UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 20-FEB-2004

SUBJECT: PP#: 0F06123. **Propamocarb Hydrochloride in/on Fruiting Vegetables, Cucurbit Vegetables, and Head and Leaf Lettuce. Health Effects Division (HED) Risk Assessment.** PC Code: 119302. DP#: D284504.

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TO: Mary Waller/Lisa Jones, PM Team 21
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The HED of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP has requested that HED evaluate hazard and exposure data and conduct dietary, occupational, residential and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from proposed uses of propamocarb hydrochloride on fruiting vegetables, cucurbit vegetables, and head and leaf lettuce.

A summary of the findings and an assessment of human risk resulting from the registered and proposed tolerances for propamocarb hydrochloride is provided in this document. The risk assessment, the residue chemistry data review, and the dietary risk assessment were provided by Jennifer Tyler (RAB1), the hazard characterization by Guruva Reddy (RAB1), the occupational/residential exposure assessment by Mark Dow (RAB1), and the drinking water assessment by Kevin Costello of the Environmental Fate and Effects Division (EFED).

Recommendation for Tolerances

The HED Hazard Identification Assessment Review Committee (HIARC) requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of propamocarb hydrochloride and inhalation margins of exposure (MOEs) >1000 for the proposed uses in this risk assessment, propamocarb hydrochloride qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses

03/04

[HED Standard Operating Procedure (SOP) 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02]. **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

Provided revised Sections B and F with the modifications specified in Section 8.1 of this risk assessment are submitted, the residue chemistry and toxicological databases support the unconditional registration and the establishment of the following tolerances for residues of propamocarb hydrochloride *per se*:

Vegetable, cucurbit, group 9	1.5 ppm
Lettuce, head	50 ppm
Lettuce, leaf	90 ppm
Vegetable, fruiting, group 8	2.0 ppm
Tomato, paste	5.0 ppm

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1.0 EXECUTIVE SUMMARY

Propamocarb hydrochloride [propyl 3-(dimethylamino) propylcarbamate hydrochloride] is a List C carbamate fungicide with specific activity against numerous Oomycete species, which cause foliar diseases and seedling, seed, root, foot and stem rot in various edible and ornamental crops. It is currently registered for use on potatoes, tomatoes, as well as golf course, sod farms, and in nurseries/greenhouses. The label specifies that these products are used on golf courses by commercial applicators only.

Bayer CropScience has submitted a petition proposing the use of the fungicide propamocarb hydrochloride, formulated as Previcur® Flex Fungicide [66.5% Suspension Concentrate (SC)], to control various diseases on fruiting vegetables, cucurbit vegetables and lettuce. Bayer is proposing both field and greenhouse uses on these commodities. In conjunction with these uses, Bayer is proposing the establishment of permanent tolerances for residues of propamocarb hydrochloride in/on the following raw agricultural commodities (RACs): vegetable, cucurbit, group at 1.5 ppm; lettuce, head at 50 ppm; lettuce, leaf at 65 ppm; vegetable, fruiting, group at 2.0 ppm; tomato, paste at 5.0 ppm; wheat, grain at 0.05 ppm; wheat, straw at 0.1 ppm; wheat, forage at 0.3 ppm and wheat, hay at 0.3 ppm.

The most recent Section 3 HED human health risk assessment was conducted in conjunction with a petition for the use of propamocarb hydrochloride on potatoes (Memo, J. Rowell, *et.al.*, 6/27/00; D265426). Since the completion of this risk assessment, the following has occurred: 1) a revisit to HED HIARC on 11/6/03, where the acute and chronic Reference Doses (RfDs) were confirmed, toxicological end-points for dermal exposure as appropriate in occupational/residential exposure risk assessments were chosen, and endpoints for short- and intermediate-term incidental oral exposure and short- and intermediate-term inhalation exposure were selected; and 2) in accordance with the February 2002 OPP 10X guidance document, a revisit of the Food Quality Protection Act (FQPA) Safety Factor (SF) to evaluate the potential for increased susceptibility of infants and children to exposure to propamocarb hydrochloride.

Hazard Assessment

Propamocarb hydrochloride has low acute toxicity via the oral, dermal, and inhalation routes (Toxicity Categories III-IV). It is neither a dermal irritant nor a dermal sensitizer. It causes slight irritation to the rabbit eye. No target organ has been identified in subchronic and chronic toxicity studies. Female rats appear slightly more sensitive than male rats. In the rat subchronic studies, propamocarb hydrochloride (near the limit dose at 716 mg a.i./kg/day) caused a decrease in body weight, body weight gain, and food efficiency in female rats; while in the male rats, only a decrease in food efficiency was observed at doses greater than the limit dose (1363 mg a.i./kg/day). In the rat 2-year feeding study, decreased body weight and body weight gain, decreased food consumption, and an increased incidence of vacuolation of choroid plexus ependymal cells in the brain were noted in both sexes at the highest dose tested (682-871 mg/kg/day). In the mouse 18-month study, decreased body weight and body weight gain were observed in the females, while the Lowest-Observed-Adverse-Effect-Level (LOAEL) was not observed in the males. In contrast to the results observed in rodents, treatment with propamocarb hydrochloride posed greater toxicity to male dogs than to female dogs. In a 2-year feeding study, decreased body weight gain and food efficiency and focal or multi-focal chronic erosive gastritis

were observed in male dogs, while none of these findings were observed in the females. However, binocular ocular toxicity was observed in all dogs at the high dose; this damage was observed after 40 weeks of treatment and was not reversible for up to 30 weeks after cessation of treatment. In the rabbit 21-day dermal study, signs of toxicity included dermal irritation and depressed body weight gain in the females.

There is limited evidence of neurotoxicity potential. Vacuolization of the choroid plexus ependymal cells in the chronic rat study and ocular toxicity in the chronic dog study were observed only at very high doses, over long exposure periods, and in the presence of other toxicity. Signs of neurotoxicity were also observed in the rat developmental toxicity study, but only at doses causing mortality. In the acute neurotoxicity study, neurobehavioral effects at the limit dose (2000 mg a.i./kg) consisted of only soiled fur coat (both sexes) and decreased motor activity 8 hours post-dosing (females only). Neurobehavioral evaluation in a subchronic, 90-day neurotoxicity study did not reveal any treatment-related Functional Observation Battery (FOB) findings or changes in motor activity. In addition, although a carbamate, propamocarb hydrochloride does not cause any appreciable cholinesterase inhibition.

Based upon the available data, it does not appear that the offspring are more sensitive to propamocarb hydrochloride than the parental animals. In the rat developmental toxicity study, maternal toxicity, which included increased mortality, decreased body weight gain, and clinical observations (spastic gait, bloody snout, and bloody vaginal discharge), occurred at the same dose level as increased fetal death and possible increases in minor skeletal anomalies in the pups. At the next higher dose there was also a marked increase in resorptions and post-implantation loss. In the rabbit developmental toxicity study, there was a decrease in body weight gain and possibly increased abortions in the does at the same dose level that there was an increase in post-implantation loss. In the rat 2-generation reproduction study, maternal and reproductive toxicity included decreased body weight, body weight gain, and food consumption in both dams and pups at the same dose level.

There is no concern for mutagenic potential, and there is no evidence of carcinogenic potential in either the rat or mouse. Propamocarb hydrochloride has been classified as "not likely to be carcinogenic in humans."

Dose Response Assessment and FQPA Decision

As mentioned previously, the HED HIARC met on 11/6/03 to select endpoints for risk assessment and to evaluate the potential for increased susceptibility of infants and children from exposure to propamocarb hydrochloride according to the February 2002 OPP 10X guidance document. This was a re-evaluation of the toxicology database subsequent to the initial evaluation by the HIARC on 12/16/99. The special FQPA SF was reduced to 1X based on toxicological considerations by the HIARC (12/2/03; TXR # 0052260), the conservative residue assumptions used in the dietary and residential exposure risk assessments, and the completeness of the residue chemistry and environmental fate databases (evaluated by the risk assessment team).

Risk assessments were conducted for the following specific exposure scenarios listed below. The acute and chronic RfDs were calculated by dividing the No-Observed-Adverse-Effect-Level

(NOAEL) by 100 (10X for interspecies extrapolation, 10X for intraspecies variation). Since the special FQPA SF has been reduced to 1X, the acute and chronic population adjusted doses (aPAD and cPAD) are equal to the aRfD and cRfD, respectively. A 60% dermal absorption factor was estimated by comparing the rabbit maternal toxicity LOAEL (300 mg/kg/day) from the rabbit developmental toxicity study with the LOAEL (525 mg/kg/day) from the 21-day rabbit dermal study. The level of concern for residential dermal exposures and occupational dermal and inhalation exposures are for MOEs <100.

Exposure Scenario	Dose	Endpoint	Study/Effect
Acute dietary (females 13-50 years old)	NOAEL = 150 mg/kg/day	aRfD and aPAD = 1.5 mg/kg/day	Developmental Toxicity Study - Rabbit/ Increased post-implantation loss at the LOAEL of 300 mg/kg/day
Acute dietary (general U.S. population, including infants and children)	NOAEL = 200 mg/kg/day	aRfD and aPAD = 2.0 mg/kg/day	Acute Neurotoxicity Screening Battery - Rat/Decreased body weight gain and decreased motor activity at the LOAEL of 2000 mg/kg/day
Chronic dietary	NOAEL = 12 mg/kg/day	cRfD and cPAD = 0.12 mg/kg/day	Carcinogenicity Study - Mouse/Decreased body weight and body weight gain in females at the LOAEL of 95 mg/kg/day
Short-term dermal	dermal NOAEL = 150 mg/kg/day	Target MOE = 100 (residential and occupational)	21-Day Dermal Toxicity Study - Rabbit/decreased body weight gain in females at the LOAEL of 525 mg/kg/day
Intermediate-term dermal	dermal NOAEL = 150 mg/kg/day	Target MOE = 100 (residential and occupational)	

Residential Exposure Estimates

Short-term post-application exposures are expected for the adult and adolescent golfer. As no chemical-specific data are available to address post-application exposure to persons reentering golf courses treated with propamocarb hydrochloride, the post-application risk assessment was based on generic assumptions as specified by the Residential SOPs and recommended approaches by HED's Exposure Science Advisory Committee (ExpoSAC). Changes to the Residential SOPs have been proposed that alter the residential post-application scenario assumptions. The proposed assumptions are expected to better represent residential exposure and are still considered to be high-end, screening level assumptions. HED management have authorized the use of the revised residential SOPs that were presented to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) in September 1999. Therefore, HED has deviated from the current Residential SOP assumptions and uses the proposed assumptions to calculate exposure estimates. An MOE of 100 is adequate to ensure protection from propamocarb via the dermal and inhalation routes for residential exposures. Based on the current use patterns, the golfer scenario is expected to represent a high-end estimate for residential exposure. The calculated MOE for the golfer is **980**; and, therefore, does not exceed HED's level of concern.

Dietary Exposure Estimates

Unrefined, Tier 1 acute (separate assessments for females 13-49 years old and the general U.S. population and all other population subgroups) and chronic (general U.S. population and all other population subgroups) dietary exposure assessments were conducted using Dietary Exposure

Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3) and the following: 1) established and recommended tolerances for all plant commodities; 2) HED-calculated residues of concern (parent and metabolites) for livestock commodities; 3) 100% crop treated (CT) information for all current and proposed uses; and 4) modified processing factors for tomato paste and default processing factors for all other commodities. The acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95% percentile for females 13-49 years old (6% aPAD) and the general U.S. population (4% aPAD) and all population subgroups. The most highly exposed population subgroups are children 1-2 years old and children 3-5 years old at 5% aPAD. The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (18% cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old at 36% cPAD.

