pesticides that have a common mechanism of toxicity. When the Agency determines that aggregate risks are not of concern and concludes that there is a reasonable certainty of no harm from aggregate exposure, the tolerances are considered reassessed. EPA decided that, for those chemicals that have tolerances and are undergoing reregistration, tolerance reassessment will be accomplished through the reregistration process.

The Food Quality Protection Act (FQPA) requires that the Agency consider available information concerning the cumulative effects of a particular pesticide's residues and other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common toxic mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the substances individually. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to piperonyl butoxide (PBO) and any other substances and PBO does not appear to produce a toxic metabolite produced by other substances that contribute to dietary exposure. For the purposes of this tolerance action, therefore, EPA has not assumed that PBO has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

The Agency made its reregistration eligibility determination based on the required data, the current guidelines for conducting acceptable studies to generate such data, and published scientific literature. The Agency has found that currently registered uses of PBO are eligible for reregistration provided the mitigation and labeling outlined in the RED are implemented. The

document consists of six sections: Section I, the introduction, contains the regulatory framework for reregistration/tolerance reassessment; Section II provides an overview of the chemical, including a profile of its use and usage; Section III gives an overview of the human health and environmental effects risk assessments; Section IV presents the Agency's reregistration eligibility, tolerance reassessment, and risk management decisions; Section V summarizes label changes necessary to implement the risk mitigation measures outlined in Section IV; and Section VI includes the appendices, related supporting documents and Data Call-In (DCI) information. The revised risk assessment documents and related addenda are not included in this document, but are available on the Agency's web page <http://www.epa.gov/pesticides>, and in the Public Docket under docket number EPA-HQ-OPP-2005-0042.

II. Chemical Overview

A. Regulatory History

Piperonyl butoxide (PBO) is a pesticide active ingredient that acts as a synergist. Synergists are chemicals which, while lacking pesticidal properties of their own, enhance the pesticidal properties of other active ingredients. PBO was first registered in the United States in the 1950s. Currently there are approximately 1500 end-use products registered in the United States containing PBO as a synergist with other active ingredients for use on agricultural and residential sites. PBO is never used alone. There are 69 tolerances for PBO listed in the Code of Federal Regulations. The reregistration of PBO is being supported by the PBO Task Force II whose members include: Endura S.P.A., S.C. Johnson & Son, Incorporated, McLaughlin Gormley King Company, Prentiss Incorporated, Takasago International Corporation USA, and Valent BioSciences Corporation.

PBO is the only active ingredient in List B reregistration case 2525. A Phase IV Data Call-In was issued for the PBO in January 1991. This DCI mainly required environmental fate and residue chemistry data. An agricultural re-entry DCI was issued in October of 1995.

This Reregistration Eligibility Decision document evaluates risks from all currently registered uses.

B. Chemical Identification

PBO is classified as a synergist. As a synergist, PBO works by inhibiting the detoxification of the pesticide by the insect pests.

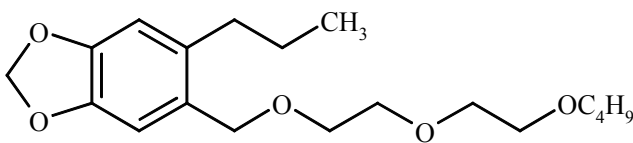
Table 1: PBO Nomenclature	
Compound	Chemical Structure 
Common name	Piperonyl butoxide (PBO)

Table 1: PBO Nomenclature	
IUPAC name	5-[2-(2-butoxyethoxy)ethoxymethyl]-6-propyl-1,3-benzodioxole or 2-(2-butoxyethoxy)ethyl 6-propylpiperonyl ether
CAS name	5-[[2-(2-butoxyethoxy)ethoxy]methyl]-6-propyl-1,3-benzodioxole
CAS #	51-03-6
EPA PC Code	067501

Table 2: Physicochemical Properties of the Technical Grade of PBO		
Parameter	Value	Reference
Boiling point	202-204 EC at 1.9 mm/Hg	D207185, 1/27/99, T. Morton
	180 EC at 1.0 mm/Hg	2002 Farm Chemicals Handbook
Molecular Weight	338.433	2002 Farm Chemicals Handbook
pH	Not applicable because the TGAI has low solubility in water	
Density, bulk density, or specific gravity	1.059 g/mL at 20°C	D172854, 11/30/92, A. Aikens
Water solubility	14.34 µg/mL at 25 °C	RD Memorandum, 12/31/90 (cited under D207185, 1/27/99, T. Morton)
Solvent solubility	Completely miscible (95% solution) in acetone, methanol, petroleum distillate, petroleum ether, methylene chloride, and isooctane	D207185, 1/27/99, T. Morton
Vapor pressure	<1 x 10 ⁻⁷ mm Hg at 25 EC (extrapolated from 1.59 x 10 ⁻⁷ mm Hg at 60 EC)	D172854, 11/30/92, A. Aikens
Dissociation constant, pK _a	Not applicable because the TGAI has low solubility in water	
Octanol/water partition coefficient	4.51 x 10 ⁴	RD Memorandum, 12/31/90 (cited under D207185, 1/27/99, T. Morton)
	log K _{ow} = 4.95	D172854, 11/30/92, A. Aikens
UV/visible absorption spectrum	Not available	

C. Use Profile

PBO comes in many chemical formulations and is found in numerous end-use products with a wide range of use patterns. PBO is used in combination with a variety of insecticides such as the natural pyrethrins and synthetic pyrethroids, and is an ingredient in about 1500 registered products. To capture the use parameters for the large number of products and use sites, the Piperonyl Butoxide Task Force II (PBOTFII) created a master label for PBO. A copy of the PBO master label is available at <http://www.epa.gov/oppsrrd1/reregistration/piperonyl/ucm.pdf>.

The following is information on the currently registered uses including an overview of use sites and application methods. Appendix A contains a detailed table of the uses of PBO eligible for reregistration. There are more than 12 crop groups and several miscellaneous commodities supported for reregistration.

1. PBO Use Profile

Type of Pesticide: Synergist

Summary of Use: PBO is used in these four general ways: (i) preharvest and postharvest uses on many agricultural crops; (ii) direct and indirect treatments of livestock animals and premises; (iii) treatments of commercial and industrial facilities and storage areas where raw and processed food/feed commodities are stored or processed; and (iv) mosquito abatement areas.

Target Organisms: PBO is used with insecticides such as the pyrethrins, pyrethroids, and some organophosphates to target a large numbers of pests including ants, worms, beetles, mites, flies, gnats, spiders, weevils, caterpillars, grubs, moths, ticks, lice, wasps, aphids, midges, and fish.

Mode of Action: PBO inhibits microsomal enzymes in target organisms by direct binding to these enzymes and inhibits the breakdown of other pesticides including pyrethrins and pyrethroids.

Tolerances: PBO currently has 69 tolerances (40 CFR §180.127 and §180.905) including 62 tolerances on raw agricultural commodities, 3 tolerances for processed food, 2 for stored dried feed, 1 for milled fractions, and 1 exemption.

Use Classification: General Use

Formulation Types: Aerosol, liquid, ready-to-use solution, dust, wettable powder, microencapsulate, impregnated material, pressurized gas, pressurized liquid, pressurized spray, combustible coil, micro-emulsion, dilutable concentrate, shampoo, towelette, pour-on (spot-on), and water-based concentrate. PBO is usually formulated with insecticides and other synergists.

Application Methods: Aerosol can, mist blower, metered aerosol unit, total release aerosol, fixed wing aircraft, helicopter, truck-mounted ultra low volume (ULV) equipment, cold aerosol generators, hand held sprayers (high or low pressure handwands), thermal fogging equipment, conventional dusting equipment (e.g., power duster, shaker can), gas operated liquid dispenser systems, and irrigation systems.

Application Rates: Application rates vary significantly by use sites. Maximum rates from 0.56 lb ai/ 1000 ft² (surface applications to commercial and domestic structures) to 3.5 lb ai/acre (commercial and domestic outdoor sites).

Usage of Pyrethrins: An estimated 100,000 to 200,000 pounds are used annually in the U.S. for non-crop use sites including wide area mosquito adulticide applications. Approximately 5,000 to 10,000 pounds of PBO are used annually in the U.S. on agricultural crops, with highest usage on potatoes (30% crop treated).

III. Summary of PBO Risk Assessments

The following is an overview of EPA's human health and environmental effects risk assessments and conclusions for PBO. For additional information on the human health risk assessment, see the *Piperonyl Butoxide HED Revised Risk Assessment for Reregistration Eligibility Document (RED)* (Daiss, February 21, 2006). For additional information on the environmental effects risk assessment, see the *Piperonyl Butoxide EFED's Response to Public Comments and our Revised Ecological Risk Assessment* (Eckel, September 6, 2005).

The purpose of this section is to summarize the key features and findings of the risk assessment to help the reader better understand EPA's risk management decisions. The revised risk assessments incorporate input received during the two 60-day public comment periods for PBO. EPA provided two public comment periods to allow interested stakeholders to provide feedback on EPA's methodology and results prior to issuing its reregistration eligibility and risk mitigation decisions. This RED and the revised risk assessments can be accessed online at <http://www.regulations.gov>, under docket number EPA-HQ-OPP-2005-0042.

A. Human Health Risk Assessment

The Agency evaluated the toxicology, product and residue chemistry, and occupational and residential exposure studies submitted and determined that the data are adequate to support a reregistration eligibility decision. The risk assessments and separate supporting disciplinary documents are available in the electronic docket. A summary of the human health risk assessment findings and conclusions are provided below.

1. Toxicity Profile

The toxicological database is adequate to support the reregistration of PBO. Data are sufficient for all exposure scenarios and for FQPA evaluation.

Acute Toxicity Profile

PBO has a low acute toxicity by oral, inhalation and dermal routes. It has been assigned toxicity Category III by oral and dermal and Category IV by inhalation exposure routes. In the acute studies, PBO has been identified as minimally irritating to eyes and skin, and is a dermal sensitizer. See Table 3 below for a summary of the acute toxicity data.

Study/ Species	MRID	Results	Classification
870.1100 Acute Oral, Rats	41969001	LD ₅₀ = 4570 mg/kg (m)7220 mg/kg (f)	Category III
870.1200 Acute Dermal, Rabbits	41969002	LD ₅₀ = >2000 mg/kg	Category III
870.1300 Acute Inhalation, Rats	41990001	LC ₅₀ = >5.9 mg/L	Category IV
870.2400 Primary Eye Irritation, Rabbits	41969004	Minimally irritating	Category IV
870.2500 Primary Skin Irritation, Rabbits	41969003	Minimally irritating	Category IV
870.2600 Dermal Sensitization, Guinea pig	44194602	Skin Sensitizer	Skin Sensitizer

Toxic Effects

The major target organ for PBO is the liver. Subchronic studies in rats showed PBO treatment caused increases in liver weight and clinical parameters such as cholesterol and enzyme activity compared to controls. Liver histopathological effects such as enlargement of hepatocytes with glassy cytoplasm, oval cell proliferation, bile duct hyperplasia, and focal necrosis were observed in treated rats. In ICR mice, similar effects (increased liver weight, cholesterol and enzyme activity as well as liver histopathological effects) were observed. A one-year study in dogs with PBO also resulted in pronounced liver effects, such as increased liver weight, hepatocyte hypertrophy and elevated serum alkaline phosphatase activity.

Toxic Effects of Mixtures

Because evidence indicates that PBO does not effectively act as a synergist in mammals, EPA did not assess risks to humans of combined exposures to PBO and other active ingredients. PBO inhibits microsomal enzymes in insects. It also inhibits the microsomal enzymes in several other species (e.g., rats, rabbits, mice). However, evidence indicates that enzyme inhibition in mammals is transient and occurs at high doses. PBO has also been used as a compound in several pharmacological experiments to compare the toxicological effects of several drugs before and after metabolism in rodents. These drug interaction studies suggest that the inhibition of microsomal enzymes is a transient effect in the mammalian system. The kinetics of PBO inhibition and/or stimulation of microsomal enzymes in humans has not been established.

Developmental

No developmental toxic effects were noted in guideline studies using rats and rabbits. A few developmental studies in the open literature reported limb deformities, increased resorption and decreased number of viable fetuses in rodents at doses close to or higher than the highest dose tested in the guideline studies.

Neurotoxicity

Neurotoxic effects of PBO are not evident from the clinical signs reported in developmental, reproductive, and chronic studies submitted to the Agency.

Mutagenicity

PBO tested negative in bacterial gene mutation assays. The *in vitro* mammalian cell mutation assays indicate a questionable positive effect for mutation. PBO tested negative for chromosomal aberration and sister chromatid exchange in CHO cells, and no induction of unscheduled DNA synthesis was observed in rat primary hepatocytes.

Cancer

PBO is classified as a Group C-possible human carcinogen with no cancer quantification required for PBO risk assessments.

In a combined chronic/carcinogenic study in rats, positive carcinogenic effects were reported at doses where a high incidence of ileocecal ulcers were noticed in test mammals. Liver adenomas and carcinomas were reported in Fischer 344 rats only when tested at very high doses. A slight increase in thyroid follicular cell tumors was reported in Sprague-Dawley rats. A 1979 National Toxicology Program (NTP) study reported negative effects for carcinogenicity in the same strain of rats and in B6C3F1 mice. In CD-1 mice, PBO tested positive for liver tumor effects.

Toxicity Endpoints

The toxicological endpoints used in the human health risk assessment for PBO are listed in Table 4.

Table 4: Endpoints for Assessing Occupational and Residential Risks for PBO			
Exposure Scenario	Dose, Uncertainty Factors (UFs), and Safety Factors (SFs)	Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)	Study and Toxicological Effects
Acute Dietary General Population	NOAEL= 630 mg/kg/day UF = 100 (inter- and intra-species UF) FQPA SF = 1X Total UF = 100 Acute RfD = 6.3 mg/kg/day	aPAD = $\frac{\text{acute RfD}}{\text{FQPA SF}}$ aPAD = 6.3 mg/kg/day	Developmental toxicity study, rats LOAEL = 1065 mg/kg/day based on decrease in maternal body weight gain (Tanaka et al., 1995)

Table 4: Endpoints for Assessing Occupational and Residential Risks for PBO			
Exposure Scenario	Dose, Uncertainty Factors (UFs), and Safety Factors (SFs)	Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)	Study and Toxicological Effects
Chronic Dietary (All populations)	NOAEL= 15.5 mg/kg/day UF = 100 (inter- and intra-species UF) FQPA SF = 1X Total UF = 100 Chronic RfD = 0.16 mg/kg/day	cPAD = <u>chronic RfD</u> FQPA SF cPAD = 0.16 mg/kg/day	Chronic oral toxicity study, dogs LOAEL = 52.8 mg/kg/day based on decrease in body weight gain, and increases in alkaline phosphatase activity, liver weight and hepatocellular hypertrophy (MRID: 42926001, 42926002)
Short-Term Incidental Oral (1-30 days); Intermediate-Term Incidental Oral (1- 6 months)	NOAEL= 89 mg/kg/day UF = 100 (inter- and intra-species UF) FQPA SF = 1X Total UF = 100	Residential LOC for MOE = 100 Occupational LOC for MOE = 100	Two generation reproduction study, rats LOAEL = 469 mg/kg/day based on the decrease in body weight gain of F ₁ and F ₂ pups at postnatal day 21 (MRID: 00161118)
Short-Term Dermal (1 to 30 days); Intermediate-Term Dermal (1 to 6 months); Long-Term Dermal (>6 months)	No systemic, developmental or neurotoxicity concerns at the limit dose. Therefore, no quantification is required. PBO is classified as mild irritant. (MRID: 42218201)		
Acute Inhalation (≤ 2 hrs) (inhalation absorption rate = 100 %)	NOAEL= 630 mg/kg/day UF = 100 (inter- and intra-species UF) FQPA SF = 1X Total UF = 100	Residential LOC for MOE = 100	Developmental toxicity study, rats LOAEL = 1065 mg/kg/day based on decrease in maternal body weight gain (Tanaka et al., 1995)
Short-Term Inhalation (1 to 30 days); Intermediate-Term Inhalation (1 to 6 months)	Respiratory LOAEL= 3.91 mg/kg/day (0.015 mg/L) UF = 100 (inter- and intra-species UF) FQPA SF = 1X Lack of NOAEL UF = 3X Total UF = 300	Residential LOC for MOE = 300 Occupational LOC for MOE = 300	Subchronic inhalation toxicity study, rats Respiratory LOAEL = 3.91 mg/kg/day (0.015 mg/L) based on laryngeal hyperplasia and metaplasia (MRID: 42477101)

Table 4: Endpoints for Assessing Occupational and Residential Risks for PBO			
Exposure Scenario	Dose, Uncertainty Factors (UFs), and Safety Factors (SFs)	Population Adjusted Dose (PAD) or Target Margin of Exposure (MOE)	Study and Toxicological Effects
Long-Term Inhalation (>6 months)	Respiratory LOAEL= 3.91 mg/kg/day (0.015 mg/L) UF = 100 (inter- and intra-species UF) FQPA SF = 1X Lack of NOAEL UF = 10X Total UF = 1000	Residential LOC for MOE = 1000 Occupational LOC for MOE = 1000	Subchronic inhalation toxicity study, rats Respiratory LOAEL = 3.91 mg/kg/day (0.015 mg/L) based on laryngeal hyperplasia and metaplasia (MRID: 42477101)
Cancer	Classified as “Group C carcinogen” with no quantification.		

NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic), RfD = reference dose, MOE = margin of exposure, LOC = level of concern

2. FQPA Safety Factor

The Food Quality Protection Act (FQPA) directs the Agency to use a tenfold (10X) safety factor to protect for special sensitivity of infants and children to specific pesticide residues in food, drinking water, or residential exposures, or to compensate for an incomplete database. FQPA authorizes the Agency to modify the tenfold safety factor only if reliable data demonstrate that another factor would be appropriate.

There are no residual uncertainties for potential exposures to infants and children. The highly refined dietary food exposure assessment uses residue data from the USDA Pesticide Data Program, actual percent crop treated data from BEAD where available, and processing factors from processing study data. The drinking water assessment is based on water concentration values derived from the drinking water model. Modeling parameters were selected to provide protective, high-end estimates of water concentrations; these estimates are not likely to be exceeded by actual values. Use of PBO-specific dietary food exposure data enhances the accuracy of the assessment, and will not result in an underestimation of actual exposures.

Therefore, after evaluating hazard and exposure data for PBO, EPA reduced the 10X FQPA special safety factor to 1X due to low degree of concern for the fetal susceptibility effects and no evidence of residual uncertainties for pre- and postnatal toxicity.

3. Endocrine disruption

EPA is required under the FFDCFA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following recommendations of its Endocrine Disruptor and Testing Advisory Committee

(EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

In the database for PBO, there was no toxicologically significant evidence of endocrine disruptor effects. When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, PBO may be subject to further screening and/or testing to better characterize effects related to endocrine disruption.

4. Dietary Risk

Dietary risk assessment incorporates both exposure to and toxicity of a given pesticide. Dietary risk is expressed as a percentage of a level of concern. The level of concern is the dose predicted to result in no unreasonable adverse health effects to any human population subgroup, including sensitive members of such population subgroups. This level of concern is referred to as the population adjusted dose (PAD), which reflects the reference dose (RfD), either acute or chronic, adjusted to account for the FQPA safety factor. Estimated risks that are less than 100% of the PAD are below EPA's level of concern.

Acute and chronic dietary exposure assessments were conducted using two models, the Lifeline™ model (Version 2.0) and the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.03), both of which use food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. USDA Pesticide Data Program (PDP) data were used for commodities which have pre-harvest registered uses and for cereal grain crops which have a stored grain use. All other commodities were assigned residues from either the simulated warehouse space spray experiment or a simulated restaurant experiment. Residue data from dermal treatment of livestock were used as input values for meat, milk poultry, and eggs because dermal treatment of livestock could result in dietary exposure for humans.

For risk assessment purposes, the residues of concern for plants include the parent, PBO, and a two-fold factor to account for metabolites, unless field trial data for metabolites on related crops indicated a lower factor was appropriate. Percent crop treated data were used for all commodities for which percent crop treated data are available. Where no percent crop treated data were available, the dietary analyses assumed 100 percent crop treated.

Acute (Food Only)

The highly refined PBO acute dietary assessment incorporates both exposure to and toxicity of PBO considering what may be consumed in one day and maximum or high-end

residue values in food. The acute dietary endpoint, seen at the lowest observed adverse effect level (LOAEL) of 1065 mg/kg/day, was decrease in maternal body weight gain in rats. The no observed adverse effect level (NOAEL) was 630 mg/kg/day. An uncertainty factor of 100 (10X for inter-species extrapolation, 10X for intra-species variation, and 1X Special FQPA Safety Factor) was applied to the NOAEL to calculate the acute Population Adjusted Dose (aPAD). The aPAD is the highest predicted dose an individual could be exposed to in one day with no expected adverse health effects. The aPAD was calculated as $630 \text{ mg/kg/day} \div 100 = 6.3 \text{ mg/kg/day}$. Risk is expressed as a percentage of the aPAD. A risk estimate less than 100% of the aPAD does not exceed the Agency's level of concern.

Dietary risk estimates were calculated for the general U.S. population and various population subgroups. PBO acute dietary exposure estimates (food + water) for the U.S. population (6% of the aPAD) and for the most highly exposed population subgroups, children 1-2 years of age (20% of the aPAD), are below the Agency's level of concern. The dietary assessment could be further refined with additional residue data and additional percent crop treated information.

Chronic (Food Only)

A highly refined assessment was conducted to assess the chronic dietary exposure to PBO. The chronic dietary endpoint, seen at the lowest observed adverse effect level (LOAEL) of 52.8 mg/kg/day, was decreased weight gain and increased enzyme activity, liver weight and liver cell size in dogs. The no observed adverse effect level (NOAEL) was 15.5 mg/kg/day. An uncertainty factor of 100 (10X for inter-species extrapolation, 10X for intra-species variation, and 1X Special FQPA Safety Factor) was applied to the NOAEL to calculate the chronic Population Adjusted Dose (cPAD). The cPAD is the highest predicted dose at which an individual may be exposed over the course of a lifetime with no expected adverse health effects. The cPAD was calculated as $15.5 \text{ mg/kg/day} \div 100 = 0.16 \text{ mg/kg/day}$. Risk is expressed as a percentage of the cPAD. A risk estimate less than 100% of the aPAD does not exceed the Agency's level of concern. The exposure estimate for the US population is 5% of the cPAD and 12 % for the highest exposed subpopulation, children (1-2 years of age).

Population Subgroup	Acute Dietary (99.9th Percentile)			Chronic Dietary		
	aPAD, mg/kg/day	Exposure, mg/kg/day	% aPAD	cPAD, mg/kg/day	Exposure, mg/kg/day	% cPAD
General U.S. Population	6.3	0.3761	6	0.155	0.0075	5
All Infants (< 1 yr)		0.3908	6		0.0057	4
Children 1-2 yrs		1.2296	20		0.0185	12
Children 3-5 yrs		0.8027	13		0.0163	11
Children 6-12 yrs		0.4112	7		0.0117	8
Youth 13-19 yrs		0.3446	5		0.0059	4
Adults 20-49 yrs		0.3030	5		0.0064	4

Population Subgroup	Acute Dietary (99.9th Percentile)			Chronic Dietary		
	aPAD, mg/kg/day	Exposure, mg/kg/day	% aPAD	cPAD, mg/kg/day	Exposure, mg/kg/day	% cPAD
Adults 50+ yrs		0.2865	5		0.0066	4
Females 13-49 yrs		0.3467	6		0.0070	5

¹ Both Lifeline and DEEM-FCID were used to produce exposure values for the dietary risk assessment, but only the Lifeline values are listed in the table above because they resulted in the most conservative dietary exposure estimates.

2. Drinking Water

For more detail on the drinking water assessment see the *Drinking Water Assessment for PBO* (Eckel, May 17, 2004).

Drinking water exposure to pesticides can occur through groundwater and surface water contamination. EPA considers both acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. To determine the maximum allowable contribution from water in the diet, EPA first looks at how much of the overall allowable risk is contributed by food and then determines a “drinking water level of comparison” (DWLOC) to ascertain whether modeled or monitored concentration levels exceed this level.

The Agency uses the DWLOC calculation to estimate risk associated with exposure from pesticides in drinking water. The DWLOCs represent the maximum contribution to the human diet (in ppb or µg/L) that may be attributed to residues of a pesticide in drinking water after dietary exposure is subtracted from the aPAD or the cPAD. Risks from drinking water are assessed by comparing the DWLOCs to the estimated drinking water concentrations (EDWC) in surface water and groundwater. EDWCs less than the DWLOC are not of concern. Drinking water modeling is considered to be an unrefined assessment and generally provides high-end estimates.

