January 6, 1998

MEMORANDUM

SUBJECT: Propachlor, The HED Chapter of the Reregistration Eligibility Decision Document (RED), Case 0177, Chemical 019101

PRAT DP Barcode Numbers: D233568

FROM: Kathryn Boyle, Chemist /s/
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THROUGH: Whang Phang, Branch Senior Scientist /s/
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TO: Walter Waldrop, Chief
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Special Review and Reregistration Division (7508W)

The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Special Review and Reregistration Division of OPP has requested that HED evaluate toxicology and residue chemistry data, and then perform dietary, and occupational risk assessments to estimate the mitigation measures and tolerance reassessments necessary for the reregistration of propachlor. Propachlor does not have any residential uses.

The Human Health Assessment for the Reregistration Eligibility Decision Document for propachlor is attached. The following individuals in OPP have contributed to this assessment: Christina Swartz (chemistry), William Hazel (secondary review - chemistry), Sid Abel (water), Linda Taylor (toxicology), Whang Phang (secondary review - toxicology), Kathryn Boyle (occupational), Jeffrey Dawson (secondary review - occupational), Steve Funk (anticipated residues), and Felicia Fort (DRES). A draft of this risk assessment was reviewed by the Risk Assessment Science Advisory Review Committee on November 20, 1997. Their comments have been incorporated.

Required Data:

Toxicology
21 day dermal study (and/or)
dermal penetration study

Product Chemistry
UV/visible absorption for the PAI

Label Requirements:

Label amendments are required to support uses of propachlor on sorghum and crops which can be rotated. Grazing and feeding restrictions are no longer considered to be practical by the Agency, and must be removed from labels allowing application to sorghum. Registered labels must be amended to include a statement restricting crop rotation to either corn or sorghum, crops for which there are registered uses of propachlor, pending submission of limited field rotational crop studies.

When end-use product DCIs are developed (e.g., at issuance of the RED), RD should require that all end-use product labels (e.g., MAI labels, SLNs, and products subject to the generic data exemption) be amended such that they are consistent with the basic producer labels.

The registrant must amend the product labels to add a rotational crop restriction stating that only crops for which there are registered propachlor uses may be rotated to treated fields.

PROPACHLOR

HED CHAPTER

Introduction

In this document, which is for use in EPA's development of the Propachlor Reregistration Eligibility Decision Document (RED), Health Effects Division (HED) presents the results of its risk assessment/characterization of the potential human health effects of dietary and occupational exposure to propachlor. Propachlor is a restricted-use pesticide; therefore, there are no residential uses of propachlor. Included is a discussion of the available product chemistry data, toxicological studies, residue chemistry data, and surface and ground water modeling that have been submitted and reviewed.

It should be emphasized that the results of the risk assessment presented in this document could change as a result of additional information or new data submissions. Changes to the risk assessment could also result if changes in labeled uses are made to achieve risk reduction.

The Food Quality Protection Act (FQPA) was signed on August 3, 1996. FQPA amended both FIFRA (Federal Insecticide, Fungicide, and Rodenticide Act) and FFDCA (Federal Food, Drug and Cosmetic Act). FQPA requires the Agency to consider aggregate exposure in its decision-making process for dietary (food source and drinking water), residential, and other non-occupational exposures. The propachlor risk assessment presented in this document is a single chemical/multi-pathway assessment. Note that under FQPA occupational exposure is prohibited from being aggregated with any other exposures for the purpose of tolerance setting.

FQPA requires that the Agency consider the cumulative effects of propachlor and other chemicals that have a common mechanism of toxicity. This requires that the Agency first determine that a common mechanism of toxicity exists for a group of chemicals, decides on the appropriate methodology for combining exposures, and then, after reviewing use information/patterns, determines which of the exposures/scenarios for which chemicals are to be added together, (i.e. aggregate exposure does occur). Propachlor is structurally similar to four other pesticides: acetochlor, butachlor, alachlor and metolachlor. However, the Agency has not yet completed its assessment of whether or not these chemicals actually have a common mechanism of toxicity. Additionally, the single chemical/multi-pathway assessments of each of the other chemicals must be completed before the Agency could perform the multi-chemical/multi-pathway assessment.

I. SUMMARY of RISKS

Acute Dietary (Food Source): Acute MOEs range from 18,000 for infants < 1 year to 180,000 for males 13+.

Chronic Dietary (Food Source): This assessment was performed with % crop treated data for corn and sorghum and anticipated residues for meat and milk. For all population sub-groups, less than 1% of the RfD is occupied.

Carcinogenic Dietary (Food Source): This assessment was performed with % crop treated data for corn and sorghum and anticipated residues for meat and milk. Carcinogenic risk for adult males is 3.5×10^{-7}, and for adult females is 2.9×10^{-7}.

Acute Dietary (Drinking Water): Acute MOEs are 82,000 for adult females, 96,000 for adult males, and 27,000 for children (1 - 6 years).

Chronic Dietary (Drinking Water): All % RfDs are less than 1%.

Carcinogenic Dietary (Drinking Water): Carcinogenic risk for adult males is 5.4×10^{-7}, and for adult females is 6.3×10^{-7}.

Total Acute Dietary (Food and Water): Acute MOEs are 53,000 for adult females, 62,000 for adult males, and 17,000 for children (1- 6 years).

Total Chronic Dietary (Food and Water): For all population sub-groups, less than 1% of the RfD is occupied.

Total Carcinogenic Dietary (Food and Water): Carcinogenic risk for adult males is 9.0×10^{-7}, and for adult females is 9.3×10^{-7}.

Residential: There are no residential uses of propachlor.

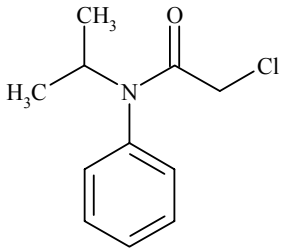
Occupational: MOEs of greater than 100 or carcinogenic risk in the 10^{-5} or 10^{-6} risk range can be achieved for all scenarios if appropriate mitgation measures are used.

