United States Environmental Protection Agency

Office of Prevention, Pesticides and Toxic Substances (7501C)

Pesticide Fact Sheet

Name of Chemical: **PT807-HCl**
Reason for Issuance: **New Chemical Registration**
Date Issued: **December 30, 1999**

DESCRIPTION OF CHEMICAL

Generic Name:	N-N-diethyl-2-(4-methylbenzyloxy)ethylamine hydrochloride
Common Name:	PT807-HCl
Trade Names:	Ecolyst
EPA Chemical Code:	069089
Chemical Abstracts Service (CAS) Number:	
Year of Initial Registration:	1999
Pesticide Type:	Plant Growth Regulator
Chemical Family:	
U.S. and Foreign Producers:	GMJA Specialties

USE PATTERNS AND FORMULATIONS

PT807-HCl is a systemic plant growth regulator which has been shown to be effective in shortening the time to maturation of oranges when applied during spring bloom. This Section 3 registration is being requested for an end-use product (Product Name - Ecolyst) which contains PT807-HCL as the sole active ingredient. The product is a 3.3% a.i. soluble concentration formulation (concentration equivalent to 1 g. ai/fl oz solution).

Additionally, a Section 3 registration is being issued for PT807-HCl Manufacturing Use Product. This product is 29.4% active ingredient, registered for formulation purposes only.

SCIENCE FINDINGS

Summary Science Statements

Toxicology

The toxicology data base is complete, and the quality of the data is high and sufficient to characterize the toxicity of this chemical. There is high confidence in the hazard and dose-response assessments conducted.

PT807-HCl has low acute toxicity by the oral, dermal, and inhalation routes (Toxicity Categories III, IV, and IV, respectively). Although it is a slight to moderate eye irritant (Toxicity Category III), it is not a notable dermal irritant or sensitizer. There is no sex-related difference in sensitivity. There is little evidence of cumulative toxicity, even when acute, subchronic, and chronic data are compared. This is most likely due to the fact that PT807-HCl is rapidly excreted, primarily in the urine and secondarily in the feces.

Neurotoxicity was observed in several studies, but only in adult animals. No developmental effects were observed in rats or rabbits, even at doses far in excess of the maternal No Observed Adverse Effect Levels (NOAELs). In the rat reproductive toxicity study, anomalies were found in the pups, but at a parentally toxic dose. There is no evidence of increased developmental or neurologic susceptibility in the prenatal and pre/postnatal studies.

At the dose levels tested, no tumors were observed in the chronic mouse study. The high-dose in the mouse study exceeded the limit dose (1000 mg/kg/day). An increased incidence of hepatocellular adenomas and carcinomas in the high-dose male rats was attributed to the fact that the high-dose animals lived significantly longer than the other groups, that is, they lived long enough to develop more tumors. PT807-HCl is clastogenic in an in *vitro* study in Chinese hamster ovary cells; however, there is no evidence of clastogenic potential in whole animals.
In the subchronic feeding dog study, the NOAEL was 2500 PPM (equivalent to 71/78 mg/kg/day, M/F). The LOAEL was 7500 PPM (equivalent to 211/233 mg/kg/day, M/F), based on pathological changes to the male reproductive organs and possibly the uterus in females.

The Agency's Hazard Identification Assessment Review Committee (HIARC) met on 9/16/99 to determine appropriate toxicological endpoints and to evaluate the Food Quality Protection Act (FQPA) aspects of PT807-HCl. Since PT807-HCl will be applied using an air-blast sprayer, the most likely routes of worker exposure are dermal and inhalation. The HIARC has determined that no dermal risk assessments are necessary since no systemic toxicity was observed in a 21-day dermal toxicity limit test in rats at 2.5-times the limit dose, but inhalation and dietary risk assessments will be required.

The HIARC selected an **acute dietary Reference dose RfD of 0.5 mg/kg/day** based on a No Observed Adverse Effect Level (NOAEL) of 50 mg/kg/day in an acute neurotoxicity study in rats, and an uncertainty factor of 100. The Lowest Observed Adverse Effect Level (LOAEL) was 200 mg/kg/day based on slight ataxia in 1 of 11 males. The HIARC selected a **chronic dietary RfD of 0.14**

mg/kg/day based on a NOAEL of 14 mg/kg/day in a reproductive toxicity study in rats, and an uncertainty factor of 100. The systemic LOAEL is 114 mg/kg/day based on decreased body weight and body weight gain. In the absence of acceptable inhalation data, inhalation risk assessments for all time periods will use the oral NOAEL of 30 mg/kg/day from the 90-day gavage toxicity study in rats. The HIARC classified PT807-HCl as a "not likely human carcinogen" according to the EPA *Proposed Guidelines for Carcinogen Risk Assessment* (4/10/96) so a cancer risk assessment is not required.