The drinking water assessment included the parent PBO, as well as the three major degradates which are PBO-alcohol, -aldehyde, and -acid. These degradates are expected to be more soluble in water and therefore more mobile in soil-water systems than the parent, and for that reason are included in the drinking water assessment. The three major degradates will likely share the same toxicity as the parent. There are no specific toxicity concerns for all other minor metabolites. No drinking water monitoring data were available for PBO.

Surface Water

FIRST (FQPA Index Reservoir Screening Tool) was used to estimate surface water concentrations. FIRST is a Tier I screening level model used to provide high-end values for the concentrations that might be found in a small drinking water reservoir. FIRST is a single-event

model (one run-off event), but can account for spray drift from multiple applications. FIRST makes adjustments for regional percent crop area but makes conservative assumptions including modeling a runoff-prone watershed, the use of the maximum use rate, no buffer zone, and a single large rainfall. FIRST input parameters are based on 10 applications at the agricultural use rate of 0.5 lb a.i./acre and a re-application interval of 3 days. These parameters result in calculated acute surface water EDWC of 240 µg/L and a chronic surface water EDWC of 60 µg/L.

Groundwater

The Screening Concentration in Ground Water (SCI-GROW) model was used to estimate ground water concentrations. The SCI-GROW screening model is a Tier I assessment that provides a high-end estimate. SCI-GROW generates a single EDWC value of pesticide concentration in ground water used for drinking water and provides a ground water screening concentration for use in determining potential risk to human health from drinking water contaminated with a pesticide. EPA used the Tier I SCI-GROW model and a percent crop area of 87%, mean soil half-life of 73 days, and a K_{oc} of 599, to calculate an EDWC of 0.26 µg/L in ground water.

3. Residential Exposure and Risk

For more detail on the residential exposure and risk assessment, see the *Revised Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision for PBO*, (Daiss, September 8, 2005), and for more detail on the residential outdoor misting system assessment, see the *Occupational and Residential Exposure Assessment for the Use of PBO in Residential Outdoor Automatic Mister Systems*, (Crowley, August 30, 2005).

Based on the Master Label, 14 residential exposure scenarios have been assessed for this RED. Only inhalation and incidental ingestion exposure assessments have been conducted for the residential scenarios. Dermal exposures were not assessed because no adverse effects were seen at the highest dose tested (1000 mg/kg/day) in the dermal studies. Acute-, short-, and intermediate-term exposures were assessed for residential exposure scenarios based on use and exposure patterns. Acute exposures were assessed for post-application inhalation exposure to aerial and curbside mosquito abatement applications and for exposures during and after application of aerosol space sprays indoors. Short- and intermediate-term exposures were assessed for all other handler and post-application exposure scenarios.

Residential risk is expressed as a Margin of Exposure (MOE), which is a ratio of the NOAEL selected from a toxicity study to the residential exposure value derived from exposure studies or standard values. MOEs greater than 100 are considered to be protective for acute exposure via inhalation and for short- and intermediate-term incidental ingestion exposures. MOEs greater than 300 (additional 3X uncertainty factor for lack of a NOAEL) are considered adequate for short- and intermediate-term inhalation exposures.

Residential Routes of Exposure	Duration of Exposures		
	Acute	Short	Intermediate
Incidental Oral	-	100	100
Inhalation	100	300	300

a. Toxicity

The toxicological endpoints used in the residential risk assessment for PBO are listed in Table 7 below.

Exposure Scenario	Dose Used in Risk Assessment, UF	Level of Concern for Risk Assessment	Study and Toxicological Effects
Short-Term Incidental Oral (1-30 days); Intermediate-Term Incidental Oral (1- 6 months)	NOAEL= 89 mg/kg/day	Residential LOC for MOE = 100	Two generation reproduction study, rats LOAEL = 469 mg/kg/day based on the decrease in body weight gain of F ₁ and F ₂ pups at postnatal day 21 (MRID: 00161118)
Short-Term Dermal (1 to 30 days); Intermediate-Term Dermal (1 to 6 months)	No systemic, developmental or neurotoxicity concerns at the limit dose. Therefore, no quantification is required. PBO is classified as mild irritant.		
Acute Inhalation (≤ 2 hrs) (inhalation absorption rate = 100 %)	NOAEL= 630 mg/kg/day	Residential LOC for MOE = 100	Developmental toxicity study, rats LOAEL = 1065 mg/kg/day based on decrease in maternal body weight gain (Tanaka et al., 1995)
Short-Term Inhalation (1 to 30 days); Intermediate-Term Inhalation (1 to 6 months)	Respiratory LOAEL= 3.91 mg/kg/day (0.015 mg/L)	Residential LOC for MOE = 300	Subchronic inhalation toxicity study, rats Respiratory LOAEL = 3.91 mg/kg/day (0.015 mg/L) based on laryngeal hyperplasia and metaplasia (MRID: 42477101)

NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, MOE = margin of exposure, LOC = level of concern

b. Residential Exposure Scenarios

The residential exposure assessment includes four handler and twelve post-application residential exposure scenarios. The term “handler” applies to individuals who mix, load, and apply the pesticide product. The term “post-application” describes individuals who may be exposed to pesticides after entering areas previously treated with pesticides. Based on

information for supported uses provided in the Master Label, the Agency assessed the residential exposure scenarios for PBO.

i. Residential Handler Scenarios

The quantitative residential handler exposure/risk assessment developed for residential handlers is based on these scenarios:

- 1) Mixing, loading, and applying liquid spray formulation by low-pressure handwand for indoor surface spray application
- 2) Mixing, loading, and applying liquid spray formulation by low-pressure handwand for indoor crack and crevice treatment
- 3) Mixing, loading, and applying liquid spray formulation by hose-end sprayer for lawn and garden application
- 4) Mixing and loading liquid formulations for the systems' holding tanks for outdoor automatic mister systems

ii. Residential Post Application Scenarios

The quantitative residential post application exposure/risk assessment developed for residential handlers is based on these scenarios:

- 1) Inhalation exposure from application of mosquito adulticide from fixed wing aircraft and/or helicopter
- 2) Inhalation exposure from application of mosquito adulticide from ultra-low volume (ULV) truck mounted sprayer
- 3) Toddler incidental ingestion of residue from treated turf grass via hand-to-mouth activities
- 4) Toddler incidental ingestion of residue via object-to-mouth activity while on treated turf grass
- 5) Toddler incidental ingestion of soil from treated area
- 6) Toddler incidental ingestion of residues deposited on carpet via hand-to-mouth activities after use of total release foggers
- 7) Toddler incidental ingestion of residues deposited on vinyl flooring via hand-to-mouth activities after use of total release foggers
- 8) Toddler incidental ingestion of residues on pets via hand-to-mouth activities after pet treatment
- 9) Inhalation exposure to aerosol spray during and after space spray application
- 10) Bystander acute inhalation exposure during outdoor automatic mister applications
- 11) Bystander short-term inhalation exposure during outdoor automatic mister applications
- 12) Bystander short- and intermediate-term exposure following indoor metered release applications

Due to lack of data, the risks associated with broadcast dust applications to carpet were not calculated. A qualitative description of the possible risk concerns is included in Section IV.

c. Exposure Data and Assumptions

Handler Exposure Data

Data from the Pesticide Handler Exposure Database (PHED) and Occupational Residential Exposure Task Force (ORETF) database were used to assess residential handler exposures. Default application assumptions regarding areas treated or amounts applied for residential handler scenarios are documented in the HED Science Advisory Committee on Exposure SOP 12: Recommended Revisions to The Standard Operating Procedures For Residential Exposure Assessment (February 22, 2001). Other residential exposure standard operating procedures (SOPs) may be viewed at the following website: <http://www.epa.gov/oscpmont/sap/1997/september/sopindex.htm> .

Post Application Exposure Data

The Agency used default factors from the Exposure Science Advisory Committee SOP 12, Non-Dietary Exposure Task Force (NDETF) data, and Spray Drift Task Force exposure data throughout the post application risk assessment. Refer to the Occupational and Residential Exposure Assessment for further information.

Exposure Parameters and Assumptions

The parameters and assumptions used in estimating risks from residential exposure to PBO are described in section 6.2 of the Occupational and Residential Exposure Assessment. This information was used to assess all scenarios including mosquito abatement, incidental oral, aerosol space sprays, and outdoor residential misting systems.

d. Residential Risk Estimates

The results of the residential exposure assessment indicate that most residential handler and post-application exposure scenarios assessed result in MOEs greater than the applicable target MOEs. All residential handler scenarios are not of concern with MOEs ranging from 2,700 to 51,000.

The quantified post-application risks of concern to the Agency include: (1) the short-term residential bystander inhalation risk from outdoor residential misting systems; and (2) the short-term inhalation risk from indoor metered release devices. While exposures are expected from short-term (1-30 days) durations, the toxicological end point is the same for intermediate-term exposure (1-6 months), so the risk calculations represent both short- and intermediate-term exposures.

There were no data to estimate the exposure from applications of dusts to wide areas of carpet, therefore, this scenario could not be assessed, but is described qualitatively in section IV.

Outdoor residential misting systems have been modified from existing dairy barn misting systems and installed in residential areas as likely due to homeowners concerns about West Nile Virus. These systems are set to dispense pesticide at specific times throughout a day, depending on how the system is set up.

The outdoor residential misting system scenario triggers bystander short-/intermediate-term inhalation risk for toddlers when two 1-minute spray durations are estimated ($MOE_{\text{Toddlers}} = 190$). When exposure is to two 30-second spray durations, risk is not of concern ($MOE_{\text{Toddlers}} = 370$). Table 8 below summarizes the results of the outdoor residential misting systems assessment.

Population Sub-Group	Application Rate (lb PBO/ft ³ -min)	Inhalation Rate (m ³ /hour)	Spray Duration (minutes)	Air Concentration (mg PBO/m ³)	Daily Dose (mg/kg/day)	MOE (Target MOE =300)
Adult	0.000000469	1	1	0.150195	0.010728	360
			0.5	0.0750974	0.005364	730
Toddler	0.000000469	0.7	1	0.150195	0.0210273	190
			0.5	0.0750974	0.0105136	370

The indoor metered release device scenario was based on the Multi-Chamber Concentration and Exposure Model (MCCEM) single chamber model to predict the air concentrations that would result from application to a whole house with multiple units. Products used in metered release devices are usually formulated in ready to use aerosol cans with a special nozzle that fits into the device. A battery-powered timer system allows a spray of PBO to dispense regularly throughout a day. These systems are registered for use to control flying insects in residential areas, food handling establishments, animal premises, and other areas. The PBO short- and intermediate-term MOEs for indoor residential metered release devices range from 12 to 240 and are below the target MOE of 300.

Exposed Population	MCCEM Execution Mode	Air Changes per Hour	Inhalation Exposure (mg/day)	Inhalation Dose (mg/kg/day)	Short/Intermediate Term MOE
Adults	Single Chamber (Units are installed throughout house)	0.18 (Summer House)	5.7	0.081	50
Children			4.7	0.313	12
Adults		0.45 (Fall/Spring House)	3.0	0.042	90
Children			1.95	0.130	30
Adults	Use Interzonal Air Flow Rates (Unit installed in kitchen only)	0.18 (Summer Hous)	2.85	0.041	100
Children			1.85	0.123	30
Adults		0.45 (Fall/Spring House)	1.15	0.016	240
Children			0.75	0.050	80

The application rates are based upon the Clean Air Purge II Label (9444-161). This product contains 1% pyrethrins by weight in a 232 gram container. One container will apply 3000 sprays per month at fifteen minute intervals and is sufficient for a 6000 cubic feet interior space.

e. Aggregate Risk

In accordance with the FQPA, the Agency must consider pesticide exposures and risks from all potential sources when assessing non-occupational sources. These exposures usually include food, drinking water, and residential exposures. In an aggregate assessment, exposures from all relevant sources are added together. When aggregating exposures and risks from various sources, the Agency considers both the route (oral, dermal, and inhalation) and duration (short-, intermediate-, or long-term) of exposure.

For PBO, aggregate risk assessments were conducted for acute (one day) and chronic (one year or more) food and drinking water exposures. The short-term aggregate exposures from food, water, and residential (incidental oral) routes associated with application of PBO were also calculated for PBO since there was a common toxicity endpoint of decreased weight gain identified for those routes of exposure.

Acute Aggregate Risk (Food + Drinking Water)

Acute DWLOCs were calculated based on acute dietary exposure estimates and default body weights and water consumption figures. The EDWCs for both surface water and groundwater are well below the acute DWLOCs for the general U.S. population and all other population subgroups indicating that acute aggregate exposure to PBO in food and water is not a concern. The lowest acute DWLOC is 51000 µg /L for children 1-2 years old, which is higher than the surface water EDWC of 240 µg/L and the ground water EDWC of 0.26 µg/L.

Short term Aggregate Risk (Food + Drinking Water + Incidental Oral)

Short term aggregate risk is the estimated risk associated with the combined risks from average food exposures, average drinking water exposures, and short-term oral, dermal and inhalation exposures. The PBO toxicity endpoints selected for the dietary, drinking water, and incidental oral routes of exposure may be aggregated because decreased body weight gain was the common toxicity endpoint for all of these exposure routes.

The inhalation endpoint was different from the other endpoints selected and no endpoint was identified for dermal exposure, so dermal and inhalation exposures were not considered in the aggregate assessment.

The short term aggregate risk for PBO was calculated by adding exposure estimates from dietary, drinking water, and incidental oral exposure pathways for children age 1-2 and comparing them with model based EDWCs. The lowest short term DWLOC is 8500 µg/L for children 1-2 years old which is higher than the surface water EDWC of 60 µg/L and the ground water EDWC of 0.26 µg/L. The aggregate short term exposure to PBO does not result in a risk of concern. Due to a high degree of uncertainty in the risk assessment some post-application short-term scenarios, including outdoor residential misting systems and metered release device scenarios, were not included in the short-term aggregate assessment. However, because of the conservative exposure assumptions used in the individual assessments, and with the exposure

mitigation requirements described herein, the Agency does not expect aggregate exposures to pose risks of concern.

Chronic Aggregate Risk (Food + Drinking Water)

Chronic DWLOCs were calculated based on the chronic dietary exposure estimates and default body weights and water consumption figures. The EDWCs for both surface water and groundwater are well below the chronic DWLOCs for the general U.S. population and all other population subgroups indicating that chronic aggregate exposure to PBO in food and water is not of concern. The lowest chronic DWLOC is 1400 µg/L for children 1-2 years old, which is higher than the surface water EDWC of 60 µg/L and the ground water EDWC of 0.26 µg/L.

4. Cumulative Risk Assessment

The Food Quality Protection Act (FQPA) requires that the Agency consider available information concerning the cumulative effects of a particular pesticide's residues and other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common toxic mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the substances individually. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to PBO and any other substances and, PBO does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance reassessment action, therefore, EPA has not assumed that PBO has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

5. Occupational Risk

For more detail on the occupational assessment, see the *Revised Occupational and Residential Exposure Assessment and Recommendations for the Reregistration Eligibility Decision for PBO*, (Daiss, September 8, 2005).

Since the last Occupational and Residential PBO risk assessment was available for public comment on September 21, 2005, the following scenarios were included in the occupational risk assessment:

- Mixing and loading liquids for aerial applications to forestry areas at a rate of 2.5 lb ai/acre.
- Liquid aerial applications to forestry areas at the rate of 2.5 lbs ai/acre.
- Post-application exposure from metered release devices spraying in institutional or non-residential areas.

a. Occupational Toxicity

Table 10 provides a listing of the toxicological endpoints used in the PBO occupational risk assessment.

Table 10: Endpoints and Doses Used in the Occupational Risk Assessment			
Exposure Scenario	Dose Used in Risk Assessment, UF	Level of Concern for Risk Assessment	Study and Toxicological Effects
Short-Term Inhalation (1 to 30 days); Intermediate-Term Inhalation (1 to 6 months)	Respiratory LOAEL= 3.91 mg/kg/day (0.015 mg/L)	Occupational LOC for MOE = 300	Subchronic inhalation toxicity study, rats Respiratory LOAEL = 3.91 mg/kg/day (0.015 mg/L) based on laryngeal hyperplasia and metaplasia (MRID: 42477101)
Short-Term Dermal (1 to 30 days); Intermediate-Term Dermal (1 to 6 months)	No systemic, developmental or neurotoxicity concerns at the limit dose. Therefore, no quantification is required.		

NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, MOE = margin of exposure, LOC = level of concern

b. Occupational Handler Exposure

Workers can be exposed to a pesticide through mixing, loading, or applying the pesticide, and through re-entering a treated site. Worker risk is measured by a Margin of Exposure (MOE) which determines how close the occupational exposure comes to the NOAEL taken from animal studies. In the case of PBO, MOEs that are greater than 300 for short- and intermediate-term exposure and 1000 for long-term exposure do not exceed the Agency’s level of concern. A summary of occupational target MOEs is below in Table 11.

Table 11: Target MOEs for Occupational Exposure			
Occupational Routes of Exposure	Duration of Exposures		
	Acute	Short	Intermediate
Inhalation	100	300	300

Data from the PHED or ORETF databases were used to assess occupational handler exposures. Standard assumptions regarding areas treated or amounts applied for agriculture and mosquito abatement handler exposure scenarios are documented in the HED Science Advisory Committee on Exposure’s SOP 9, “Standard Values for Daily Acres Treated in Agriculture” (July 5, 2000). Information on how pest control operators use pesticide products was obtained from a survey conducted by the National Pest Management Association (NPMA). NPMA sponsored a “Pest Control Operators (PCO) Product Use and Usage Information Survey.” Further information on data utilized in the occupational risk assessment can be found in the PBO occupational risk assessment, (Daiss, September 8, 2005).

i. Agricultural Handler Scenarios

- 1) mixing and loading liquids for aerial and/or chemigation application to field crops
- 2) mixing and loading liquids for groundboom application to field crops
- 3) mixing and loading liquids for airblast application to field crops
- 4) mixing and loading wettable powders for aerial and/or chemigation application to field crops
- 5) mixing and loading wettable powders for groundboom application to field crops
- 6) mixing and loading wettable powders for airblast application to field crops
- 7) applying liquids aerially to field crops
- 8) applying liquids with ground boom sprayer to field crops
- 9) applying liquids with airblast sprayer to field crops
- 10) mixing, loading and applying liquids with high pressure hand wand for greenhouse application
- 11) mixing, loading and applying liquids with backpack sprayer or low pressure handwand for greenhouse application
- 12) mixing loading and applying wettable powder with backpack sprayer or low pressure hand wand for greenhouse application
- 13) mixing, loading and applying liquids with backpack sprayer or low pressure hand wand for agricultural premise and equipment application
- 14) flagging for aerial spray application

ii. Forestry Handler Scenarios

- 1) mixing and loading liquids for aerial forestry applications
- 2) applying liquids for aerial forestry applications

iii. Pesticide Control Operator Handler Scenarios

- 1) mixing, loading and applying liquids indoors for surface spray application with low pressure handwand;
- 2) mixing, loading and applying liquids indoors for crack and crevice application with low pressure handwand;
- 3) mixing, loading and applying wettable powders indoors for surface spray application with low pressure handwand;
- 4) mixing, loading and applying wettable powders indoors for crack and crevice application with low pressure handwand;
- 5) mixing, loading and applying liquids with backpack sprayer or low pressure hand wand for general outdoor sites;
- 6) mixing, loading and applying liquids for hand gun sprayer application to lawns;
- 7) mixing, loading and applying liquids for groundboom application to golf courses
- 8) mixing, loading and applying liquids for back pack sprayer or low pressure handwand application to stored grain
- 9) mixing, loading and applying liquids for high pressure handwand application to stored grain

- 10) mixing, loading and applying liquids for low pressure handwand application to warehouse stored produce
- 11) applying liquids to golf courses with groundboom sprayer
- 12) aerosol spray application indoors
- 13) mixing and loading liquid formulations for the systems' holding tanks for outdoor automatic mister systems

iv. Mosquito Abatement Scenarios

- 1) mixing, loading liquids for aerial application
- 2) mixing, loading liquids for ULV truck mounted spray application
- 3) mixing, loading, applying liquids with truck mounted ULV ground spray (airblast sprayer unit exposure used as surrogate)
- 4) mixing, loading, applying liquids with back pack sprayer

v. Direct Application to Pets and Farm Animals

- 1) spray application by veterinarians and groomers

c. Occupational Handler Risk Summary

Based on the supported uses provided in the Master Label, thirty-four occupational exposure scenarios were assessed for agricultural, forestry, professional pest control operator, and mosquito control applications of PBO. Short-, intermediate-, and long-term exposures were assessed for occupational scenarios based on use patterns. Agricultural and forestry handler scenarios were assessed as short- and intermediate-term exposures. Pesticide control operator scenarios were assessed as short-, intermediate- and long-term exposures. Mosquito abatement scenarios were assessed as short- and intermediate-term exposures for aerial and backpack spray applications and short-, intermediate-, and long-term exposures for truck mounted ULV spray applications. Only inhalation exposures have been assessed for each of the occupational scenarios because no dermal assessment was conducted since no adverse effects were seen at the highest dose tested in dermal toxicity studies.

The majority of occupational handler scenarios are not of concern at baseline attire (long-sleeved shirt, long pants, shoes and socks) with MOEs ranging from 300 to 23,000. The following agricultural, forestry, pesticide control operator, and mosquito abatement scenarios do not reach their target MOEs (300 for short- and intermediate-term and 1000 for long-term exposures) at baseline attire, and are potentially of concern.

Table 12: Scenarios of Potential Concern for Agricultural Handlers				
Agricultural Handler Exposure Scenarios of Concern	Crop	Application Rate	Daily Area Treated	Inhalation MOE* (Short & Inter Term Target = 300)
Wettable Powders Mixing/Loading for Aerial application and/or Chemigation Application	Field Crops	0.50 lb ai/acre	350 Acres/day	40
	High Acre Crops	0.50 lb ai/acre	1200 Acres/day	11
Wettable Powders Mixing/Loading for Groundboom Application	Field Crops	0.50 lb ai/acre	80 Acres/day	160
Wettable Powders Mixing/Loading/Applying for Low-Pressure Handwand or Backpack Sprayer Application	Greenhouse	1.5 lb ai/acre	2 Acres/day	85
Liquids Mixing/Loading/Applying for High-Pressure Handwand Application	Greenhouse	1.5 lb ai/acre	10 Acres/day	160

*Assumes baseline PPE (long-sleeved shirt, long pants, shoes and socks). No respirator is included in these calculations.

Table 13: Scenarios of Potential Concern for Handlers for Forestry Application				
Forestry Exposure Scenarios	Site	Rate in Assessment	Daily Area Treated	Inhalation MOE (Short & Inter Term Target = 300)
Liquid Mixing/Loading for aerial application with baseline PPE (no respirator)	Forestry	2.5 lb ai/acre (Master Label Rate)	1200 acres/day	160
Liquid Mixing /Loading for aerial application with PF 5 respirator	Forestry	2.5 lb ai/acre	1200 acres/day	770
Aerial spray application with baseline PPE (no respirator)	Forestry	2.5 lb ai/acre	1200 acres/day	2200

Table 14: Scenarios of Potential Concern for Pesticide Control Operators				
Pesticide Control Operator Exposure Scenarios	Use	Application Rate	Daily Area Treated	Inhalation MOE* (Short & Inter Term Target = 300) (Long Term Target = 1000)
Wettable Powders Mixing/Loading/Applying for Low Pressure Handwand application - Surface Spray	Indoor Surface Spray	0.56 lb ai per 1000 ft ²	7 buildings avg area treated - 1600 ft ²	40
Wettable Powders Mixing/Loading/Applying for Low Pressure Handwand application - Crack & Crevice Treatment	Indoor Crack & Crevice	2.2 lb ai per 1000 ft ²	7 buildings avg area treated - 1600 ft ²	10
Liquids Mixing/Loading/Applying for Low Pressure Handwand application - Crack & Crevice Treatment	Indoor Crack and Crevice	2.2 lb ai per 1000 ft ²	7 buildings avg area treated - 1600 ft ²	380
Applying Aerosol Sprays	Indoor Space Spray	0.025 lb ai per 16 oz can	7 homes per day 2 cans per home	615

*Assumes baseline PPE (long-sleeved shirt, long pants, shoes and socks). No respirator is included in these calculations.