Post-Application: Based on the current uses of propachlor, post-application exposure will be low. No post-application exposure studies are required at this time. Note that Monsanto is a member of the Agricultural Re-entry Task Force (ARTF).

II. SCIENCE ASSESSMENT

A. Physical and Chemical Properties Assessment

Propachlor [2-chloro-N-isopropylacetanilide] is a selective herbicide used for the preemergence control of grasses and certain broadleaf weeds in corn and sorghum.



Empirical Formula:	$C_{11}H_{14}ClNO$
Molecular Weight:	211.69
CAS Registry No.:	1918-16-7
Shaughnessy No.:	019101

1. Identification of Active Ingredient

Propachlor is a light tan/brown solid with a melting point of 67-76 C. Propachlor is practically insoluble in water (0.058 g/100 g at 20 C) and readily soluble in organic solvents including acetone, benzene, chloroform, ethanol, ethyl ether, toluene, and xylene.

2. Manufacturing-use Products

A search of the Reference Files System (REFS) conducted 2/27/97 identified two manufacturing-use products (MPs): the Monsanto Agricultural Company 96.5% technical product (T; EPA Reg. No. 524-310) and the Drexel Chemical Company 93% T (EPA Reg. No. 19713-163). The Drexel 93% T is repackaged from an EPA-registered product.

3. Regulatory Background

The Propachlor Guidance Document dated 12/84 required additional generic and product-specific product chemistry data for the Monsanto 96.5% T. The Propachlor Reregistration Standard Update dated 4/10/90 reviewed data submitted in response to the Guidance Document and summarized the product chemistry database for the Monsanto 96.5% T; data for the Drexel 93% T were not reviewed in the Update because this product was registered subsequent to issuance of the Guidance Document. Additional data were required concerning GLNs 61-3, 62-2, and 63-20 (now OPPTS 830.1670, 830.1750, and 830.6320) for the Monsanto 96.5% T.

The current status of the product chemistry data requirements for the propachlor MPs is presented in the attached data summary tables. Refer to Tables 1 and 2 for a listing of the

outstanding product chemistry data requirements.

4. Conclusions

All pertinent data requirements are satisfied for the Monsanto and Drexel propachlor Ts, except for a new data requirement concerning UV/visible absorption for the PAI (OPPTS 830.7050) which applies to the Monsanto 96.5% T. Provided that Monsanto submits the data required in the attached data summary table for the 96.5% T and either certifies that the suppliers of beginning materials and the manufacturing process have not changed since the last comprehensive product chemistry review or submits a complete updated product chemistry data package, HED has no objections to the reregistration of propachlor with respect to product chemistry data requirements.

Table 1: Propachlor - Product Chemistry Data Summary
Registrant: Monsanto Agricultural Company
Product: 96.5% T (EPA Reg. No. 524-310)

Guideline Number	Requirement	Are Data Requirements Fulfilled? [1]	MRID Number
830.1550	Product Identity and Disclosure of Ingredients	Y	00104354, CSF 12/18/91, CSF 9/16/92
830.1600 830.1620 830.1650	Starting Materials and Manufacturing Process	Y	00104354, 00152340
830.1670	Discussion of Formation of Impurities	Y	00104354, 00152340, letter 12/18/91
830.1700	Preliminary Analysis	Y	00152340
830.1750	Certification of Ingredient Limits	Y	00152340, CSF 12/18/91, CSF 9/16/92
830.1800	Analytical Methods to Verify the Certified Limits	Y	00104310, 00104354, 00152340
830.6302	Color	Y	00104354, 00152340
830.6303	Physical State	Y	00104354, 00152340
830.6304	Odor	Y	00152340
830.6313	Stability	Y	00104354, 00152340
830.6314	Oxidation/Reduction	Y	00152340
830.6315	Flammability	Y	00152340
830.6316	Explodability	Y	00152340
830.6317	Storage Stability	Y	00152340
830.6319	Miscibility	N/A [2]	
830.6320	Corrosion Characteristics	Y	00152340, 42828101
830.7000	pH	Y	00152340
830.7050	UV/Visible Absorption	N [3]	
830.7100	Viscosity	N/A [2]	
830.7200	Melting Point/Melting Range	Y	00104354, 00152340
830.7220	Boiling Point/Boiling Range	N/A [2]	
830.7300	Density/Relative Density/Bulk Density	Y	00104354, 00152340

830.7370	Dissociation Constant in Water	Y	00104354
830.7550 830.7560 830.7570	Partition Coefficient (Octanol/Water)	Y	00152340
830.7840 830.7860	Solubility	Y	00104354, 00152340
830.7950	Vapor Pressure	Y	00104354, 00152340

[1] Y = Yes; N = No; N/A = Not Applicable.

[2] Data are not required because the TGAI/MP is a solid at room temperature.

[3] The OPPTS Series 830, Product Properties Test Guidelines require data pertaining to UV/visible absorption for the PAI.

Table 2: Propachlor - Product Chemistry Data Summary

Registrant: Drexel Chemical Company
Product: 93% T (EPA Reg. No. 19713-63)

Guideline Number	Requirement	Are Data Requirements Fulfilled? [1]	MRID Number
830.1550	Product Identity and Disclosure of Ingredients	Y [2]	CSF 10/15/82 [3]
830.1600 830.1620 830.1650	Starting Materials and Manufacturing Process	N/A	
830.1670	Discussion of Formation of Impurities	N/A	
830.1700	Preliminary Analysis	N/A	
830.1750	Certification of Ingredient Limits	Y [2]	CSF 10/15/82 [3]
830.1800	Analytical Methods to Verify the Certified Limits	N/A	
830.6302	Color	N/A	
830.6303	Physical State	N/A	
830.6304	Odor	N/A	
830.6313	Stability	N/A	
830.6314	Oxidation/Reduction	N/A	
830.6315	Flammability	N/A	
830.6316	Explodability	N/A	
830.6317	Storage Stability	N/A	
830.6319	Miscibility	N/A	
830.6320	Corrosion Characteristics	N/A	
830.7000	pH	N/A	
830.7050	UV/Visible Absorption	N/A	
830.7100	Viscosity	N/A	
830.7200	Melting Point/Melting Range	N/A	
830.7220	Boiling Point/Boiling Range	N/A	
830.7300	Density/Relative Density/Bulk Density	N/A	
830.7370	Dissociation Constant in Water	N/A	