On 10/4/99, the FQPA Safety Factor Committee met to determine the FQPA Safety Factor needed to protect infants and children. **The FQPA Safety Factor for enhanced sensitivity of infants and children was reduced to 1x** (the Agency's FQPA Safety Factor Committee, memo of 10/15/99). Rationales for removing the FQPA factor include: 1) the toxicology database is complete for the assessment of the effects following *in utero* and/or postnatal exposure to PT807-HCl; 2) the toxicity data provided no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure; 3) the requirement of a developmental (DNT) study is not based on the criteria reflecting some special concern which are generally used for requiring a DNT study and an FQPA safety factor (e.g.: neuropathy in adult animals; Central Nervous System (CNS) malformations following prenatal exposure; brain weight or sexual maturation changes in offspring; and/or functional changes in offspring) and therefore does not warrant an FQPA safety factor; and 4) the exposure assessment will not underestimate the potential dietary(food and water) exposures for infants and children from the use of PT807-HCl (currently no residential exposure is expected).

On 9/21/99, the Agency's Metabolism Assessment Review Committee (MARC) determined that only parent compound needs to be included in the tolerance expression and used for dietary risk assessment purposes for oranges. The nature of the residue in plant and animal is adequately understood for the purpose of this use on oranges.

The crop field trials submitted by the petitioner are not adequate to support the proposed zero day Pre-Harvest Interval (PHI) on oranges. About 40% of oranges (i.e., Valencia oranges) have mature fruit from the previous year still present at the time the trees bloom and thus potentially may have fruit harvested immediately after treatment with Ecolyst. The normal data requirement for oranges is 16 field trials or, if residues are below the method's limit of quantitation, 12 trials. Only two of the trials included samples with a zero day PHI. The Agency has concluded that at least three more studies reflecting the zero day PHI are required. Unless these additional crop trials supporting 0-day PHI are submitted, the PHI should be increased to 14 days for which more data are available to allow a conclusion that residues are not likely to exceed the 0.01 ppm tolerance.

Acute Reference Dose (RfD): 0.5 mg/kg/day. The systemic NOAEL of 50 mg/kg/day in the acute neurotoxicity study in rats is based on slight ataxia in 1/11 males at the LOAEL of 200 mg/kg/day. The FQPA Safety Factor for enhanced sensitivity of infants and children was reduced to 1x. The acute population adjusted dose (**aPAD**) is determined by dividing the acute RfD by the FQPA factor: **aPAD** = 0.5 / 1 = **0.5 mg/kg /day**. Since the HED FQPA Safety Factor Committee determined to remove the 10X safety factor, the acute RfD is identical to the aPAD. This aPAD applies to all population

subgroups.

Chronic RfD: 0.14 mg/kg/day. The systemic NOAEL of 14.1 mg/kg/day in the reproductive toxicity study in rats is based on decreased body weight and body weight gain at the LOAEL of 114 mg/kg/day. This is the lowest NOAEL in the most sensitive species. The FQPA Safety Factor for enhanced sensitivity of infants and children was reduced to 1x. The chronic population adjusted dose (cPAD) is determined by dividing the chronic RfD by the FQPA factor: **cPAD** = 0.14 / 1 = **0.14 mg/kg/day**. Since the Agency's FQPA Safety Factor Committee determined to remove the 10X safety factor, the chronic RfD is identical to the cPAD. This cPAD applies to all population subgroups.

Occupational Dermal Exposure

This risk assessment **is not required** because no systemic toxicity was seen at the limit dose in a 21-day dermal toxicity study and because no developmental effects were observed in rats or rabbits..

Occupational Inhalation Exposure. In the absence of acceptable inhalation data, the Agency's HIARC used oral data as a surrogate. The oral NOAEL of 30 mg/kg/day from the 90-day gavage toxicity study in rats has been selected for use in inhalation risk assessments. Neurotoxic signs were observed at the LOAEL of 300 mg/kg/day in that study.