Drinking Water Exposure Estimates

EFED provided Tier 1, surface and ground water Estimated Drinking Water Concentrations (EDWCs) for propamocarb hydrochloride using FQPA Index Reservoir Screening Tool (FIRST) and Screening Concentration in Ground Water (SCI-GROW) models, respectively. The EDWCs were based on the currently registered turf use, which has the highest yearly application rate. For surface water, and acute (peak) and chronic (average annual) EDWCs are 972 ppb and 77 ppb, respectively. The groundwater EDWC is 2.99 ppb. These values are meant to represent upper-bound estimates of the concentrations that might be found in surface water and groundwater due to the use of propamocarb hydrochloride on turf. All EEC values are less than the lowest drinking water level of comparison (DWLOC) values of 19,000 ppb (children 1-2 years old, children 3-5 years old and children 6-12 years old), 40,000 ppb (females 13-49 tears old), and 760 ppb (children 1-2 years old) determined for the acute, short-term, and chronic scenarios, respectively. Therefore, the EECs do not exceed HED's level of concern.

Aggregate Exposure Scenarios and Risk Conclusions

Aggregate exposure risk assessments were performed for the following scenarios: acute aggregate exposure (food + drinking water), short-term aggregate exposure (food + drinking water + residential), and chronic aggregate exposure (food + drinking water). Intermediate-term aggregate risk assessment was not performed because the short-term aggregate assessment adequately addresses both the short- and intermediate-term golfer dermal exposures. A long-term aggregate risk assessment was not performed because, based on the current use patterns, HED does not expect exposure durations that would result in long-term exposures. A cancer aggregate risk assessment was not performed because propamocarb hydrochloride is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment. Dietary (food and drinking water) and post-application residential exposures were considered, as necessary, because there is a potential for individuals to be exposed concurrently through these routes. **All aggregate exposure and risk estimates do not exceed HED's level of concern for the scenarios listed above.**

Occupational Exposure Estimates
Based on the proposed use patterns, short-term (1-30 days) dermal and inhalation exposures are expected for commercial and private (i.e., grower operators) applicators. The application techniques that are assessed include a mixer/loader using open pour of liquids supporting aerial operations; an applicator using open-cab, ground-boom machinery; and a mixer/loader/ applicator using open-pour loading and low-pressure hand-wand equipment. No chemical-specific data are available with which to assess potential exposure to pesticide handlers (i.e., mixer/loaders and applicators). Therefore, estimates of exposure are based on study data available in the Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate Exposure Guide, 8/98). A MOE ≥ 100 is adequate to protect occupational pesticide handlers. **Provided all handlers wear protective gloves (pilots are not required to wear protective gloves)**, all MOEs are >100; and, therefore, do not exceed HED's level of concern. It should be noted that although short-term exposures are typically expected, guidance from ExpoSAC indicates that intermediate-term exposures (1 - 6 months) may be possible. However, the NOAELs for short-term and intermediate-term exposures are the same. Therefore, the estimated risk is the same for intermediate-term exposures as is estimated for short-term exposures.

Short-term (1-30 days) dermal exposures are expected for post-application agricultural activities. Post-application inhalation exposure is expected to be negligible. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur. HED has also identified Transfer Coefficients (TC) (expressed as cm^2/hr) relative to the various activities. There are no chemical-specific data with which to estimate post-application exposure of agricultural workers to dislodgeable residues of pesticide. Therefore, post-application worker exposure is estimated using HED procedure that assumes 20% of the application rate is available as dislodgeable foliar residue (DFR) on the day of treatment. The HED ExpoSAC Policy 003.1, Rev. 7 Aug. 2000, Regarding Agricultural Transfer Coefficients; Amended ExpoSAC Meeting notes - 13 Sept 01 lists a number of possible post-application agricultural activities relative to some of the subject crops that result in potential pesticide exposure to agricultural workers. For most of the proposed crop uses, the activities with the highest TCs are typically hand harvesting and hand thinning. An MOE of 100 is adequate to protect agricultural workers from post-application exposures to propamocarb. The estimated MOE is based upon conservative assumptions and is > 100; therefore, estimated risks from post-application exposures do not exceed HED's level of concern.

Recommendations for Tolerances
The HED HIARC requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of propamocarb hydrochloride and inhalation MOEs >1000 for the proposed uses in this risk assessment, propamocarb hydrochloride qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses (HED SOP 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02). **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

Provided revised Sections B and F with the modifications specified in Section 8.1 of this risk

assessment are submitted, the residue chemistry and toxicological databases support the unconditional registration and the establishment of the following tolerances for residues of propamocarb hydrochloride *per se*:

Vegetable, cucurbit, group 9	1.5 ppm
Lettuce, head	50 ppm
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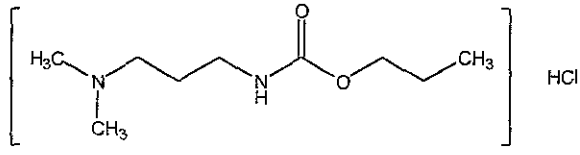
Vegetable, fruiting, group 8	2.0 ppm
Tomato, paste	5.0 ppm

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

2.1 Identification of Active Ingredient

Registrant:	Bayer CropScience
Common name:	Propamocarb Hydrochloride
Pesticide Type:	Fungicide
Chemical Class:	Carbamate
Target Pests:	Phytophthora blight (late blight), Phytophthora fruit rot, Downy mildew
Formulation:	Previcur Flex
% a.i.:	66.5
Trade Names:	Previcur® Flex
EPA Reg Nos.:	264-678
CAS Number:	25606-41-1
PC Code:	119302
Chemical name:	propyl[3-(dimethylamino)propyl]carbamate monohydrochloride
Empirical Formula:	$C_9H_{21}ClN_2O_2$
Molecular Weight:	224.7

2.2 Structural Formula



Propamocarb Hydrochloride

2.3 Physical and Chemical Properties

The review of product chemistry data associated with this petition is under the purview of RD. Product chemistry data in support of this petition have been submitted by the petitioner and were forwarded by RD to their Product Chemistry Review Section on 8/12/96. All applicable product chemistry data requirements must be met for a Section 3 registration of the proposed use of propamocarb hydrochloride on potatoes. The following data for propamocarb hydrochloride were provided in the HED RED signed in September, 1995:

Appearance:	Colorless to yellow
Vapor Pressure:	$8x10^{-5}$ Pa at 25°C
Water Solubility:	>700 g/L
Partition Coefficient (Octanol/Water):	-2.6 (pH 4.1)
Melting Point:	64.2°C

Propamocarb hydrochloride is a solid at room temperature with a low vapor pressure; thus, any losses due to volatilization/sublimation are expected to be minimal.

3.0 HAZARD CHARACTERIZATION

The existing toxicological database for propamocarb hydrochloride supports the establishment of permanent tolerances for residues of propamocarb hydrochloride in/on the RACs resulting from the proposed uses.

3.1 Hazard Profile

The toxicological database for propamocarb hydrochloride is complete. The HIARC did request a 28-day inhalation study to characterize the direct effects of propamocarb hydrochloride on the pulmonary system and any systemic effects via the inhalation route. The HED HIARC requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of propamocarb hydrochloride and inhalation MOEs >1000 for the proposed uses in this risk assessment, propamocarb hydrochloride qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses (HED SOP 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02). **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

Propamocarb hydrochloride has low acute toxicity via the oral, dermal, and inhalation routes (Toxicity Categories III-IV). It is not dermal irritant nor a dermal sensitizer. It causes slight irritation to the rabbit eye. No target organ has been identified in subchronic and chronic toxicity studies. Female rats appear slightly more sensitive than male rats. In the rat subchronic studies, propamocarb hydrochloride (near the limit dose at 716 mg a.i./kg/day) caused a decrease in body weight, body weight gain, and food efficiency in female rats; while in the male rats, only a decrease in food efficiency was observed at doses greater than the limit dose (1363 mg a.i./kg/day). In the rat 2-year feeding study, decreased body weight and body weight gain, decreased food consumption, and an increased incidence of vacuolation of choroid plexus ependymal cells in the brain were noted in both sexes at the highest dose tested (682-871 mg/kg/day). In the mouse 18-month study, decreased body weight and body weight gain were observed in the females, while the LOAEL was not observed in the males. In contrast to the results observed in rodents, treatment with propamocarb hydrochloride posed greater toxicity to male dogs than to female dogs. In a 2-year feeding study, decreased body weight gain and food efficiency and focal or multi-focal chronic erosive gastritis were observed in male dogs, while

none of these findings were observed in the females. However, binocular ocular toxicity was observed in all dogs at the high dose; this damage was observed after 40 weeks of treatment and was not reversible for up to 30 weeks after cessation of treatment. In the rabbit 21-day dermal study, signs of toxicity included dermal irritation and depressed body weight gain in the females.

There is limited evidence of neurotoxicity potential. Vacuolization of the choroid plexus ependymal cells in the chronic rat study and ocular toxicity in the chronic dog study were observed only at very high doses, over long exposure periods, and in the presence of other toxicity. Signs of neurotoxicity were also observed in the rat developmental toxicity study, but only at doses causing mortality. In the acute neurotoxicity study, neurobehavioral effects at the limit dose (2000 mg a.i./kg) consisted of only soiled fur coat (both sexes) and decreased motor activity 8 hours post-dosing (females only). Neurobehavioral evaluation in a subchronic, 90-day neurotoxicity study did not reveal any treatment-related FOB findings or changes in motor activity. In addition, although a carbamate, propamocarb hydrochloride does not cause any appreciable cholinesterase inhibition.

Based upon the available data, it does not appear that the offspring are more sensitive to propamocarb hydrochloride than the parental animals. In the rat developmental study, maternal toxicity, which included increased mortality, decreased body weight gain, and clinical observations (spastic gait, bloody snout, and bloody vaginal discharge), occurred at the same dose level as increased fetal death and possible increases in minor skeletal anomalies in the pups. At the next higher dose there was also a marked increase in resorptions and post-implantation loss. In the rabbit developmental toxicity study, there was a decrease in body weight gain and possibly increased abortions in the does at the same dose level that there was an increase in post-implantation loss. In the rat 2-generation reproduction study, maternal and reproductive toxicity included decreased body weight, body weight gain, and food consumption in both dams and pups at the same dose level.

There is no concern for mutagenic potential, and there is no evidence of carcinogenic potential in either the rat or mouse. Propamocarb hydrochloride has been classified as "not likely to be carcinogenic in humans."

Table 1. Acute Toxicity Profile of Propamocarb Technical.