830.7550 830.7560 830.7570	Partition Coefficient (Octanol/Water)	N/A
830.7840 830.7860	Solubility	N/A
830.7950	Vapor Pressure	N/A

[1] Y = Yes; N = No; N/A = Not Applicable. This product is repackaged from an EPA-registered product; all product chemistry data requirements will be satisfied by data for the technical source product.

[2] The CSF should be amended to reflect the nominal concentration and upper and lower certified limits of the active ingredient in the product.

[3] The CSF was obtained from the product jacket.

B. HUMAN HEALTH RISK ASSESSMENT

1. Hazard Identification

Toxicology data are used by HED to assess the hazards to humans and domestic animals. The data are derived from a variety of acute, subchronic, and chronic toxicity tests; developmental/reproductive tests; and tests to assess mutagenicity and pesticide metabolism. Reregistration eligibility decisions require that HED have sufficient information to select the appropriate end-points for performing a human health risk assessment. This requires a toxicological database that is not only complete, but of acceptable quality.

The toxicology profile for propachlor is summarized in Table 3. The toxicology database on propachlor is complete and will support reregistration eligibility.

Table 3: Toxicology Profile

Guideline	Study Type	MRID #	Required	Satisfied
81-1	acute oral - rats	00104350	yes	yes
81-2	acute dermal - rabbits	00104351	yes	yes
81-3	acute inhalation - rats	41986001	yes	yes
81-4	primary eye irritation	00151787	no	yes
81-5	primary dermal irritation	00104353	no	yes
81-6	dermal sensitization	00151789	no	yes
81-7	acute delayed neurotoxicity - hen	-	no	no
81-8	acute neurotoxicity - rat	42584702	yes	yes

82-1	subchronic feeding - rats subchronic feeding - mice	00152151 00152865	yes no	no[1] no[2]
82-1	subchronic feeding - dog	00157852	yes	yes
82-2	21-day dermal - rabbits	-	yes	no
82-5	subchronic neurotoxicity - rats	43575701	yes	yes
83-1(a)	chronic toxicity - rats	44168301	yes	yes
83-1(b)	chronic toxicity - dog	40081601	yes	yes
83-2	carcinogenicity - mice	40162501 40248701 44069801 44158001	yes	yes
83-3(a)	developmental toxicity - rat	00115136	yes	yes
83-3(b)	developmental toxicity - rabbits	00150936 40113801 40398301 42348002 42584701	yes	yes
83-4	2-generation reproduction - rats	00157168 43226701 43862901	yes	yes
83-5	chronic toxicity/carcinogenicity - rat	40473101 44168301	yes	yes
84-2	gene mutation	00153939	yes	yes
84-2	chromosomal aberration	00153940 40312701	yes	yes
84-2	other genotoxic effects	00144512 40068401 43221801	yes	yes
85-1	metabolism	00157496- 00157500 00157502- 00157507	yes	yes
85-2	dermal penetration	-	no[3]	no
86-1	domestic animal safety	-	waived	no

1 classified unacceptable, but there is a chronic toxicity study available and a repeat of the subchronic study is not required
2 classified unacceptable, but there is a carcinogenicity study available and a repeat of the subchronic study is not required
3 Generally, a dermal penetration study is required for a chemical with a significant route of human exposure for which the assumption of 100% absorption does not produce an adequate margin of exposure. For propachlor additional information, such as a dermal absorption factor is necessary to refine the occupational assessment.

a. GLN 81: Acute Toxicity

Sufficient data are available on the acute toxicity of propachlor. Acute toxicity values and categories for propachlor are summarized in Table 4. The acute toxicity data requirements [§81-1 through §81-8] are satisfied.

TABLE 4: Acute Toxicity of Propachlor

Guideline/ Study Type	MRID	Results	Toxicity Category
81-1 Acute Oral - rat	00104350	LD_{50} = 1.8 g/kg	III
81-2 Acute Dermal - rabbit	00104351	LD_{50} > 20 g/kg	IV
81-3 Acute Inhalation - rat	41986001	LC_{50} = > 1.2 mg/L	III
81-4 Primary Eye Irritation - rabbit	00151787	severe irritant	I
81-5 Primary Skin Irritation - rabbit	00104353	slight irritant	IV
81-6 Dermal Sensitization - guinea pig	00151789	strong dermal sensitizer	-
81-8 Acute Neurotoxicity - rat	42584702	systemic NOEL = 175 mg/kg, systemic LOEL = 350 mg/kg, based on an increase in landing foot splay at 7 hours [peak effect time]	-

Propachlor is highly toxic via the ocular route of exposure. In a primary eye irritation study with rabbits, the test material was a severe irritant. This is toxicity category I. In a dermal sensitization study in guinea pigs, propachlor was found to be a strong dermal sensitizer. The acute oral neurotoxicity study in the rat is discussed in the section on Neurotoxicity Studies.

b. GLN 82: Subchronic Toxicity

Although the mouse and rat studies were classified as unacceptable, sufficient data for the purposes of reregistration are available on the subchronic toxicity of propachlor. However, a 21-day dermal toxicity study is required as confirmatory data.