Carcinogenicity

PT807-HCl has been classified by the Agency's HIARC as a “not likely human carcinogen.” A cancer risk assessment **is not required**.

Aggregate Risk

The risk assessments conducted in this review are acute and chronic aggregates. In conducting the acute and chronic exposure assessment for food, the Agency used Dietary Exposure Evaluation Model (DEEM) program and Tier 1 approach. Tier 1 assumptions are: tolerance level residues and 100% crop treated. This DEEM analysis concluded that both acute and chronic exposures to PT807-HCl from food for the general US population, infants and children are all **less than 1%** of the **aPAD/cPAD .**

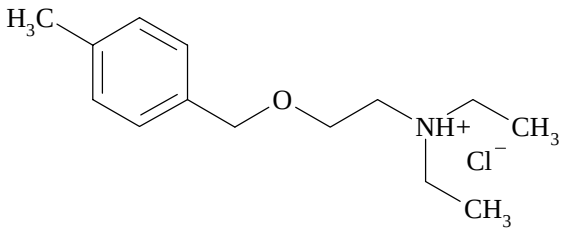
EFED provided the environmental fate analysis and the results of maximum estimated environmental concentrations (EECs) of PT807-HCl in surface and ground water for acute exposure. This chemical is very soluble in water and stable in the environment. Based on its chemical properties it is likely that this chemical will move to surface water and groundwater, and it may accumulate in the environment. According to information included in the proposed Ecolyst label, the maximum application rate for this chemical is 0.013 lb a.i./acre/year. Using PRZM/EXAMS model, the surface water acute EEC is **4.0 ppb** and the surface water chronic EEC is **3.9 ppb**. These values represent the 1-in-10 year peak surface water concentration and 1-in-10 year mean yearly concentration. The calculated concentration in surface water increases over time as the compound builds up in the

environment, and continued use may result in increasing concentration over time. The groundwater screening concentration, calculated using SCI-GROW is **0.02 ppb**. However, the properties of this compound are outside the range of values used to develop SCI-GROW. Because of its stability in the environment this chemical may be expected to accumulate in groundwater and the actual concentrations may be much higher.

Ecolyst currently has no registered or proposed residential uses . Therefore a residential exposure assessment is not required at this time.

Chemical Characteristics

The chemical structure of PT807-HCl is as follows:



Some of the physical properties of PT-807 HCl are summarized below:

Color: Colorless
Physical State: Slightly viscous liquid
Odor: Like sweet alcohol
B.P.: $105.9^0 \pm 1.5^0$C
Density: 1.0596 ± 0.0001 g/cm^3
Vapor pressure: 8.93×10^{-8} Torr
Dissociation Constant: pKa = 9.55 ± 0.08
pH: Neat 1.98±0.01 @ 25^0C
: 1% aq. Soln. 4.57±0.03 @ 25.1^0C
Octanol/Water Partition Coefficient:
$K_{o/w}$ at pH 5 and 7 = < 1.0
$K_{o/w}$ at pH 9 based on total ^{14}C-activity = 94.4±06.3
$K_{o/w}$ at pH 9 based on total ^{14}C-PT807-HCl = 235.0±16.0
Solubility:
Aqueous Buffer solution: pH 5-9 100%
Organic solvents: Acetonitrile 100% at 25^0C
Methanol 100%
Methylene chloride 100%

	Octanol	100%
Hydrolysis:	Stable	
Half-life:	Stable (photolysis)	
	335 days (aerobic soil metabolism)	
	No data submitted so assumed stable (aerobic aquatic metabolism)	

Toxicological Profile

PT807-HCl has been classified as a "not likely human carcinogen" Prenatal developmental toxicity studies in rats and rabbits provided no indication of quantitative or qualitative increased susceptibility to *in utero* exposure to PT807-HCl.

Subchronic Feeding - mouse. The No Observed Adverse Effect Level (NOAEL) was 7000 PPM (1004/1272 mg/kg/day, M/F); limit dose. **Note:** Due to faulty dose concentration analyses, the regulatory usefulness of this NOAEL is in doubt.