GDLN	Study Type	MRID	Results	Tox Category
870.1100	Acute Oral	41278115	LD_{50} =2900 mg/kg (M) LD_{50} = 2000 mg/kg (F)	III
870.1200	Acute Dermal	41278116	LD_{50} > 3,000 mg/kg	III
870.1300	Acute Inhalation	93193044	LC_{50} > 7.90 mg/L (Limit Test)	IV
870.2400	Primary Eye Irritation	41278117	Slight irritation, resolved within 72 hrs	III
870.2500	Primary Skin Irritation	41278118	No erythema after 24 hours	IV
870.2600	Dermal Sensitization	00083808	Non-sensitizer	N/A

Table 2. Toxicity Profile of Propamocarb Hydrochloride.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100 90-Day oral toxicity in rodents	44810401 (1998) Acceptable/guideline 0, 5000, 10,000 or 20,000 ppm M: 0, 318, 646, or 1363 mg/kg/day F: 0, 363, 716, or 1549 mg/kg/day	NOAEL = 363 mg/kg/day in females and 646 mg/kg/day in males LOAEL = 716 mg/kg/day in females, based on decreased body weight and body weight gain and decreased food efficiency. LOAEL in males is 1363 mg/kg/day based on decreased food efficiency
870.3150 90-Day oral toxicity in nonrodents	41278119 (1977) and 43044201 (1985) Acceptable/guideline M: 0, 22.75, 70.81, or 243.32 mg ai/kg/day F: 0, 22.752, 72.91, or 228.31 mg ai/kg/day	NOAEL was not achieved LOAEL = 22.75 mg/kg/day based upon body weight gain depression, decreased food efficiency and focal or multi-focal chronic erosive gastritis
870.3200 21/28-Day dermal toxicity in rabbits	00071526 (1980) Acceptable/guideline M & F: 0, 150, 525 or 1500 mg/kg/day	NOAEL≥150 mg/kg/day for both sexes LOAEL = 525 mg/kg/day based on dose-related skin irritation and depressed body weight gain
870.3250 90-Day dermal toxicity in rats	NA	NA
870.3465 90-Day inhalation toxicity in rats	NA	NA
870.3700a Prenatal developmental toxicity in rats	00101641 (1981) and 93193042 (1990) Acceptable/guideline F: 0, 74, 221, 740 or 2210 mg/kg/day	**Maternal** NOAEL = 221 mg/kg/day LOAEL = 740 mg/kg/day based on mortality **Developmental** NOAEL = 221 mg/kg/day LOAEL = 740mg/kg/day based on GD 20 fetal death and a possible increase in minor skeletal anomalies
870.3700b Prenatal developmental toxicity in rabbits	00072574 (1981), 93193043 (date not available) Acceptable/guideline F: 0, 15, 45, 150, 300, 600 mg/kg/day	**Maternal** NOAEL = 150 mg ai/kg/day LOAEL = 300 mg /kg/day based on decreased body weight gains for GD 6-18 and possible increased abortions **Developmental** NOAEL = 150 mg/kg/day LOAEL = 300 mg/kg/day based on increased post-implantation loss

Table 2. Toxicity Profile of Propamocarb Hydrochloride.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3800 Reproduction and fertility effects in rats	44730103 (1998), 44730102 (1998) Acceptable/guideline F_0 M: 9.95, 65.41 or 406.69 mg/kg/day, F_0 F: 12.79, 76.78, or 467.13 mg/kg/day F_1 M: 12.08, 75.36 or 484.90 mg/kg/day F_1 F: 14.22, 85.32 or 541.78 mg/kg/day	**Parental/Systemic** NOAEL = 65.41 mg/kg/day for males and 76.78 mg/kg/day for females LOAEL = 406.69 mg/kg/day for males and 467.13 mg/kg/day for females based on decreased body weights **Reproductive/Offspring** NOAEL = 65.41 mg/kg/day for males and 76.78 mg/kg/day for females LOAEL = 406.69 mg/kg/day for males and 467.13 mg/kg/day for females based on reduced pup weights
870.4100a Chronic toxicity in rodents	00101638 (1981) Acceptable/guideline M: 0, 1.0, 5.1, or 25.6 mg/kg/day F: 0, 1.3, 6.5, or 31.9 mg/kg/day	NOAEL = ≥25.6 mg/kg/day LOAEL = >25.6 mg/kg/day. There were no signs of toxicity attributable to treatment at any dose level
870.4100b Chronic toxicity in dogs	41278119 (1977) and 43044201 (1985) Acceptable/guideline M: 0, 22.75, 70.81, or 243.32 mg ai/kg/day F: 0, 22.752, 72.91, or 228.31 mg ai/kg/day	NOAEL was not achieved. LOAEL = 22.75 mg/kg/day based upon body weight gain depression, decreased food efficiency and focal or multi-focal chronic erosivegastritis
870.4200a Carcinogenicity in rats	44730101 (1998) Acceptable/guideline M: 0, 10.4, 84, or 682 mg/kg/day F: 0, 14.0, 112, or 871 mg/kg/day	NOAEL = 84 mg/kg/day in males, 112 mg/kg/day in females LOAEL = 682 mg/kg/day in males, 871 mg/kg/day in females based on decreased body weight and body weight gain, decreased food consumption, and an increased incidence of vacuolation of choroid plexus ependymal cells in the brain in both sexes and decreased water consumption in the females **no evidence of carcinogenicity**
870.4200b Carcinogenicity in mice	44693801 (1998) Acceptable/guideline M: 0, 11, 84, or 690 mg/kg/day F: 0, 12, 95, or 883 mg/kg/day	NOAEL = 12 mg/kg/day in females and ≥ 690.0 mg a.i./kg/day in males LOAEL = 95mg/kg/day in females based on decreased body weight and body weight gains **no evidence of carcinogenicity**
Gene Mutation 870.5100 reverse gene mutation assay in bacteria	41278121 (1987) Acceptable/guideline	There was *no evidence* of induced mutant colonies over background
Cytogenetics 870.5375 *in vitro* mammalian cytogenetics assay	41278122 (1987) Acceptable/guideline	Increases in aberrant metaphases were within the historical control range
870.5395, bone marrow micronucleus assay	00101642 (1980) Acceptable/guideline with 00101643	There was no significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow at any dose tested.
870.5395, bone marrow micronucleus assay	00101643 (1980) Acceptable/guideline with 00101642	There was no significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow after any treatment time.

Table 2. Toxicity Profile of Propamocarb Hydrochloride.

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
Other Genotoxicity 870.5575, *Saccharomyces cerevisiae*, mitotic recombination, gene conversion assay	41278124 (1985) Acceptable/guideline with 00101645	There was no evidence of gene conversion in the tested strains with activation.
870.5575, *Saccharomyces cerevisiae*, mitotic recombination, gene conversion assay	00101645 (1980) Acceptable/guideline with 41278124	There was no evidence of gene conversion in the tested strains without activation.
870.5575, *Saccharomyces cerevisiae*, mitotic recombination, gene conversion assay	00101624 (1977) Acceptable/guideline with 00101645	Under the conditions of the study there was no evidence of gene conversion.
870.6200a Acute neurotoxicity screening battery in rats	43062301 (1993) and 43013101 (1993) Acceptable/guideline M & F: 0, 20, 200 or 2000 mg/kg/day	NOAEL = 200 mg/kg/day LOAEL =2000 mg/kg/day based on soiled fur coat (both sexes) and decreased motor activity 8 hours post-dosing (females only)
870.6200b Subchronic neurotoxicity screening battery in rats	43013102 (1993) Acceptable/guideline M: 0, 12.9, 134.6, or 1320.8 mg/kg/day F: 0, 14.2, 148.5, or 1485.6 mg/kg/day	NOAEL = 1320.8 mg/kg/day in males and 1485.6 mg/kg/day in females LOAEL = not observed
870.6300 Developmental neurotoxicity in rats	NA	NA
870.7485 Metabolism in rats	00101640 (1978) Unacceptable/guideline M & F: 0.5 mg/kg	A higher dose (at least equivalent to levels of human exposure) should have been tested, and the metabolites should have been identified.
870.7600 Dermal penetration	NA	NA
Special studies	00130267 (1981) Unacceptable/non-guideline *In vitro*: Rat and dog plasma incubated for 30 min at 37°C Dose: 0.925 to 74 mg a.i./ml plasma *In vivo*: Dog Dose: Single oral Preivcur N (67.5%)= 674 mg a.i./kg b.w.	1 male & 1female died within 43 min; exhibited tremors, convulsions, respiratory, standstill, and death. ChE inhibition dead animals, plasma - no effect; RBC - 19 - 54%, and brain decrease 10x the controls. No appreciable decrease in ChE in the surviving dog. Conclusion: The cholinesterase inhibition studies were of questionable quality. The chemical does not cause any appreciable inhibition of cholinesterase.

3.2 FQPA Considerations

On 11/6/2002, the HED HIARC evaluated the potential for increased susceptibility of infants and children from exposure to propamcarb hydrochloride according to the February 2002 OPP 10X guidance document. The HIARC concluded that the toxicology database was complete for FQPA purposes and that there are no residual uncertainties for pre-/post-natal toxicity (Memo, G. Reddy, 12/2/03; TXR NO. 0052260). Based on the on the hazard data, the HIARC recommended the special FQPA SF be reduced to 1X. The propamocarb hydrochloride assessment team evaluated the quality of the exposure data; and, based on these data, recommended that the special FQPA SF be reduced to 1X. The recommendation is based on the following:

- There is no quantitative or qualitative evidence of increased susceptibility of rat and rabbit fetuses to *in utero* exposure to propamocarb hydrochloride in developmental toxicity studies. There is no quantitative or qualitative evidence of increased susceptibility to propamocarb hydrchloride following pre-/post-natal exposure to a 2-gerneration reproduction study.
- There is no concern for developmental neurotoxicity resulting from exposure to propamocarb hydrochloride. A developmental neurotoxicity study (DNT) study is not required.
- The toxicological database is complete for FQPA assessment.
- The acute and chronic dietary food exposure assessment utilizes existing and HED-recommended tolerance level residues and 100% CT information for all commodities. By using these screening-level assessments, actual exposures/risks will not be underestimated.
- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.
- The residential handler assessment is based upon the residential SOPs in conjunction with chemical-specific study data in some cases and PHED unit exposures in other cases. The majority of the residential post-application assessment is based upon chemical-specific data or other chemical-specific post-application exposure study data. The chemical-specific study data as well as the surrogate study data used are reliable and also are not expected to underestimate risk to adults as well as to children. In a few cases where chemical-specific data were not available, the SOPs were used alone. The residential SOPs are based upon reasonable "worst-case" assumptions and are not expected to underestimate risk. These assessments of exposure are not likely to underestimate the resulting estimates of risk from exposure to propamocarb hydochloride.

3.3 Dose-Response Assessment

Acute Dietary Endpoint: The rabbit developmental toxicity study was used to select the endpoint for the acute RfD of 1.5 mg/kg/day for females 13-50 years old. The NOAEL of 150 mg ai/kg/day (developmental) was based on increased post-implantation loss in rabbits at the LOAEL of 300 mg ai/kg/day. This endpoint is considered appropriate for females of child bearing age (13-50 years old) since the effects could occur due to a single *in utero* exposure. An uncertainty factor of 100 was applied to the NOAEL to derive the RfD. The special FQPA SF of 1X is applicable for the acute dietary risk assessment. Thus, the aPAD for females 13-50 years old is 1.5 mg/kg/day.

The rat acute oral neurotoxicity study was used to select the endpoint for the acute RfD of 2.0 mg/kg/day for the general U.S. population (including infants and children). The NOAEL of 200 mg ai/kg/day was based on decreased body weight gain and decreased motor activity 8 hrs post-dosing in females at the LOAEL of 2000 mg ai/kg/day. These effects occurred following a single

dose in the acute neurotoxicity study and therefore are appropriate for use in the acute dietary risk assessment. An uncertainty factor of 100 was applied to the NOAEL to derive the RfD. The special FQPA SF of 1X is applicable for the acute dietary risk assessment. Thus, the aPAD for the general U.S. population (including infants and children) is 2.0 mg/kg/day.

Chronic Dietary Endpoint: The mouse carcinogenicity study was used to select the endpoint for establishing the chronic RfD of 0.12 mg/kg/day. The NOAEL of 12 mg ai/kg/day was based on decreased body weight and body weight gain in females at the LOAEL of 95 mg ai/kg/day. An uncertainty factor of 100 was applied to the NOAEL to derive the RfD. The FQPA SFC determined that the safety factor of 1X is applicable for chronic dietary risk assessment. Thus, the cPAD is 0.12 mg/kg/day.

Carcinogenicity: In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July, 1999), the HIARC classified propamocarb hydrochloride as "not likely to be carcinogenic to humans" by all routes of exposure based upon lack of evidence of carcinogenicity in rats and mice, therefore, a cancer risk assessment is not required.

Short- and Intermediate-Term Incidental Oral Endpoint: Short- and intermediate-term incidental oral endpoints were selected from the 2-generation rat reproduction study. The NOAEL of 65.41 mg/kg/day was chosen based upon significant reduction in body weights of F_0 and F_1 pups during days 14 - 21 of lactation at the offspring LOAEL of 406.7 mg/kg/day. This study and endpoint are appropriate for the population of concern (infants and children) and the route and durations of exposure.

Dermal Penetration:
Dermal Absorption Factor: 60%
No dermal absorption study was submitted. Dermal absorption was estimated by comparing the rabbit maternal toxicity LOAEL (300 mg/kg/day) from the rabbit developmental toxicity study (870.3700b) with the LOAEL (525 mg/kg/day) from the 21-day rabbit dermal study (870.3250). The dermal absorption factor is: 300 mg/kg/day ÷ 525 mg/kg/day X 100 = 60%.