In a subchronic feeding study [MRID 00152151], 30 Sprague-Dawley rats/sex/group were administered propachlor [96.1%] via the diet at dose levels of 0, 300 ppm [≈15 mg/kg/day], 1500 ppm [75 mg/kg/day], and 7500 ppm [375 mg/kg/day] for 90 days [standard conversion ratio]. There were no deaths. During the first month only, hyperactivity was displayed by the high-dose rats. There was a dose-related decrease in body weight throughout the study [terminal sacrifice: males 90% and 39% of control/females 92% and 63% of control for the mid- and high-dose, respectively]. There was a negative body-weight gain during the first week in both sexes at the high-dose level, and overall [males 13% of control/females 31% of control]. Food consumption was decreased during the first 4-5 weeks at the high-dose level [both sexes]. Effects [increasing cholesterol, decreasing glucose, decreasing protein, decreasing organ weights] observed at the high dose are attributed to poor nutrition, due to the poor palatability of the test material and not to a toxic effect. No adverse effects were observed at the mid- and low-dose levels in either sex. **The NOEL is 1500 ppm [≈75 mg/kg/day].** This guideline [§82-1] study is classified **Unacceptable** due to the lack of effects at dose levels that were palatable and the lack of pair-fed controls for comparison with the dose level that was not palatable. Since sufficient data from a chronic toxicity study in rats are available, an additional subchronic feeding study in rats is not required.

In a subchronic feeding study [MRID 00157852], 6 Beagle dogs/sex/group were administered propachlor [96.1%] via the diet at dose levels of 0, 100 ppm [≈2.5 mg/kg/day; standard conversion factor used], 500 ppm [≈12.5 mg/kg/day], and 1500 ppm [≈37.5 mg/kg/day] for 90 days. There were no deaths. Throughout the study, decreased body weight was observed at all dose levels in both sexes, although there was no dose-response. The mid-dose level of both sexes displayed the lowest terminal body weight [males 85%/females 87% of control]. Overall, decreased body-weight gain was observed at all dose levels of both sexes [males: 46%, 26%, and 37%/females: 91%, 18%, and 27% of control at the low-, mid-, and high-dose levels, respectively]. At the high-dose level in both sexes, food consumption was decreased throughout the study. There were no dose-related effects observed in hematology, clinical chemistry, urinalysis, ophthalmoscopic, gross, or microscopic examinations in either sex. **The NOEL is 37.5 mg/kg/day, the highest dose tested (HDT).** This guideline [§82-1] subchronic toxicity study in dogs is classified Acceptable.

In a subchronic feeding study [MRID 00152865], 30 Crl:CD®-1 (ICR)BR mice/sex/group were administered Propachlor [96.1%] via the diet at dose levels of 0, 500 ppm [≈75 mg/kg/day], 1500 ppm [≈225 mg/kg/day], and 5000 ppm [≈750 mg/kg/day] for 90 days. There were no deaths. There was a dose-related decrease in body weight of the males throughout the study [week 13: 95.6% and 91.1% of control for the mid- and high-dose, respectively]. In females, there was a dose-related decrease in body weight during the first 6 weeks [week 6: 93.3% and 91.6% of control at the mid- and high-dose levels, respectively], but during the last half of the study, the mid-dose females displayed the lowest body weight compared to the control [week 13: 92.2% and 95.8% of control at the mid- and high-dose levels, respectively]. Food consumption was decreased mainly in females at the high dose. There was a dose-related decrease in leukocytes in both sexes at week 7, and a decrease was observed in the mid- and high-dose males at study termination. There was a dose-related decrease in kidney weight in males that was statistically significant at all dose levels and relative kidney weight was significantly decreased in the high-dose males. Liver weight was increased in the mid- and high-dose males and in the high-dose females. There was a dose-related increase in relative liver weights in both sexes. Centrilobular hepatocyte enlargement was observed at all dose levels in the males [dose-related] and in the high-dose females.

There is no NOEL for this study. This guideline [§82-1] subchronic feeding study in the mouse is classified Unacceptable, because a NOEL could not be set due to questions regarding liver effects raised during a data audit that were not addressed by the study author. Since there are sufficient data available on long-term exposure [mouse carcinogenicity study] in the mouse, no additional mouse subchronic study is required.

c. Chronic Toxicity and Carcinogenicity

Sufficient data are available to assess the chronic toxicity and carcinogenic potential of propachlor. Propachlor has been classified as a "**Likely**" human carcinogen, based on the (a) rare stomach tumor in male Fischer 344 rats; (b) thyroid tumors in male and ovarian granulosa/theca cell tumors in female Sprague-Dawley rats at doses that were not adequate to assess carcinogenicity; (c) hepatocellular tumors in male CD-1 mice; (d) in vitro clastogenic activity; and (e) tumors observed at one or more of the same sites with three structurally-related chloroacetanilide compounds.

GLN 83-5: Combined Chronic Toxicity/Carcinogenicity Study in Rats

In the combined chronic toxicity/carcinogenicity study in rats [MRID 44168301], Propachlor [97.83% a.i.] was administered to 60 F-344 rats/sex/dose via the diet at dose levels of 0, 100, 300, 1000, and 2500 [males]/5000 [females] ppm [males 0, 5.4, 16.1, 53.6, and 125.3/females 0, 6.4, 19.3, 65.5, and 292.1 mg/kg/day, respectively] for 24 months. Due to palatability problems, the high dose level was attained by ramping the dose from 1000 ppm initially to the desired level by increasing by 500 ppm each week.