Subchronic Gavage - rat. The NOAEL was 30 mg/kg/day. The Lowest Observed Adverse Effect Level (LOAEL) was 300 mg/kg/day based on increased mortality; tremors, convulsions, and increased salivation in males and females; and elevated urinary protein in males.

Subchronic Feeding - dogs. The NOAEL was 2500 PPM (equivalent to 71/78 mg/kg/day, M/F). The LOAEL was 7500 PPM (equivalent to 211/233 mg/kg/day, M/F), based on pathological changes to the male reproductive organs and possibly the uterus in females.

21-Day Dermal - rat. The systemic NOAEL was >1000 mg/kg/day (limit dose). The dermal NOAEL was 1000 mg/kg/day (nonadverse dermal irritation was observed at 1000 mg/kg/day).

Developmental Toxicity - rat. The maternal NOAEL was 50 mg/kg/day. The maternal LOAEL was 250 mg/kg/day, based on clinical signs (post-dosing rooting in the bedding and lethargy) and reduced body weight gains. The developmental NOAEL was 500 mg/kg/day and the developmental LOAEL was not observed.

Developmental Toxicity - rabbit. The maternal NOAEL was 10 mg/kg/day. The Maternal LOAEL was 100 mg/kg/day, based on increased mortality in the mid- and high-dose animals. The developmental NOAEL was >200 mg/kg/day and the developmental LOAEL was not observed.

Reproductive Toxicity -rat. The systemic NOAEL was 14.1 mg/kg/day. The systemic LOAEL was 114 mg/kg/day based upon the body weight and body weight gains. The reproductive NOAEL was 14.1 mg/kg/day for both sexes. The Reproductive LOAEL was 114 mg/kg/day for both sexes based on decreased pup body weight and body weight gains, delayed sexual development, reductions in absolute and relative uterus and ovary weights, and histological changes in the uterus, vagina, and ovaries in the females.

Chronic Toxicity - dog. The NOAEL was >5000 ppm (135.7/151.5 mg/kg/day, M/F). The LOAEL was not observed.

Carcinogenicity - mouse (18 months). The NOAEL was 7000 ppm (1010/1250 mg/kg/day, M/F). The LOAEL was not observed. Mice were dosed at greater than the limit dose of 1000 mg/kg/day with no evidence of carcinogenic potential.

Chronic Toxicity/Carcinogenicity - rat. The NOAEL was 500 ppm (20/28 mg/kg/day, M/F). The LOAEL was 5000 ppm (213/308 mg/kg/day, M/F) based on decreased body weight and body weight gains. An increased incidence of hepatocellular adenomas and carcinomas in the high-dose males (5000 ppm) was attributed to significantly increased survival. There was no clear evidence of carcinogenic potential.

Bacterial Reverse Gene Mutation Test. Negative for cytotoxicity and genotoxic response at the limit dose (5000 ug/plate) with and without metabolic activation in *S. typhimurium* strains TA98, TA100, TA1535, and TA1537, and *E. coli* WP2 *uvr*A strain.

CHO/HGPRT/Mammalian Activation Assay. Negative for induction of forward mutation at the HGPRT locus in this *in vitro* assay with or without metabolic activation.

In vivo Mammalian Chromosome Aberrations in CHO Cells. Clastogenic with or without metabolic activation in Chinese hamster ovary cells cultured *in vitro*.

In vivo Mammalian Cytogenetics - Micronucleus Assay in Mice. Testing at toxic concentrations, with mortality at $\geq$116.5 mg/kg, did not induce significant increases in micronucleated polychromatic erythrocytes (MPCEs).

Unscheduled DNA Synthesis in Rat Hepatocytes. Unscheduled DNA Synthesis was not induced.

Acute Neurotoxicity - rats. The neurotoxicity NOAEL was 50 mg/kg/day. The neurotoxicity LOAEL was 200 mg/kg based on slight ataxia in 1 of 11 males. The neurotoxicity at 400 mg/kg included increases in FOB clinical signs and decreases in motor activity.

Subchronic Neurotoxicity - rats. The neurotoxicity NOAEL is >5000 ppm. (323/386 mg/kg/day; M/F). The neurotoxicity LOAEL was not observed.