Table 15: Scenarios of Potential Concern for Mosquito Abatement Handlers				
Mosquito Abatement Exposure Scenarios of Concern	Use	Application Rate	Daily Area Treated	Inhalation MOE (Short & Inter Term Target = 300) (Long Term Target = 1000)
Liquids Mixing/Loading for Aerial Application	Mosquito Control	0.08 lb ai per acre	7500 acres per day	390
Mix/Load/Apply Sprays for ULV truck mounted spray (Airblast Surrogate Unit Exposure)	Mosquito Control	0.08 lb ai per acre	3000 acres per day	260

There were no risks of concern with professional applications to pets or other animals. Due to lack of data, application of dust with bulb duster, and power dusters were not assessed. Also, handlers applying with handheld foggers could not be assessed due to lack of use and application information.

d. Occupational Post-Application Risk Summary

Inhalation exposures are thought to be negligible in outdoor post-application scenarios, since PBO has low vapor pressure and the dilution factor outdoors is considered infinite. As a result, inhalation post-application exposures from outdoor applications were not considered in this assessment. There is potential for post-application inhalation exposure from indoor metered release applications.

According to the Master Label, PBO is used as a space spray in a wide variety of indoor areas such as barns, greenhouses, food storage areas, food processing areas, restaurants and residences. A scenario that involves a metered release into a dairy barn was evaluated to assess these exposures because PBO is commonly used in dairy barns and because the ventilation characteristics of dairy barns are relatively well defined. The MOE for short- and intermediate-term exposure is 62, which does not reach the target MOE of 300 as shown in Table 16.

The indoor metered release device scenario used the same model, the MCCEM single chamber model, as the residential metered release device scenario, except the occupational assessment assumed a ventilation rate of six air changes per hour, while the residential scenario assumed less than half an air change per hour. The risk estimates for the metered release scenarios are conservative because it was assumed that the aerosol particles would remain airborne until they were removed by ventilation and the effect of aerosol particle settling was not considered. Aerosol particle settling could be a major factor depending upon the aerosol particle size and rate of evaporation. Data will be required to better characterize this exposure.

Table 16: PBO Occupational Post-Application Estimated Risks Following Metered Release		
Exposure Scenario	Location	Short/Intermediate Term MOE (Target MOE = 300)
Metered Release Space Spray	Dairy Barns	62

The restricted entry interval (REI) for PBO will remain at 12 hours for all post-application scenarios that fall under the Worker Protection Standard. In addition, under the Worker Protection Standard for Agricultural Pesticides - WPS-(40 CFR 170) greenhouses must be appropriately ventilated following pesticide applications so that post-application inhalation exposures are minimal.

6. Human Incident Data

Based on data from Poison Control Centers, there appears to be a greater risk of moderate or major symptoms among those exposed to products containing PBO and pyrethrins than those exposed to pyrethrins alone. A detailed review of symptoms found that respiratory symptoms (bronchospasm, cough/choke, and dyspnea) and selected dermal symptoms (dermal irritation/pain, itching, and rash) were more likely reported if the exposure included PBO. These symptoms are likely the reason for increased risk of moderate effects which typically would require medical attention. The findings from analysis of symptoms from Poison Control Centers suggest that PBO added to a product with pyrethrins increases the reported effects.

However, other evidence indicates that PBO does not effectively act as a synergist in mammals. PBO is well known to inhibit microsomal enzymes in insects. It also inhibits the microsomal enzymes in several other species (e.g., rats, rabbits, mice) based on available toxicological data. However, evidence indicates that enzyme inhibition in mammals is transient and occurs at high doses. These studies also indicate that initial inhibition in mammals is followed by stimulations of microsomal enzymes upon continued exposure. PBO has also been used as a classical compound in several pharmacological experiments to compare the therapeutic or toxicological effects of several drugs before or after metabolism in rodents. These drug interaction studies also suggest that the inhibition of microsomal enzymes is a transient effect in mammalian systems. The kinetics of PBO inhibition and stimulation of microsomal enzymes in humans is not established. However, one study in humans reports no inhibition of microsomal enzymes at a relatively low dose.

B. Environmental Risk Assessment

A summary of the Agency's environmental risk assessment for PBO is presented below. More detailed information associated with the environmental risk from the use of PBO can be found in the document *PBO EFED's Response to Public Comments and our Revised Ecological Risk Assessment* (Davy, September 6, 2005).

Agricultural and public health (mosquito control) uses were estimated to result in the most likely environmental exposure for PBO. Exposure analyses focused on the use of PBO in post-crop emergence sprays to control insects. Both ground and aerial spray applications were considered. The use of PBO in mosquito control was examined with the standard Rice Paddy Model, which estimates environmental concentrations from direct water applications.

PBO was evaluated for its ecological and environmental effects independently from any other active ingredient, but because PBO is never used alone, its adverse effects should be considered in light of the other active ingredients with which it is formulated, typically insecticides like pyrethroids or natural pyrethrins. PBO alone is generally less toxic to the species of concern, such as aquatic invertebrates, than pyrethrins and pyrethroids. Depending on the different fate characteristics of PBO and other active ingredients in formulated products, the chemicals may separate in the environment, affecting the potential for adverse effects to species at risk. Risk quotients (RQs) discussed in this section reflect PBO alone. The available toxicity data from PBO plus other active ingredients like pyrethrins or pyrethroids show greater toxicity to invertebrates than if exposure was to the pyrethrin/pyrethroid alone.

1. Environmental Fate and Transport

The environmental fate database is adequate to characterize the environmental fate, drinking water, and ecological exposure of PBO. However, EPA does intend to issue a Data Call-In as part of this RED to address remaining areas of uncertainty.

PBO degrades rapidly (8.4-hour half-life) in the environment by photolysis in water, and is metabolized by soil microorganisms. Other tested routes of degradation, such as hydrolysis,

aerobic and anaerobic aqueous metabolism, are very slow or have questionable rates due to experimental difficulties, as in the case of soil photodegradation. The estimated atmospheric half-life of PBO is 3.4 hours, based on the estimated reaction rate with hydroxyl radicals. PBO is moderately mobile in soil-water systems ($K_{oc} = 399 - 830$). Little volatilization from soil or water is expected, but PBO may enter the atmosphere as an aerosol when applied by spraying.

The major degradates PBO-alcohol, PBO-aldehyde, and PBO-acid are expected to be more soluble in water than the parent and therefore more mobile in soil-water systems. Exposure to both parent PBO and its major degradates (PBO-alcohol, PBO-aldehyde, and PBO-acid) were considered in the assessment. The toxicity of the degradates was considered to be equivalent to that of the parent in the absence of data.

2. Ecological Risk

The Agency’s ecological risk assessment compares toxicity endpoints from ecological toxicity studies to estimated environmental concentrations (EECs) based on environmental fate characteristics and pesticide use data. PBO lacks pesticide properties of its own, and must be used with other active ingredients to be effective, but in this assessment PBO alone was considered. To evaluate the potential risk to non-target organisms from the use of PBO alone, the Agency calculates a Risk Quotient (RQ), which is the ratio of the EEC to the most sensitive toxicity endpoint values, such as the median lethal dose (LD_{50}) or the median lethal concentration (LC_{50}). These RQ values are then compared to the Agency’s levels of concern (LOCs), which are listed below in Table 17 and indicate whether a pesticide, when used as directed, has the potential to cause adverse effects to non-target organisms. When the RQ exceeds the LOC for a particular category, the Agency presumes a risk of concern. These risks of concern may be addressed by further refinements of the risk assessment or risk mitigation measures. Use, toxicity, fate, and exposure are considered when characterizing the risk, as well as the uncertainty in the assessment. EPA further characterizes ecological risk based on any reported incidents to non-target terrestrial or aquatic organisms in the field (e.g., fish or bird kills).

Table 17: EPA’s Levels of Concern and Associated Risk Presumptions			
Risk Presumption	LOC Terrestrial Animals	LOC Aquatic Animals	LOC Plants
<i>Acute Risk</i> - there is potential for acute risk	0.5	0.5	1
<i>Acute Endangered Species</i> - endangered species may be adversely affected	0.1	0.05	1
<i>Chronic Risk</i> - there is potential for chronic risk	1	1	N/A

The ecological risk assessment for PBO focuses on maximum application rates for agricultural and mosquito abatement uses, which combined make up roughly about 20% of the total PBO use. Consideration was also given to PBO entering water from sources like lice shampoos and flea sprays that may contaminate water going down the drain and run into water

treatment facilities. This “Down-the-Drain” scenario was included in a response memo from EFED addressing water quality concerns (Davy, January 30, 2006). However, no analogous exposure model has been developed to allow a similar screening assessment for pesticides applied in an outdoor urban setting. As a result, the Agency has taken a qualitative approach to characterize the potential aquatic risk from urban and suburban use of PBO.

a. Risk to Aquatic Organisms

i. Fish and Invertebrate Toxicity and Exposure

1. Toxicity

A summary of the toxicity results for aquatic organisms exposed to PBO is below in Table 18.

Freshwater Fish

PBO is moderately toxic to freshwater fish on an acute basis ($LC_{50} = 1.9$ ppm).

A no observed effect concentration (NOEC) of 0.04 ppm was estimated from a chronic early life stage of fish study with fathead minnow in which embryo survival at hatch and length and weight of larvae was observed at the lowest observed effect concentration (LOEC) of 0.11 ppm.

Freshwater invertebrates

PBO ranges from moderately toxic ($LC_{50} = 12.0$ ppm) to highly toxic ($LC_{50} = 0.51$ ppm) to freshwater invertebrates on an acute basis. The species selected for RQ calculation was *Daphnia magna* with an LC_{50} of 0.51 ppm.

A NOEC of 0.030 ppm was estimated from a chronic life cycle study where *Daphnia magna* exhibited reproduction affects at the lowest observed effect concentration (LOEC) of 0.047 ppm.

Estuarine fish

PBO is moderately toxic ($LC_{50} = 3.94$ ppm) to estuarine/marine fish based on observed effects to sheepshead minnow on an acute basis.

There are no chronic data available for estuarine fish.

Estuarine/Marine invertebrates

PBO is highly toxic to estuarine invertebrates ($LC_{50} = 0.49$ ppm). There are no chronic data available for estuarine/marine invertebrates.

Amphibians

PBO is highly toxic to amphibians on an acute basis ($LC_{50} = 0.21$ ppm).

Table 18: Toxicity reference values for aquatic organisms exposed to PBO		
Exposure Scenario	Species	Toxicity Reference Value
Freshwater Fish		
Acute	Rainbow trout (<i>Oncorhynchus mykiss</i>)	$LC_{50}^a = 1.9$ ppm
Chronic	Fathead minnow (<i>Pimephales promelas</i>)	NOEC ^b = 0.04 ppm LOEC ^c = 0.11 ppm Effect: Survival and growth
Freshwater Invertebrates		
Acute	Waterflea (<i>Daphnia magna</i>)	$LC_{50} = 0.51$ ppm
Chronic	Waterflea (<i>Daphnia magna</i>)	NOEC = 0.03 ppm LOEC = 0.047 ppm Effect: reproduction
Esuarine/Marine Fish		
Acute	Sheepshead minnow (<i>Cyprinodon variegatus</i>)	$LC_{50} = 3.94$ ppm
Estuarine/Marine Invertebrates		
Acute	Mysid shrimp (<i>Mysidopsis bahia</i>)	$LC_{50} = 0.49$ ppm
Amphibians		
Acute	Western chorus frog tadpole (<i>Pseudacris triseriata</i>)	$LC_{50} = 0.210$ ppm

^a LC_{50} = Median Lethal Concentration

^b NOEC = No Observed Effect Concentration

^c LOEC = Lowest Observed Effect Concentration

2. Exposure

Environmental exposure from PBO was modeled in four ways. Exposures from terrestrial agricultural applications were assessed using the standard farm pond scenario in the PRZM-EXAMS models. All PRZM-EXAMS exposure analyses were done at maximum application rates and frequency. The EFED Interim Rice Paddy Model was used to calculate acute exposure due to direct application to water from mosquito abatement uses. Spray drift

from terrestrial agricultural applications was assessed using the AgDrift model to calculate exposures in the EFED standard farm pond and standard wetland models. Finally, the Down-the-Drain model in E-FAST was used to address water quality impacts from disposal of PBO down drains.

Comments were submitted from PBOTFII stating that the aquatic exposure assessment for PBO should include only the parent compound and no degradates. To demonstrate the effect of considering only parent PBO, a revised assessment for Florida peppers was run considering the parent compound only. Although the results of the revised parent only Florida peppers assessment, which is found in the *Piperonyl Butoxide: EFED's Response to Public Comments and Revised Ecological Risk Assessment* (Davy, September 6, 2005), resulted in lower RQs, the results were not large enough to change the original risk conclusions for acute or chronic levels-of-concern for any organism. Considering the parent only or the parent plus degradates, did not change the risk conclusions for PBO.

Agricultural Exposure

For exposure to fish and aquatic invertebrates, EPA considers surface water only, since most aquatic organisms are not found in ground water. The aquatic exposure assessment for PBO relied on the PRZM and EXAMS Tier II models. The Pesticide Root Zone Model (PRZM version 3.12) simulates fate and transport on the agricultural field, while the water body is simulated with Exposure Analysis Modeling System (EXAMS version 2.98). Simulations are run for multiple (usually 30) years and the reported EECs represent the values that are expected once every ten years based on the thirty years of daily values generated during the simulation. The half-life values used in the PRZM/EXAMS model reflect the combined residues of parent PBO and its major degradates PBO-alcohol, PBO-aldehyde, and PBO-acid, expressed as PBO equivalents.

PRZM/EXAMS modeling of PBO was done for 23 crop scenarios using the current maximum label rate of 0.5 lbs a.i. per acre, ten applications per year, and a 3-day re-application interval. The peak EECs ranged from 22.1 ppb (CA grapes) to 160 ppb (FL peppers) for aerial application. For ground application, the peak EECs ranged from 8.4 ppb (CA grapes) to 159 ppb (FL peppers). A complete listing of EECs, including those used for PBO RQ calculations can be found in table 6a and 6b in the EFED risk assessment (September 2005).

Mosquito Abatement Exposure

The EFED interim standard Rice Paddy Model (October 29, 2002) was used as a measure of exposure for mosquito abatement applications. This model estimates the exposure concentration in a four-inch deep water body at the time of application, and accounts for partitioning to sediment, but not dissipation. Overall, the model yields a conservative measure of exposure. The PBO Master Label indicates that the application rate of PBO for mosquito abatement applications can be up to 0.08 lb/acre to control *Aedes taeniorhynchus* and other difficult species. No maximum number of applications is indicated. The minimum soil-water distribution coefficient ($K_d = 0.98$) measured for PBO was used to provide maximum partitioning to the water phase, and resulting in a conservative measure of exposure in the water column. The Rice Paddy EEC for a single application is 75 ppb.

Spray Drift

Ground Application

The AgDrift model was used to calculate aquatic exposures in the EPA standard pond and standard wetland, from spray drift from a single agricultural application. A ground spray Tier I aquatic assessment was performed, assuming high boom application with very fine to fine spray, 90th percentile drift, and a zero-foot buffer, at an application rate of 0.5 lb a.i./acre. AgDrift calculated that 6.16% of the applied mass would reach the pond or wetland, resulting in an initial average concentration of 1.7 ppb in the pond, and 23 ppb in the wetland.

Aerial Application

Tier 1 aerial analysis, assuming fine to very fine spray and a zero-foot buffer, resulted in the pond and wetland EECs of 6.8 ppb and 90.6 ppb, respectively.

Aquatic Exposure – “Down-the-Drain” Assessment

In order to address the issue of PBO release to domestic wastewater treatment, the Agency relied on the Office of Pollution Prevention and Toxics (OPPT) consumer exposure model, Exposure and Fate Assessment Screening Tool (E-FAST) (USEPA, 1999). This screening level Down-the-Drain model E-FAST is specifically designed to address all sources of PBO, such as from pet shampoos and other uses that could potentially contribute to domestic wastewater from a “down-the-drain” application.

The model uses input parameters to estimate the highest amount of PBO that could be released down a drain before a significant concentration of PBO is reached. In this case, it was assumed that synergistic effects from PBO would be insignificant at levels less than 1 ppb. The model assumes that in a given year, a certain amount of PBO is parceled out on a daily per capita basis to the U.S. population and diluted into the average daily volume of wastewater prior to entering a treatment facility. It is assumed that the sewage treatment removal efficiency is zero for PBO, and that it is instantaneously diluted when mixing with surface water. Two dilution scenarios were modeled assuming low (75 times) and average (980 times) dilution into surface water.

Assuming a sewage treatment removal efficiency of 0%, then 6,033,688 pounds PBO per year disposed down a drain would be required to reach 1 ppb in receiving waters for the low dilution case (75 times), and 79,568,289 pounds PBO per year are required for the average dilution case (980 times). The annual production of PBO, estimated at 210,000 lbs per year for agricultural and non-agricultural applications, is well below this level and the Agency concluded that there was no risk of concern from the Down-the-Drain scenario.

ii. Aquatic Risk

A summary of the RQs for acute exposure to PBO is summarized in Table 19 below. The LOC for endangered species was slightly exceeded for most species and application methods. The RQ for amphibians exposed to PBO from agricultural applications was the highest estimated RQ at 0.76.

Table 19: Acute Aquatic Risk Quotient (RQ) Summary			
Species	Application Type		
	Agriculture	Mosquito Use	Spray Drift
Freshwater fish	<0.05 - 0.08	<0.05	<0.05 - 0.05
Freshwater invertebrates	<0.05 - 0.31	0.15	<0.05 - 0.18
Estuarine/Marine Fish	<0.05	<0.05	<0.05
Estuarine/Marine Invertebrates	<0.05 - 0.33	0.15	<0.05 - 0.18
Amphibians	<0.05 - 0.76	0.36	<0.05 - 0.43

Bold values indicate exceedance for Endangered Species LOC (RQ \geq 0.05).

Data were only available to assess chronic risk to freshwater fish and invertebrates exposed to PBO from agricultural applications. Some RQs exceeded the target LOC of 1.0, with the highest RQ estimated for freshwater invertebrates at 5.1. There were no data available to assess chronic risk to other species. The chronic RQ summary is in Table 20 below.

Table 20: Chronic Aquatic Risk Quotient (RQ) Summary	
Species	Agricultural Applications
Freshwater fish	<1.0 - 3.6
Freshwater invertebrates	<1.0 - 5.1
Estuarine/Marine Fish	Not assessed because no data were available.
Estuarine/Marine Invertebrates	
Amphibians	

Bold values indicate exceedance for chronic LOC (RQ \geq 1.0).

Wide Area Mosquito Adulticide Monitoring Data

In a Sacramento County monitoring study for PBO and pyrethrins, water samples were collected after mosquito adulticide applications in the Sacramento metropolitan area. In samples collected up to 10 hours after application there were detections of PBO and pyrethrins in the ppb range, that were similar to modeling predictions in the PBO and the pyrethrins mosquito adulticide assessment. Samples were also collected the day after application and measured lower or no concentrations for both active ingredients. This indicates both chemicals appear to dissipate fairly rapidly in the water column. The co-occurrence of PBO and pyrethrins in some of these first samples is an indication of direct transport to water from pesticide application and not transport by runoff.

b. Risk to Terrestrial Organisms

i. Birds, Mammals, and Insects Toxicity and Exposure

1. Toxicity

Birds

PBO is practically nontoxic to birds on an acute basis. There were no mortalities observed at the highest concentration tested for acute oral (2250 mg/kg bw) or for the sub-acute dietary studies (5620 ppm). EPA did not calculate RQs from the acute toxicity data because no mortality was seen at very high concentrations indicating minimal adverse acute effects to birds.

From chronic avian toxicity data, a NOEC of 300 ppm was estimated from an avian reproduction study in which adult and hatchling body weight and food consumption, number of eggs laid, number of eggs cracked, and eggshell thickness effects were observed at the lowest observed effect concentration (LOEC) of 1200 ppm.

Mammals

PBO is practically nontoxic to mammals on an acute basis. At higher concentrations mortalities were observed; therefore, RQs were calculated based on the LD₅₀ of 4570 mg/kg bw.

From chronic mammal toxicity data, a NOAEC of 1,000 ppm (89 mg/kg bw) was estimated from a 2-generation rat reproductive study in which decreased body weight gain in the maternal rats and offspring was observed at the LOAEC of 5,000 ppm (469 mg/kg bw).

Beneficial insects

PBO is practically nontoxic to honey bees on an acute oral basis (LD₅₀ > 25 µg/bee). Due to the uncertainty of estimating environmental exposure to the honey bee, EPA did not attempt to calculate an RQ.

Table 21: Toxicity reference values for mammals and birds exposed to PBO		
Exposure Scenario	Species	Toxicity Reference Value
Mammals		
Acute	Rat (Rattus norvegicus)	LD50 = 4570 mg/kg bw
Chronic	Rat (Rattus norvegicus)	Maternal NOAEC = 1000 ppm (89 mg/kg bw) Maternal LOAEC = 5000 ppm (469 mg/kg) Offspring NOAEC = 1000 ppm (89 mg/kg bw) Offspring LOAEC = 5000 ppm (469 mg/kg)
Birds		

Table 21: Toxicity reference values for mammals and birds exposed to PBO		
Exposure Scenario	Species	Toxicity Reference Value
Acute	Bobwhite quail (<i>Colinus virginianus</i>)	LD50 > 2250 mg a.i./kg bw (no mortalities at highest dose) NOEC = 486 mg a.i./kg bw
Acute	Bobwhite quail (<i>Colinus virginianus</i>) and Mallard duck (<i>Anas platyrhynchos</i>)	Dietary LC50 > 5620 ppm (no mortalities) NOEC = 1000 ppm (toxicosis)
Chronic	Mallard duck (<i>Anas platyrhynchos</i>)	NOEC = 300 ppm LOEC = 1200 ppm (adult and hatchling body weight and food consumption, number of eggs laid, number of eggs cracked, and eggshell thickness)
Insects		
Acute	Honey Bee	LD50> 25 µg /bee; NOAEC = 25 µg/bee

2. Exposure

Birds and mammals may be exposed after application through oral or dietary exposure to vegetative plant material or insects when foraging in the treated fields for nesting material or food. The EFED terrestrial exposure model, T-REX, Version 1.1, is used to estimate exposures and risks to avian and mammalian species. Input values for avian and mammalian toxicity as well as use parameters and foliar half-life data are required to run the model. The model provides estimates of both exposure concentrations and risk quotients (RQs). Specifically, the model provides estimates of concentrations (maximum and average) of chemical residues in different types of food sources that may be sources of dietary exposure to avian, mammalian, reptilian, or terrestrial-phase amphibian receptors. By comparing these estimated concentrations to acute and chronic toxicity reference values, acute and chronic RQs are calculated.

It was assumed that PBO was applied ten times at the maximum agricultural use rate (0.5 lb/acre) with 3-day intervals. In the absence of foliage residue data, the default assumption for the decay rate on foliage (35-day half-life) was used. The maximum EEC on food items available for wildlife ranged from 58 ppm to 932 ppm. The Hoerger-Kenaga nomogram also has mean values for residues on food items. The mean EEC on food items available for wildlife ranges from 17 ppm to 330 ppm.

ii. Bird Risk

Since PBO is practically non-toxic to birds and no mortality was observed at the highest concentrations, no RQ calculation is necessary for acute exposures to birds.

Chronic risk quotients for birds range from less than 1.0 to 3.1, and exceed the Agency's level of concern of 1.0 for chronic risks. The EECs used to calculate the RQs are based on an

application rate of 0.5 lb ai/A applied ten times during a season at 3-day intervals between applications.

Using the maximum Kenaga residue EEC, chronic LOCs are exceeded for birds that consume short grass, tall grass, and broadleaf plants/small insects (RQs range 1.4 to 3.1). Using the mean Kenaga residue EEC, chronic LOCs are exceeded for birds that consume short grasses (RQ = 1.1).

iii. Mammal Risk

Acute risk quotients for mammals are all below the Agency's level of concern of 0.1 for endangered mammalian species.

Chronic risk quotients for mammals range from less than 1.0 to 4.5 for maximum Kenaga EEC values and from less than 1.0 to 1.6 for mean Kenaga EEC values. The Agency's level of concern is 1.0 for chronic exposures to mammals.

Using the maximum Kenaga residue EEC, chronic LOCs are exceeded for all mammal weight classes except for those animals that only consume the fruit/pods/large insects food category. Using the mean Kenaga residue EEC, chronic LOCs are exceeded for only 15-gram and 35-gram mammal weight classes that only consume short grass food category.

iv. Non-Target Insect Risks

Currently, the Agency does not estimate RQs for terrestrial non-target insects.

v. Synergistic Risk Effects

Antagonistic Effects with Organophosphate Insecticides

Table 10 in the *EFED Risk Assessment* (Eckel, September 2005) lists 12 organophosphate (OP) insecticides and one carbamate insecticide that have been tested for PBO antagonism, that is, whether they are made toxic by simultaneous exposure to PBO.