There were no adverse effects on survival or clinical signs in either sex. Both sexes at the

highest dose level displayed decreased body weight throughout most of the study [males 93%/females 72% of control value at study termination], which was accompanied by a decreased food intake [attributable to poor palatability of the test material]. Small decreases in body weight [males 96-97%/females 93-97% of control] and food consumption were observed in both sexes at the 1000 ppm dose level also. Body-weight gains at the two highest dose levels of both sexes were significantly decreased throughout much of the study, with the deficit for the first 3-month interval being 93%/89% of the control for males/females at 1000 ppm and 82%/79% of the control for males/females at the highest dose level, respectively. Several clinical pathology findings [initial decrease in red cell indices suggesting a mild anemia, increases in platelets/WBC in females, decreases in serum enzymes, increased GGT levels] may be treatment-related, although wide variability occurred in both sexes. At both the 12-month and terminal sacrifices, increased liver weight [absolute and relative-to-brain] was observed in females at the highest dose level, but males at the highest dose level displayed increased liver weight only at the interim sacrifice. At the highest dose level, kidney weights [absolute and relative-to-brain] were decreased in both sexes at the terminal sacrifice. At study termination, increased testicular weight was observed in males at the highest dose level and decreased thyroid weight was observed in females at the highest dose level. In the stomach, herniated mucosal glands [submucosa/tunica muscularis], mucosal hyperplasia of the pylorus, and pyloric cyst(s) were observed only in treated rats of both sexes, and the incidence and severity increased with dose in males. Females at the 65.5 mg/kg/daydose level and both sexes at the highest dose level also displayed erosion/ulceration of the glandular mucosa of the stomach. The incidence and severity of hepatocellular hypertrophy (centrilobular/midzonal) were increased in a dose-related manner in both sexes. There was no increase in the incidence of hepatocellular tumors in either sex. One male at the highest dose level displayed a glandular stomach carcinoma and, because of the other lesions observed in this organ, it could not be ruled out and appeared to be treatment related. At the doses tested, with the exception of the uncommon stomach tumor in one high-dose male, there was no apparent treatment-related increase in tumors in the treated rats when compared to the control rats. Dosing was considered adequate, based on the known poor palatability of propachlor and the demonstrated decrease in food consumption and a concomitant decrease in body-weight gain.

The NOEL in males is 5.4 mg/kg/day and in females is 6.4 mg/kg/day. The LOEL in males is 16.1 mg/kg/day and in females is 19.3 mg/kg/day, based on stomach lesions in males and liver lesions in both sexes. This guideline [§83-5] chronic toxicity/carcinogenicity study in the rat is Acceptable.

In another 2-year feeding study [MRID 40473101], 60 Sprague-Dawley CD®-Crl:CD(SD)BR rats/sex/group were administered propachlor [96.1%] via the diet at dose levels of 0, 10 ppm [males 0.48/females 0.60 mg/kg/day], 50 ppm [males 2.39/females 3.04 mg/kg/day], and 500 ppm [males 23.88/females 30.05 mg/kg/day] for 104 weeks. Survival was comparable among the groups of both sexes, and there were no adverse effects observed on any parameter monitored, with the exception of a slight increase in the incidence of thyroid and ovarian tumors. It was concluded that the dose levels were not adequate, and a repeat study [cited above] was performed. This study was considered in the weight of evidence

considerations on propachlor.

GLN 83-1(b): Chronic Toxicity Study in Dogs

In a chronic feeding study [MRID 40081601], 6 Beagle dogs/sex/ group were administered Propachlor [97.1%] via the diet at dose levels of 0, 25 ppm [≈0.025 mg/kg/day], 250 ppm [≈6.25 mg/kg/day], and 1000 ppm [≈25 mg/kg/day] for 12 months. There were no deaths. Estrus occurred more frequently in the treated females than in the controls. Throughout the study, decreased body weight was observed at the mid- and high-dose levels in males and at the high-dose level in females. At termination, the decreases in body weight were 94% of control for the mid-dose males and high-dose females and 84% of control for the high-dose males. At the high-dose level in both sexes, food consumption was decreased throughout the study. Low-dose females and mid-dose males consumed less food than the controls from week 6 on, and the mid-dose females consumed less food from week 13 on. There was a dose-related decrease in body-weight gain in both sexes [high-dose males were 37% of control during the 1-92 day interval; high-dose females were 47% of control for the same interval]. There were no dose-related effects observed in hematology, clinical chemistry, urinalysis, ophthalmoscopic, gross, or microscopic examinations in either sex. **The NOEL is 6.25 mg/kg/day. The LOEL is 25 mg/kg/day, based on decreased body weight, body-weight gain, and food consumption.** This guideline [§83-1(b)] chronic dog study is classified Acceptable.

GLN 83-2: Carcinogenicity Study in Mice

In a carcinogenicity study (MRID 44069801), propachlor [97.8% a.i.] was administered in the diet to 60 CD-1 mice/sex/dose for 18 months at dose levels of 0, 100, 500, 1500, or 6000 ppm (0, 14.6, 75.0, 222.9, or 847.3 mg/kg/day, respectively, in males; 0, 19.3, 100.0, 276.7, or 1006.9 mg/kg/day, respectively, in females). Due to palatability problems, the high-dose level was attained by ramping the dose from 1500 initially to the desired level of 6000 ppm by increasing by 500 ppm each week.

There were no adverse effects on survival or clinical signs in either sex. Decreased body weight [males 89%/females 86% of control value at study termination] and body-weight gains [overall gain males 72%/females 68% of control] were observed in males at 276.7 mg/kg/day and in both sexes at the highest dose level throughout most of the study following the ramping phase of the dosing procedure. These decreases were accompanied by decreases in food consumption. This latter effect can be attributed to the known poor palatability of the test material. Comparable increases in platelet counts were observed in both sexes at the highest dose level compared to the controls. At both the 12-month and terminal sacrifices in both sexes, there was a dose-related increase in liver weight. At the highest dose level, kidney weights [absolute and relative-to-brain] were decreased in males at both the 12-month and terminal sacrifices and in females at the terminal sacrifice. In the stomach, herniated mucosal glands into the submucosa/tunica muscularis were observed in both sexes at the highest dose level and in some males at the next highest dose level. Males at the highest dose level also

displayed erosion/ulceration of the glandular mucosa of the stomach. Several non-neoplastic lesions indicative of liver toxicity were observed in the liver in both sexes at the highest dose level and in males at the next highest dose level. These included hepatocellular hypertrophy (centrilobular/midzonal), necrosis of individual hepatocytes, eosinophilic foci, telangiectasis, and pigment deposition in Kupffer cells in the males and hepatocellular hypertrophy (periportal), mononuclear cell infiltrate, and pigment deposition in Kupffer cells in the females. Treatment-related increases in liver tumors [hepatocellular adenomas, carcinomas, adenomas and/or carcinomas combined]. There were no treatment-related tumors in female mice. Dosing was considered adequate, based on the known poor palatability of propachlor and the demonstrated decrease in food consumption and a concomitant decrease in body-weight gain. **The NOEL in males is 14.6 mg/kg/day and in females is 19.3 mg/kg/day. The LOEL in males is 75 mg/kg/day and in females is 100 mg/kg/day, based on increased liver weights and microscopic lesions in the liver.** This guideline [§83-2] carcinogenicity study in the mouse is Acceptable.