Short- and Intermediate-Term Dermal Endpoint: Short- and intermediate-term dermal endpoints were selected from a rabbit 21-day dermal toxicity study. The NOAEL of 150 mg ai/kg/day was based on decreased body weight gain in females at the LOAEL of 525 mg ai/kg/day. For the intermediate-term dermal endpoint, it should be noted that the NOAEL from the 90-day neurotoxicity study in the rat is slightly lower (134.6 mg ai/kg/day male, 148.5 mg ai/kg/day female) than 150 mg/kg/day, but the LOAEL is greater than 1300 mg ai/kg/day. When these values are compared to a new 90-day rat feeding study in the same strain (NOAEL 646 mg ai/kg/day males, 363 mg ai/kg/day females; LOAEL 1363 mg ai/kg/day males, 716 mg ai/kg/day females), with the same toxicity endpoint, it is evident that the NOAEL in the neurotoxicity study is artificially low due to inadequate dose selection. The dermal NOAEL/study was selected because the route of exposure in animals is appropriate for the exposure scenario. This dose/endpoint is appropriate for the route and durations of exposure.

Long-term Dermal Endpoint: The long-term dermal endpoint was selected from the mouse carcinogenicity study. The NOAEL of 12 mg ai/kg/day was based on decreased body weight and body weight gain in females at the LOAEL of 95 mg ai/kg/day. No long-term dermal study was submitted. A dermal absorption factor of 60% was applied for route-to-route extrapolation. This dose/endpoint is appropriate for long-term exposure risk assessment.

Short- and Intermediate-term Inhalation Endpoint: Short- and intermediate-term inhalation endpoints were selected from the 2-generation rat reproduction study. The NOAEL of 65.41 mg/kg/day was chosen based upon significant reduction in body weights of F_0 and F_1 pups during days 14 - 21 of lactation at the offspring LOAEL of 406.7 mg/kg/day. Due to the lack of a repeated exposure inhalation study, an oral dose was selected. Absorption via inhalation is assumed to be equivalent to oral absorption. An inhalation absorption factor of 100% should be applied. This dose/endpoint is appropriate for short- and intermediate-term exposure risk assessments.

Long-term Inhalation Endpoint: The long-term inhalation endpoint was selected from the mouse carcinogenicity study. The NOAEL of 12 mg ai/kg/day was based on decreased body weight and body weight gain in females at the LOAEL of 95 mg ai/kg/day. Due to the lack of repeated exposure inhalation study, an oral dose was selected. Absorption via inhalation is assumed to be equivalent to oral absorption. An inhalation absorption factor of 100% should be applied. This dose/endpoint is appropriate for long-term exposure risk assessment.

MOE for Occupational/Residential Risk Assessments: The level of concern for dermal and inhalation occupational and oral, dermal and inhalation residential (non-dietary) exposure risk assessments are for MOEs less than 100. The MOEs are based on the conventional uncertainty factor of 100x (10x for intraspecies extrapolation and 10x for interspecies variation). The doses and toxicological endpoints selected for various exposure scenarios are summarized in Table 3.

Table 3. Summary of Toxicological Dose and Endpoints for Propamocarb Hydrochloride for Use in Human Health Risk Assessment [1]

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Special Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary females 13-50 years of age	NOAEL = 150 mg ai/kg/day UF = 100 **Acute RfD** = 1.5 mg ai/kg/day	FQPA SF = 1X **aPAD** = acute RfD / FQPA SF = 1.5 mg/kg/day	Developmental Toxicity Study - Rabbit Developmental LOAEL = 300 mg ai/kg/day based on increased post-implantation loss
Acute Dietary general population including infants and children	NOAEL= 200 mg ai/kg/day UF = 100 **Acute RfD** = 2.0 mg/kg/day	FQPA SF = 1X **aPAD** = acute RfD / FQPA SF = 2.0 mg/kg/day	Acute Neurotoxicity Screening Battery - Rat LOAEL = 2000 mg ai/kg/day, based on decreased body weight gain and decreased motor activity

Table 3. Summary of Toxicological Dose and Endpoints for Propamocarb Hydrochloride for Use in Human Health Risk Assessment [1]

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Special Level of Concern for Risk Assessment	Study and Toxicological Effects
Chronic Dietary all populations	NOAEL= 12 mg ai/kg/day UF = 100 **Chronic RfD** = 0.12 mg/kg/day	FQPA SF = 1X **cPAD** = chronic RfD / FQPA SF = 0.12 mg/kg/day	Carcinogenicity Study - Mouse LOAEL = 95 mg ai/kg/day, based on decreased body weight and body weight gain in females
Short-Term Oral (1 - 30 days) (Residential)	NOAEL = 65.41 mg ai/kg/day	**Residential LOC for MOE** = 100	2-Generation Reproduction Toxicity Study - Rat Offspring LOAEL = 406.7 mg ai/kg/day, based on reduced pup weights in F_0 & F_1 during Day 14 - 21 of lactation
Intermediate-Term Oral (1 - 6 months) (Residential)	NOAEL = 65.41 mg ai/kg/day	**Residential LOC for MOE** = 100	2-Generation Reproduction Toxicity Study - Rat Offspring LOAEL = 406.7 mg ai/kg/day, based on reduced pup weights in F_0 & F_1 during Day 14 - 21 of lactation
Short-Term Dermal (1-30 days) (Occupational/ Residential)	dermal NOAEL= 150 mg ai/kg/day	**Occupational LOC for MOE** = 100 **Residential LOC for MOE** = 100	21-day Dermal Toxicity Study - Rabbit LOAEL = 525 mg/kg/day, based on decreased body weight gain in females
Intermediate-Term Dermal (1 - 6 months) (Occupational/ Residential)	dermal NOAEL= 150 mg ai/kg/day	**Occupational LOC for MOE** = 100 **Residential LOC for MOE** = 100	21-day Dermal Toxicity Study - Rabbit LOAEL = 525 mg/kg/day, based on decreased body weight gain in females
Long-Term Dermal (> 6 months) (Occupational/ Residential)	oral NOAEL= 12 mg ai/kg/day (dermal absorption rate = 60%)	**Occupational LOC for MOE** = 100 **Residential LOC for MOE** = 100	Carcinogenicity Study - Mouse LOAEL = 95 mg ai/kg/day, based on decreased body weight and body weight gain in females
Short-Term Inhalation (1-30 days) (Occupational/ Residential)	oral NOAEL= 65.41 mg ai/kg/day (inhalation absorption rate = 100%)	**Occupational LOC for MOE** = 100 **Residential LOC for MOE** = 100	2-Generation Reproduction Toxicity Study - Rat Offspring LOAEL = 406.7 mg ai/kg/day, based on reduced pup weights in F_0 & F_1 during Day 14 - 21 of lactation
Intermediate-Term Inhalation (1 - 6 months) (Occupational/ Residential)	oral NOAEL= 65.41 mg ai/kg/day (inhalation absorption rate = 100%)	**Occupational LOC for MOE** = 100 **Residential LOC for MOE** = 100	2-Generation Reproduction Toxicity Study - Rat Offspring LOAEL = 406.7 mg ai/kg/day, based on reduced pup weights in F_0 & F_1 during Day 14 - 21 of lactation

Table 3. Summary of Toxicological Dose and Endpoints for Propamocarb Hydrochloride for Use in Human Health Risk Assessment [1]

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Special Level of Concern for Risk Assessment	Study and Toxicological Effects
Long-Term Inhalation (> 6 months) (Occupational/ Residential)	oral NOAEL= 12 mg/kg/day (inhalation absorption rate = 100%)	**Occupational LOC for MOE** = 100 **Residential LOC for MOE** = 100	Carcinogenicity Study - Mouse LOAEL = 95 mg ai/kg/day, based on decreased body weight and body weight gain in females
Cancer (oral, dermal, inhalation)	"not likely to be carcinogenic to humans"		

[1] UF = uncertainty factor, FQPA SF = FQPA safety factor, 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

3.4 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (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 the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases 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 has 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).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, propamocarb hydrochloride may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Proposed Uses

Registered Uses

Section 3 registrations for use of propamocarb hydrochloride on potatoes have been established for the end-use product Tattoo C (30.5% propamocarb hydrochloride and 30.5% chlorothalonil; EPA File Symbol No. 264-676) and Previcur® Flex Fungicide [66.5% SC, EPA Reg. No. 264-

678]. In addition, Section 18 Emergency Exemptions have been established for use on tomatoes. In conjunction with these registrations, a permanent tolerance has been established for residues of propamocarb hydrochloride in/on potatoes at 0.06 ppm [40 CFR §180.499(a)] and temporary tolerances, with an expiration date of 12/31/03, have been established for residues in/on tomatoes and tomato paste at 2.0 and 5.0 ppm, respectively [40 CFR §180.499(b)].

Section 3 registrations for uses on golf courses, sod farms, and in nurseries/greenhouses have been established for the end-use products Banol® (66.5% propamocarb hydrochloride; EPA File Symbol No. 432-942) and Banol® C (30.5% propamocarb hydrochloride and 30.5% chlorothalonil; EPA File Symbol No. 432-961). Banol® and Banol® C are SC formulations. The label specifies that these products are used by commercial applicators on golf courses.

Proposed Uses

Propamocarb hydrochloride, formulated as Previcur® Flex Fungicide, is being proposed for use on fruiting vegetables, cucurbit vegetables and lettuce. Bayer is proposing both field and greenhouse uses on these commodities to control such diseases as downy mildew and tomato late blight. A proposed label for a Previcur® Flex Fungicide lists separate directions for the field and greenhouse uses (see Tables 4 and 5). The following crop rotation restrictions are listed:

All Labeled Crops	Crops on this label may be rotated anytime following the last application of Previcur® Flex Fungicide.
Root and Leafy Vegetables	Do not rotate to root and leafy vegetables for 30 days following the last application of Previcur® Flex Fungicide.
Winter Wheat and All Other Non-Labeled Crops	Do not rotate to winter wheat and all other crops for 120 days following the last application of Previcur® Flex Fungicide.

Field Uses: Previcur® Flex is recommended for broadcast and aerial applications to tomato, lettuce, cucurbit vegetables, and peppers for the control of such diseases as downy mildew and tomato late blight. Previcur® Flex should be applied preventatively as a foliar spray in sufficient water to obtain coverage. Ground applications should be made with a tractor-mounted boom sprayer with 3 nozzles per row (with 2 nozzles directed at lower portion of plant). The shorter spray intervals should be used with moderate to heavy disease pressure. Chemigation is allowed (see Application Through Irrigation Systems section on label). Previcur® Flex can be tank mixed with other registered fungicides (see label for specific directions).

Table 4. Summary of Directions for Field Use of Propamocarb Hydrochloride.

Application Method. (gallons/A)[4]	Formulation (EPA Reg. No.)	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	RTI [1] (days)	PHI [2] (days)	Directions/Restrictions
Tomatoes							
Ground (15-100) Aerial (min. 5)	Previcur® Flex (264-678)	1.125	5	5.625	7-10	5	- Use a min. of 1.2 pt/A when tank mixing. The guidelines listed on the label should be followed when adjusting time and rate based on local late blight conditions. Under conditions favoring rapid disease development and severe disease conditions, apply at 1.5 pt/A with a tank-mix partner on a 10-day schedule alternating on the 5th day with a contact fungicide.
Peppers							
Ground (15-100) Aerial (min. 5)	Previcur® Flex (264-678)	0.9	5	4.5	7-14	5	- Use a min. of 1.2 pt/A when tank mixing .
Cucurbits							
Ground (15-100) Aerial (min. 5)	Previcur® Flex (264-678)	0.9	5	4.5	7-14	2	- Use a min. of 1.2 pt/A when tank mixing.
Lettuce							
Ground (15-100) Aerial (min. 10)	Previcur® Flex (264-678)	1.5	4	6.0	5-10	2	- Use a min. of 1.33 pt/A when tank mixing.