Nine OP insecticides (azinphos-methyl, chlorpyrifos, diazinon, dioxabenzophos, fenitrothion, malathion, methyl parathion, parathion, and phenthoate) that require metabolic activation were less toxic when PBO was present in most sensitive species. The remaining three OP insecticides (chlorfenvinphos, dichlorvos, mevinphos) did not require metabolic activation, and did not exhibit decreased toxic effects when mixed with PBO.

PBO's mechanism of action increases the toxicity of insecticides by preventing them from breaking down by blocking the action of mixed-function oxidase (MFO) enzymes. By the same mechanism, PBO blocks the action of OP insecticides that require activation by MFO enzymes to convert them to their more-toxic forms.

Synergistic Effects with Pyrethroid Insecticides

A study comparing the toxic effects to fish of the pyrethroid resmethrin alone, compared to the toxic effects from resmethrin mixed with PBO concluded that PBO increases the toxicity of resmethrin to fish following short exposures (6 hours). No differences in toxicity between synergized and non-synergized resmethrin were detected with longer exposures (24 hours or longer).

In another study with permethrin it appears that PBO does not increase the toxicity of permethrin to fish. Any mortality of fish in the study seems to be due to permethrin rather than PBO.

The presence of PBO in a water body may either increase or decrease the toxicity of a mixture of insecticides, depending on which ones are present. PBO increases the toxicity of pyrethroids/pyrethrins, decreases the toxicity of OP insecticides that require metabolic activation, and has no effect on OP insecticides that do not require activation.

3. Ecological Incidents

According to the Ecological Incident Information System (EIIS) database summarizing 6(a)2 incident reports, for PBO, there are three alleged terrestrial animal incidents (bee, butterflies, and birds), seven alleged plant incidents (mostly ornamental flowers) and one alleged aquatic organisms incident (fish and invertebrates). The PBO products involved in the incidents were all applied as co-formulated sprays or through tank mixed mist blowers with pyrethrins, pyrethroids or rotenone. The Agency can not attribute any of the incidents to PBO by itself since as an insecticide synergist, it is never used by itself but always with another insecticide. However, the incidents do show that PBO in conjunction with an insecticide has the potential to cause adverse effects to aquatic species and to beneficial insect.

4. Endangered Species Concerns

The Agency's screening level assessment results in the determination that PBO will have no direct acute effects on threatened and endangered estuarine fish, mammals, and birds. Chronic RQs were estimated up to 3.1 for birds and 4.5 for mammals, and chronic RQs were not calculated for estuarine/marine fish due to lack of chronic data. The preliminary risk assessment for endangered species indicates that RQs exceed endangered species LOCs for freshwater fish, freshwater invertebrates, freshwater amphibians, and estuarine/marine invertebrates. Further, potential indirect effects to any species dependent upon a species that experiences effects from use of PBO can not be precluded based on the screening level ecological risk assessment. These findings are based solely on EPA's screening level assessment and do not constitute "may affect" findings under the Endangered Species Act.

5. Endocrine Disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other

ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate.” Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCa authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

In the available ecological toxicity studies on PBO, an avian reproduction study shows that PBO may cause decreases in adult and hatchling body weight and food consumption, number of eggs laid, and eggshell thickness. In addition, PBO may cause increases in number of eggs cracked. When additional appropriate screening and/or testing protocols being considered under the Agency’s EDSP have been developed, PBO may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

IV. Risk Management, Reregistration, and Tolerance Reassessment Decision

A. Determination of Reregistration Eligibility and Tolerance Reassessment

Section 4(g)(2)(A) of FIFRA calls for the Agency to determine, after submission of relevant data concerning an active ingredient, whether or not products containing the active ingredient are eligible for reregistration. The Agency has previously identified and required the submission of the generic data to support reregistration of products containing PBO. The Agency has completed its review of these generic data, and has determined that the data are sufficient to support reregistration of all products containing PBO.

The Agency has completed its assessment of the dietary, occupational, residential, and ecological risk associated with the use of pesticide products containing the active ingredient PBO. Based on a review of these data and on public comments on the Agency’s assessments for the active ingredient PBO, the Agency has sufficient information on the human health and ecological effects to make decisions as part of the tolerance reassessment process under FFDCa and reregistration process under FIFRA, as amended by FQPA. The Agency has determined that products containing PBO are eligible for reregistration provided that: (i) the risk mitigation measures outlined in this document are adopted and (ii) label amendments are made to reflect these measures. Label changes are described in Section V. Appendix A summarizes the uses of PBO that are eligible for reregistration. Appendix B identifies the generic data requirements that the Agency reviewed as part of its determination of reregistration eligibility of PBO, and lists the submitted studies that the Agency found acceptable. Data gaps are identified as generic data requirements that have not been satisfied with acceptable data.

Based on its evaluation of PBO, the Agency has determined that PBO products, unless labeled and used as specified in this document, would present risks inconsistent with FIFRA and

FQPA. Accordingly, should a registrant fail to implement any of the reregistration requirements identified in this document, the Agency may take regulatory action to address the risk concerns from the use of PBO. If all changes outlined in this document are incorporated into the product labels, then all current risks for PBO will be adequately mitigated for the purposes of this determination. Once an Endangered Species assessment is completed, further changes to these registrations may be necessary as explained under “Endangered Species Concerns” above.

B. Regulatory Position

Through the Agency’s public participation process, EPA worked with stakeholders and the public to reach the regulatory decisions for PBO. EPA released its PBO preliminary risk assessments for public comment on April 27, 2005 for a 60-day public comment period (Phase 3 of the 6 Phase public participation process). Where appropriate, the PBO risk assessments were revised in response to the comments received, and the assessments were released for an additional 60 day public comment period on September 21, 2005 (Phase 5 of the 6 Phase public participation process). During both public comment periods, the Agency received comments from the PBO Task Force II, stakeholder groups, such as the American Mosquito Control Association, State and Local government entities in California, California Water Boards, Publicly Owned Treatment Works, Mosquito and Vector Control Districts, and several private citizens. All of the preliminary and revised PBO risk assessments, public comments, response to comments, and this RED document are available in the public docket (OPP-2005-0043) at EPA’s docket and in the EPA’s electronic docket at www.regulations.gov.

1. Food Quality Protection Act Findings

a. “Risk Cup” Determination

As part of the FQPA tolerance reassessment process, EPA assessed the risks associated with PBO. EPA has determined that risk from dietary (food + water) exposure is within its own “risk cup.” An aggregate assessment was conducted for PBO for exposures through dietary and residential exposures. The Agency has determined that the human health risks from these combined exposures are within acceptable levels. In other words, EPA has concluded that the tolerances for PBO meet FQPA safety standards. In reaching this determination, EPA has considered the available information on the special sensitivity of infants and children, as well as aggregate exposure from food, drinking water, and residential sources.

b. Determination of Safety to U.S. Population

The Agency has determined that the established tolerances for PBO, with amendments and changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(D) of the FFDCA, as amended by FQPA, and that there is a reasonable certainty no harm will result to the general population or any subgroup from the use of PBO. In reaching this conclusion, the Agency has considered all available information on the toxicity, use practices, and the environmental behavior of PBO. As discussed in Section III, the acute, chronic, short-term, intermediate-term, and long-term risks from food, drinking water, and residential exposures do not exceed the Agency’s level of concern.

c. Determination of Safety to Infants and Children

EPA has determined that the established tolerances for PBO, with amendments and changes as specified in this document, meet the safety standards under the FQPA amendments to section 408(b)(2)(C) of the FFDCA, that there is a reasonable certainty of no harm for infants and children. The safety determination for infants and children considers the toxicity, use practices and environmental behavior of a chemical for the general population, but also takes into account the possibility of increased dietary exposure due to the specific consumption patterns of infants and children, as well as the possibility of increased susceptibility to the toxic effects of PBO residues in this population subgroup.

In determining whether or not infants and children are particularly susceptible to toxic effects from exposure to residues of PBO, the Agency considered the completeness of the hazard database for developmental and reproductive effects, the nature of the effects observed, and other information. The FQPA Safety Factor has been reduced to 1X, because there are no residual uncertainties for pre- and/or post-natal toxicity, exposure is not underestimated, and there is no evidence of increased susceptibility.

2. Endocrine Disruptor Effects

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) “may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other endocrine effects as the Administrator may designate.” Following recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC’s recommendation that EPA include evaluations of potential effects in wildlife. For pesticides, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

In the available human health toxicity studies on PBO, there was no toxicologically significant evidence of endocrine disruptor effects. In the available ecological toxicity studies on PBO, an avian reproduction study shows that PBO may cause decreases in adult and hatchling body weight and food consumption, number of eggs laid, and eggshell thickness. In addition, PBO may cause increases in number of eggs cracked.

When the appropriate screening and/or testing protocols being considered under the EDSP have been developed, PBO may be subject to additional screening and/or testing.

3. Cumulative Risks

The Food Quality Protection Act (FQPA) requires that the Agency consider available information concerning the cumulative effects of a particular pesticide’s residues and other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common toxic mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the substances individually. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding for PBO and any other substances. For information regarding EPA’s efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA’s Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA’s website at <http://www.epa.gov/pesticides/cumulative/>.

C. Tolerance Reassessment Summary

Table 22, 23, and 24 provide a summary of the PBO tolerance reassessment decision. Further tolerance explanation is provided after the table.

All references that indicate use in combination with another active ingredient, such as pyrethrins or n-octyl bicycloheptene dicarboximide (MGK-264), are removed, or decoupled from the tolerance expressions for PBO. All tolerances established for use on bags are being revoked as the last active product supporting this use was cancelled on October 10, 1989, and there are no data to support this use. The 40 CFR should be updated to reflect all of these changes as summarized below.

Current 40 CFR Citation	Action	Comment
§180.127(a)(2)(i) all parts	Remove	This section refers to PBO being used in conjunction with pyrethrins. All references to use with multiple chemicals is being removed from the CFR.
§180.127(a)(2)(ii) all parts	Remove	This section refers to PBO being used in conjunction with pyrethrins and MGK-264. All references to use with multiple chemicals is being removed from the CFR.
§180.127(a)(2)(iii)(A)	Retain	This tolerance for cereal grain will be kept as indicated in Table 23 below. Recodify under §180.127 (a)(2)
§180.127(a)(2)(iii)(B)	Remove	This is a tolerance for use on bags. The last registration for this use was cancelled in 1989 and there are no data to support this use.
§180.127(a)(2)(iii)(C)	Retain	This citation refers to another part of the CFR for MGK-264 that is being revised. In order to clarify the statement it will be stated in its entirety here. The exact statement and section number are indicated in Table 23 below. Recodify under §180.127 (a)(3)

§180.127(a)(2)(iii)(D)	Remove	This is a tolerance for use on bags. The last registration for this use was cancelled in 1989 and there are no data to support this use.
§180.127(a)(2)(iii)(E)	Remove	This refers to other sections that are being removed, so this section is not relevant once the other parts are revised.
§180.127(a)(2)(iv)	Remove	Old language not used in the CFR currently.
§180.127(a)(2)(v)	Retain	Recodify under §180.127 (a)(4)
§180.127(a)(3) all parts	Remove	This is a tolerance for use on bags. The last registration for this use was cancelled in 1989 and there are no data to support this use.

Table 23: Tolerance Reassessment Summary for PBO

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment [Correct Commodity Definition]
Tolerances Listed Under 40 CFR §180.127 (a)(1)			
Almond, postharvest	8	TBD ¹	
Apple, postharvest	8	TBD	
Barley, postharvest	20	TBD	[<i>Barley, grain, postharvest</i>]
Bean, postharvest	8	TBD	[<i>Bean, succulent, postharvest</i>]
Birdseed, mixtures, postharvest	20	TBD	
Blackberry, postharvest	8	TBD	
Blueberry (huckleberry), postharvest	8	TBD	[<i>Blueberry, postharvest</i>]
Boysenberry, postharvest	8	TBD	
Buckwheat, grain, postharvest	20	TBD	
Cattle, fat	0.1 (N)	TBD	
Cattle, meat byproducts	0.1 (N)	TBD	
Cattle, meat	0.1 (N)	TBD	
Cherry, postharvest	8	TBD	
Cocoa bean, postharvest	8	TBD	[<i>Cocoa bean, dried bean, postharvest</i>]
Coconut, copra, postharvest	8	TBD	
Corn (including popcorn), postharvest	20	TBD	[<i>Corn, field and pop, grain, postharvest</i>]
Cottonseed, postharvest	8	TBD	[<i>Cotton, undelinted seed, postharvest</i>]
Crabapple, postharvest	8	TBD	
Currant, postharvest	8	TBD	
Dewberry, postharvest	8	TBD	
Egg	1	TBD	
Fig, postharvest	8	TBD	
Flaxseed, postharvest	8	TBD	[<i>Flax, seed, postharvest</i>]

¹ TBD = To be determined. EPA notes that while additional data are needed to support certain tolerances, conservative assumptions have been used in the risk assessment and no dietary risks have been identified. Thus, EPA considers the tolerances reassessed.

Table 23: Tolerance Reassessment Summary for PBO

Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment [Correct Commodity Definition]
Goat, fat	0.1 (N)	TBD	
Goat, meat byproducts	0.1 (N)	TBD	
Goat, meat	0.1 (N)	TBD	
Gooseberry, postharvest	8	TBD	
Grape, postharvest	8	TBD	
Guava, postharvest	8	TBD	
Hog, fat	0.1 (N)	TBD	
Hog, meat byproducts	0.1 (N)	TBD	
Hog, meat	0.1 (N)	TBD	
Horse, fat	0.1 (N)	TBD	
Horse, meat byproducts	0.1 (N)	TBD	
Horse, meat	0.1 (N)	TBD	
Loganberry, postharvest	8	TBD	
Mango, postharvest	8	TBD	
Milk fat (reflecting negligible residues in milk)	0.25	TBD	
Muskmelon, postharvest	8	TBD	
Oat, postharvest	8	TBD	[<i>Oat, grain, postharvest</i>]
Oranges, postharvest	8	TBD	[<i>Orange, sweet, postharvest</i>]
Peach, postharvest	8	TBD	
Peanut (with shell removed), postharvest	8	TBD	[<i>Peanut, nutmeat, postharvest</i>]
Pear, postharvest	8	TBD	
Pea, postharvest	8	TBD	[<i>Pea, dry, seed, postharvest</i>]
Pineapple, postharvest	8	TBD	
Plum, prune, fresh, postharvest	8	TBD	
Potato, postharvest	0.25	0.25	The reassessed tolerance is based on data reflecting residues of PBO <i>per se</i> . Additional data may be required if PBO metabolites are included in the tolerance expression
Poultry, fat	3	TBD	
Poultry, meat byproducts	3	TBD	
Poultry, meat	3	TBD	
Raspberry, postharvest	8	TBD	
Rice, postharvest	20	TBD	[<i>Rice, grain, postharvest</i>]
Rye, postharvest	20	TBD	[<i>Rye, grain, postharvest</i>]
Sheep, fat	0.1 (N)	TBD	
Sheep, meat byproducts	0.1 (N)	TBD	

Table 23: Tolerance Reassessment Summary for PBO			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment [Correct Commodity Definition]
Sheep, meat	0.1 (N)	TBD	
Sorghum, grain, postharvest	8	TBD	
Sweet potato, postharvest	0.25	0.25	The preharvest use on stored raw sweet potatoes are supported by residue data translated from potatoes.
Tomato, postharvest	8	TBD	
Walnut, postharvest	8	TBD	
Wheat, postharvest	20	TBD	[Wheat, grain, postharvest]
Tolerance Listed Under 40 CFR §180.127(a)(2)(iii)(A)			
Grains, Cereal, Milled Fractions	10	10	
Tolerance Listed Under 40 CFR §180.127(a)(2)(iii)(B)			
Stored Dried Food (Multiwall paper bags (50 lbs +))	10	Revoke	This is a tolerance for use on bags. The last registration for this use was cancelled in 1989 and there are no data to support this use.
Tolerance Listed Under 40 CFR §180.127(a)(2)(iii)(C)			
Processed Food (food handling establishments)	10	10	Decouple pyrethrins tolerance from MGK-264 and PBO. The new tolerance should be stated as: “A tolerance of 10 ppm is established for residues of the insecticide synergist piperonyl butoxide in or on all food items in food handling establishments where food and food products are held, processed, prepared and/or served. Food must be removed or covered prior to use.”
Tolerance Listed Under 40 CFR §180.127(a)(2)(iii)(D)			
Processed Food (Cotton bags (50 lbs +) with waxed paper liners containing Stored Dried Food (4% fat or less))	10	Revoke	This is a tolerance for use on bags. The last registration for this use was cancelled in 1989 and there are no data to support this use.
Tolerance Listed Under 40 CFR §180.127(a)(3)(iii)(A)			
Processed Food (Stored Feed (Dried Feed from use on outer ply of multiwall paper bags 50 lbs or more))	10	Revoke	This is a tolerance for use on bags. The last registration for this use was cancelled in 1989 and there are no data to support this use.
Tolerance Listed Under 40 CFR §180.127(a)(3)(iii)(B)			
Stored Feed (Dried Feed (containing 4% fat or less) from use on cotton bags with waxed paper liners 50 lbs or more)	10	Revoke	This is a tolerance for use on bags. The last registration for this use was cancelled in 1989 and there are no data to support this use.
Tolerances Listed Under 40 CFR §180.905(a)(6)			

Table 23: Tolerance Reassessment Summary for PBO			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment [Correct Commodity Definition]
Raw Agricultural Commodities	Exemption	Revoke	Formerly established under 180.1001 (b). The Agency will not revoke this tolerance immediately, but will issue a DCI for the data. When the data have been reviewed and approved by the Agency, the appropriate crop group tolerances will be established concomitant with revocation of the exemption.

Table 24: PBO Tolerances to be Established Under 40 CFR §180.127			
Commodity	Current Tolerance (ppm)	Tolerance Reassessment (ppm)	Comment [Correct Commodity Definition]
Tolerances to be Established Under CFR §180.127(a)(1)			
Aspirated grain fractions	None	TBD ¹	

¹ TBD = To be determined. EPA notes that while additional data are needed to support certain tolerances, conservative assumptions have been used in the risk assessment and no dietary risks have been identified.

Tolerance exemption under CFR §180.1001(b)(4)

PBO is currently exempt from the requirements of tolerances when applied to growing crops in accordance with good agricultural practices [40 CFR §180.1001(b)(4)]. Based on the results of limited field trials reflecting preharvest uses, EPA recommends for the revocation of this tolerance exemption. The results of preharvest trials show detectable and variable residues of PBO *per se* (or PBO plus PBO metabolites, assayed collectively as hydroxymethyl dihydrosafrol) in/on nearly all raw agricultural commodities following applications of one formulation class (EC) at 1.0X the maximum seasonal rate the PBO Task Force II wishes to support for preharvest uses. Additional residue data reflecting preharvest uses will be required to confirm the tolerance reassessment. When the requested data have been evaluated, EPA will recommend for the revocation of the tolerance exemption in 40 CFR §180.1001(b)(4) concomitant with the establishments of crop group tolerances, if appropriate, in 40 CFR §180.127 to support all uses.

Tolerances Established Under CFR §180.127

Tolerances are established in 40 CFR §180.127 for residues of PBO *per se* [(butylcarbityl)(6-propyl piperonyl)ether] in/on: (i) plant commodities resulting from postharvest uses; (ii) livestock commodities; and (iii) food/feed items while in storage areas. The CAS name for PBO is: 5-[[2-(2-butoxyethoxy)ethoxy]methyl]-6-propyl-1,3-benzodioxole. EPA recommends the chemical name of PBO listed in 40 CFR §180.127 be changed to the CAS name. The tolerance expression will be updated in the CFR to read as follows: “Tolerances for residues of the insecticide synergist piperonyl butoxide [5-[[2-(2-butoxyethoxy)ethoxy]methyl]-6-propyl-1,3-benzodioxole] are established in or on the following food commodities:”. A list of

tolerances established for PBO along with our recommendations of changes to correct commodity definitions are presented in Table 22, 23, and 24.

The qualitative nature of the residue in plants has not yet been determined although the registrants have submitted acceptable plant metabolism studies conducted on three dissimilar crops (lettuce, cotton, and potatoes). The nature of the residue in livestock (poultry and ruminants) remains inadequately understood because additional data are required to upgrade previously submitted studies. The EPA Metabolism Assessment Review Committee (MARC) concluded the terminal residue of concern in plants and livestock (i.e., residues that need to be regulated or included in the tolerance expression) is PBO *per se*.

An improved method, HPLC/fluorescence method has been proposed to replace the existing colorimetric method listed in PAM Volume II for the enforcement of plant commodity tolerances. The new method can separately measure residues of PBO *per se* and PBO metabolites collectively determined as hydroxymethyl dihydrosafrol (HMDS). The HPLC/fluorescence method has been subjected to a successful independent laboratory validation and has been forwarded to ACL/BEAD for a method validation by Agency chemists. There are also several methods listed in PAM Volume II which can measure residues of PBO *per se* in livestock commodities.

The PBO tolerances for plant commodities, resulting from post-harvest uses [40 CFR §180.127(a)(1)], range from 0.25 ppm (potato and sweet potato) to 20 ppm (most cereal grains). The available data are inadequate to support many of the established tolerances resulting from post-harvest uses (except those uses for potato and sweet potato), and additional data are required for tolerance reassessment. The required post-harvest data for cereal grains will be translated to birdseed mixture since the use rate for birdseed mixture and cereal grains are identical.

PBO tolerances of 0.25 ppm for milk fat, reflecting negligible residues in milk, and 0.1 ppm for the fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep are established [40 CFR §180.127(a)(1)]. Tolerances of 1 ppm for eggs and 3 ppm for the fat, meat, and meat byproducts of poultry are also established [40 CFR §180.127(a)(1)]. Additional data are required to confirm the livestock commodity tolerances and to estimate residues expected from all possible exposure scenarios which include direct application to livestock, premise treatment, and oral treatment.

The remainder of tolerances and tolerance exemptions established in CFR §180.127 pertain to uses of PBO in food/feed storage areas.

- According to 40 CFR §180.127(a)(2)(i), PBO may be safely used in combination with pyrethrins for control of insects when used according to conditions specified in the same 40 CFR section.
- According to 40 CFR §180.127(a)(2)(ii), PBO may be safely used in combination with pyrethrins and N-octylbicycloheptene dicarboximide for insect control in accordance with 21 CFR 178.3730.

- According to 40 CFR §180.127(a)(2)(iii), a tolerance of 10 ppm is established for residues of PBO *per se* in/on: (A) milled fractions derived from cereal grains when present therein as a result of its use in cereal grain mills and in storage areas for milled cereal grain products; (B) dried foods when present as a result of migration from its use on the outer ply of multiwall paper bags of 50 pounds or more capacity; (C) foods treated in accordance with 21 CFR 178.3730; (D) dried foods that contain 4 % fat, or less, when present as a result of migration from its use on the cloth of cotton bags of 50 pounds or more capacity constructed with waxed paper liners; and (E) foods from treated food processing and storage areas provided the food is removed or covered prior to such use.

- According to 40 CFR §180.127(a)(2)(iv), to assure safe use of the pesticide, its label and labeling shall conform to that registered with the U.S. Environmental Protection Agency, and it shall be used in accordance with such label and labeling.

- According to 40 CFR §180.127(a)(2)(v), where tolerances are established on both raw agricultural commodities and processed foods made therefrom, the total residues of PBO in/on the processed food shall not be greater than that permitted by the larger of the two tolerances.

- According to 40 CFR §180.127(a)(3), PBO may be safely used in accordance with the following prescribed conditions: (i) It is used or intended for use in combination with pyrethrins for control of insects: (A) On the outer ply of multiwall paper bags of 50 pounds or more capacity in amounts not exceeding 60 milligrams per square foot; or (B) On cotton bags of 50 pounds or more capacity in amounts not exceeding 55 milligrams per square foot of cloth. Such treated bags are constructed with waxed paper liners and are to be used only for dried feeds that contain 4 percent fat or less; or (ii) It is used in combination with pyrethrins, whereby the amount of PBO is equal to 10 times the amount of pyrethrins in the formulation. Such treated bags are to be used only for dried feeds.

The tolerance regulations contained in 40 CFR §180.127(a)(2)(i) and 40 CFR §180.127(a)(2)(ii) establish that PBO may be safely used in combination with pyrethrins and N-octylbicycloheptene dicarboximide, respectively, for control of insects in food/feed processing areas and food/feed storage areas provided that the food/feed is removed or covered prior to use of the products. EPA concludes that no additional data for PBO are required to maintain the above tolerance regulations. This conclusion does not apply to pyrethrins and N-octylbicycloheptene dicarboximide because the labels for these pesticide chemicals were not examined in the generation of this Residue Chapter.