In another mouse study [MRID 40162501], 60 CD-1 mice/sex/group were administered propachlor [96.1%] via the diet at dose levels of 0 ppm, 10 ppm [males 1.62/females 2.01 mg/kg/day], 50 ppm [males 8.12/females 10.03 mg/kg/day], and 500 ppm [males 81.25/females 104.89 mg/kg/day] for 78 weeks. There were no treatment-related effects observed on survival, body weight/gain, food consumption, hematology, gross pathology, or histopathology in either sex, and there were no apparent treatment-related increases in tumors in either sex compared to the controls. The dose levels were determined to be inadequate for assessing the carcinogenic potential of propachlor. A repeat study [cited above] was performed. This study was considered in the weight of evidence considerations on propachlor.

Other Carcinogenic Issues

Propachlor induced tumors in rats at the same sites [stomach and thyroids] as structurally-related alachlor [stomach/thyroids], acetochlor [thyroids], and butachlor [stomach/thyroids] but not in the liver, as observed with metolachlor and SAN 582H, or nose/ turbinates, as seen with acetochlor, alachlor, and butachlor. The hepatocellular tumors seen with propachlor in mice were observed only with acetochlor.

d. Developmental Toxicity Studies

Developmental studies are designed to identify possible adverse effects on the developing organism which may result from the mother's exposure to the pesticide during pre-natal development.

GLN 83-3(a): Developmental Toxicity in Rats

Under the conditions of the study [MRID 00115136], 25 pregnant Charles River COBS CD rats [mated 1:1] were administered propachlor [technical] at dose levels of 0 [corn oil], 20, 60, and 200 mg/kg/day via gavage from day 6 through 19 of gestation. On day 20 of gestation,

the dams were sacrificed via CO_2 inhalation. The one death that occurred [at 200 mg/kg/day] was attributed to intubation error. Body weights were comparable among the groups. There were no significant differences observed in the mean number of viable fetuses, postimplantation loss, total implantations, corpora lutea, fetal body weights, or sex ratio. Soft tissue and skeletal malformations were comparable among the groups, and the occurrence of unossified sternebrae, 14th rudimentary ribs, and renal papillae not developed and/or distended ureter were comparable among the groups also. Although no effects were observed in this study, it was determined that a repeat rat study was not required in light of the fact that maternal toxic effects were observed in the rabbit developmental toxicity study at 100 mg/kg/ day and the rabbit developmental NOEL was 50 mg/kg/day compared to the rat NOEL for maternal and developmental toxicity in this study was 200 mg/kg/day. Additionally, severe maternal toxicity [moribund appearance, loss of righting reflex,, inactivity, dilated pupils,cool to touch] was observed in a range-finding study in rats at 600 mg/kg/day. **The NOEL is 200 mg/kg/day, the highest dose tested.** This guideline [§83-3(a)] rat developmental toxicity study is classified Acceptable.

GLN 83-3(b): Developmental Toxicity Study in Rabbits

Under the conditions of the study [MRID 42348002 and 42584701], 20 artificially inseminated New Zealand female rabbits were administered pPropachlor [96.8%] at dose levels of 0 [0.5% aqueous methylcellulose], 5, 50, and 100 mg/kg/day [analytical doses of 5.8, 58.3, and 116.7 mg/kg/day] via gavage from day 7 through 19 of gestation. On day 29 of gestation, the does were sacrificed via an i.v. injection of T-61®. There were 2 deaths at the high-dose level [on day 10], and both were considered treatment-related. One control doe died on day 12, and this was attributed to intubation error. Salivation was displayed immediately after dosing in several high-dose does, and reduced defecation occurred in the majority of these does during the treatment period. Thrashing, vocalization, prostration, labored breathing, and convulsions were displayed prior to death by the two does that died at the high dose. Negative body-weight gain occurred at the high-dose level throughout the dosing period, and the corrected overall gain was ≈27% of the control value. The high-dose does displayed decreased food consumption throughout the dosing period and for 5 days thereafter [77% of control]. Gravid uterine weight was decreased at the high-dose level [86% of control] compared to the control. There were no significant differences observed in the pregnancy rate among the groups. One low- and one high-dose does aborted [day 24], but only the abortion at the high dose was considered treatment-related, since none of the mid-dose does aborted and the high-dose doe displayed considerable weight loss and reduced food intake during treatment. One high-dose doe delivered prematurely on day 29. The number of corpora lutea were comparable among the groups, but the number of implantation sites and live fetuses were decreased at the high-dose level, and the mid- and high-dose does displayed an increased number [dose related] of resorptions [total and per doe] compared to the control. Postimplantation loss was increased in a dose-related manner, but statistical significance was not attained. A subsequent assessment of the data with respect to resorptions/postimplantation losses determined that the apparent increase was due to total litter resorption in one mid-dose doe and two high-dose does, which was within the historical control incidence. Although the

number of fetuses per litter and fetal body weight were comparable among the groups, the high dose displayed the smallest number and weight. There were no statistically significant increases in the incidence of any external, visceral, or skeletal malformation or variation at any dose level that could be attributed to treatment. **The developmental toxicity NOEL is 58.3 mg/kg/day. The developmental toxicity LOEL is 116.7 mg/kg/day, based on the slightly reduced mean fetal body weight. The maternal NOEL is 58.3 mg/kg/day. The maternal LOEL is 116.7 mg/kg/day, based on decreased body-weight gain and food consumption.** This guideline [§83-3(b)] developmental toxicity study is classified Acceptable.