1. RTI = retreatment interval.
2. PHI = preharvest interval.

Greenhouse Uses: Previcur® Flex is recommended for tomato, lettuce, cucurbit vegetables, and peppers for the prevention of root rot and damping-off caused by *Phythium* spp. and *Phytophthora* spp. It does not require agitation after initial mixing and is recommended to all stages of propagation and development, including seeding, transplanting, and potting. Stock solution should be used within 1 day of mixing. Do not tank mix with other products. Previcur® Flex should be used in rotation with other effective labeled fungicides. Contact with intense sunlight after application should be prevented.

Table 5. Summary of Directions for Field Use of Propamocarb Hydrochloride.	
Use Pattern	**Use Directions**
PRESEEDING AND/OR SEEDLING TREATMENT [1]	**ROCK WOOL CUBE SATURATION** Prepare a 1:1000 stock solution; apply as a soil drench at a rate of 3.4-6.8 fl oz per cube to saturate (100 gallons will treat 3800 to 1900 plants, respectively).
	SEED BEDS - SOIL OR SOILLESS In a min. of 50 gallons of water/1000 sq. ft apply: At seeding - 1.5 lbs ai/1000 sq. ft. (32 fl oz product/1000 sq. ft.) After emergence - 0.75 lb ai/1000 sq. ft. (16 fl. oz. product/1000 sq. ft.)
GREENHOUSE TREATMENT (after transplanting) [2]	**DRIP SYSTEM or DRENCH** Prepare a 1:1000 stock solution; apply stock solution through drip system at a rate of 3.4-6.8 fl oz per cube through drip system to avoid runoff and cover root area (100 gallons will treat 3800 to 1900 plants, respectively. Evening applications by drip irrigation will reduce leaching or washing of the product from the root zone and may improve control
	FOLIAR TREATMENT (Tomato and Lettuce only) See field use directions. Do not harvest lettuce for 14 days after greenhouse foliar treatment. Do not harvest tomatoes for 5 days following foliar treatment.

MAXIMUM USE RATES	NUMBER OF PLANTS/ACRE	AMOUNT PRODUCT PER APPLICATION PER ACRE (lb ai/A)	AMOUNT PRODUCT PER CROPPING CYCLE (lb ai/A)
	6,000 10,000 14,000	1.94 3.23 4.52	11.6 9.4 27.1

Note: Up to 6 total applications are allowed as follows:
[1] Do not apply more than 2 preseeding and/or seeding applications per cropping cycle.
[2] Do not apply more than 4 greenhouse applications (after transplanting) per cropping cycle.

The proposed field use directions adequately reflect the use patterns from the available crop field trials. The greenhouse use directions do not adequately reflect the use patterns from the available residue data. **The available residue data do not support the greenhouse uses on leaf lettuce and tomatoes. The petitioner should submit a revised Section B with these uses removed.**

4.2 Dietary Exposure/Risk Pathway

The residue chemistry data submitted in support of proposed petition were reviewed in the HED-memorandum dated 2/20/04 (J. Tyler; D267921). The drinking water assessment was completed by EFED on 11/10/03 (Memo, K. Costello, D267925). The acute and chronic dietary exposure assessment was completed in a HED-memorandum dated 2/20/03 (J. Tyler, D297250). A residential exposure assessment was prepared in an HED memorandum dated 2/20/04 (Memo, M. Dow; 297387).

4.2.1 Residue Profile

Background
Bayer CropScience is proposing the establishment of permanent tolerances for residues of propamocarb hydrochloride in/on the following RACs: vegetable, cucurbit, group at 1.5 ppm; lettuce, head at 50 ppm; lettuce, leaf at 65 ppm; vegetable, fruiting, group at 2.0 ppm; tomato, paste at 5.0 ppm; wheat, grain at 0.05 ppm; wheat, straw at 0.1 ppm; wheat, forage at 0.3 ppm; and wheat, hay 0.3 ppm.

In an additional submission dated 3/22/01, the company has requested to reduce the current rotational crop interval for wheat from 120 to 60 days. This request was reviewed in a memo dated 12/29/03 (Memo, J.Tyler; D274264). In that memo, HED determined that the available data do not support the establishment of a 60-day rotational crop restriction for wheat, or the proposed tolerances for inadvertent residues of propamocarb hydrochloride *per se* in/on wheat RACs. The petitioner should submit the following data: 1) limited rotational residue data on wheat from Regions 5 (3 trials), and 11 (1 trial); 2) the results of a poultry feeding study; and 3) the results of a wheat processing study.

Nature of the Residue in Plants and Livestock
Plants: The nature of propamocarb hydrochloride residues in potatoes, cucumbers and spinach is adequately understood. These data were presented to the HED Metabolism Assessment Review Committee (MARC) on April 6, 2000 (Memo, J. Rowell and D. Nixon; D264291). The Committee determined that the parent is the only residue of concern in these crops (Memo, J. Rowell, 5/3/00; D264293).

Ruminants: The nature of the residue in ruminants is adequately understood based on acceptable studies on dairy cattle. These data were presented to the HED MARC on April 6, 2000 (Memo, J. Rowell and D. Nixon; D264291). In the absence of toxicological evidence to the contrary, it was concluded that the metabolites N-oxide propamocarb, 2-hydroxy propamocarb, and oxazolidine could be of comparable toxicity to the parent. Since these metabolites are a major portion of the residue in livestock commodities, they need to be included in the risk assessment. The Committee recommended that the following metabolites be determined in the livestock feeding study: N-oxide propamocarb, 2-hydroxy propamocarb, and oxazolidine. The appropriate tolerance expression will be determined once the results of this feeding study are available (Memo, J. Rowell, 5/3/00; D264293).

Poultry: No poultry metabolism study has been submitted in support of the subject petition. A poultry metabolism study will be required in order to support tolerances for inadvertent residues in/on wheat commodities.

Residue Analytical Methods
Plants: An adequate gas chromatography/nitrogen-phosphorus detection (GC/NPD) method (Xenos Report Number: XEN97-37) has been submitted. This method has undergone a successful independent laboratory validation (ILV) and petition method validation (PMV) by Analytical Chemistry Branch (ACB)/Biological and Economics Analysis Division (BEAD; Memo, J. Rowell, 10/3/00, D268955). The GC/NPD has been sent to the Food and Drug Administration

(FDA) and is currently listed in the Pesticide Analytical Manual (PAM) Vol. II for determining residues of propamocarb hydrochloride in plant commodities (Memo, J. Tyler, 4/25/02; D282694). The limit of quantitation (LOQ) for this method is 0.05 ppm.

Samples collected in the pepper and tomato field trial studies and the tomato processing study were analyzed for residues of propamocarb hydrochloride using a GC/NPD method, which has been found to be adequate for data collection and enforcement purposes. Samples collected from the cucurbit and lettuce field trial studies were analyzed for residues of propamocarb hydrochloride using a GC method with a thermionic-specific detector (TSD; XAM-47). The reported LOQ for propamocarb cucurbit vegetables and lettuce was 0.05 ppm; the limit of detection (LOD) was not reported. Method XAM-47 is essentially the same as the method used to analyze propamocarb residues in rotational crops (PP#6F04707; Memo, J. Rowell, 4/28/00; D252751), which was found to be adequate for data collection. Samples from the greenhouse field trial studies were analyzed for residues of propamocarb hydrochloride using a high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) method. A complete description of the HPLC-MS/MS method used in the greenhouse trials was not provided. A copy of the complete HPLC-MS/MS method should be submitted. The reported LOD and LOQ for the method were 0.003 and 0.01 ppm, respectively. Based on concurrent recoveries from fortified control samples, the GC/NPD, GC/TSD, and HPLC-MS/MS method used for determining residues of propamocarb in the field trials are adequate for data collection. Concurrent method recoveries fortified with propamocarb at various levels were all within the acceptable 70-120% range. Adequate sample calculations and chromatograms were provided.

Livestock: Based on the anticipated dietary burden from proposed inadvertent residues on wheat and the results of the ruminant metabolism study, a ruminant feeding study is required. Conclusions about the need for livestock tolerances and appropriate enforcement analytical methods are deferred until receipt of the ruminant feeding study and determination of the residues of concern in livestock.

The petitioner is proposing tolerances for wheat grain, which is considered to be a poultry feed item. Therefore, a poultry metabolism study is now required. Conclusions about the need for poultry tolerances and appropriate enforcement analytical methods are deferred until receipt of the poultry feeding study and determination of the residues of concern in livestock.

Multiresidue Method (MRM)

The results of a multiresidue testing study was submitted in support of a Section 3 permanent registration for the use of propamocarb hydrochloride on potatoes, and have been reviewed by HED (Memo, J. Rowell, 3/23/00; D258626). The compound was not recovered by any of the protocols. The report has been forwarded to FDA for inclusion in the PAM Vol. I (Memo, J. Rowell, 3/23/00; D258629). The submitted results are adequate for the parent propamocarb hydrochloride only. If, in the future, tolerances are established which include propamocarb hydrochloride metabolites, then multiresidue testing of such metabolites will be required.

Storage Stability

Samples from the crop field trials and processing study are supported by the available storage stability data. The available plant storage stability data indicate that propamocarb hydrochloride is stable at -20 °C for at least 785 days (approximately 26 months) in potatoes, cabbage, and tomatoes.

Magnitude of Residues in Plants

In support of the field uses, residue data were submitted on tomatoes, bell and non-bell peppers, cucumbers, cantaloupe, summer squash and head and leaf lettuce. In support of the greenhouse uses, residue data were submitted on tomatoes, bell (sweet) peppers, cucumbers, and head lettuce. A summary table of the results of the crop field trial studies can be found in Attachment 2 of this risk assessment.

Proposed Field Uses: The submitted residue data are sufficient to support the proposed field uses. The number and location of the submitted lettuce (head and leaf) field trials do not match those recommended in current HED guidelines. Four residue trials were performed in Region 10 instead of the recommended six. However, as residue data were submitted for both Regions 1 and 2, they are sufficient to support the proposed use on leaf and head lettuce.

Greenhouse Uses: The submitted greenhouse residue data are adequate to support the use of propamocarb hydrochloride on cucurbit vegetables, bell and non-bell peppers, and head lettuce. The lettuce and tomato residue data are not adequate to support the proposed use on greenhouse grown leaf lettuce and tomatoes.

It should be noted that the majority of the trials were not conducted in accordance with the proposed label. According to the proposed label, propamocarb hydrochloride can be applied as a soil drench to greenhouse-grown tomatoes, lettuce, cucurbit vegetables and peppers at maximum application rate of 4.52 lb. ai/A, and as a foliar spray to greenhouse-grown tomatoes and lettuce at 1.125 and 1.5 lbs. ai/A, respectively. The total application rate of 27.1 lb ai/A/cropping cycle (for 14,000 plants/A). A total of six applications are allowed as follows: 1) no more than 2 preseeding and/or seeding applications per cropping cycle, and 2) no more than 4 greenhouse applications (after transplanting) per cropping cycle. The label states that the greenhouse applications (after transplanting) can be applied foliarly to tomatoes and lettuce only, and can be applied to all proposed crops via drip system or soil drench. The submitted greenhouse trials were performed at total application rates ranging from 33.2 to 111 lb ai/A (1.2-4.1x the proposed maximum application rate).

In the cucumber trials, HED notes that for the establishment of a tolerance on the cucurbit crop group, current guidelines recommend that residue data be submitted on cucumbers, a muskmelon, and summer squash. No greenhouse residue data were provided for a representative muskmelon and summer squash. However, propamocarb hydrochloride will be applied to greenhouse-grown cucurbit vegetables via soil drench only. As propamocarb hydrochloride was applied foliarly in the greenhouse trials, the greenhouse data represent a worst-case estimate of residues of propamocarb hydrochloride on cucurbit vegetables. Additionally, the crop field trial data submitted in support of the field use were performed using foliar and soil drench applications. HED is willing to translate the residue data submitted in support of the field use on cucurbit

vegetables to support the greenhouse use. Therefore, the residue data support application of propamocarb hydrochloride on cucurbit vegetables for soil drench applications only. If in the future the petitioner desires to include a foliar use for greenhouse-grown cucurbit vegetables, then additional data will be required in which propamocarb hydrochloride is applied in accordance with label directions.