Adequate data depicting the magnitude of residues of PBO *per se* in food-handling establishments and food storage areas are available. These data indicate that the established tolerance of 10 ppm will not be exceeded in representative food commodities and surfaces that had been covered during space, contact, and intermittent spray aerosol treatments using representative soluble concentrate/liquid and pressurized liquid formulations. The submitted PBO master label provides adequate instructions which specify that food should be removed or

covered during treatment, and that all food processing surfaces should be covered during treatment or thoroughly cleaned before use.

No data are available to support uses of PBO on foods stored in multi-walled paper or cloth bags. The last active product with this use was cancelled in October 15, 1989. Therefore, the stored dried food tolerance in section 180.127(a)(2)(iii)(B), the two processed food tolerances in sections 180.127(a)(2)(iii)(D) and 180.127(a)(3)(iii)(A), and the stored feed tolerance in section 180.127(a)(3)(iii)(B) should be revoked.

Tolerances to be Established Under 40 CFR §180.127

The data requirements to support pre-harvest uses, that are recommended in this RED Chapter, are designed to support the establishments of crop group tolerances. Therefore, several crop group tolerances, if appropriate, will likely be proposed when the requested data have been reviewed. In addition, a tolerance for aspirated grain fraction needs to be proposed upon receipt of the requested residue data for this commodity.

Codex/International Harmonization

The Codex Alimentarius Commission has established several maximum residue limits (MRLs) for residues of PBO. The Codex MRLs are expressed in terms of PBO *per se* which is identical to the current U.S. tolerance expression. A numerical comparison of the Codex MRLs and the corresponding current U.S. tolerances for PBO is presented in Table 25. Canadian MRLs are presented in Table 26. Following completion of the RED the Agency will take steps to determine if harmonization of U.S. tolerances and certain Codex and Canadian MRLs can be achieved.

Codex		Current U.S. Tolerance, ppm
Commodity, As Defined	MRL (mg/kg)	
Cattle, kidney	0.3	0.1 for meat byproducts of cattle, goat, hog, horse, and sheep
Cattle liver	1	
Cattle meat	5 (fat)	0.1 for meat of cattle, goat, hog, horse, and sheep
Cereal grains	30 (Po ²)	8 ppm for oat and sorghum resulting from postharvest uses; 20 ppm for barley, buckwheat, corn, (including popcorn), rice, rye, and wheat resulting from postharvest uses
Citrus fruits	5	8 ppm for oranges resulting from postharvest uses
Citrus juice	0.05	
Dried fruits	0.2 (Po)	
Eggs	1	1

² Po = Postharvest

Table 25: Codex MRLs and Applicable U.S. Tolerances for PBO

Codex		Current U.S. Tolerance, ppm
Commodity, As Defined	MRL (mg/kg)	
Fruiting vegetables, cucurbits	1	
Kidney of cattle, goats, pigs, and sheep	0.2 (excluding cattle)	0.1 for meat byproducts of cattle, goat, hog, horse, and sheep
Lettuce, leaf	50	
Liver of cattle	1	0.1 for meat byproducts of cattle, goat, hog, horse, and sheep
Maize, oil, crude	80 (Po)	
Meat (mammalian) fat	2 (excluding cattle meat)	0.1 for fat of cattle, goat, hog, horse, and sheep
Milks	0.05	0.25 ppm for milk fat
Mustard greens	50	
Pea hay	200	8 ppm for pea resulting from postharvest uses
Pea vines (green)	400	
Peanut, whole	1 (Po)	8 ppm for peanut resulting from postharvest uses
Peppers	2	
Poultry meat	7 (fat)	3
Poultry, edible offal	10	3
Pulses	0.2 (Po)	
Radish leaves	50	
Root and tuber vegetables	0.5	0.25 ppm for potato and sweet potato resulting from postharvest uses
Spinach	50	
Tomato	2	8 ppm resulting from postharvest uses
Tomato juice	0.3	
Wheat	10 (Po)	20 ppm for barley, buckwheat, corn (including popcorn), rice, rye, and wheat resulting from postharvest uses
Wheat bran, unprocessed	80 (Po)	
Wheat flour	10 (Po)	
Wheat germ	90 (Po)	
Wheat wholemeal	30 (Po)	

¹ Po = Postharvest**Table 26: Canadian MRLs for PBO**

Commodity, As Defined	MRL (ppm)	Current U.S. Tolerance, ppm
Raw Cereals	20	8 ppm for oat and sorghum resulting from postharvest uses; 20 ppm for barley, buckwheat, corn, (including popcorn), rice, rye, and wheat resulting from postharvest uses

Table 26: Canadian MRLs for PBO		
Commodity, As Defined	MRL (ppm)	Current U.S. Tolerance, ppm
Almonds, apples, beans, blackberries, blueberries, boysenberries, cherries, cocoa beans, copra, crabapples, currants, dewberries, figs, gooseberries, grapes, guavas, huckleberries, loganberries, mangoes, muskmelons, oranges, peaches/nectarines, peanuts, pears, peas, pineapple, plums, raspberries, tomatoes, and walnuts.	8	8 ppm from postharvest uses
Dried codfish	1	none

Updated 40 CFR

The 40 CFR should be updated to incorporate all the changes specified above. Once these changes are made the CFR should be in the format listed below.

§180.127 Piperonyl butoxide; tolerances for residues

(a) General.

(1) Tolerances for residues of the insecticide synergist piperonyl butoxide [5-[[2-(2-butoxyethoxy)ethoxy]methyl]-6-propyl-1,3-benzodioxole] are established in or on the following food commodities:

[Insert list as specified in the tables above after all data to support these tolerances have been submitted and reviewed.]

(2) A tolerance of 10 ppm is established for residues of the insecticide synergist piperonyl butoxide in or on milled fractions derived from Grain, cereal when present as a result of its use in cereal grain mills and in storage areas for milled cereal grain products.

(3) A tolerance of 10 ppm is established for residues of the insecticide synergist piperonyl butoxide in or on all food items in food handling establishments where food and food products are held, processed, prepared and/or served. Food must be removed or covered prior to use.

(4) Where tolerances are established on both the raw agricultural commodities and processed foods made there-from, the total residues of piperonyl butoxide in or on the processed food shall not be greater than that permitted by the larger of the two tolerances.

(b) Section 18 emergency exemptions.

[Reserved]

(c) Tolerances with regional registrations.

[Reserved]

(d) Indirect or inadvertent residues.

[Reserved]

D. Regulatory Rationale

The Agency has determined that PBO is eligible for reregistration provided that the risk mitigation measures and label amendments specified in this RED are implemented. The following is a summary of the rationale for managing risks associated with the use of PBO.

1. Human Health Risk

a. Dietary (Food Only) Risk Mitigation

Acute Risk

Acute dietary (food only) risk does not exceed the Agency's level of concern; acute dietary risk estimates are 6% of the aPAD for the general U.S. population, and 20% for children 1-2 years old, the subgroup most exposed. Therefore, no mitigation is necessary for this scenario.

Chronic Risk

The chronic dietary (food and drinking water) risk is below the Agency's level of concern; risk estimated are 5% of the cPAD for the general U.S. population, and 12% of the cPAD for children 1-2 years old, the most exposed subpopulation. Therefore, no mitigation is necessary for this scenario.

b. Residential Risk Mitigation

i. Handler

In the residential handler exposure assessment a number of scenarios were assessed to estimate the exposure to homeowners handling products containing PBO. From the results of the residential handler assessment, there are no residential risks of concern when PBO is mixed, loaded, applied, or handled by homeowners. Therefore, no mitigation is necessary for these scenarios.

ii. Post-Application

A number of post-application residential scenarios were assessed either quantitatively or qualitatively for adults and children exposed to PBO indirectly after application. Of these scenarios, three post-application residential scenarios assessed were potentially of concern to the Agency including: 1) broadcast dust applications to carpets, 2) applications from indoor metered release devices, and 3) applications from outdoor residential misting systems. To address the potential risks associated with these post-application scenarios, the following mitigation measures are to be implemented.

Dusts - Broadcast Applications to Carpets

Applying dusts to carpets over a wide area can lead to exposure to children through incidental oral exposures. Most of the labels containing this type of application indicate that

the dust needs to be vacuumed after application. The Agency has concerns form the potential incidental oral exposure children could have from this type of broadcast application to large carpeted areas since there is no information to determine how much PBO is removed from the carpet after vacuuming and an unknown amount of dust available for exposure to children. To reduce exposure to children from broadcast dust applications to carpets, the PBOTF II has agreed to restrict carpet applications to spot treatments no greater than 3 feet by 3 feet in area.

PBO is also used on turf, and so an incidental oral assessment was conducted for use on turf which is considered a conservative risk estimate including 3 separate incidental oral exposure activities and assumes the exposures occur simultaneously. The turf scenario methodology, which has been peer reviewed and is better understood than the carpet dust scenario, includes incidental oral exposure to pesticide on turf from (1) hand to mouth activities, (2) object to mouth activities, and (3) ingesting soil particles. The aggregate of all three of these incidental oral turf exposures is above the Agency's target MOE of 100 with an MOE of 4800. Given the conservative nature of the turf exposure scenario, it is unlikely that the magnitude and frequency of exposure to small spot treatments (3 sq ft) of dust formulations of PBO would result in exposure estimates equal or greater than estimated for the residential lawns. Since there are no incidental oral risks of concern from the turf scenario, and the PBOTFII has agreed to reduce the amount of potential exposure to children by restricting applications to spots only, the Agency is not requiring and additional data at this time.

Indoor Metered Release Devices

There are potential risk concerns for post-application short- and intermediate-term exposures following indoor applications with metered release devices. The MOEs range from 12 to 240 and are less than the target MOE of 300. The risk calculations for the metered release scenarios are conservative because it was assumed that the aerosol spray would remain airborne until they were removed by ventilation and the effect of aerosol spray settling was not considered. Aerosol spray settling could be a major factor depending upon the aerosol droplet size and rate of evaporation. Information regarding the aerosol droplet size and evaporation rate could be used to refine the risks, particularly for the residential scenarios where the ventilation removal rate is probably slower than the settling rate.

The master label indicates that the metered release system application rate of 0.05 lb ai/1000 ft³/day can be used in domestic dwellings and indoor sites. Commercially available aerosol dispensers that appear to be intended for the residential areas apply much less than the master label rate. These dispensers apply aerosols from 6.4 oz cans at 15 minute intervals and each can will deliver approximately 3000 applications in a month to a 6000 ft³ space. The application rate for these dispensers is approximately 0.0001375lb ai/1000 ft³/day if continuous operation is assumed.

Therefore, to reduce the risks to bystanders of sensitive population, the PBOTFII has agreed to prohibit the use in residential areas and remove the following use sites from their metered release device product labels: day care centers, nursing homes, and schools.

Outdoor Residential Misting Systems

As stated in Section 3, the Agency considered post-application exposure to adults and toddlers who are exposed to PBO from an outdoor residential misting system pesticide application. These systems are fairly new to the pesticide market, and vary in their system design. Based on available information at the time and outreach to the PBO registrants, other stakeholders, and review of labels currently registered for use in these systems, the Agency used the following assumptions in the PBO risk assessment:

- The spray droplets would be inhaled over a period of 5 hours for adults or 3 hours for toddlers, based on information from the Exposure Factors Handbook (EPA, 1997) on how much time individuals spend outside.
- The initial concentration is based upon instantaneous release and mixing into a fixed space with a height of 8 feet.
- The exposure is assumed to encompass 2 spray events that occur in the morning or evening.

Based on these assumptions, the Agency has identified a potential risk of concern for toddlers over the short-/intermediate-term exposure duration. The target short-/intermediate-term inhalation MOE is 300, and the toddler bystander assessment calculated an MOE of 190.

The inhalation exposure durations used for the mosquito mister scenarios (5 hours/day for adults, 3 hours/day for toddlers) represent the 95th percentile values for time spent outdoors at a restaurant/picnic area (USEPA, 1997). During this exposure period the individual is assumed to be exposed to 2 spray events each lasting a period of 1 minute. Although this spray duration is considered reasonable, lower spray durations (i.e., 20- or 30-second durations) may be more representative of actual system rates, particularly for extended exposure durations. Standard label language for use rates could provide a more refined risk assessment. Currently, the labels do not specify the maximum daily application rates.

The Consumer Specialty Products Association (CSPA) submitted a discussion paper outlining some use information associated with these outdoor residential misting systems. Mosquito mister risks were calculated based on automatic applications of 4 sprays per day. It was noted in the CSPA discussion paper that the systems could be manually activated by the homeowner to apply additional sprays. Although re-filling and maintenance costs would likely limit homeowner use, label language indicating appropriate daily spray cycles and maximum daily application rates is also needed to address current concerns over excessive use.

Therefore, to mitigate the risks for toddler bystander exposure from intermediate-term outdoor residential misting systems, the PBOTF II has agreed to restrict the maximum allowable daily rate to 0.00058 lbs PBO/1000 cubic feet/day, which is the rate where risks to children are not a concern to the Agency. Further, the PBOTF II has agreed to submit data to allow the Agency to better understand these systems and refine the risk assessment. Information on use and usage of outdoor residential misting systems, as well as air concentration and droplet size data will be submitted. The PBOTF II has also agreed to add the label statements listed in the label table in Section V of this document. These label statements will restrict the maximum allowable daily rate that can be applied, specify how the systems should be installed to reduce

off-site drift, and specify measures to make the system reservoirs less accessible to children or other individuals.

Future Steps for Outdoor Residential Misting Systems

The distribution or sale, and use of pesticides in outdoor residential misting systems are subject to several statutory requirements. At this time, PBO, pyrethrins, and permethrin appear to be the only chemicals known to be used in outdoor residential misting systems; however, it is possible that other pesticide registered for residential outdoor use might also be used in similar systems. Section 2(ee)(3) of FIFRA permits the use of any application methods that are not prohibited by the pesticide's labeling; however, the application must only be to sites specified by the labeling and at no more than the maximum dosage rates specified by the labeling. Since most pesticide labels do not explicitly prohibit use in outdoor residential misting systems, other chemicals that target similar pests could be used in these misting systems. The Agency is not aware of other pesticides being used in outdoor residential misting systems, and therefore, has not assessed the potential risks to homeowners associated with use of pesticides other than PBO, pyrethrins, and permethrin.

All PBO, pyrethrins, and permethrin registrants that do not support outdoor residential misting systems use for their products will be expected to amend their Manufacturing Use Product label to state the following, "This product must not be formulated into an end use product for use in outdoor misting systems." Additionally, all registrants of PBO end-use products must either include a statement prohibiting use in an outdoor residential misting system, for example, "This product must not be used in an outdoor residential misting system," or include separate and specific instructions for use in outdoor residential misting systems, including the maximum application rate per day, use directions, and restrictions specified in Section V. Although this action will only address PBO, pyrethrins, and permethrin products, the Agency plans to issue broader guidance pertaining to use of outdoor misting systems and the pesticides which can be used in these systems as part of its on-going effort to standardize the way in which these systems are used.

By definition in FIFRA Section 2(e)(1) and (gg), leaving unapplied pesticide at a use site constitutes the distribution or sale of a pesticide. In order to be in compliance with FIFRA, companies which sell, install, and service outdoor residential misting systems must ensure that one of the following transactions occur when providing these services:

- The unopened registered pesticide is distributed or sold to the use-site owner prior to mixing and loading into the equipment; or
- The diluted registered pesticide is distributed or sold as a custom blend in accordance with EPA's custom blending policies at FIFRA Compliance Program Policies Nos. 3.4 and 7.1 of the FIFRA Compliance Program Policy Compendium; or
- The diluted pesticide is registered and is distributed or sold to the use-site owner prior to loading into the equipment.

Several issues, in addition to those discussed above, have been raised to EPA Regions through State FIFRA Issues Research and Evaluation Group (SFIREG) issue papers, stakeholder forums and comments, and other sources regarding the use of these systems. These issues include, but are not limited to, the potential for inadvertent exposure and risks to residents, misuse of the systems and pesticide products, offsite drift and potential exposure to non-target organisms, and pest resistance issues. The Agency is aware of a cooperative effort lead by the National Pest Management Association involving state and industry stakeholders, and pest management professionals to standardize these systems and address the issues raised above, and intends to continue to address these on-going issues through continued involvement and discussions with the States, industry and stakeholder groups.

The Agency will have a 60-day comment period after the publication of the RED to solicit feedback on the label language in Section V and the issues discussed above.

c. Aggregate Risk Mitigation

For PBO, aggregate risk assessments were conducted for acute (one day) and chronic (one year or more) food and drinking water exposures. The short-term aggregate exposures from food, water, and residential routes associated with application of PBO was also calculated since there was a common toxicity endpoint of decreased weight gain identified for those routes of exposure.

i. Acute and Chronic Aggregate Risk (Food + Water)

Acute DWLOC

Acute DWLOCs were calculated based on acute dietary exposure estimates and default body weights and water consumption figures. The EDWCs for both surface water and groundwater are well below the acute DWLOCs for the general U.S. population and all other population subgroups indicating that acute aggregate exposure to PBO in food and water is not a concern. Therefore, no mitigation is necessary for this scenario.

Chronic DWLOC

Chronic DWLOCs were calculated based on the chronic dietary exposure estimates and default body weights and water consumption figures. The EDWCs for both surface water and groundwater are well below the chronic DWLOCs for the general U.S. population and all other population subgroups indicating that chronic aggregate exposure to PBO in food and water is below the Agency's level of concern for these populations. Therefore, no mitigation is necessary for this scenario.

ii. Short-Term Aggregate (Food + Water + Residential)

The short term aggregate risk for PBO was calculated by adding exposure estimates from dietary, drinking water, and incidental oral exposure pathways for children age 1-2, the highest exposed sub-population, and comparing them with model based EDWCs. The lowest short term

DWLOC (8500 µg/L) for children 1-2 years old, which is higher than the surface water EDWC (60 µg/L) and the ground water EDWC (0.26 µg/L), and therefore does not result in a risk of concern. Therefore, no mitigation is necessary for this scenario.

d. Occupational Risk Mitigation

Occupational exposure assessments are completed by the Agency considering the use of baseline PPE and, if warranted, for handlers, increasing levels of PPE and engineering controls in order to estimate the potential impact on exposure and risk. The target MOEs for PBO are 300 for short- and intermediate-term inhalation exposures, and 1000 for long-term inhalation exposures.

i. Handler Risk Mitigation

Wettable Powders – Agricultural

There are inhalation risk concerns for agricultural mixers and loaders using wettable powder PBO products at baseline attire. Therefore, to mitigate the risks to mixers and loaders of wettable powders in agricultural settings, the PBOTFII has agreed to package wettable powders only in water soluble bags. When wettable powder products are packaged in water soluble bags, there are no risks of concern for mixers and loaders in agricultural settings. At this time, the Agency is not aware of any wettable powder products being actively marketed in the U.S. If wettable powders are sold in the future all products must comply with the water soluble bag and other requirements established in this decision document.

Wettable Powders – PCO Handlers

There are inhalation risk concerns for pest control operators (PCO) mixers and loaders handling wettable powder PBO products at baseline attire. Therefore, to mitigate the risks to PCO mixers and loaders of wettable powders, the PBOTFII has agreed to repackage wettable powders in water soluble bags. Even when water soluble packages are used by PCOs, there is still a risk of concern for crack and crevice applications with wettable powders. Therefore, to mitigate this risk, the PBOTFII has agreed to reduce the indoor crack and crevice treatment rate from 2.2 lbs ai/1000 square feet, to 0.56 lbs ai/1000 square feet. At this lower rate and with water soluble bags, there will be no risks of concern for PCO mixing, loading, and applying wettable powders.

Indoor Handheld Equipment (including thermal, cold, and ULV foggers)

Hand held fogging equipment was not included in the Phase 5 PBO risk assessment. Two studies measuring exposure from fogging have since been considered by the Agency. The exposure values estimated from the two studies differ greatly depending on the type of equipment, duration of application, size of fogging area, and air flow. One study with the pyrethroid prallethrin (MRID 45869301) was conducted to estimate exposure from a short (6 minute) fogging application in a small space. Another study conducted in a Florida greenhouse (MRID 40350501) reflected applications in greenhouses, and may be more appropriate to estimate exposure for greenhouse and warehouse applications. Due to the uncertainty in fogging

practices with PBO, the Agency is requiring use and usage information to show if the existing data is satisfactory to calculate exposure values from fogging with PBO. Based on the review of this use and usage data, the Agency will determine if further fogging exposure data is needed.

Therefore, to further characterize the inhalation risk to applicators using handheld fogging equipment, the Agency is requiring use and usage data on fogging applications. Based on review of this data the Agency may require additional exposure data in the future. A dust-mist respirator (PF10) will be required in the interim to address the Agency's immediate inhalation risk concerns.

Dusts Applied through Power Dusters - Agricultural and PCO Handlers

The Agency was not able to assess scenarios involving dust applications with power dusters because there are no exposure data to represent this application method. Power dusters could potentially pose inhalation risk. Due to a lack of data on this exposure scenario and no interest in supporting this application method from the PBOTFII, EPA has determined that this application scenario is not eligible for reregistration. If data are submitted to support this application method, EPA will reconsider this decision in the future. Dust product labels must prohibit use of power dusters.

Dusts Applied through Bulb Dusters

The Agency was not able to assess scenarios involving dust applications with bulb dusters because of a lack of data. Bulb dusters are only used for crack and crevice treatments, which reduces the possible exposure to an applicator. Due to small amounts of dust used in this application method, the exposure is expected to be negligible. Therefore, no mitigation or data are required for this scenario.

Forestry Applications

Applications to forest areas are made at a higher rate than was assessed for any other scenario. Other agricultural applications are made at the rate of 0.5 lbs ai/acre, while applications to forest areas are made at the rate of 1.25 lbs ai/acre. There are inhalation risks of concern for mixers and loaders supporting aerial applications with liquid and wettable powder formulations at baseline attire. The addition of a dust-mist (PF5) respirator would eliminate inhalation concerns from this scenario. Therefore, the Agency is requiring all mixers and loaders supporting aerial application to forests with liquids to wear a dust-mist (PF5) respirator. All applications to forest areas with wettable powder formulations will be prohibited.

Indoor Crack and Crevice Treatments with Low Pressure Handwand

There are inhalation risks of concern for PCO mixers, loaders, and applicators using a low pressure handwand making indoor crack and crevice treatments. Therefore, to mitigate these concerns the PBOTFII has agreed to reduce the rate from 2.2 lbs ai/1000 square feet to 0.56 lbs ai/1000 square feet. At this new rate, there will be no risks of concern for PCO handlers of making crack and crevice applications.

High Pressure Handwand Applications in Enclosed Areas (Greenhouses) - Agricultural

There are inhalation risks of concern for agricultural mixers, loaders, and applicators using a high pressure handwand for applications to enclosed areas like greenhouses. Therefore, to mitigate these concerns the PBOTFII has agreed to require applicators to wear a dust-mist (PF5) respirator when making applications in enclosed areas like greenhouses. With this additional PPE, there will be no risks of concern for agricultural handlers making high pressure handwand applications in enclosed areas.

PCO Long-Term Handler Assessments

There are inhalation risks of concern for PCO handlers in some of the assessed long-term scenarios including making applications with low pressure handwands for crack and crevice treatments, and aerosol applications for indoor space spray applications.

PBO is used to control a large number and a wide variety of pests and labels do not restrict or preclude repeated applications or long-term use. Given the potential for multiple applications and long-term use for occupational handlers, inclusion of a repeated use/long-term exposure for pest control operator and mosquito abatement scenarios is considered reasonable. The results of the worker exposure assessment indicate that certain pest control operator scenarios (i.e., mixing/loading/applying and/or aerosol application) result in MOEs less than the target MOE of 1000 for long-term exposure.

However, it is important to note that for pest control operators and mosquito abatement scenarios, assuming full day, long-term application for each application method is likely to significantly overestimate actual exposure. Based on data on usage of likely PBO containing pesticides presented in the National Pest Management Association Survey, these assumptions would result in a significant overestimate of exposure for PCOs. Similarly, assuming continuous usage of PBO containing pesticides for mosquito abatement applications would also significantly overestimate total exposure based on personal communication with mosquito control district officials regarding current usage of these products. Therefore, no mitigation is necessary for these scenarios.

Aerosol Applications for Indoor Space Sprays – PCO Handlers

The registrants have requested a rate increase for aerosol cans applied by PCOs, from 0.025 lbs ai/ 16 oz can, to 0.05 lbs ai/ 16 oz can.