In the range-finding study [MRID 42348002] in rabbits, dose levels of 0, 25, 75, 125, 175, and 225 mg propachlor [96.8%]/kg body weight/day to 7 artificially inseminated New Zealand rabbits/group during days 7 through 19 of gestation via gavage resulted in (1) death and gross pathological lesions of the stomach and liver at dose levels of 125 mg/kg/day and greater; (2) reduced defecation and soft stool at doses of 125 mg/kg/day and greater; and (3) decreased body-weight gain and, corrected body weight at 175 mg/kg/day and above. Pregnancy rate was 57.1% at 175 and 225 mg/kg/day. There were no differences observed in any Cesarean section parameter monitored among groups with gravid does at the scheduled sacrifice. No external malformation or developmental variation was observed in any of the fetuses. Maternal toxicity was observed at 125 mg/kg/day and above, expressed mainly as deaths. Developmental toxicity was not observed at any dose level with available animals [25, 75, and 125 mg/kg/day]. From these results, dose levels of 5, 50, and 100 mg/kg/day were chosen for the definitive study [cited above].

Under the conditions of the study [MRID 00150936], 16 artificially inseminated New Zealand female rabbits were administered Propachlor [96.5%] at dose levels of 0 [corn oil], 5, 15, and 50 mg/kg/day via gavage from day 7 through 19 of gestation. On day 29 of gestation, the does were sacrificed. There were numerous deaths [all groups], apparently due to disease. There were no maternal toxic effects reported at any dose level, and the clinical observations and necropsy findings [nasal and ocular discharge, lung congestion, foci] suggest a possible infection [or dosing problem]. There was no adverse effect on body weight due to treatment, and in fact the control group showed a negative body-weight gain compared to positive gains in the treated groups. There was no apparent adverse effect on pregnancy rate, although due to deaths and abortions, the low-dose group had only 8 litters. The number of corpora lutea were comparable among the groups, but the number of implantation sites/doe and live fetuses/doe were decreased at the mid- and high-dose levels. Preimplantation loss was increased at all dose levels, and the incidence exceeded historical control. Postimplantation loss was also increased, with the incidence being the highest at the mid-dose level. Because there was an insufficient number of litters at the low-dose level, no developmental toxicity NOEL could be set. The rabbit developmental toxicity study was repeated [cited above].

e. Reproduction Toxicity Studies

The reproduction study is designed to provide general information concerning the effects

of a test substance on mating behavior, conception, parturition, lactation, weaning, and growth and development of the offspring.

GLN 83-4: Two-Generation Reproduction Study in Rats

In a two-generation reproduction study [MRID 43862901], propachlor [97.83%] was administered to Sprague-Dawley (CD) rats [30 rats/sex/group] via the diet during pre-mating [F_0 10 weeks/F_{1A} 11 weeks] and through gestation and lactation [one litter/generation] at dose levels of 0, 100 ppm [males 7.1/females 8.2 mg/kg/day], 1000 ppm [males 69.6/females 80.1 mg/kg/day], and males 2500 ppm/females 5000 ppm [males 140.7/females 315.1 mg/kg/day]. Maternal toxicity was observed at the high-dose level, as evidenced by (1) decreased body weight [86% of control at mating; 75% of control at day 21 of gestation; 72% of control at day 21 of lactation], (2) decreased body-weight gain (60% of control for premating period; 48% of control during gestation; 56% of control during lactation), (3) decreased food consumption, and (4) decreased litter size at birth. This dose level was discontinued after the first generation due to severe toxicity. Reproductive effects occurred at the high-dose level, as evidenced by decreased (1) litter size at birth, (2) F_{1A} pup body weight, and (3) pup viability. Offspring viability and growth were adversely affected at the highest dose level, as evidenced by the fact that at day 21, the pups were too small [body weight ≈32% of the control] to be weaned, and the majority [11/14] of those weaned at day 21 died within one day. At the 1000 ppm dose level, slight maternal toxicity was observed, as evidenced by a decrease in body weight [90% of control] in the F_{1A} females at mating and a decrease in body-weight gain in both the F_0 [86% of control] and F_{1A} [82% of control] females during the mating period. No consistent decrease in body weight or body-weight gain was displayed by the F_0 and F_{1A} dams at 1000 ppm during gestation or lactation. At 1000 ppm in both generations, decreased pup body weight was observed at weaning [88% of control]. There were no adverse effects on mating or fertility at any dose level. At terminal sacrifice, centrilobular hepatocellular hypertrophy was observed in the liver of the adults in both sexes in both generations at the 69.6 mg/kg/day dose level. **The NOEL for maternal/paternal toxicity in males is 7.1 mg/kg/day and in females is 8.2 mg/kg/day. The LOEL in males is 69.6 mg/kg/day and in females is 80.1 mg/kg/day based on decreased body weight/gain and food consumption. The NOEL for effects on the offspring in males is 7.1 mg/kg/day and in females is 8.2 mg/kg/day. The LOEL in males is 69.6 mg/kg/day and in females is 80.1 mg/kg/day based on decreased body weight at weaning. The NOEL for reproductive/ developmental effects in males is 69.6 mg/kg/day and in females is 80.1 mg/kg/day. The LOEL for reproductive/developmental effects in males is 140.7 mg/kg/day and in females is 315.1 mg/kg/day based on reduced litter size, decreased offspring growth, and decreased pup viability at the highest dose level in the first generation.**