In the pepper trials, although the trials were not performed in accordance with the proposed label, the residues were less than those seen in the submitted field trial studies. No residue data were provided on non-bell peppers grown in greenhouses. However, propamocarb hydrochloride will be applied to greenhouse-grown peppers via soil drench only, and the crop field trial data submitted in support of the field use on peppers were performed using foliar and soil drench applications. HED is willing to translate the residue data submitted in support of the field use on non-bell peppers to support the greenhouse use. Therefore, the residue data support application of propamocarb hydrochloride on bell and non-bell peppers. If in the future the petitioner desires to include a foliar use for greenhouse-grown non-bell peppers, then additional data will be required in which propamocarb hydrochloride is applied in accordance with label directions.

In the lettuce trials, although the trials were not performed in accordance with the proposed label, the residues were less than those seen in the submitted field trials. No residue data were provided on leaf lettuce grown in greenhouses. As demonstrated in the lettuce residue data submitted in support of the field use on lettuce, residues are typically higher in leaf lettuce than in head lettuce. Therefore, the available data do not support the proposed greenhouse use of propamocarb hydrochloride on leaf lettuce. **A revised Section B should be submitted with this use removed.**

In the tomato trials, propamocarb hydrochloride was applied as soil drenches only. However, the proposed label states that foliar treatments are allowed. As majority of the residues would be expected to be a result of the foliar application, the available data do not support the proposed use on greenhouse-grown tomatoes. **A revised Section B should be submitted with this use removed.** In order to support a greenhouse use on tomatoes, the petitioner should provide additional residue data in which propamocarb is applied according to the label directions. It should be noted that current residue chemistry guidelines require data on all major varieties of tomatoes, including cherry and/or grape.

The available residue data support the proposed tolerances on fruiting vegetables, cucurbit vegetables, peppers (bell and non-bell), and lettuce (head). However the proposed tolerance on leaf lettuce it too low. The available residue data support a tolerance of 90 ppm for residues of propamocarb on lettuce, leaf. **A revised Section F should be submitted.**

Magnitude of Residues in Processed Commodities

An adequate processing study was submitted to support the proposed use on tomatoes. Although propamocarb was shown to concentrate slightly in tomato puree (1.3x), the recommended tolerance of 2.0 ppm for fruiting vegetables will adequately cover residues in tomato puree. Therefore, a tolerance is not required for this processed commodity. However, residue concentrations were observed in tomato paste (3.1x). Based on the observed 3.1x processing factor for tomato paste and highest average field trial (HAFT) residue of 1.53 ppm from the tomato field trials, the maximum expected propamocarb residues in tomato paste would be 4.74

ppm. Therefore, the available tomato processing data support the proposed tolerance of 5.0 ppm for residues in tomato, paste.

Magnitude of Residues in Meat, Milk, Poultry and Eggs (MMPE)

Ruminants: No ruminant feeding study has been submitted in support of the subject petition. Based on the anticipated dietary burden and the results of the ruminant metabolism study, a ruminant feeding study is required. Conclusions about the need for livestock tolerances and appropriate enforcement analytical methods are deferred until receipt of the ruminant feeding study and determination of the residues of concern in livestock.

In a submission in support of the use of propamocarb hydrochloride on potatoes, the petitioner proposed tolerances of 0.05 ppm for residues of propamocarb hydrochloride in/on meat, meat byproducts, fat of cattle, goats, hogs, horses, and sheep; and milk. In the HED human health risk assessment performed in conduction with this petition (Memo, J. Rowell, *et. al.*, 6/27/00; D265426), HED used the proposed livestock tolerances and the results of the ruminant metabolism study in order to determine the appropriate residue levels (parent and metabolites of concern) to be included in the dietary exposure assessment (see Table 6). This approach was used in the current risk assessment as well.

Table 6. Summary of residue levels (parent and metabolites) for livestock commodities to be used in HED's risk assessment.

Commodity	Residues (parent and metabolites) [1] (ppm)
meat	0.15
liver	0.60
kidney	0.20
meat by-products (except liver and kidney)	0.15
fat [2]	0.05
milk	0.85

1. For livestock commodities, the residues of concern are the parent propamocarb hydrochloride and the metabolites N-oxide propamocarb, 2-hydroxy propamocarb, and oxazolidine.
2. For fat, the total radioactive residue (TRR) in the ruminant metabolism study was <0.01 ppm, and not extracted. Therefore, the recommended tolerance (0.05 ppm) will be used.

Poultry: No poultry feeding studies have been submitted in support of the subject petition. A poultry metabolism study is required to support tolerances for inadvertent residue of propamocarb hydrochloride on wheat commodities. The need for a poultry feeding study will be determined upon submission of the poultry metabolism study.

Confined and Field Accumulation in Rotational Crops

Adequate confined and field rotational crop studies have been submitted and reviewed by HED (Memo, J. Rowell, D266084; 5/15/00). As mentioned above, the company recently submitted a request to shorten the rotational crop restriction for wheat from 120 to 60 days. HED reviewed the request in a memo dated 12/29/03 (Memo, J. Tyler; D274264), and determined that the available data do not support a 60-day plantback interval (PBI) for wheat, and the proposed

tolerances for inadvertent residues of propamocarb hydrochloride *per se* (see 12/29/03 memo for further details).

Tolerance Recommendation
The available residue data support the proposed tolerances on fruiting vegetables, cucurbit vegetables, peppers (bell and non-bell), and lettuce (head) (see Table 7). However the proposed tolerance on leaf lettuce is too low. The available residue data support a tolerance of 90 ppm for residues of propamocarb on lettuce, leaf. **A revised Section F should be submitted.**

Table 7. Tolerance Summary for Propamocarb Hydrochloride.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (correct commodity definition)
Vegetable, cucurbit group	1.5	1.5	Vegetable, cucurbit, group 9
Lettuce, head	50	50	
Lettuce, leaf	65	90	
Vegetable, fruiting, group	2.0	2.0	Vegetable, fruiting, group 8
Tomato, paste	5.0	5.0	
Wheat, grain	0.05	Not Supported	See 860.1900 Field Accumulation in Rotational Crops and Memo, J. Tyler, 2/29/03; D266084
Wheat, straw	0.1	Not Supported	
Wheat, forage	0.3	Not Supported	
Wheat, hay	0.3	Not Supported	

4.2.2 Dietary Exposure Analyses

Propamocarb hydrochloride acute and chronic dietary exposure assessments were conducted using DEEM-FCID™, Version 1.30), which incorporates consumption data from USDA's CSFII, 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food-form is summed with the residue consumption estimates for all other food/food-forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic (Tier 1 or Tier 2) exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic (Tier 3/4) assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (i.e., those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. However, for Tiers 1 and 2, significant differences in user vs. per capita exposure and risk are identified and noted in the risk assessment.

The results of the acute and chronic assessments are listed in Table 8. DEEM-FCID™ (Ver. 1.30) estimates the dietary exposure for the U.S. population and 28 population subgroups. Based on an analysis of 1994-96, 98 CSFII consumption data which took into account dietary patterns and number of survey respondents, HED determined that the following population groupings were appropriate for regulatory purposes (only the exposure estimates for these populations are reported in this document): U.S. Population, all infants (<1 year old), children 1-2 years old, children 3-5 years old, children 6-12 years old, youth 13-19 years old, females 13-49 years old, adults 20-49 years old, and/or adults 50+ years old.

4.2.2.1 Acute Dietary Exposure Analysis

Separate unrefined, Tier 1 acute dietary exposure assessments were conducted for females 13-49 years old and the general U.S. population using the following: 1) established and recommended tolerances for all plant commodities; 2) HED-calculated residues of concern (parent and metabolites) for livestock commodities (see Table 6); 3) 100% CT information for all current and proposed uses; and 4) modified processing factors for tomato paste and default processing factors for all other commodities. The acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95% percentile for females 13-49 years old (6% aPAD) and the general U.S. population (4% aPAD) and all population subgroups. The most highly exposed population subgroups are children 1-2 years old, children 3-5 years old and children 6-12 years old at 5% aPAD.

4.2.2.2 Chronic Dietary Exposure Analysis

An unrefined, Tier 1 chronic dietary exposure assessment was conducted for the general U.S. population and various population subgroups using the following: 1) established and recommended tolerances for all plant commodities; 2) HED-calculated residues of concern (parent and metabolites) for livestock commodities; 3) 100% CT information for all current and proposed uses; and 4) modified processing factors for tomato paste and default processing factors for all other commodities. The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (18% aPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old at 36% cPAD.

Table 8. Summary of Dietary Exposure and Risk for Propamocarb Hydrochloride.

Population Subgroup	Acute Dietary [1]		Chronic Dietary [2]	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD
U.S. Population (total)	0.083061	4	0.020997	18
All Infants (< 1 year old)	0.045372	2	0.012559	11
Children 1-2 years old	0.108470	5	0.043522	36
Children 3-5 years old	0.102640	5	0.035688	30
Children 6-12 years old	0.089743	5	0.026535	22
Youth 13-19 years old	0.075640	4	0.019059	16
Adults 20-49 years old	0.084951	4	0.019378	16
Adults 50+ years old	0.073044	4	0.017353	15
Females 13-49 years old	0.091653	6	0.019952	17

1. Separate endpoints were chosen for the general U.S. population (including infants and children) and the females 13-50 years old population subgroup for propamocarb hydrochloride. Acute dietary endpoint of 1.5 mg/kg/day applies to females 13-49 years old, and acute dietary endpoint of 2.0 mg/kg/day applies to the general U.S. population.
2. Chronic dietary endpoint of 0.12 mg/kg/day applies to the general U.S. population and all population subgroups.

4.3 Water Exposure/Risk Pathway

Tier I EDWCs were for surface water and groundwater using FIRST and SCI-GROW, respectively (Memo, K. Costello, 11/10/03; D267925). The EDWCs were based on the currently registered turf use, which has the yearly application rate (25 lb ai/A). For surface water, and acute (peak) and chronic (average annual) EDWCs are 972 ppb and 77 ppb, respectively. The groundwater EDWC is 2.99 ppb. These values are meant to represent upper-bound estimates of the concentrations that might be found in surface water and groundwater due to the use of propamocarb hydrochloride on turf.

4.4 Residential Exposure/Risk Pathway

4.4.1 Residential Use Pattern

Propamocarb hydrochloride, formulated as Banol® (66.5% propamocarb hydrochloride; EPA File Symbol No. 432-942) and Banol® C (30.5% propamocarb hydrochloride and 30.5% chlorothalonil; EPA File Symbol No. 432-961), may be applied to golf courses by commercial applicators only. Banol® is a water miscible fungicide concentrate applied as a spray at a rate of 8.2 lbs ai/Acre to golf courses at 7-21 day intervals. Therefore, there is a potential for golfer post-application exposure to propamocarb-hydrochloride. HED considered this potential exposure in the human health risk assessment performed in conjunction with the request for the use of propamocarb hydrochloride on potatoes (Memo, J. Rowell *et. al.*, 6/27/00; D265426 and Memo, D.Vogel, 6/27/00; D266413). The following post-application exposure assessment was taken

from the 6/27/00 risk assessment.

4.4.1.1 Residential Post-Application Exposure

An MOE of 100 is adequate to ensure protection from propamocarb hydrochloride via the dermal and inhalation routes for residential exposures. No chemical-specific data are available to address post-application exposure to persons reentering golf courses treated with propamocarb hydrochloride. The post-application risk assessment is based on generic assumptions as specified by the newly proposed Residential SOPs and recommended approaches by HED's ExpoSAC. Changes to the Residential SOPs have been proposed that alter the residential post-application scenario assumptions. The proposed assumptions are expected to better represent residential exposure and are still considered to be high-end, screening level assumptions. HED management have authorized the use of the revised residential SOPs that were presented to the FIFRA SAP in September 1999. Therefore, HED has deviated from the current Residential SOP assumptions and uses the proposed assumptions to calculate exposure estimates.