At this higher rate, the MOE for the aerosol space spray scenario would still fall above our target for short-term risk. No intermediate-term exposure is expected from this use based on use information provided by the PBOTFII. The assessment assumed each PCO handler applied 14 cans of PBO pesticide containing PBO everyday for both a short-term (30 day) and an intermediate-term (30 day to 6 month) duration. This is a conservative estimation of the amount of PBO a PCO handles over the intermediate term. Therefore, for the aerosol application scenario the Agency will allow the PBOTFII to raise the rate to 0.05 lbs ai/16 oz can.

The 0.025 lbs ai/16 oz can rate for the aerosol application was also used in the residential post-application assessment. The MOE for this scenario was 600 for children. A rate increase would still result in an MOE above our target of 100 and not a concern for the Agency.

ii. Post-Application Worker Risk Mitigation

Metered Release Devices – Dairy Barns

The Agency has similar concerns for post-application short- and intermediate-term exposures from these systems as described in the occupational post-application section of this chapter. According to the PBO Master Label, PBO is used as space sprays in a wide variety of indoor areas such as barns, greenhouses, food storage areas, food processing areas, restaurants and residences. A scenario that involves a metered release into a dairy barn was evaluated to assess these exposures because PBO is commonly used in dairy barns and because the ventilation characteristics of dairy barns are relatively well defined. The MOE for metered release devices in occupational areas like dairy barns was calculated to be 62 with a target of 300 for both short- and intermediate-term exposures. Risks are lower for these occupational scenarios than for residential settings due to the fact that the occupational areas generally have a greater ventilation capacity and the risk assessment assumes a higher number of air changes per hour in these settings.

Therefore, in order to refine the risk assessment for metered release devices in occupational settings, the Agency is requiring additional usage information about metered release device products, as well as requiring label changes which are included in Section V. Some products labeled for use in occupational areas are also labeled for use in residential settings and areas where children may be present. Therefore, as mentioned in the residential metered release device section above, the PBOTF II has agreed to remove the following use sites from metered release device product labels: day-care centers, nursing homes, schools, and hospitals.

2. Non-Target Organism (Ecological) Risk Management

a. Aquatic Organisms

Agriculture

There were exceedences for acute exposure for several aquatic species exposed to PBO from agricultural applications including amphibians (RQs 0.76 to 1.1), estuarine/marine invertebrates (RQs <0.05 to 0.33), freshwater fish (RQs <0.05 to 0.08), and freshwater invertebrates (RQs <0.05 to 0.31).

There were also chronic exceedences for aquatic organisms exposed from agricultural applications including freshwater fish (RQs <1.0 to 3.6) and freshwater invertebrates (RQs <1.0 to 5.1).

A sensitivity analysis was conducted with the scenario that produced the highest EECs (Florida peppers with aerial application). The EEC appears to be proportional to both the application rate (lb/acre) and the number of applications. A decrease from 0.5 lb/acre to 0.25 lb/acre decreased the EEC by about half. Similarly, a decrease in number of application from 10 to 5 decreased the EEC by about half.

An increase in the application interval from 3 to 6 days had little effect on the EEC, but the longer time averages dropped somewhat (21-day average from 153 ppb to 140, and 60-day average from 142 ppb to 120). An increase to ten-day application intervals reduced the 21-day average EEC to 104 ppb, and the 6-day average to 90.5 ppb. The relatively small changes in time-averaged concentrations versus changed application intervals are likely due to the large number of applications allowed (10).

The maximum rate for all agricultural crops (0.5 lbs ai/acre) is not expected to be typically applied at this rate on all crops. PBO is used on a wide variety of crops, and the typical application parameters can vary greatly depending on the commodity, but will never exceed the modeled maximum agricultural rate of 0.5 lbs ai/acre. Applying PBO at rates and re-application intervals lower than the maximum assessed values will decrease the potential risk to aquatic organisms.

Currently there are label restrictions on some, but not all product labels indicating the application frequency and rate. All product labels will be revised to include the following information:

- No more than 10 applications per season.
- Do not reapply within 3 days except under extreme pest pressure.
- In case of extreme pest pressure, do not reapply within 24 hours.

Stating these imitations on all product labels will promote more judicious use and will likely reduce the amount of PBO in the environment.

Wide Area Mosquito Abatement

There were slight exceedences for acute exposure for several aquatic species exposed to PBO from mosquito abatement applications including freshwater invertebrates (RQ = 0.15), estuarine/marine invertebrates (RQ = 0.15), and amphibians (RQ = 0.36).

Currently there are label restrictions on some, but not all product labels with specific application parameters. Therefore, to address the risks from wide area mosquito adulticide applications, the PBOTFII agreed to the following restrictions in accordance with PR 2005-1:

- Droplet size for aerial applications: $Dv_{0.5} < 60$ microns and $Dv_{0.9} < 80$ microns
- Droplet size for ground applications: $Dv_{0.5} < 30$ microns and $Dv_{0.9} < 50$ microns
- Release height: 100 feet for airplane, 75 feet for helicopter
- Yearly application rate: 2.0 lbs ai/acre/year
- Wind Speed: Apply only when wind speed is greater than or equal to 1 mph.

Down the Drain

There were no risks of concern identified in EPA's assessment attributed to PBO in domestic wastewaters. Therefore, no mitigation is needed.

Spray Drift

As a result of AgDrift modeling for aerial applications to both pond and wetland scenarios, there were listed species LOC exceedences for freshwater invertebrates (RQ = 0.18), amphibians (RQ = 0.43), and estuarine invertebrates (RQ = 0.18). There was also an exceedence for listed amphibian species from ground spray applications (RQ = 0.11).

All labels are being required to be updated with the following spray drift language to address concerns of drift to non-target organisms:

- Wind speed: "Do not apply at wind speeds greater than 10 mph at the application site."
- Droplet size: "Apply as a medium or coarser spray (ASABE standard 572)."
- Temperature inversions: "Do not make any type of application into temperature inversions."
- Release height for ground applications: "Do not release spray at a height greater than 4 feet above the ground or crop canopy."
- Release height for aerial applications: "Do not release spray at a height greater than 10 feet above the ground or crop canopy."

Other Non-Agricultural Uses

The Office of Pesticide Programs (OPP) generally tries to estimate pesticide exposure through all significant routes of exposure from both agricultural and non-crop uses. However, the ecological risk assessments for pyrethrins, pyrethroids, and the synergists like PBO, focus predominantly on the agricultural uses for these insecticides, because pesticide transport models are available to estimate potential aquatic exposure. Based on laboratory toxicity tests with terrestrial and aquatic animals, aquatic exposure would be more likely to cause adverse effects in the environment.

However, sales data indicate that non-crop uses of PBO comprise a much larger fraction of total use than agricultural uses. The use of pyrethrins, pyrethroids, and synergists in urban and suburban settings has increased since the phase-out of these uses of the organophosphate insecticides diazinon and chlorpyrifos. Outdoor non-crop uses of PBO include landscape maintenance and homeowner lawn and garden use. Indoor uses include insect control, and treatment of pets and clothing.

The Agency uses a "Down-the-Drain" model to perform a screening aquatic risk assessment for indoor uses of pesticides. In these simulations, waste water containing pesticide residue from pet shampoos or treated clothing flows into a building drain and passes through a sanitary sewer and publicly owned treatment works (POTW) before being discharged to surface

water. However, no analogous exposure model has been developed to allow a similar screening assessment for pesticides applied in an outdoor urban setting. As a result, the Agency has had to take a qualitative approach to characterize the potential aquatic risk from urban and suburban use of pyrethrins, pyrethroids, and synergists.

For outdoor urban uses it is assumed that runoff water from rain and/or lawn watering may remove pesticide to storm sewers and then directly to surface water. Conceptually, a greater contribution to contamination of surface water bodies would be expected from application to impervious surfaces such as walkways, driveways or the sides of buildings than to lawns or bare ground. This is especially so for the pyrethrins and pyrethroids, given their strong affinity to bind to organic carbon in soils. However, the Agency has not identified a model which can simulate the different application methods for urban use and the physical representation of the urban landscape, storm sewer and receiving water configuration.

There are models available that can be calibrated to simulate sites and pesticides for which extensive flow and pollutant data have been collected in advance. The HSPF/NPSM model, for instance, which is included in the Office of Water's BASINS shell, has been used to calibrate stream flow and copper pesticide use data to simulate loading of these pesticides consistent with concentrations measured in surface water monitoring. Risk assessors with the California Department of Environmental Protection confirmed in conversations with the Agency that they also have used watershed models calibrated to previously collected flow and pesticide monitoring data, but that they did not know of any models capable of predicting concentrations of pyrethrins and pyrethroids that might occur because of outdoor urban uses.

Development of a screening model which could simulate the fate and transport of pesticides applied in an urban setting would require a large body of data which is currently unavailable. For instance, an urban landscape cannot be simulated as easily as an agricultural field. The PRZM model simulates runoff from an agricultural field using readily available data describing surface soil characteristics and laboratory data detailing the persistence and mobility of pesticides in these soils. The agricultural field simulated is homogeneously planted to a single crop, and soil and water are transported from the field to a receiving water body with dimensions consistent with USDA farm-pond construction guidelines.

By contrast, an urban landscape or suburban housing development consists of impervious surfaces such as streets and sidewalks, and permeable surfaces such as lawns and parkland. One could expect much greater mobility for pesticides applied to impervious surfaces, but laboratory soil metabolism studies may not provide an accurate measure of the persistence of pesticides on these surfaces. The path runoff water and eroded sediment might take is less obvious for an urban setting than an agricultural field. First, an urban landscape cannot be considered homogeneous, as the proportion of impervious and pervious surfaces varies for different locations. In addition, the flow path of runoff water and sediment is not necessarily a direct path over land, but can pass below ground through storm sewer networks, or be directed or slowed by pumping stations or temporary holding ponds.

The timing and magnitude of urban uses is less well defined than agricultural uses. While agricultural uses would occur within a predictable window during the growing season, the

need for urban uses could occur at different times each year, and might occur at different times within the same watershed. In addition, since records of how and to what extent pyrethrins and pyrethroids are applied by homeowners are less well defined than for professional applications, it is harder to estimate the total load to model.

Monitoring Data

The Agency considers surface water monitoring data in addition to modeling results when they are available. However, surface water monitoring for PBO has been limited. PBO is always used with another chemical, commonly either pyrethrins or the synthetic pyrethroids.

In a Sacramento County monitoring study targeting PBO and pyrethrins, water samples were collected after mosquito adulticide applications in the Sacramento metropolitan area. In samples collected up to 10 hours after application there were detects of PBO and pyrethrins from in the ppb range, similar to modeling predictions in the PBO and the pyrethrins mosquito adulticide assessment. Samples were also collected the day after application and measured lower or no concentrations for both active ingredients. This indicates both chemicals appear to dissipate fairly rapidly in the water column. The co-occurrence of PBO and pyrethrins in some of these first samples is an indication of direct application to water and not transport by runoff.

There has been limited monitoring for the pyrethroids, but recently researchers from the University of California- Berkeley have published studies which reported transport of pyrethroids to stream bed sediment as a result of urban uses. In 2004, Weston, et al. collected sediment from creeks draining a residential area in Rosedale, California. The sediments were analyzed for 7 pyrethroids (including two currently in the reregistration process), as well as for other insecticides. All of the pyrethroids were detected in the bed sediment from at least one sampling location. The researchers exposed the aquatic amphipod *Hyalella azteca* to the 21 sediment samples they collected; pesticide concentrations in 9 of these samples were sufficient to cause 90% mortality in the amphipods after a 10-day exposure. The concentrations of pyrethroids detected in the sediments were above the level expected to cause 50% mortality in *H. azteca*, suggesting that the pyrethroids were responsible for the observed toxicity.

In a subsequent study, Weston, et al. collected samples from 15 urban creeks in California and 12 in Tennessee. Toxicity to *H. azteca* was observed at least once with sediments taken from 12 of the 15 California sampling sites. In most cases, the toxicity could be accounted for by the concentrations of pyrethroids detected in the sediment. Pyrethroids were rarely detected in the Tennessee sediment samples, and exposure to the Tennessee sediments did not prove to be toxic to *H. azteca*. The Weston studies did not sample for PBO.

The Weston, et al. studies indicate that urban uses of pesticides can lead to surface-water contamination, including contamination by pesticides that would bind almost completely to soil in an agricultural setting. Since PBO is commonly formulated with the pyrethrins or the synthetic pyrethroids, efforts to better understand the conditions under which pyrethroids and pyrethrins might be transported to surface water would help improve our assessment of the scenarios in which PBO might contribute to increased risk to aquatic organisms.

The results of the Weston, et al. studies have led a number of organizations, such as the California State Water Resources Control Board (SWRCB) to submit comments to the Agency calling for mitigation measures to prevent surface-water contamination. However, the lack of data and information to develop an urban pesticide transport model also makes it difficult to identify whether risks may exceed some LOCs, and appropriate mitigation at this time. The Agency is committed to develop mitigation options during the reregistration process, and to identify steps which can be taken to allow a greater understanding of potential ecological risk from urban use.

One reason that broad mitigation measures cannot be adopted during reregistration is that not all of the chemicals of concern are going through reregistration at this time. If use restrictions were placed on only a few of these chemicals, it would likely be replaced with another chemical with a similar registered use. It would be useful, as some commenters have suggested, performing a risk assessment for all of the pyrethrins, pyrethroids, and synergists at the same time. The Weston papers indicated that the sediments which proved toxic to the tested aquatic invertebrate were contaminated not only with the chemicals undergoing reregistration, but also pyrethroids such as bifenthrin and lambda-cyhalothrin.

A number of steps are planned for the intervening years which should improve the Agency's ability to assess the level of aquatic exposure to pesticides such as pyrethrins, pyrethroids, and synergists from urban use. One step is to better identify what conditions in an urban setting might lead to greater vulnerability to transport to urban water bodies. Although the Weston paper reported sediment toxicity from samples from California but not Tennessee, the authors could only speculate what differences in use or geography made an area more vulnerable to exposure than the other.

Further investigation into the dominant urban uses and application practices of pyrethroids and pyrethrins, and PBO by association, around the country would also help provide a clearer picture of relative vulnerability. The California SWRCB commented that structural pest control is likely a major source of pyrethroids in urban runoff, and suggested best management practices (BMP). The Pyrethroid Working Group (PWG) indicated that irrigation of lawns in areas of California with little rainfall during the application season could be a major contributor, and has contacted organizations such as Responsible Industry for a Sound Environment (RISE) and the Coalition for Urban/Residential Environmental Stewardship (CURES) to develop BMPs as part of their product stewardship plan. As further sediment monitoring studies are published reflecting various parts of the country with different weather and pest pressures, more detailed usage data will make it easier to correlate the causes of pyrethrins, pyrethroids, and synergist contamination of surface water with use practices.

The Agency will also continue in its efforts to develop a screening model for urban pesticide uses. Advances in the resolution of GIS databases may allow better representation of the impervious and pervious portions of a typical urban landscape. As it becomes clearer which uses are most likely to lead to transport of pyrethrins, pyrethroids, and synergists to surface water, the conceptual model of how urban transport should be simulated will be more focused.

The Agency will evaluate available published literature and call-in data to resolve data gaps to ensure a robust comparison of the potential ecological risk of all the pyrethrins, pyrethroids, and synergists during Registration Review. Toxicity data cited by several commenters from published literature are included in the Agency's ECOTOX database. The Agency will evaluate the quality of studies to identify those to be included in the risk assessments during Registration Review.

Stewardship Language

While the Agency cannot currently assess the potential risks to aquatic organisms from non-agricultural uses of PBO, the Agency is still seeking to reduce the potential drift and run-off of PBO into aquatic habits through explicit directions for use on both professional and consumer use products for use in residential settings. These use directions include best management and stewardship practices which are formulation specific, and will serve to reduce the potential run-off and drift that can occur from applications of these products. Label statements implementing these measures are listed in the "direction for use" section of the label table in Section V of this RED document.

b. Terrestrial Organisms

There are LOC exceedences using the maximum application rate of 0.5 lbs ai/acre for chronic exposure to birds (RQs <1.0 to 3.1), and chronic exposures for mammals using both the maximum Kenaga EEC values (RQs <1.0 to 4.5) and the average Kenaga EEC values (RQs <1.0 to 1.6).

All product labels will be revised to include the maximum application rate, application frequency, and maximum applications per season. These measures will reduce the amount of PBO in the environment.

c. Ecological Risk from Mixtures

The Agency has reviewed data that show the toxicity and risk from PBO formulated with other insecticides, specifically the pyrethrins or synthetic pyrethroids, appeared to be higher than the toxicity or risk from either of the individual active ingredients separately for certain species. When PBO is mixed with organophosphate insecticides, the toxic effect observed depends upon the mechanism that causes the OP to break down. In some cases the toxicity of the OP insecticide can be either increased or decreased in the presence of PBO. Due to the uncertainty in predicting the possible effects a synergist would have to the environment when mixed with another chemical, the Agency is requiring product specific ecotoxicity data on formulated products of PBO.

V. What Registrants Need to Do

The Agency has determined that PBO is eligible for reregistration provided that the mitigation measures and label changes identified in this RED are implemented. Registrants will need to amend their product labeling to incorporate the label statements set forth in the Label Changes Summary Table (Table 27). The Agency intends to issue Data Call-Ins (DCIs) requiring generic and product specific data. Generally, the registrant will have 90 days from receipt of a DCI to complete and submit response forms or request time extensions and/or waivers with a full written justification. For product-specific data, the registrant will have eight months to submit data and amended labels.

A. Manufacturing Use Products

1. Additional Generic Data Requirements

The generic data base supporting the reregistration of PBO for currently registered uses has been reviewed and determined to be substantially complete. However, the data listed below are necessary to confirm the reregistration eligibility decision documented in this RED.

Environmental Fate and Ecological Effects Data Needs

- Guideline 72-5 Full Life Cycle Fish (freshwater) is required to understand the chronic toxicity of PBO to fish beyond that found in the fish early life stage study.
- Eco-toxicity data on fish, invertebrates, and sediment dwelling organisms, and honeybees must be submitted in order to address concerns for synergistic toxic effects for typical end use products containing PBO.
- The exposure of birds and mammals is required to better understand the dissipation of total foliar residues (guideline 132-1a). Due to lack of this data, a default half-life of 35 days on foliage has been assumed. A measured foliar dissipation rate, if shorter than 35 days, might remove the presumption of chronic risk to mammals.
- 72-4 Life-cycle estuarine invertebrate using shrimp.
- 122-1 Tier I Terrestrial Plant Study - Field incidents reported under section 6(a)(2) indicate that PBO with pyrethrin and pyrethroid insecticides may cause plant mortality. Since this is an area of great uncertainty due to lack of data, Tier I terrestrial plant studies with typical end use products (Vegetative Vigor) are needed to decrease this uncertainty.
- In the avian reproduction toxicity studies on PBO, there was toxicologically significant evidence for PBO to be a potential candidate to test for endocrine disruptor effects once the endocrine disruptor program is formalized.

Human Health Data Requirements

The following product and residue chemistry data are required to support the registration of PBO:

Product Chemistry

- Product chemistry data as listed in the Product Chemistry Chapter is needed for TGAI of PBO.

Residue Chemistry

- Label revisions and clarifications will be required for some crops in order to reflect the use pattern parameters for which adequate residue data are available.
- Further analytical work to upgrade the previously submitted oral metabolism studies with ruminant and poultry. Representative egg, milk, and tissue samples from the dermal or oral ruminant/poultry metabolism studies must be analyzed using the enforcement method or any preferred data-collection method to determine whether the method(s) adequately recover PBO residues of concern. Data are under review.
- Additional storage stability data for plant (and processed) and livestock commodities to upgrade previously submitted studies or to support new studies.
- Data to support uses of PBO on foods stored in multi-walled paper or cloth bags.
- A magnitude of the residue study with ruminants reflecting premise treatment and further analysis on milk samples from the dermal and oral studies.
- A magnitude of the residue study with poultry reflecting direct applications to laying hens using a 10% dust formulation.
- Magnitude of the residue studies reflecting preharvest uses on representative commodities of all crop groups (and a few miscellaneous commodities) which are being supported for reregistration.
- Magnitude of the residue studies reflecting postharvest uses for all crops (except potato and sweet potato) which are being supported for reregistration
- Processing studies on apple, barley, coconut, corn (field), fig, flax, oat, peanut, pineapple, plum, potato, rice, rye, sorghum, and wheat.
- A confined rotational crop study. A field accumulation study in rotational crops (OPPTS 860.1900) is required if the level of the total radioactive residue in the confined rotational crops is equal to or exceeds 0.01 ppm at the desired rotational interval or at 12 months, and once the nature of the residue in the rotational crops is understood.

Occupational and Residential Exposure

- Metered release devices: use and usage information, as well as air concentration and particle size data.
- Outdoor residential misting systems: use and usage information, as well as air concentration and droplet size data.

- Applicators using handheld fogging equipment: use and usage data on application practices, as well as exposure data held in reserve pending review of the use and usage data.

2. Labeling Requirements

To ensure compliance with FIFRA, manufacturing use product (MUP) labeling should be revised to comply with all current EPA regulations, PR Notices, and applicable policies. The MUP labeling should bear the labeling contained in Table 27.

3. Spray Drift Management

The Agency has been working closely with stakeholders to develop improved approaches for mitigating risks to human health and the environment from pesticide spray drift. As part of the reregistration process, the EPA will continue to work with all interested parties on this important issue.

Specific spray drift language for PBO is outlined in the “spray drift management” section of Table 27.

B. End-Use Products

1. Additional Product-Specific Data Requirements

Section 4(g)(2)(B) of FIFRA calls for the Agency to obtain any needed product-specific data regarding the pesticide after a determination of eligibility has been made. The Registrant must review previous data submissions to ensure that they meet current EPA acceptance criteria and if not, commit to conduct new studies. If a registrant believes that previously submitted data meet current testing standards, then the study MRID numbers should be cited according to the instructions in the Requirement Status and Registrants Response Form provided for each product. The Agency intends to issue a separate product-specific data call-in (PDCI), outlining specific data requirements. For any questions regarding the PDCI, please contact Veronica Dutch at (703) 308-8585.

In addition, efficacy data for all applications that target public health pests must be submitted, including data for outdoor residential misting systems. Additional information on the efficacy data can be found in the Series 810 Product Performance Test Guidelines on the Agency’s website.

(http://www.epa.gov/opptsfrs/publications/OPPTS_Harmonized/810_Product_Performance_Test_Guidelines/index.html)

2. Labeling for End-Use Products

To be eligible for reregistration, labeling changes are necessary to implement measures outlined in Section IV above. Specific language to incorporate these changes is specified in Table 27. Generally, conditions for the distribution and sale of products bearing old labels/labeling will be established when the label changes are approved. However, specific

existing stocks time frames will be established case-by-case, depending on the number of products involved, the number of label changes, and other factors.

Labeling Changes Summary Table 27

In order to be eligible for reregistration, all product labels must be amended to incorporate the risk mitigation measures outlined in Section IV. The following table describes how language on the labels should be amended.