Metabolism - rat. [^{14}C]PT807-HCl was readily absorbed from the GI tract of male and female rats. Within 24 hours of dosing, 75.2 and 66.5% of the administered dose was recovered in urine (plus cage wash) from males and females, respectively. Within 168 hours, 79.3% of the dose was recovered in urine (plus cage wash) and 13.8% was recovered in feces from males, and 73.8% was recovered in urine

(plus cage wash) and 18.3% was recovered in feces from females. Only ≤0.34% of the dose was associated with tissues, and no radioactivity was found in expired air.

Radioactivity was generally 2-3x higher in tissues and blood of females than males, except in kidney and spleen. However, the pattern of distribution among tissues was similar between the sexes. With the exception of the uterus, radioactivity was highest in liver, spleen, and carcass and lowest in fat and gonads. In females, radioactivity was highest in the uterus and was >2.3x higher than the liver and carcass.

The metabolism of PT807-HCl in male and female rats was qualitatively similar. Only minor amounts of parent, PT807 (0.400.8% dose), were identified in urine and feces. The primary metabolite identified in excreta was the carboxylic acid metabolite (M-7) which then undergoes conjugation to glucuronic acid (m-3) or hydroxylation on the alkyl portion of the molecule (RU-10b). Other secondary reactions involved in the metabolism of PT807 included deamination, N-de-ethylation, hydroxylation of the N-ethyl group, and oxidation of the benzyl carbon.

Ecological Characteristics

Avian Acute Toxicity:

Bobwhite Quail: LD_{50} = 765 mg/kg

Avian Dietary Toxicity:

Bobwhite Quail: 8-day LC_{50} > 5,600 ppm
Mallard Duck: 8-day LC_{50} > 5,600 ppm

Reproductive Toxicity:

Bobwhite Quail NOEC = 1,500
LOEC =>1,500
Mallard Duck NOEC = 1,500
LOEC = >1,500

Mammalian Acute and Chronic Toxicity

Laboratory rat LD_{50} = 531 mg/kg/day (acute oral)
Laboratory rat NOAEL =14.1 (chronic dietary 1
2-generation study)
LOAEL = 114 mg/kg/day

Insect Toxicity

Honey bee LD_{50} >25 (ug/bee)

Freshwater Fish Acute Toxicity:

Bluegill Sunfish 96-hr LC_{50} > 12.6 mg/L ai/1
Rainbow Trout: 96-hr LC_{50} 6.7 mg/L ai/l

Fish Early Life Stage Test:

Rainbow trout NOEC/LOEC = 0.125/0.252 mg/L

Freshwater Invertebrate Acute Toxicity:

Daphnia magna 24-hr LC50 = 24 mg ai/l

Aquatic Invertebrate Life Cycle: Chronic Toxicity

Daphnia magna NOEC = 1.1 mg ai/L

Estuarine and Marine Organisms Toxicity:

Sheepshead
Minnow 96-hr LC50 = 16 mg ai/l
Eastern Oyster 96-hr EC50 = 7.0 mg ai/l
Mysid Shrimp 96-hr LC50 = 20 mg ai/l

Seedling Emergence and Vegetative Vigor

Seedling Emergence:

Monocot-Corn EC_{25} > 0.014 lbs ai/A
Monocot-Onion
Monocot-ryegrass
Monocot-Wheat
Dicot-Root Crop/
Radish
Dicot-Soybean
Dicot-Bean
Dicot-Cabbage
Dicot-lettuce
Dicot-tomato

Vegetative Vigor:

Monocot-corn EC_{25} 0.014 Lbs ai/A
Monocot-onion
Monocot-ryegrass
Monocot-wheat
Dicot-radish
Dicot-soybean
Dicot-bean
Dicot-cabbage
Dicot-lettuce
Dicot-tomato

The vegetative vigor studies conducted using the equivalent application rate of 0.014 lbs. a.i./A
revealed that none of the species tested exhibited any effect greater than 10%. Similar to the seedling emergence studies, the radish was the most sensitive species with 10% of the plants exhibiting phytotoxicity. The most sensitive monocot was corn with 6% of the plants showing reduced dry weight. The vegetative vigor toxicity testing guideline is fulfilled.