Short-term post-application exposures are expected for the adult and adolescent golfer. Golfer exposure is expected through minimal hand contact with the golf ball and dermal contact to the lower legs from treated plant surfaces. Since it is assumed that the adolescent golfer would have a proportionally similar exposure to adults, a dermal post-application assessment was performed for the adult golfer only. A TC of 500 cm^2/hr has been used to estimate post-application exposure and all exposure estimates were assessed on the day of treatment. The golfer post-application exposures estimate is presented in Table 9.

Table 9. Golfer Post-application Exposure.

Exposure Scenario	Transfer Coefficient [1] (cm^2/hr)	DFR [2] (ug/cm^2)	Hrs exposed/day	ADD[3] (mg/kg/day)	MOE[4]
Adult Golfer to turf	500	4.6	4	0.15	980

1. TC (HED Exposure SAC Meeting Minutes, 2/24/00).
2. Surrogate DFR_0 = AR X 5% Available as dislodgeable residue X 4.54E8 ug/lb X 2.47E-8 A/cm^2;
3. Dermal ADD-golf course =DFR (ug/cm^2) X TC (cm^2/hr) X 4 Hours/day X 0.001 mg/ug X 1/BW ; BW= (60kg for adults)
4. MOE = NOAEL/ADD; (short- and intermediate- term dermal NOAEL = 150 mg/kg/day)

level of concern is for MOEs below 100

The calculated MOE for the golfer is 980 and, therefore, does not exceed HED's level of concern. Since the short and intermediate-term toxicological endpoints are the same, the golfer post-application exposure assessment is expected to provide adequate exposure estimates for both the short- and intermediate-term. In the event of intermediate-term exposure, propamocarb hydrochloride residues are expected to dissipate over time. Therefore, this assessment is expected to present a high-end conservative estimate of actual exposure.

4.4.2 Non-occupational Off-Target Exposure

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential

source of exposure from groundboom application methods. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new database submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

Aggregate exposure risk assessments were performed for the following scenarios: acute aggregate exposure (food + drinking water), short-term aggregate exposure (food + drinking water + residential), and chronic aggregate exposure (food + drinking water). Intermediate-term aggregate risk assessment was not performed because the short-term aggregate assessment adequately addresses both the short- and intermediate-term golfer dermal exposures. A long-term aggregate risk assessment was not performed because, based on the current use patterns, HED does not expect exposure durations that would result in long-term exposures. A cancer aggregate risk assessment was not performed because propamocarb hydrochloride is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment. Dietary (food and drinking water) and post-application residential exposures were considered, as necessary, because there is a potential for individuals to be exposed concurrently through these routes.

Since HED does not have ground and surface water monitoring data to calculate a quantitative aggregate exposure, DWLOCs were calculated. A DWLOC is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxicity endpoint, drinking water consumption, body weights, and pesticide uses. Different populations will have different DWLOCs. HED uses DWLOCs in the risk assessment process to assess potential concern for exposure associated with pesticides in drinking water. DWLOC values are not regulatory standards for drinking water.

To calculate DWLOCs, the dietary food estimates (from DEEM-FCID™) were subtracted from the PAD value to obtain the maximum water exposure level. DWLOCs were then calculated using the standard body weights and drinking water consumption figures: 70kg/2L (US Population, adult male, and youth), 60 kg/2L (adult female), and 10kg/1L (infants and children).

For acute and chronic dietary exposure, HED is concerned when estimated dietary risk exceeds 100% of the aPAD and cPAD, respectively. HED's level of concern for residential oral, dermal and inhalation exposures are for MOEs <100. An MOE of 100 is adequate to ensure protection from propamocarb hydrochloride via the dermal route for residential exposures.

5.1 Acute Aggregate Risk Assessment (Food and Drinking Water)

The acute aggregate risk assessment takes into account exposure estimates from dietary consumption of propamocarb hydrochloride (food and drinking water).

The Tier 1 [conservative, deterministic assessment using registered and HED-recommended tolerance level residues (plant commodities) and residues of concern (livestock commodities); 100% CT information for registered and proposed commodities; and modified DEEM™ (version 7.76) processing factors for some commodities based on guideline processing studies] acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95th exposure percentile for females 13-49 years old (6% of the aPAD), the general U.S. population (4% of the aPAD), and all other population subgroups. The most highly exposed population subgroups are children 1-2 years old, children 3-5 years old and children 6-12 years old at 5% aPAD. The EECs generated by EFED are less than HED's calculated DWLOCs for acute exposure to propamocarb hydrochloride in drinking water. Therefore, the acute aggregate risk associated with the proposed use of propamocarb hydrochloride does not exceed HED's level of concern for the general U.S. population or any population subgroups. Table 10 summarizes the acute aggregate exposure estimates to propamocarb hydrochloride residues.

Table 10. Acute Aggregate Exposures to propamocarb Hydrochloride Residues.

Population Subgroup	aPAD (mg/kg/day)	Acute Food Exposure (mg/kg/day)	Maximum Acute Water Exposure [1] (mg/kg/day)	Ground Water EEC [2] (µg/L)	Surface Water EEC [2] (µg/L)	Acute DWLOC [3] (µg/L)
U.S. Population	2.0	0.083061	1.916939	2.99	972	67000
All infants (< 1 year old)	2.0	0.045372	1.954628	2.99	972	19000
Children (1-2 years old)	2.0	0.108470	1.891530	2.99	972	19000
Children (3-5 years old)	2.0	0.102640	1.897360	2.99	972	19000
Children (6-12 years old)	2.0	0.089743	1.910257	2.99	972	19000
Youth (13-19 years old)	2.0	0.075640	1.924360	2.99	972	67000
Adults (20-49 years old)	2.0	0.084951	1.915049	2.99	972	67000
Adults (50+ years old)	2.0	0.073044	1.926956	2.99	972	67000
Females (13-49 years old)	1.5	0.091653	1.408347	2.99	972	42000

1. Maximum water exposure (mg/kg/day) = aPAD (mg/kg/day) - food exposure (mg/kg/day)
2. The crop producing the highest level was used.
3. DWLOC calculated as follows:

$$\text{DWLOC} = \frac{(\text{maximium water exposure (mg / kg / day)}) * (\text{body weight (kg)}) * (1000\ \mu\text{g / mg})}{\text{water consumption (liter / day)}}$$

5.2 Short-Term Aggregate Risk Assessment

The short-term aggregate risk assessment estimates risks likely to result from 1- to 30-day exposure to propamocarb hydrochloride residues from food, drinking water, and residential pesticide uses. High-end estimates of the residential exposure are used in the short-term assessment, and average values are used for food and drinking water exposures.

Short-term aggregate risk assessments are required for adults as there is potential for dermal post-application exposure from the golf course use of propamocarb hydrochloride. The short-term residential post-application exposure potential from the golf course use for the adult golfer can be found in Table 9. As the MOEs are greater than 100, the short-term aggregate risks are below HED's level of concern. For surface and ground water, the estimated average concentrations of propamocarb hydrochloride are less than HED's calculated DWLOCs for propamocarb hydrochloride in drinking water as a contribution to short-term aggregate exposure. Therefore, HED concludes with reasonable certainty that residues of propamocarb hydrochloride in drinking water do not contribute significantly to the short-term aggregate human health risk at the present time.

Table 11. Short-Term Aggregate Risk and DWLOC Calculations for Propamocarb Hydrochloride.

Population Subgroups	Short-Term Scenario									
	NOAEL (mg/kg/day)	Level of Concern[1]	Max Exposure[2] (mg/kg/day)	Average Food Exposure (mg/kg/day)	Residential Exposure [3] (mg/kg/day)	Aggregate MOE (food and residential)[4]	Max Water Exposure[5] (mg/kg/day)	Ground Water EEC[6] (ug/L)	Surface Water EEC[6] (ug/L)	Short-Term DWLOC[7] (µg/L)
General US Population	150	100	1.5	0.020997	0.1316	980	1.347403	2.99	77	47000
Females 13-49 years old	150	100	1.5	0.019952	0.1533	870	1.326748	2.99	77	40000
Youth 13-19 years old	150	100	1.5	0.019059	0.1316	1000	1.3574941	2.99	77	48000

1. The level of concern (target MOE) includes 10X for interspecies extrapolation and 10X for intraspecies variation.
2. Maximum Exposure (mg/kg/day) = NOAEL/Target MOE
3. Residential Exposure = Dermal exposure.
4. Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]
5. Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)
6. The crop producing the highest level was used.
7. DWLOC calculated as follows:

$$\text{DWLOC} = \frac{\left(\text{maximium water exposure (mg / kg / day)}\right) * \left(\text{body weight (kg)}\right) * \left(1000\ \mu\text{g / mg}\right)}{\text{water consumption (liter / day)}}$$

5.3 Chronic Aggregate Risk Assessment (Food and Drinking Water)

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of propamocarb hydrochloride (food and drinking water) and residential uses. However, due to the use patterns, no chronic residential exposures are expected. Therefore, the chronic aggregate risk assessment will consider exposure from food and drinking water only.

The Tier 1 [conservative, deterministic assessment using registered and HED-recommended tolerance level residues (plant commodities) and residues of concern (livestock commodities); 100% CT information for registered and proposed commodities; and modified DEEM™ (version 7.76) processing factors for some commodities based on guideline processing studies] chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (11% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 35% of the cPAD. The Tier 1 EECs generated by EFED are less than HED's calculated chronic DWLOCs for chronic exposure to propamocarb hydrochloride. Therefore, the chronic aggregate risk associated with the proposed use of propamocarb hydrochloride does not exceed HED's level of concern for the general U.S. population or any population subgroups. Table 12 summarizes the chronic aggregate exposure estimates to propamocarb hydrochloride residues.

Table 12. Chronic Aggregate Exposures to Propamocarb Hydrochloride Residues.

Population Subgroup	cPAD (mg/kg/day)	Chronic Food Exposure (mg/kg/day)	Maximum Chronic Water Exposure[1] (mg/kg/day)	Ground Water EEC[2] (µg/L)	Surface Water EEC (µg/L)	Chronic DWLOC[3] (µg/L)
U.S. Population	0.12	0.020997	0.099003	2.99	77	3500
All infants (< 1 year old)	0.12	0.012559	0.107441	2.99	77	1100
Children (1-2 years old)	0.12	0.043522	0.076478	2.99	77	760
Children (3-5 years old)	0.12	0.035688	0.084312	2.99	77	840
Children (6-12 years old)	0.12	0.026535	0.093465	2.99	77	930
Youth (13-19 years old)	0.12	0.019059	0.100941	2.99	77	3500
Adults (20-49 years old)	0.12	0.019378	0.100622	2.99	77	3500
Females (13-49 years old)	0.12	0.019952	0.100048	2.99	77	3000
Adults (50+ years old)	0.12	0.017353	0.102647	2.99	77	3600

1. maximum water exposure (mg/kg/day) = cPAD (mg/kg/day) - food exposure (mg/kg/day)
2. NR = not recorded.
3. DWLOC calculated as follows:

$$\text{DWLOC} = \frac{\left(\text{maximium water exposure (mg / kg / day)}\right) * \left(\text{body weight (kg)}\right) * \left(1000\ \mu g / \text{mg}\right)}{\text{water consumption (liter / day)}}$$

6.0 CUMULATIVE RISK

FQPA (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to 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 mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

HED did not perform a cumulative risk assessment as part of this tolerance action for propamocarb hydrochloride because HED has not yet initiated a review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of propamocarb hydrochloride. For purposes of this tolerance action, EPA has assumed that propamocarb hydrochloride does not have a common mechanism of toxicity with other substances.