Description	PBO Required Labeling Language	Placement on Label
<i>Manufacturing-Use Products</i>		
Required on all MUPs	<p>“Only for formulation into a synergist for the following use(s) [fill blank only with those uses that are being supported by MP registrants].”</p> <p>“Not for formulation into wettable powder end use products (EUP), unless the EUP is packaged in water soluble bags.”</p> <p>“Not for formulation into granular End Use Products.”</p> <p>>>Delete any reference to tolerance exemptions on labels.</p> <p>If Registrants are not supporting outdoor residential misting systems use for their products, the following statement must appear on the MUP label of all liquid or wettable powder products: “Not for formulation into an end use product for use in outdoor residential misting systems.”</p> <p>Direct Application to Non-domestic Animals/Livestock</p> <p><u>Formulated products eligible for reregistration may not contain a percentage of a.i. that exceeds the following:</u></p> <ul style="list-style-type: none"> Dusts for application to livestock only– 10% ai Liquids for application to livestock only – 0.35 lb ai/gallon Towelettes for application to livestock only – 2% ai Spot-on applications – 10% ai Liquids for applications to poultry only – 0.1% ai 	Directions for Use

Description	PBO Required Labeling Language	Placement on Label
	<p>Pet Care</p> <p><u>Formulated products eligible for reregistration may not contain a percentage of a.i. that exceeds the following:</u> Shampoos – 3% ai Sprays – 0.1% ai Spot-on or Pour-on – 10% ai Dust – 10% ai Towelettes-2% ai</p>	
<p>One of these statements may be added to a label to allow reformulation of the product for a specific use or all additional uses supported by a formulator or user group.</p>	<p>“This product may be used to formulate products for specific use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s).”</p> <p>“This product may be used to formulate products for any additional use(s) not listed on the MP label if the formulator, user group, or grower has complied with U.S. EPA submission requirements regarding support of such use(s).”</p>	<p>Directions for Use</p>
<p>Environmental Hazards Statements Required by the RED and Agency Label Policies</p>	<p>“This product is toxic to aquatic organisms, including fish and invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA. Do not contaminate water when disposing of equipment wash-waters.”</p>	<p>Directions for Use</p>
<p><i>End-Use Products Intended for Occupational Use (WPS and non-WPS) and Wide Area Mosquito Adulticide Applications</i></p>		
<p>Handler PPE Requirements for Wettable Powders Formulations Packaged in Water Soluble Packaging</p> <p>[Note: Wettable Powders</p>	<p>“Personal Protective Equipment (PPE)”</p> <p>“Mixers, loaders, applicators, and other handlers must wear: - long-sleeve shirt, - long pants, and - shoes and socks.”</p> <p>“In addition to the above PPE, applicators using a high pressure handwand in an enclosed area must</p>	<p>Precautionary Statements: Hazards to Humans and Domestic Animals</p>

Description	PBO Required Labeling Language	Placement on Label
<p>must be packaged in water soluble bags to be eligible for reregistration.]</p>	<p>wear at least a NIOSH-approved respirator with: -- a dust/mist filter with MSHA/NIOSH approval number prefix TC-21C or -- any N, R, P, or HE filter.”</p> <p>“In addition to the above PPE, applicators using hand held foggers in an enclosed area must wear at least a half face NIOSH-approved respirator with: -- a dust/mist filtering cartridge (MSHA/NIOSH approval number prefix TC-21C), or -- a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or -- a cartridge or canister with any N,R,P or HE filter.</p> <p>“See engineering controls for additional requirements.”</p> <p><i>Instruction to Registrant:</i></p> <p>Drop the “N” type prefilter from the respirator statement, if the pesticide product contains, or is used with, oil.</p>	
<p>Handler PPE Requirements for Liquid Formulations¹ [including: liquid concentrates, total release foggers, microencapsulated concentrates, foams, aerosols, gels, pastes, and pressurized liquids]</p> <p>Note: The statement may be omitted if the end-use product is labeled only for use on pets.</p> <p>Note: If aerial application to forests or use of a high</p>	<p>“Personal Protective Equipment (PPE)”</p> <p>“Mixers, loaders, applicators, and other handlers must wear the following: - long-sleeve shirt, - long pants, - shoes and socks.”</p> <p>“In addition to the above PPE, mixers and loaders supporting aerial applications to forests and/or applicators using a high pressure handwand in an enclosed area must wear at least a NIOSH-approved respirator with: -- a dust/mist filter with MSHA/NIOSH approval number prefix TC-21C or -- any N, R, P, or HE filter.”</p> <p>“In addition to the above PPE, applicators using hand held foggers in an enclosed area must wear a half-face, full-face, or hood-style NIOSH-approved respirator with:</p>	<p>Precautionary Statements: Hazards to Humans and Domestic Animals</p>

Description	PBO Required Labeling Language	Placement on Label
<p>pressure handwand sprayer is not permitted or not feasible for the end-use product, the statement requiring respirators for those uses may be omitted.</p> <p>Note If aerial application is not permitted or not feasible for the end-use product, the reference to engineering control statements may be omitted.</p> <p>Note: If the use of handheld foggers in enclosed areas is not permitted or not feasible for the end-use product, the statement requiring respirators for those uses may be omitted.</p>	<p>-- a dust/mist filtering cartridge (MSHA/NIOSH approval number prefix TC-21C), or -- a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or -- a cartridge or canister with any N,R,P or HE filter.</p> <p>“See engineering controls for additional requirements.”</p> <p>Instruction to Registrant: Drop the “N” type filter from the respirator statement, if the pesticide product contains, or is used with, oil.</p> <p>Products that prohibit aerial applications may omit the reference to engineering control statements.</p>	
<p>Handler PPE Requirements for Dusts</p>	<p>“Personal Protective Equipment (PPE)”</p> <p>“Loaders, applicators, and other handlers must wear the following:</p> <ul style="list-style-type: none"> - long-sleeve shirt, - long pants, - shoes and socks.” <p>“ In addition, applicators using power duster equipment must wear a half-face, full-face, or hood-style NIOSH-approved respirator with:</p> <p>-- a dust/mist filtering cartridge (MSHA/NIOSH approval number prefix TC-21C), or</p>	<p>Precautionary Statements: Hazards to Humans and Domestic Animals</p>

Description	PBO Required Labeling Language	Placement on Label
	-- a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or -- a cartridge or canister with any N,R, P, or HE filter.”	
User Safety Requirements	“Follow manufacturer’s instructions for cleaning/maintaining PPE. If no such instructions for washables exist, use detergent and hot water. Keep and wash PPE separately from other laundry.” “Discard clothing and other absorbent material that have been drenched or heavily contaminated with the product’s concentrate. Do not reuse them.”	Precautionary Statements: Hazards to Humans and Domestic Animals immediately following the PPE requirements
Engineering Controls: Wettable Powders packaged in Water-Soluble Bags [Note: Wettable Powders must be packaged in water soluble packages to be eligible for reregistration.] Note If aerial application is not permitted or not feasible for the end-use product, the to engineering control statements referring to pilots or human flaggers may be omitted.	“Engineering Controls:” “Water-soluble packets when used correctly qualify as a closed mixing/loading system under the Worker Protection Standard for Agricultural Pesticides [40 CFR 170.240(d)(4)]. Mixers and loaders using water-soluble packets must : -- wear the personal protective equipment required in the PPE section of this labeling for mixers and loaders, and -- be provided and must have immediately available for use in an emergency, such as a broken package, spill, or equipment breakdown a half-face, full-face, or hood-style NIOSH-approved respirator with: -- a dust/mist filtering cartridge (MSHA/NIOSH approval number prefix TC-21C), or -- a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G), or -- a cartridge or canister with any N,R,P or HE filter. “Pilots must use an enclosed cockpit that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(6)].” “Human flagging is prohibited. Flagging to support aerial application is limited to use of the Global Positioning System (GPS) or mechanical flaggers.” <i>Instructions to Registrant:</i> Drop the “N” type prefilter from the respirator statement, if the pesticide product contains, or is used with, oil.	Precautionary Statements: Hazards to Humans and Domestic Animals (Immediately following PPE and User Safety Requirements.)

Description	PBO Required Labeling Language	Placement on Label
<p>Engineering Controls for all liquid formulations.</p> <p>Note if aerial application is not permitted or not feasible for the end-use product, the to engineering control statements referring to pilots or human flaggers may be omitted.</p>	<p>“Engineering Controls:”</p> <p>“Pilots must use an enclosed cockpit that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(6)].”</p> <p>“Human flagging is prohibited. Flagging to support aerial application is limited to use of the Global Positioning System (GPS) or mechanical flaggers.”</p>	<p>Precautionary Statements: Hazards to Humans and Domestic Animals (Immediately following PPE and User Safety Requirements.)</p>
<p>User Safety Recommendations</p>	<p>“USER SAFETY RECOMMENDATIONS”</p> <p>“Users should wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.”</p> <p>“Users should remove clothing/PPE immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.”</p> <p>“Users should remove PPE immediately after handling this product. Wash the outside of gloves before removing. As soon as possible, wash thoroughly and change into clean clothing.”</p>	<p>Precautionary Statements under: Hazards to Humans and Domestic Animals immediately following Engineering Controls</p> <p>(Must be placed in a box.)</p>
<p>Environmental Hazards Statements for products labeled for outdoor uses other than as a wide area mosquito adulticide:</p> <p>(PR Notice 2005-1 recommends separating labels intended for wide area mosquito adulticide applications.)</p>	<p>“ENVIRONMENTAL HAZARDS”</p> <p>“This product is toxic to aquatic organisms, including fish and invertebrates. Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas. This product may contaminate water through runoff. This product has a potential for runoff for several weeks after application. Poorly draining soils and soils with shallow water tables are more prone to produce runoff that contains this product.”</p> <p>“Do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment wash-waters or rinsate.”</p>	<p>Precautionary Statements under Environmental Hazards</p>
<p>Environmental</p>	<p>“ENVIRONMENTAL HAZARDS”</p>	<p>Precautionary</p>

Description	PBO Required Labeling Language	Placement on Label
<p>Hazards Statements for products labeled solely for use as a wide area mosquito adulticide:</p> <p>(PR Notice 2005-1 recommends separating labels intended for wide area mosquito adulticide applications.)</p>	<p>“This pesticide is toxic to aquatic organisms, including fish and invertebrates. Runoff from treated areas or deposition of spray droplets into a body of water may be hazardous to fish and aquatic invertebrates.”</p> <p>“Before making the first application in a season, it is advisable to consult with the state or tribal agency with primary responsibility for pesticide regulation to determine if other regulatory requirements exist.”</p> <p>“Do not apply over bodies of water (lakes, rivers, permanent streams, natural ponds, commercial fish ponds, swamps, marshes or estuaries), except when necessary to target areas where adult mosquitoes are present, and weather conditions will facilitate movement of applied material away from the water in order to minimize incidental deposition into the water body. Do not contaminate bodies of water when disposing of equipment rinsate or washwaters.”</p>	<p>Statements under Environmental Hazards</p>
<p>Environmental Hazards Statements for products labeled as a wide area mosquito adulticide and is labeled for other outdoor uses as well:</p> <p>(PR Notice 2005-1 recommends separating labels intended for wide area mosquito adulticide applications.)</p>	<p>“ENVIRONMENTAL HAZARDS for TERRESTRIAL APPLICATIONS”</p> <p>“This product is toxic to aquatic organisms, including fish and invertebrates. Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas. This product may contaminate water through runoff. This product has a potential for runoff for several weeks after application. Poorly draining soils and soils with shallow water tables are more prone to produce runoff that contains this product.”</p> <p>“Except as specified in the directions for use, do not apply directly to water, to areas where surface water is present or to intertidal areas below the mean high water mark. Do not contaminate water when disposing of equipment wash-waters or rinsate.”</p> <p>“ENVIRONMENTAL HAZARDS for WIDE AREA MOSQUITO ADULTICIDE APPLICATIONS”</p> <p>“This pesticide is toxic to aquatic organisms, including fish and invertebrates. Runoff from treated areas or deposition of spray droplets into a body of water may be hazardous to fish and aquatic invertebrates.”</p> <p>“When applying as a wide area mosquito adulticide, before making the first application in a season,</p>	<p>Precautionary Statements under Environmental Hazards</p>

Description	PBO Required Labeling Language	Placement on Label
	<p>it is advisable to consult with the state or tribal agency with primary responsibility for pesticide regulation to determine if other regulatory requirements exist.”</p> <p>“When applying as a wide area mosquito adulticide, do not apply over bodies of water (lakes, rivers, permanent streams, natural ponds, commercial fish ponds, swamps, marshes or estuaries), except when necessary to target areas where adult mosquitoes are present, and weather conditions will facilitate movement of applied material away from the water in order to minimize incidental deposition into the water body.</p>	
<p>Environmental Hazards for Products labeled only for Indoor Use EXCEPT ready to use impregnated materials (e.g. flea collars, ear tags, coils, mats)</p> <p>(Note: Products used on domestic animals like flea collars and ear tags, generally do not require an Environmental Hazards statement. In addition, products containing the statement: “For indoor use only,” may also omit the environmental hazards statement.)</p>	<p>“ENVIRONMENTAL HAZARDS”</p> <p>“This product is toxic to fish and aquatic invertebrates. Do not contaminate water when disposing of equipment, washwater, or rinsate. See Directions for Use for additional precautions and requirements.”</p> <p>For indoor products packaged in containers equal to or greater than 5 gallons or 50 lbs add the following statement:</p> <p>“Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the requirements of a National Pollution Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.”</p>	<p>Precautionary Statements under Environmental Hazards</p>
<p>Restricted-Entry Interval for WPS products as required by Supplement Three of PR Notice 93-7</p>	<p>“Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 12 hours.”</p>	<p>Directions for Use, Agricultural Use Requirements Box</p>
<p>Early Entry Personal Protective Equipment for Products subject to WPS as required by Supplement</p>	<p>“PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as soil or water, is:</p> <ul style="list-style-type: none"> - coveralls, - chemical-resistant gloves made of any waterproof material, and 	<p>Directions for Use, Agricultural Use Requirements Box</p>

Description	PBO Required Labeling Language	Placement on Label
Three of PR Notice 93-7	- shoes plus socks.”	
<p>Entry Restrictions for products with non-WPS uses on the label</p> <p>Note: This excludes products labeled for use when people are permitted to be present (e.g. wide-area mosquito adulticide applications, metered release devices, and pet applications)</p>	<p>Entry Restriction for products applied as a spray (does not apply to products applied directly to domestic animals):</p> <p>“Do not enter or allow others to enter until sprays have dried.”</p> <p>Entry Restriction for products applied dry:</p> <p>“Do not enter or allow others to enter until dusts have settled.”</p> <p>Entry Restriction for products applied as a space spray or as a fog::</p> <p>“Do not enter or allow others to enter until vapors, mists, and aerosols have dispersed, and the treated area has been thoroughly ventilated.”</p>	<p>If no WPS uses on the product label, place the appropriate statement in the Directions for Use Under General Precautions and Restrictions. If the product also contains WPS uses, then create a Non-Agricultural Use Requirements box as directed in PR Notice 93-7 and place the appropriate statement inside that box.</p>
<p>Entry Restrictions for products labeled solely for use when people are present (e.g. wide-area mosquito adulticide applications, metered release devices, and applications to pets)</p>	<p>Note to Registrants: No entry restrictions are required. See below under Use Restrictions for further requirements.</p>	
<p>Entry Restrictions for products labeled for use when people are present (e.g. wide-area mosquito adulticide applications, metered release devices, and applications to pets) and for use on other sites as a directed or space spray.</p>	<p>Products labeled for use as a directed spray (does not apply to products applied directly to domestic animals):</p> <p>“Except when (insert application method or site that allows people to be present), do not enter or allow others to enter until sprays have dried.”</p> <p>Products labeled for use as a space spray:</p> <p>“Except when (insert application method or site that allows people to be present), do not enter or allow others to enter until vapors, mists, and aerosols have dispersed, and the treated area has been thoroughly ventilated.”</p>	<p>If no WPS uses on the product label, place the appropriate statement in the Directions for Use Under General Precautions and Restrictions. If the product also contains WPS uses, then create a Non-Agricultural Use Requirements box as directed in PR Notice</p>

Description	PBO Required Labeling Language	Placement on Label
	Note to Registrant: An example is as follows: Except when applying in a metered release system, do not enter or allow others to enter until sprays have dried.	93-7 and place the appropriate statement inside that box.
<p>General Application Restrictions for products with WPS or non-WPS uses on the label</p> <p>Note: This excludes products that contain any directions for uses when people are permitted to be present in the treated area (e.g. . wide-area mosquito adulticide applications, metered release devices, and applications to pets)</p>	<p>“Do not apply this product in a way that will contact workers or other persons, either directly or through drift.”</p> <p>“Only protected handlers may be in the area during application.”</p>	Place in the Direction for Use.
<p>General Application Restrictions for products with WPS and non-WPS uses on the label AND contain directions for uses when people are permitted to be present in the treated area (e.g. . wide-area mosquito adulticide applications, metered release devices, and applications to pets)</p>	<p>“Except when” (insert application method or site that allows people to be present) “do not apply this product in a way that will contact workers or other persons, either directly or through drift.”</p> <p>“Except when” (insert application method or site that allows people to be present) “only protected handlers may be in the area during application.”</p>	Place in the Direction for Use.
<p>General Application Restrictions for products</p>	<p>Note to Registrants: No entry restrictions are required. See below under Use Restrictions for further requirements.</p>	Place in the Direction for Use.

Description	PBO Required Labeling Language	Placement on Label
<p>labeled for use solely when people are permitted to be present in the treated area (e.g. wide-area mosquito adulticide applications, metered-release devices, and applications to pets)</p>		
<p>Other Application Restrictions</p>	<p>Note to Registrants: Delete any reference to tolerance exemptions on labels.</p> <p>In addition add the following restrictions depending on the registered product uses and formulation:</p> <p>Wettable powder formulations: “Do not apply this product as a dust.” “Do not apply in forestry areas.”</p> <p>Dust formulations: “Aerial applications are prohibited.” “Applications with power duster equipment is prohibited, except when making applications to agricultural commodities.”</p> <p>Products labeled for use as a space spray: “Do not remain in treated area. Exit area immediately and remain outside the treated area until aerosols, vapors, and/or mists have dispersed.”</p> <p>Products labeled for spray applications to plants: “Do not wet plants to point of runoff or drip.”</p> <p>Products labeled for spray applications to articles: “Do not wet articles to point of runoff or drip.” “Do not use treated article until spray has dried.”</p>	<p>Directions for Use under General Precautions and Restrictions and/or Application Instructions</p>

Description	PBO Required Labeling Language	Placement on Label
	<p>Products labeled for applications to clothing articles: “Dry clean treated clothes before wearing.”</p> <p>Products labeled for dip applications: “Do not use treated article before it is dry.”</p> <p>Products labeled for crack and crevice, surface or space spray, fogging or dust applications indoors: “Remove or cover exposed food and drinking water before application.” “Remove or cover dishes, utensils, food processing equipment, and food preparation surfaces, or wash them before use.”</p> <p>Products labeled for applications to non-residential indoor sites: “Do not use in aircraft cabins except in compliance with PR Notice 96-3.” “When used in dairy barns or facilities: Close milk bulk tank lids to prevent contamination from spray and from dead or falling insects. Remove or cover milking utensils before application. Wash teats of animals before milking.”</p> <p>Products labeled for use in food handling and processing facilities: “Do not make space spray applications when facility is in operation.” “During space spray applications, cover or remove food.” “During space spray applications, cover food processing surfaces or clean after treatment with a suitable detergent and rinse with potable water before use.”</p>	
<p>Rate Related Application Restrictions</p> <p>(Note: The maximum application rate and maximum seasonal rates specified in this table must be listed as pounds or gallons of formulated</p>	<p>Food Crops Grown Outdoors or in Greenhouses in Agricultural Settings</p> <p><u>Maximum application rates:</u> Field and orchard– 0.5 lbs ai/acre or 0.012 lb ai /1000 square feet Hydroponically grown crops – 1.0 ppm ai in water Greenhouse space sprays - 0.0014 lbs ai/1000 cubic feet Greenhouse surface spray – 0.012 lbs per 1000 square feet or 0.5 lbs ai per acre</p> <p><u>Use restrictions:</u></p>	<p>Directions for Use under General Precautions and Restrictions and/or Application Instructions</p>

Description	PBO Required Labeling Language	Placement on Label
<p>product per acre/square ft/ppm/cubic feet etc., not just as pounds active ingredient)</p>	<p>“Do not apply more than 10 times per season.” “Do not reapply within 3 days except under extreme pest pressure.” “In case of extreme pest pressure do not reapply within 24 hours.” “Do not apply to cotton within 14 days of seed harvest.” (For labels with cotton only)</p> <p>Forestry</p> <p><u>Maximum application rate:</u> 1.25 lb ai per acre</p> <p>Sod farms</p> <p><u>Maximum application rate:</u> 1 lb ai per acre</p> <p>Rice Fields</p> <p>“A 10 day water hold is required for all pyrethrins applications when rice fields are flooded.”</p> <p>Greenhouse Grown Ornamental, Flowering and Foliage Plants:</p> <p><u>Maximum application rates:</u> Surface applications – 0.036 lbs ai/1000 square feet (or 1.5 lb ai/acre) Space sprays (including space, total release, and fogger applications) – 0.0042 lbs ai/1000 cubic feet</p> <p><u>Use restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>Post-harvest Application to Vegetables (Potato, Tomato, Pea, Sweet Potato), Fruits (Apple, Blackberry, Blueberry, Boysenberry, Cherry, Crabapple, Currant, Dewberry, Fig, Gooseberry, Grape, Guava, Loganberry, Mango, Muskmelon, Orange, Peach, Pear, Pineapple, Plum, Raspberry) Nuts (Almonds, Walnuts) and Other Commodities (Copra and Peanut</p>	

Description	PBO Required Labeling Language	Placement on Label
	<p><u>Maximum application rates:</u> Surface applications – 0.10 lb ai/ 1000 square feet Surface application to fruits or tomatoes in baskets or hampers – 1.6 x 10-6 lbs ai/ lb of fruit (or 1.6 ppm)</p> <p>Space spray to fruits, vegetables, copra – 0.001 lbs ai/1000 cubic feet Dip or spray – 0.004 lbs ai/ gallon</p> <p><u>Use restrictions:</u> “Do not apply more than 1 time per day.” “Do not reapply within 7 days.” “Do not apply more than 10 times to sweet potatoes.”</p> <p>Post-harvest Applications to Stored Grain and Seed (Barley, Beans, Lima Beans, Birdseed, Buckwheat, Cocoa beans, Corn, Cottonseed, Flax, Grain sorghum, Oats, Field Peas, Rice, Rye, Wheat)</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications – 0.50 lbs ai/1000 square feet Direct application to bulk grain and seed – 1.0 lb ai/1000 bushels grain</p> <p><u>Maximum application rates:</u> Barley – 0.033 oz ai per cwt Beans – 0.027 oz ai per cwt Lima beans – 0.029 oz ai per cwt Birdseed – 0.032 oz ai per cwt Buckwheat – 0.033 oz ai per cwt Cocoa beans – 0.037 oz ai per cwt Corn – 0.029 oz ai per cwt Cottonseed – 0.057 oz ai per cwt Flax – 0.029 oz ai per cwt Grain sorghum – 0.029 oz ai per cwt Oats – 0.050 oz ai per cwt Field peas – 0.027 oz ai per cwt</p>	

Description	PBO Required Labeling Language	Placement on Label
	<p>Rice – 0.036 oz ai per cwt Rye – 0.029 oz ai per cwt Wheat (club, common, durham) – 0.027 oz ai per cwt What (emmer, spelt) – 0.040 oz ai per cwt)</p> <p><u>Use restrictions:</u> “Do not reapply within 30 days.”</p> <p>Food Stored in Bags</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Space sprays may be made to the surfaces of bags of stored food products at the rate of 0.025 lbs ai/1000 cubic foot.</p> <p><u>Use restrictions:</u> “Direct application to food contact surfaces is prohibited.”</p> <p>Direct Application to Non-domestic Animals/Livestock</p> <p><u>Use restrictions:</u> “Do not apply more than 1 time per day.” “Do not apply microencapsulated product to lactating or food animals.”</p> <p>Indoor Agricultural Premises and Commercial Animal Housing and Equipment (when animals are NOT present)</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications – 0.56 lbs ai/1000 square feet Crack/crevice or spot surface – 0.56 lbs ai/1000 square feet Space sprays when non-domestic animals are absent– 0.025 lbs ai/1000 cubic feet (Rate changed from 0.033 lbs) Metered release device space sprays – 0.05 lbs ai/1000 cubic feet/day</p>	

Description	PBO Required Labeling Language	Placement on Label
	<p><u>Use Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>Indoor Agricultural Premises and Commercial Animal Housing and Equipment (when animals are present)</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Space sprays when non-domestic animals are present – 0.008 lb ai/ 1000 cubic feet/day</p> <p>Indoor Food Handling/Processing Facilities</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u></p> <p>Surface applications – 0.56 lbs ai/1000 square feet Crack/crevice or spot surface –0.56 lbs ai/1000 square feet Space sprays– 0.025 lbs ai/1000 cubic feet ^a Metered release device space sprays – 0.05 lbs ai/1000 cubic feet/day</p> <p><u>Use Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>In addition, these label statements should be deleted from all products registered for food handling and processing facilities: “Except in Federally inspected meat and poultry plants, food processing operations may continue when the product is applied as a general surface spray with care and in accordance with the directions and precautions on the label, at a maximum rate of 0.11 pounds of piperonyl butoxide per 1000 square feet.” “Except in Federally inspected meat and poultry plants, food processing operations may continue when the product is applied as a crack and crevice treatment with care and in accordance with the directions and precautions on the label, at a maximum rate of 0.56 pounds of piperonyl butoxide per 1000 square feet.”</p>	