Growth and Reproduction of Aquatic Plants: Acute Toxicity

Non-Vascular Plant-Green Algae

Psuedokirchnellia subcapitata 96-Hour IC_{50} = 0.40 mg/L

Skeletonema costatum 96-Hour IC50 = 0.119 mg/L

Vascular Plant

Lemma gibba *96-Hour IC 50 = >116 mg/L*

Diatoms

Navicula pelliculosa *96-Hour IC50 = 0.88 mg/L*

Environmental Characteristics

Ecolyst is a persistent, moderately mobile to immobile compound; on sandy soils, leaching and runoff are likely. The primary degradation pathway is aerobic degradation in soil to CO_2. Batch adsorption studies and model simulation indicate moderate potential for leaching and runoff in sandy soils. K_d and K_{oc} values varied (K_d:2.7-420; K_{oc}:285-11,000) depending on soil type. Soil physical characteristics other than organic carbon content, e.g.,cation exchange capacity and clay content, appear to strongly influence sorption of Ecolyst. If sandy soils are present in areas of application, some leaching and/or runoff may occur. Also, irrigation canals present in citrus groves are vulnerable to spray drift and potential runoff from sandy soils. However, this risk is mitigated by the low application rate (0.013 lb a.i./A).

The surface water acute Estimated Environmental Concentration is 4.0 part per billion (ppb). The surface water chronic EEC is 3.9 ppb. The groundwater screening concentration, calculated using SCI-GROW is 0.02 ppb. Because of PT 807-HCl's stability in the environment this chemical may be expected to have some accumulation in drinking water, however the Agency does not expect the exposure to exceed our level of concern considering the low application rate and extremely low EEC's.

Ecolyst is moderately toxic to coldwater fish and estuarine/marine molluscs and is slightly toxic to warmwater fish, estuarine/marine fish, freshwater macroinvertebrates and estuarine/marine shrimp. Ecolyst is also slightly toxic to upland game birds and small mammals on an acute oral exposure basis, however it is practically nontoxic to birds on a subacute dietary exposure basis. Ecolyst is practically nontoxic to honey bees on an acute contact basis.

Chronic toxicity testing with birds failed to demonstrate any treatment-related effects; however, in rats chronic exposure to Ecolyst resulted in decreased pup body weight and body weight gain, delayed sexual development, reductions in absolute and relative uterus and ovary weights and histopathological changes in the uterus, vagina, and ovaries of dams (NOAEL = 281 ppm). Chronic aquatic exposure to Ecolyst resulted in diminished growth in both rainbow trout and water fleas with NOEC values of 0.125 mg/L and 1.1 mg/L, respectively. Chronic exposure in water fleas also resulted in reproductive effects, i.e., reduced egg production. Although Ecolyst is a plant growth regulator, terrestrial plant studies failed to establish an EC_{25} value. Ecolyst exhibited a broad range of toxicity to aquatic plants with IC_{50} values ranging from 0.102 mg/L (freshwater diatom; Skeletonema costatum) to greater than 116 mgL (duckweed; Lemna gibba).

When compared to estimated environmental concentrations, no acute or chronic levels of concern were exceeded for either aquatic or terrestrial animals (RQ < 0.01) at the maximum proposed application rate for citrus. No levels of concern were exceeded for either terrestrial or aquatic plants.

Although it is unlikely that at the maximum proposed application rate for Ecolyst, the compound will represent an acute or chronic risk to either terrestrial or aquatic organisms, the potential accumulation of this chemical in both surface and groundwater of vulnerable areas is a

concern. While there may be some potential for PT807-HCl to accumulate in drinking water, the Agency does not expect the exposures to exceed our level of concern considering the drinking water level of concern (DWLOC) is thousands of times higher than high end estimates of drinking water exposure.

Based on Ecolyst's persistence and the likelihood that the pesticide will contaminate both surface and groundwater, the following label language is recommended:

Groundwater Label Advisory

This chemical has properties and characteristics associated with chemicals detected in groundwater. The use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination.

Surface Water Advisory

This chemical can contaminate surface water through spray drift. Also, this chemical has properties and characteristics associated with chemicals that have a potential for runoff into surface water. The use of this chemical in poorly draining or wet soils with readily visible slopes toward adjacent surface waters, frequently flooded areas, areas overlaying extremely shallow groundwater, areas with in-field canals or ditches that drain to surface water, areas not separated from adjacent surface waters with vegetated filter strips, and areas overlaying tile drainage systems that drain to surface waters may result in surface water contamination.