On this basis, the Registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether propamocarb hydrochloride shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for propamocarb hydrochloride need to be modified or revoked. If HED identifies other substances that share a common mechanism of toxicity with propamocarb hydrochloride, HED will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment.

HED has recently developed a framework that it proposes to use for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on January 16, 2002 (67 FR 2210-2214) and is available from the OPP Website at: http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf. In the guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed.

Before undertaking a cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity" (64 FR 5795-5796, February 5, 1999).

7.0 OCCUPATIONAL EXPOSURE

An occupational exposure assessment for propamocarb hydrochloride was prepared in an HED memorandum dated 2/20/04 (Memo, M. Dow; D297387).

7.1 Occupational Handler

Based upon the proposed use patterns, HED believes the most highly exposed occupational pesticide handlers are: 1) a mixer/loader using open pour of liquids supporting aerial operations 2) an applicator using open-cab, ground-boom machinery and 3) a mixer/loader/applicator using open-pour loading and low-pressure hand-wand equipment. Pilots are expected to experience less exposure than ground-boom operators however estimated exposure and risk are presented for pilots. A mixer/loader supporting ground operations is expected to experience less exposure than a loader supporting aerial operations as a smaller volume of pesticide is handled i.e., fewer acres are treated per day. Similarly, exposure is not estimated for a "chemigator." Typically, pesticides applied through irrigation systems are not "mixed and loaded" in the traditional sense of preparing a spray solution. Materials applied through irrigation systems are typically metered into the water flow via siphon-type injection systems whereby a pesticide is drawn (i.e., siphoned) from its original container into the irrigation flow. Thus, HED expects any "handler" exposure for chemigators to be less than what would be experienced by a mixer/loader supporting aerial operations.

The directions for use within a greenhouse are predominantly applications for rock wool cube saturation, for seed bed (soil or soilless) application and via drip irrigation systems. For "foliar treatment" of tomato and lettuce, the label says: "See field use directions." For all the greenhouse methods of application except "foliar," HED believes there are no "applicators" in the typical sense. That is to say, instead individuals prepare stock solutions or set up automatic metering systems that deliver the material via the various "irrigation" systems. As such, these individuals would not be exposed to a greater volume of material than would a mixer/loader supporting aerial operations. HED expects "mixing and loading" exposures for such individuals would be less than what is estimated for a mixer/loader supporting aerial operations.

The label does indicate that the highest rate of application within a greenhouse is 4.52 lb a.i./A for a plant density fo 14,000 plants per acre. The highest rate of application for field use is 1.5 lb a.i./A. HED presents estimates of exposure for a mixer/loader/applicator using low pressure handwand equipment at the highest rate of application listed for greenhouse use.

HED expects the duration of most handler exposures in this case are likely to be "short-term" exposures (i.e., 1 - 30 days). The proposed use sites are not large acreage crops in the sense of some typical row crops such as cotton, corn or soybeans. The total time required to apply is therefore comparatively reduced. Although the label allows up to five applications per season, the label suggests that when applying propamocarb with the longer treatment intervals, a contact fungicide of a different chemistry or mode, be applied **alternatively between** treatments. Although short-term exposures are typically expected, guidance from ExpoSAC indicates that "intermediate-term" exposures (1 - 6 months) may be possible. However, the NOAELs for short-term and intermediate-term exposures are the same. Therefore, the estimated "risk" is the same

for intermediate-term exposures as is estimated for short-term exposures.

It is expected that some private (i.e., grower) applicators may perform all tasks, that is, mix, load and apply the material. However, HED ExpoSAC draft SOP (29 March 2000) directs that although the same individual may perform all tasks, in some cases they shall be assessed separately.

The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the PHED Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, all handling activities are assumed to be conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, groundboom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of PPE for each aspect of the job without requiring an applicator to wear unnecessary PPE that might be required for a mixer/loader (e.g., chemical resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical specific data were available with which to assess potential exposure to pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in PHED (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline" that is, for workers wearing a single layer of work clothing consisting of a long sleeved shirt, long pants, shoes plus socks and no protective gloves and with a single layer of work clothing **and the use of protective gloves** or other PPE as might be necessary. The proposed product label involved in this assessment directs applicators and other handlers to wear long-sleeved shirt, long pants, waterproof gloves and shoes and socks.

Although HED does not expect pesticide handlers to typically be exposed to intermediate-term exposures (1 - 6 months), the endpoints identified by the HIARC for intermediate-term dermal and inhalation exposures are the same, respectively, as the endpoints identified for short-term exposures. Therefore, the estimated risks for short-term exposures are conservative to also describe possible risks from intermediate-term exposures. See Table 13 for a summary of estimated exposures and risks to occupational pesticide handlers from the proposed new uses of propamocarb hydrochloride.

Table 13. Estimated Handler Exposure and Risk from the Use of Propamocarb on Cucurbit, Lettuce, Pepper and Tomato

Unit Exposure[1] mg a.i./lb handled	Applic. Rate[2] lb a.i./A	Units Treated[3] Per Day	Average Daily Dose[4] mg a.i./kg bw/day	MOE[5]	COMBINED MOE[6]
Mixer/Loader - Liquid - Open Pour - Supporting Aerial Operation					
Dermal: No Glove 2.9 HC With Glove 0.023 HC Inhale 0.0012 HC	1.5	350 A	Dermal: No Glove 21.75 W Glove 0.173 Inhale 0.011	Dermal: No Glove 7.0 W Glove 870 Inhale 5900	No Glove 7.0 With Glove 760
Applicator - Aerial					
Dermal: No Glove 0.0050 HC With Glove 0.0022 HC Inhale 0.000068 MC	1.5	350 A	Dermal: No Glove 0.038 W Glove 0.017 Inhale 0.000595	Dermal: No Glove 3900 W Glove 8800 Inhale 110000	No Glove 3900 With Glove 8200
Applicator - Ground-boom - Open Cab					
Dermal: No Glove 0.014 HC With Glove 0.014 MC Inhale 0.00074 HC	1.5	200 A	Dermal: No Glove 0.06 W Glove 0.06 Inhale 0.0037	Dermal: No Glove 2500 W Glove 2500 Inhale 18000	No Glove 2200 With Glove 2200
Mixer/Loader/Applicator - Open Pour - Low Pressure Handan					
Dermal: No Glove 100.0 LC With Glove 0.43 MC Inhale 0.03 MC	4.52	8 A	Dermal: No Glove 51.66 W Glove 0.22 Inhale 0.02	Dermal: No Glove 3 W Glove 680 Inhale 3300	No Glove 3.0 With Glove 560

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhale. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
2. Applic. Rate. = Taken from proposed label for PREVICUR FLEX Fungicide Reg. No. 264 - 678.
3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000; greenhouse area treated taken from unpublished report "U.S. Greenhouse/Hothouse Hydroponic Tomato Timeline" by P. Selina and M. Bledsoe, Ph.D., 30 APRIL 2002; pselina@villagefarms.com and mbledsoe@villagefarms.com.
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated ÷ Body Weight (70 kg for dermal; 60 kg for inhalation since the endpoint was identified from a developmental study and there were fetal effects). There is no correction for dermal absorption since the toxicological endpoints are identified from a dermal toxicity study. It is assumed that there is 100% inhalation absorption.
5. MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. Short-term dermal NOAEL = 150 mg a.i./kg bw/day; short-term inhalation NOAEL 65.41 mg a.i./kg bw/day.
6. Since the toxicological effects are the same for each route of exposure and are identified from different studies, the MOEs are combined using the following convention:

$$\frac{1}{\frac{1}{MOE_{DERMAL}} + \frac{1}{MOE_{INHALATION}}}$$ = Combined MOE (HED SOP 97.2; 26 NOV 97).

A MOE ≥ 100 is adequate to protect occupational pesticide handlers. Since all MOEs are > 100 **provided all handlers wear protective gloves,** (pilots are not required to wear protective gloves), the proposed uses do not exceed HED's level of concern.

7.2 Occupational Post-Application Exposure

There is a potential for agricultural workers to have post-application exposure to pesticides during the course of typical agricultural activities. HED in conjunction with the ARTF has identified a number of post-application agricultural activities that may occur. HED has also identified TCs (expressed as cm^2/hr) relative to the various activities.

The transfer coefficients used in this assessment are from an interim transfer coefficient SOP developed by HED's ExpoSAC using proprietary data from the ARTF database (SOP # 3.1). It is the intention of HED's ExpoSAC that this SOP will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

For most of the proposed crop uses, the activities with the highest TCs are typically hand harvesting and hand thinning with a TC of 2,500 cm^2/hr. HED has identified TCs associated with Romaine lettuce (2,500 cm^2/hr) but not for iceberg lettuce. For tomato, the highest TC is 1,000 cm^2/hr for hand harvest, staking, tying, thinning and training of vines.

Lacking compound specific data, HED assumes 20% of the application rate is available as foliar dislodgeable residue on day zero after application. This is adapted from the ExpoSAC SOP No. 003 (7 May 1998 - Revised 7 August 2000). The following convention may be used to estimate post-application exposure.

Surrogate Dislodgeable Foliar Residue
DFR = application rate * 20% available as dislodgeable residue * $(1\text{-}D)^1$ * 4.54×10^8 µg/lb * 2.47×10^{-8} A/cm^2

and the Average Daily Dose (ADD) = DFR µg/cm^2 * TC cm^2/hr * hr/day * 0.001 mg/µg * 1/70 kg bw ∴

1.5 lb a.i./A * .20 * $(1\text{-}0)^0$ * 4.54×10^8 µg/lb * 2.47×10^{-8} A/cm^2 = 3.36 µg/cm^2 ∴

3.36 µg/cm^2 * 2,500 cm^2/hr * 8 hr/day * 0.001 mg/µg * 1/70 kg bw = 0. 96 mg/kg bw/day

Since **MOE = NOAEL ÷ ADD** then 150 mg/kg bw/day ÷ 0.96 mg/kg bw/day = **156.**

A MOE of 100 is adequate to protect agricultural workers from post-application exposures to propamocarb. The estimated MOE is based upon conservative assumptions and is > 100, therefore estimated risks from post-application exposures do not exceed HED's level of concern.

Restricted Entry Interval (REI)
Propamocarb is listed in acute Toxicity Category III for acute dermal and primary eye irritation. It is listed in Toxicity Category IV for acute inhalation and primary skin irritation. It is not a dermal sensitizer. Therefore, the interim Worker Protection Standard (WPS) restricted entry interval of 12 hours (as listed on the proposed label) is adequate to protect agricultural workers from post-application exposures of propamocarb hydrochloride.

Incidents
The OPP Incident Data System (17 NOV 2003) indicates that there are no incidents reported for the compound propamocarb.

8.0 DATA NEEDS/LABEL REQUIREMENTS

8.1 Chemistry

- As the available residue data do not support the proposed greenhouse uses on leaf lettuce or tomatoes, the uses should be removed from the label. **A revised Section B should be submitted.**

- The proposed tolerance on leaf lettuce it too low. The available residue data support a tolerance of 90 ppm for residues of propamocarb on lettuce, leaf. In addition, the available data do not support a 60-day PBI for wheat, and the proposed tolerances for inadvertent residues of propamocarb hydrochloride *per se* (Memo, J. Tyler, 12/29/03: D274264). **A revised Section F should be submitted.**

- In order to support the request to reduce the current rotational crop restriction for wheat from 120 to 60 days, the following data are required: 1) limited rotational residue data on wheat from Regions 5 (3 trials), and 11 (1 trial); 2) the results of a poultry metabolism study; and 3) the results of a ruminant feeding study; and 4) the results of a wheat processing study. The need for a livestock enforcement method will be determined upon submission of the ruminant feeding metabolism study. The need for a poultry feeding study will be determined upon submission of the poultry metabolism study.

8.2 Toxicology

- The HED HIARC requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of propamocarb hydrochloride and inhalation MOEs >1000 for the proposed uses in this risk assessment, propamocarb hydrochloride qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses (HED SOP 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02). **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

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