Description	PBO Required Labeling Language	Placement on Label
	<p>Residential Dwellings and Commercial, Institutional Indoor Sites</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications – 0.56 lbs ai/1000 square feet Crack/crevice or spot surface – 0.56 lbs ai/1000 square feet Space sprays– 0.025 lbs ai/1000 cubic feet Metered release device space sprays – 0.05 lbs ai/1000 cubic feet/day</p> <p>Outdoor Agriculture Premises</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications – 0.020 lbs ai/1000 square feet (or 1.0 lbs ai/acre) Crack/crevice or spot surface (including applications for fire ant applications or turf diagnostic aid) – 0.56 lbs ai/1000 square feet^b</p> <p><u>User Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>General Outdoor Sites (including Non-Agricultural rights-of-way, Commercial/Institutional/Industrial Premises and Outdoor Eating Establishments)</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications – 0.075 lbs ai/1000 square feet Crack/crevice or spot surface – 0.56 lbs ai/1000 square feet</p> <p><u>User Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>Outdoor Ornamental and Lawns</p> <p><u>Maximum application rates:</u></p>	

Description	PBO Required Labeling Language	Placement on Label
	<p>Surface applications – 0.020 lbs ai/1000 square feet (or 1.0 lbs ai/acre) Crack/crevice or spot surface (including applications for fire ant applications or turf diagnostic aid) – 0.56 lbs ai/1000 square feet</p> <p><u>User Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>Manholes</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications to manholes – 0.04 lbs ai per manhole over a length of 200 feet</p> <p><u>User Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>Pet Care</p> <p><u>Use restrictions:</u> “Do not apply to pets less than 12 weeks old.” “Consult a veterinarian before applying this product on medicated, debilitated, aged, pregnant, or nursing animals.” “Sensitivities may occur after using any pesticide product for pets. If signs of sensitivity occur bathe your pet with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.”</p> <p>Registrant Note: Follow instructions in PR Notice 96-6, Pet Pesticide Product Label Statements, for including reapplication restrictions on the end-use product label.</p> <p>Pet Premise Treatment</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u></p> <p>Surface – 0.56 lb per 1000 square feet Crack and crevice – 0.56 lbs per 1000 square feet</p>	

Description	PBO Required Labeling Language	Placement on Label
	Space spray – 0.033 lbs per 1000 square feet	
Application Restrictions for products used in Metered Release Devices	<p>Note to Registrants: Delete nurseries, day care centers, and nursing homes as registered use sites on all product labels.</p> <p>Add the following statements:</p> <p>“Do not use in nurseries or rooms where infants, ill, or aged persons are confined.”</p> <p>“Do not place metering device directly over or within 8 feet of exposed food, dishes, utensils, food processing equipment, and food handling or preparation.”</p> <p>“Do not install within 3 feet of air vents.”</p> <p>“Carefully follow directions for the dispenser unit when installing the dispenser and replacing cans or conducting maintenance.”</p>	Directions for Use under General Precautions and Restrictions and/or Application Instructions
<p>Use-Specific Application Restrictions for all liquid and wettable powder labels</p> <p>(Outdoor residential misting system requirement)</p> <p>(Note: The maximum allowable application rate and maximum allowable seasonal rate must be listed as pounds or gallons of formulated product per acre, not just as pounds active ingredient per acre.)</p>	<p>Outdoor Residential Misting Systems</p> <p>Products not intended for use in outdoor residential misting systems must contain the following statement:</p> <p>“Not for use in outdoor residential misting systems.”</p> <p>Products intended for use in outdoor residential misting systems must contain the following statements:</p> <p>“Directions for use in outdoor residential misting systems:”</p> <p>“When using this product installers and service technicians must comply with the license, certification, or registration requirements of the state(s), tribe(s), or local authority(ies) where they are installed.”</p> <p>“If the system works on an automatic timer, set the timing for application when people, pets, and food are unlikely to be present.”</p>	Directions for Use under General Precautions and Restrictions and/or Application Instructions

Description	PBO Required Labeling Language	Placement on Label
	<p>“If the system works when a person operates a remote activation device, then application of this pesticide when people, pets, and food are present is prohibited.”</p> <p>“Do not use in an evaporative cooling system.”</p> <p>“Direct nozzles to spray towards the target area and away from swimming pools, water bodies, or eating and cooking areas.”</p> <p>“If used in a system with a reservoir tank for the end use dilution, the system reservoir tank must be locked. Securely attach the end use pesticide label and a dilution statement to the system reservoir tank in a weather protected area or plastic sleeve. The dilution statement must be phrased as follows: this container holds __ parts [<i>product name</i>] to __ parts water”</p> <p>“If used in a direct injection system, the pesticide container must be locked. Securely attach the end use label to the pesticide container in a weather protected area or plastic sleeve.” (These instructions not applicable to wettable powder products).</p> <p>“This product must only be used in systems that have been calibrated to apply no more than the maximum application rate of” [insert product application rate that is equal to 0.00058 lbs piperonyl butoxide per 1000 cubic feet per day].</p> <p>Note to registrant: Also express this application rate as pounds or gallons of end-use product formulation.</p>	
<p>Use-Specific Application Restrictions for products labels for Wide Area Mosquito Adulticide Application by ground or air.</p> <p>(Note: The maximum allowable application rate and maximum allowable seasonal rate must be listed as pounds or gallons of</p>	<p>“For use by federal, state, tribal, or local government officials responsible for public health or vector control, or by persons certified in the appropriate category or otherwise authorized by the state or tribal lead pesticide regulatory agency to perform adult mosquito control applications, or by persons under their direct supervision.”</p> <p>The maximum application rate for wide area mosquito adulticide applications is 0.025 lbs ai/acre. When targeting <i>Aedes Taeirorhynchus</i> and other difficult species applications may be made up to 0.08 lbs ai/acre.</p> <p>“Do not apply more than 2.0 lbs ai/acre/year in any treated area. More frequent treatments may be made to prevent or control a threat to public and/or animal health determined by a state, tribal, or local health or vector control agency on the basis of documented evidence of disease causing agents</p>	<p>Directions for Use under General Precautions and Restrictions and/or Application Instructions</p>

Description	PBO Required Labeling Language	Placement on Label
formulated product per acre, not just as pounds active ingredient per acre.)	in vector mosquitoes or the occurrence of mosquito-borne disease in animal or human populations, or if specifically approved by the state or tribe during a natural disaster recovery effort.”	
Spray Drift Label Language for all products labeled for outdoor applications to agricultural use sites	<p>“SPRAY DRIFT MANAGEMENT for AGRICULTURE CROPS”</p> <p>“Avoiding spray drift at the application site is the responsibility of the applicator and the grower. The interactions of many equipment and weather-related factors determine the potential for spray drift. The applicator and the grower are responsible for considering all these factors when making decisions.”</p> <p>“Do not apply at wind speeds greater than 10 mph at the application site.”</p> <p>“Do not make any type of application into temperature inversions.”</p> <p>“Apply as a medium or coarser spray (ASABE standard 572).”</p> <p>“<u>Additional requirements for aerial applications:</u>”</p> <p>“Do not release spray at a height greater than 10 feet above the ground or crop canopy.”</p> <p>“The boom length must not exceed 75% of the wingspan or 90% of the rotor blade diameter.”</p> <p>“Aerial applicators must consider flight speed and nozzle orientation in determining droplet size.”</p> <p>“When applications are made with a cross-wind, the swath will be displaced downwind. The applicator must compensate for this displacement at the downwind edge of the application area by adjusting the path of the aircraft upwind.”</p> <p>“<u>Additional requirements for ground applications:</u>”</p> <p>“Do not release spray at a height greater than 4 feet above the ground or crop canopy.”</p> <p>“<u>Additional requirements for airblast applications:</u>”</p> <p>“Direct sprays into the canopy.”</p>	Directions for Use under General Precautions and Restrictions

Description	PBO Required Labeling Language	Placement on Label
	“Turn off outward pointing nozzles at row ends and when spraying outer rows.”	
Spray Drift Label Language for ALL Products Intended for ULV Mosquito Abatement Programs	<p>“SPRAY DRIFT MANAGEMENT for WIDE AREA MOSQUITO ABATEMENT”</p> <p>“A variety of factors including weather conditions (e.g., wind direction, wind speed, temperature, relative humidity) and method of application (e.g., ground, aerial, airblast, chemigation) can influence pesticide drift. The applicator must evaluate all factors and make appropriate adjustments when applying this product.”</p> <p>WIND SPEED: “Apply only when wind speed is greater than or equal to 1 mph.”</p>	Directions for Use under General Precautions and Restrictions
Spray Drift Label Language For End-Use Products Applied with Ground-Based Mechanical Application Equipment for ULV Mosquito Abatement Programs	<p>“Ground-based wide area mosquito abatement application:</p> <p>Spray equipment must be adjusted so that the volume median diameter is less than 30 microns ($D_v 0.5 < 30 \mu\text{m}$) and that 90% of the spray is contained in droplets smaller than 50 microns ($D_v 0.9 < 50 \mu\text{m}$). Directions from the equipment manufacturer or vendor, pesticide registrant or a test facility using a laser-based measurement instrument must be used to adjust equipment to produce acceptable droplet size spectra. Application equipment must be tested at least annually to confirm that pressure at the nozzle and nozzle flow rate(s) are properly calibrated.”</p>	Directions for Use under General Precautions and Restrictions
Spray Drift Label Language for Products Applied as an Aerial Spray for ULV Mosquito Abatement Programs	<p>“Aerial wide area mosquito abatement application:</p> <p>Spray equipment must be adjusted so that the volume median diameter produced is less than 60 microns ($D_v 0.5 < 60 \mu\text{m}$) and that 90% of the spray is contained in droplets smaller than 80 microns ($D_v 0.9 < 80 \mu\text{m}$). The effects of flight speed, and for non-rotary nozzles, nozzle angle on the droplet size spectrum must be considered. Directions from the equipment manufacturer or vendor, pesticide registrant or a test facility using a wind tunnel and laser-based measurement instrument must be used to adjust equipment to produce acceptable droplet size spectra. Application equipment must be tested at least annually to confirm that pressure at the nozzle and nozzle flow rate(s) are properly calibrated.”</p> <p>RELEASE HEIGHT:</p>	Directions for Use under General Precautions and Restrictions

Description	PBO Required Labeling Language	Placement on Label
	Fixed wing: “Apply using a nozzle height of no less than 100 feet above the ground or canopy.” Rotary wing: “Apply using a nozzle height of no less than 75 feet above the ground or canopy.”	
	<i>Products Primarily Used by Consumers/Homeowners</i>	
Entry Restrictions for products except those products that contain any directions for uses when people are permitted to be present in the treated area (e.g. . applications to pets)	<p>Entry Restriction for products applied as a spray except for sprays applied directly to domestic animals:</p> <p>“Do not allow adults, children, or pets to enter the treated area until sprays have dried.”</p> <p>Entry Restriction for products applied dry:</p> <p>“Do not allow adults, children, or pets to enter the treated area until dusts have settled.”</p> <p>Entry Restriction for products applied as a space spray or as a fog:</p> <p>“Do not allow adults, children, or pets to enter until vapors, mists, and aerosols have dispersed, and the treated area has been thoroughly ventilated.”</p>	Directions for use under General Precautions and Restrictions
Entry Restrictions for products products that only contain directions for uses when people are permitted to be present (e.g. pet applications)	<p>Note to Registrants: No entry restrictions are required. See below under Use Restrictions for further requirements.</p>	Directions for use under General Precautions and Restrictions
Entry Restrictions for products that contain directions for uses when people are permitted to be present in the treated area	<p>Products labeled for use as a surface spray (does not apply to products applied directly to domestic animals):</p> <p>“Except when applying directly to pets, do not allow adults, children, or pets to enter until sprays have dried.”</p>	Directions for use under General Precautions and Restrictions

Description	PBO Required Labeling Language	Placement on Label
(e.g. applications to pets) AND for use on other sites as a surface spray.		
General Application Restrictions for all products except those that contain any directions for uses when people are permitted to be present in the treated area (e.g. . applications to pets)	“Do not apply this product in a way that will contact adults, children, or pets, either directly or through drift.”	Place in the Direction for Use
General Application Restrictions for products that only contain directions for uses when people are permitted to be present (e.g. pet applications)	Note to Registrants: No entry restrictions are required. See below under Use Restrictions for further requirements.	Place in the Direction for Use
General Application Restrictions for products that contain directions for uses when people are permitted to be present in the treated area (e.g. applications to pets) AND for use on other sites as a surface spray.	“Except when applying directly to pets, do not apply this product in a way that will contact adults, children, or pets, either directly or through drift.”	Place in the Direction for Use
Environmental Hazards for Residential Products (Note: Products used on domestic animals like flea collars and ear tags, generally do not require an Environmental Hazards	“ENVIRONMENTAL HAZARDS” “This product is toxic to aquatic organisms, including fish and invertebrates. Do not contaminate water when disposing of equipment, washwater, or rinsate. See Directions for Use for additional precautions and requirements.” Note to Registrants: For products with outdoor uses include the following statement.	Precautionary Statements under Environmental Hazards

Description	PBO Required Labeling Language	Placement on Label
statement. In addition, products containing the statement: “For indoor use only,” may also omit the environmental hazards statement.)	“Do not apply directly to or near water. Drift and run-off may be hazardous to fish in water adjacent to treated areas.”	
Homeowner User Safety Recommendations Statements	<p>“User Safety Recommendations</p> <p>Users should wash hands with plenty of soap and water before eating, drinking, chewing gum, using tobacco, or using the toilet.</p> <p>Users should remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.”</p>	<p>Precautionary Statements under: Hazards to Humans and Domestic Animals immediately following Engineering Controls</p> <p>(Must be placed in a box.)</p>
Other Application Restrictions	<p>Note to Registrants: Delete any reference to tolerance exemptions on labels.</p> <p>In addition add the following restrictions depending on the registered product uses and formulation:</p> <p>Wettable powder formulations: “Do not apply this product as a dust.” “Do not apply in forestry areas.”</p> <p>Dust formulations: “Aerial applications are prohibited.” “Applications with power duster equipment is prohibited, except when making applications to agricultural commodities.”</p> <p>Products labeled for use as a space spray: “Do not remain in treated area. Exit area immediately and remain outside the treated area until aerosols, vapors, and/or mists have dispersed.”</p> <p>Products labeled for spray applications to plants:</p>	<p>Directions for Use under General Precautions and Restrictions and/or Application Instructions</p>

Description	PBO Required Labeling Language	Placement on Label
	<p>“Do not wet plants to point of runoff or drip.”</p> <p>Products labeled for spray applications to articles: “Do not wet articles to point of runoff or drip.” “Do not use treated article until spray has dried.”</p> <p>Products labeled for applications to clothing articles: “Dry clean treated clothes before wearing.”</p> <p>Products labeled for dip applications: “Do not use treated article before it is dry.”</p> <p>Products labeled for crack and crevice, surface or space spray, fogging or dust applications indoors: “Remove or cover exposed food and drinking water before application.” “Remove or cover dishes, utensils, food processing equipment, and food preparation surfaces, or wash them before use.”</p> <p>Products labeled for applications to non-residential indoor sites: “Do not use in aircraft cabins except in compliance with PR Notice 96-3.” “When used in dairy barns or facilities: Close milk bulk tank lids to prevent contamination from spray and from dead or falling insects. Remove or cover milking utensils before application. Wash teats of animals before milking.”</p>	
<p>Use-Specific Application Restrictions</p> <p>For products with directions for residential uses</p>	<p>Requirement for Liquid Formulations (except for Ready to Use) with outdoor uses:</p> <p>“Do not apply directly to or near water, storm drains, or drainage ditches. Do not apply when windy. To prevent product run-off, do not over water the treated area(s) or apply when heavy rain is expected. Rinse applicator over lawn or garden area only.”</p>	<p>Directions for Use under General Precautions and Restrictions and/or Application Instructions</p>

Description	PBO Required Labeling Language	Placement on Label
	<p>Requirement for Ready to Use Liquid or Dust Formulations with outdoor uses: “Do not apply directly to or near water, storm drains, or drainage ditches. Do not apply when windy. To prevent product run-off, do not over water the treated area(s) or apply prior to heavy rainfall.”</p>	
<p>Residential Use restriction</p> <p>(Note: The maximum allowable application rate and maximum allowable seasonal rate must be listed as pounds or gallons of formulated product per acre or per square feet or per cubic feet, not just as pounds active ingredient per unit area.)</p>	<p>Home Garden or Home Greenhouse Applications</p> <p><u>Maximum application rates:</u> Garden and orchard– 0.5 lbs ai/acre or 0.012 lb ai /1000 square feet Hydroponically grown crops – 1.0 ppm ai in water Greenhouse space sprays - 0.0014 lbs ai/1000 cubic feet Greenhouse surface spray – 0.012 lbs per 1000 square feet or 0.5 lbs ai per acre</p> <p><u>Use restrictions:</u> “Do not apply more than 10 times per season.” “Do not reapply within 3 days except under extreme pest pressure.” “In case of extreme pest pressure do not reapply within 24 hours.” “Do not apply to cotton within 14 days of seed harvest.” (For labels with cotton only)</p> <p>Residential Dwellings - Indoors</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications – 0.56 lbs ai/1000 square feet Crack/crevice or spot surface – 0.56 lbs ai/1000 square feet ^b Space sprays– 0.025 lbs ai/1000 cubic feet ^a</p> <p>General Outdoor Sites</p> <p><u>Products must be formulated to deliver no more than this maximum rate when used according to directions:</u> Surface applications – 0.075 lbs ai/1000 square feet Crack/crevice or spot surface – 0.56 lbs ai/1000 square feet ^b</p>	<p>Directions for Use under General Precautions and Restrictions and/or Application Instructions</p>

Description	PBO Required Labeling Language	Placement on Label
	<p><u>User Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>Outdoor Ornamental and Lawns</p> <p><u>Maximum application rates:</u> Surface applications – 0.020 lbs ai/1000 square feet (or 1.0 lbs ai/acre) spot treatment (including applications for fire ant applications or turf diagnostic aid) – 0.56 lbs ai/1000 square feet^b</p> <p><u>User Restrictions:</u> “Do not apply more than 1 time per day.”</p> <p>Pet Care</p> <p><u>Use restrictions:</u> “Do not apply to pets less than 12 weeks old.” “Consult a veterinarian before using this product on medicated, debilitated, aged, pregnant, or nursing animals.” “Sensitivities may occur after using any pesticide product for pets. If signs of sensitivity occur bathe your pet with mild soap and rinse with large amounts of water. If signs continue, consult a veterinarian immediately.”</p> <p>Dusts</p> <p><u>Use Restrictions:</u> “Only apply as a spot treatment to areas no greater than 3 feet by 3 feet per room.”</p>	
<p>Use-Specific Application Restrictions for all liquid and wettable powder labels</p> <p>(Outdoor residential misting)</p>	<p>Outdoor Residential Misting Systems</p> <p>Products not intended for use in outdoor residential misting systems must contain the following statement:</p>	<p>Directions for Use under General Precautions and Restrictions and/or Application</p>

Description	PBO Required Labeling Language	Placement on Label
<p>system requirement)</p> <p>(Note: The maximum allowable application rate and maximum allowable seasonal rate must be listed as pounds or gallons of formulated product per acre, not just as pounds active ingredient per acre.)</p>	<p>“Not for use in outdoor residential misting systems.”</p> <p>Products intended for use in outdoor residential misting systems must contain the following statements:</p> <p>“Directions for use in outdoor residential misting systems:”</p> <p>“When using this product installers and service technicians must comply with the license, certification, or registration requirements of the state(s), tribe(s), or local authority(ies) where they are installed.”</p> <p>“If the system works on an automatic timer, set the timing for application when people, pets, and food are unlikely to be present.”</p> <p>“If the system works when a person operates a remote activation device, then application of this pesticide when people, pets, and food are present is prohibited.”</p> <p>“Do not use in an evaporative cooling system.”</p> <p>“Direct nozzles to spray towards the target area and away from swimming pools, water bodies, or eating and cooking areas.”</p> <p>“If used in a system with a reservoir tank for the end use dilution, the system reservoir tank must be locked. Securely attach the end use pesticide label and a dilution statement to the system reservoir tank in a weather protected area or plastic sleeve. The dilution statement must be phrased as follows: this container holds __ parts [<i>product name</i>] to __ parts water”</p> <p>“If used in a direct injection system, the pesticide container must be locked. Securely attach the end use label to the pesticide container in a weather protected area or plastic sleeve.” (These instructions not applicable to wettable powder products).</p> <p>“This product must only be used in systems that have been calibrated to apply no more than the maximum application rate of” [insert product application rate that is equal to 0.00058 lbs piperonyl butoxide per 1000 cubic feet per day].</p>	<p>Instructions</p>

Description	PBO Required Labeling Language	Placement on Label
	Note to registrant: Also express this application rate as pounds or gallons of end-use product formulation.	

¹ PPE that is established on the basis of Acute Toxicity of the end-use product must be compared to the active ingredient PPE in this document. The more protective PPE must be placed in the product labeling. For guidance on which PPE is considered more protective, see PR Notice 93-7.

Appendix: Technical Support Documents

Additional documentation in support of this RED is maintained in the OPP docket, located in room S-4400, One Potomac Yard (South Building), 2777 S. Crystal Drive, Arlington, VA 22202. It is open Monday through Friday, excluding legal holidays, from 8:30 am to 4 pm.

All documents, in hard copy form, may be viewed in the OPP docket room or downloaded or viewed via the Internet at the following site: <http://www.regulations.gov>

These documents include:

HED Documents:

Piperonyl Butoxide HED Revised Risk Assessment for Reregistration Eligibility Document (RED). Daiss, B.; D326576; February 21, 2006.

Piperonyl Butoxide: Addendum to Occupational and Residential Exposure Assessment. Daiss, B.; D327790; July 5, 2006.

Revised Occupational and Residential Exposure Assessment and Recommendation for the Reregistration Eligibility Decision (RED) for Piperonyl Butoxide. Daiss, B.; D318743; September 8, 2005.

Occupational and Residential Exposure Assessment for the Use of Piperonyl Butoxide in Residential Outdoor Automatic Mister Systems. Crowley, M., D315334; August 30, 2005.

Piperonyl Butoxide: Risk-Based Application Rate for Residential Outdoor Automatic Mister Systems. Crowley, M.; D325918; July 5, 2006.

Piperonyl Butoxide: Toxicology Chapter for the RED. Ramasamy, S.; D296885; TXR 0052707; September 23, 2004.

Piperonyl Butoxide: Revised Anticipated Residues and Acute probabilistic and Chronic Dietary Exposure Assessment for the Reregistration Eligibility Decision. Morton, T.; D310032; November 23, 2004.

Piperonyl Butoxide-First Report of the Hazard Identification Assessment Review Committee. Ramasamy, S.; TXR 0052600; June 8, 2004.

Piperonyl Butoxide RED – Reregistration Eligibility Decision. Revised Product and Residue Chemistry Considerations. Morton, T.; D310030; November 23, 2004.

Piperonyl Butoxide: Revised Metabolism Assessment Review Committee Report. Morton, T, and Ramasamy, S.; D321269; September 1, 2005.

Review of Pyrethrins Incident Reports – Second Revisions. Blondell, J.; D320300; August 16, 2005.

Review of Piperonyl butoxide Incident Reports. Blondell, J.; D302030; May 10, 2004.

HED Response to Comments Documents:

Piperonyl Butoxide: Response to Public Comments on the HED Risk Assessment for Piperonyl Butoxide RED Chapter. Daiss, B.; D324670; January 31, 2006.

Piperonyl Butoxide: Response to Phase 3 Comments – Toxicity Document. Ramasamy, S.; D310025; September 14, 2005.

Piperonyl Butoxide: Response to Public Comments on the HED Risk Assessment for Piperonyl Butoxide RED Chapter. Daiss, B.; D321496; September 9, 2005.

Piperonyl Butoxide (PBO), Pyrethrins and MGK-264: Health Effects Division's response to the Registrant's concerns for using metaplasia seen in the larynx in subchronic inhalation studies as an endpoint for inhalation risk assessment. Ramasamy, S., et al.; D319913, D319914, and D320298; September 8, 2005.

EFED Documents:

Piperonyl Butoxide: EFED's Response to Public Comments and our Revised Ecological Risk Assessment. Davy, M., and Eckel, W.; D296889 and D296881; September 6, 2005.

Tier 1 Drinking Water Assessment for Piperonyl Butoxide (Terrestrial Agriculture). Eckel, W.; D286223, D286227, D286228, D286229; May 17, 2004.

EFED Response to Comments Documents:

Response to Comments of Phase 5 Period About Water Quality, and Other Issues on the Revised Draft EFED RED Chapters for Pyrethrins, PBO and MGK-264. Davy, M., et al.; D324663, D324664, D324667, D324662, D324671, and D324673; January 30, 2006.

EFED Response to Error-Only Review: Ecological Risk Assessment For Piperonyl Butoxide. Eckel, W.; D296879; February 24, 2005.