TOLERANCE ASSESSMENT

A tolerance has been established for the residues of PT807-HCl at 0.01 ppm in or on oranges. Data were sufficient to determine that no harm to humans or the environment will result from residues at this level.

AGGREGATE EXPOSURES

In examining aggregate exposure, Food Quality Protection Act (FQPA) directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses). In evaluating food exposures, EPA takes into account varying consumption patterns of major identifiable subgroups of consumers, including infants and children.

From Food and Feed Uses

Using the most conservative Tier I approach, it is estimated that the acute exposure to PT807-HCl from food for the general U.S. population, infants and children will utilize <1% of the aPAD. Despite the potential for exposure to PT807-HCl in drinking water, the Agency does not expect the aggregate exposure to exceed 100% of the aPAD for adults, infants and children. EFED's maximum concentration of PT807-HCl in surface and groundwater for acute exposure is well below the Drinking Water Level of Concern (DWLOC). The Agency concludes that there is a reasonable certainty that no harm will result to adults, infants and children from acute aggregate exposure to PT807-HCl residues.

Using the most conservative Tier 1 analysis, it is estimated that the chronic exposure to PT807-HCl from food for the general U.S. population, infants and children will utilize <1% of the cPAD. Despite the potential for exposure to PT807-HCl in drinking water, the Agency does not expect the aggregate exposure to exceed 100% of the cPAD. The Agency's maximum concentration of PT807-HCl is very small compared to the DWLOCs. Currently there is no registered or proposed use that could result in residential exposures. Therefore, the Agency concludes that there is a reasonable certainty that no harm will result to adults, infants and children from chronic aggregate exposure to PT807-HCl residues.

Cumulative Toxicity and Metabolism

There is little evidence of cumulative toxicity. The oral LD_{50} in rats (531 mg/kg) is not markedly greater than the oral subchronic rat LOAEL (300 mg/kg/day). Similarly, a comparison of subchronic and chronic LOAELs reveals little evidence of cumulation in the rat (300 mg/kg/day v 213/308, M/F) and dog (211/233 mg/kg/day v >135.7/141.5 mg/kg/day, HDT). The rat metabolism study reveals why there is a minimum of cumulation. Rats rapidly excrete PT807-HCl, primarily in the urine and secondarily in the feces, with very little remaining in the tissues after 7 days ($\leq$0.34%). There may also be some adaption due to enzyme induction.

DETERMINATION OF SAFETY FOR INFANTS AND CHILDREN

The FQPA Safety Factor committee has determined that the safety factor should be reduced to 1x. Rationales for removing the FQPA factor include: 1) the toxicology database is complete for the assessment of the effects following in utero and/or postnatal exposure to PT807-HCl; 2) the toxicity data provided no indication of quantitative or qualitative increased susceptibility of rats or rabbits to in utero and/or postnatal exposure; 3) the requirement of a developmental neurotoxicity study is not based on the criteria reflecting some special concern which are generally used for requiring a DNT study and an FQPA safety factor (e.g: neuropathy in adult animals; CNS malformations following prenatal exposure; brain weight or sexual maturation changes in offspring; and/or functional changes in offspring) and therefore, does not warrant an FQPA safety factor; and 4) the exposure assessment will not underestimate the potential dietary (food and water) exposures for infants and children from the use of PT807-HCl (currently no residential exposure is expected). Specifically, as to residues in drinking water, EPA took into account that residues may

accumulate over time.

OCCUPATIONAL EXPOSURE

Workers may be exposed to PT807-HCl during mixing, loading, application and postapplication activities. Based on the proposed use patterns, short and intermediate-term exposures may occur. Chronic exposures (6 months of continuous exposure) are not expected. Dermal risk assessments are not required due to the absence of systemic toxicity at the limit dose. Inhalation margins of exposure (MOE) were calculated for workers and were well above 100 (MOE <100 are of concern).

SUMMARY OF DATA GAPS

Anaerobic Soil Metabolism [GLN 163-2]

Anaerobic Aquatic Metabolism [GLN 162-3]

Aged Leaching [GLN 163-1] required if the Aquatic Metabolism study shows degradation

Terrestrial Field Dissipation (GLN 164-1)

Product Chemistry Physical Chemical Properties (end-use product)

A Developmental Neurotoxicity Study (rat) is required based on the fact that the chemical is a neurotoxicant in adult animals.

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