In another 2-generation reproduction study [MRID 00157168], Fischer 344 rats [30 rats/sex/group] were administered propachlor via the diet [F_0 for 100 days/F_1 for 120 days premating; through gestation and lactation] at dose levels of 0.3, 3.0, and 30 mg/kg/day for two generations [1 litter for F_0; 2 litters for F_1 due to low fertility at the 2 highest dose levels]. Propachlor did not produce any adverse effects on the ability of the rats to mate, reproduce,

and nurse their offspring. Although initially it was concluded that the rats had not been challenged adequately to assess the potential of propachlor to produce reproductive effects, a subsequent assessment of the data determined that the absolute and relative liver weight decreases and the increased centrilobular hepatocyte eosinophilia accompanied by very slight hypertrophy in the females demonstrated an effect level. **The maternal/systemic NOEL is 3.0 mg/kg/day. The LOEL is 30 mg/kg/day, based on liver toxicity. The reproductive NOEL is equal to or greater than 30 mg/kg/day, the highest dose tested.**

f. Mutagenicity Studies

Sufficient data are available to satisfy data requirements for mutagenicity testing. There is evidence that propachlor has genotoxic activity and analogue data are supportive of a mutagenicity concern for propachlor.

GLN 84-2: Gene Mutation

In a Chinese hamster ovary [CHO] cells HGPRT forward gene mutation assay [MRID 00153939], propachlor induced a concentration-dependent increase in mutant frequency to over a doubling of ethanol control frequency at the HGPRT locus of CHO cells at 50 μg/mL with metabolic activation only. This was supported by appropriate toxicity (14% relative survival)at this concentration, an increase in absolute colony numbers, and the relatively tight spontaneous background reported in the testing lab. There was no apparent increase without metabolic activation (dose levels of 10 - 60 ug/mL).

GLN 84-2: Chromosomal Aberration Assay

In a Chinese hamster ovary [CHO] cell/chromosomal aberration assay [MRID 40312701], propachlor was found to induce a clastogenic effect under metabolic activation conditions at the highest dose tested, 15 ug/mL, and was negative for aberrations in this in vitro assay in CHO cells without metabolic activation, dose levels of 5 - 15 ug/mL.

In an in vivo rat bone marrow cytogenetic assay [MRID 00153940], Propachlor was not shown to be clastogenic in bone marrow cells of Fischer 344 rats. Cytotoxicity was not observed at the i.p. doses tested (0.05, 0.2, or 1.0 mg/kg), and slightly higher dosing may have been appropriate. In other studies [open literature], propachlor was positive for aberrations in mouse bone marrow.

GLN 84-2: Other Genotoxic Effects

In an in vitro unscheduled DNA assay [MRID 00257647], propachlor was not shown to be genotoxic at doses up to 25 μg/mL; higher doses were cytotoxic.

In an in vivo-in vitro rat hepatocyte DNA repair assay [MRID 40068401], propachlor

was not shown to be genotoxic at the concentrations [25-1000 mg/kg] tested.

In a dominant lethal assay [MRID 43221801] in Sprague-Dawley rats, there was no indication of a dominant lethal effect associated with dietary exposure to propachlor at dose levels up to 2500 ppm for approximately 10 weeks, an acceptably high dose.

g. GLN 85: Metabolism

Sufficient data are available on the metabolism of propachlor in the rat.

In a metabolism study in rats in which single doses of 25 mg propachlor/kg of body weight were administered orally, 91% of the dose was recovered in 56 hours, with 68% of the dose being excreted in urine, 10% in the feces, and 4% was found in the carcass. Eleven metabolites were identified. The metabolic fate of propachlor depends to a large extent on the presence of the intestinal microflora. Propachlor metabolites can make 3 or more cycles in the enterohepatic circulation. In the first cycle, propachlor is metabolized via the mercapturic acid pathway and the conjugates are excreted in the bile. The second cycle is initiated when the biliary mercapturic acid pathway metabolites are metabolized by a microflora C-S lyase to reabsorbable metabolites, which are then metabolized to glucuronides that are secreted with the bile. Subsequent cycles result from microfloral β-glucuronidase activity. Propachlor appears to undergo rapid absorption, distribution, metabolism, and excretion with little, if any, tissue retention in rats. From the studies available [MRID 00157496-00157500, 00157501-00157507], it can be stated that, following initial glutathione conjugation, metabolism proceeds primarily via the mercapturic acid pathway with concurrent oxidative reactions and glucuronic acid conjugation. Initially-formed metabolites undergo extensive excretion and enterohepatic circulation.

h. Neurotoxicity Studies

GLN 81-8: Acute Neurotoxicity Study

In an acute neurotoxicity study [MRID 42584702], 10 Sprague-Dawley CD rats/sex/group were administered a single dose of propachlor via gavage at dose levels of 0, 175, 350, and 700 mg/kg. At the 700 mg/kg dose level, deaths occurred in both sexes, and several clinical signs suggestive of general systemic toxicity and/or neurological involvement [increased foot splay, myoclonic jerks, slightly abnormal gait, and decreased forelimb grip strength] were observed at the mid- and/or high-dose levels. **The NOEL is 175 mg/kg, and the LOEL is 350 mg/kg, based on an increase in landing foot splay at 7 hours [peak effect time] in females.** This guideline [§81-8] acute neurotoxicity study in rats is classified Acceptable.

GLN 82-5: Subchronic Neurotoxicity Study

In a subchronic neurotoxicity study [MRID 43575701], 10 Sprague-Dawley CD rats/sex/group were administered propachlor at dose levels of 100 ppm [males 5.5/females 6.8

mg/kg/day], 1000 ppm [males 55.8/females 6.3 mg/kg/day], and 2500 ppm [males 120.6 mg/kg/day]/5000 ppm [females 316.4 mg/kg/day] for at least 13 weeks. There were decreases in (1) body weight of both sexes [males 86%/females 77% of control] at their respective high-dose levels, (2) overall body-weight gain in both sexes at the same dose levels [males 76%/females 57% of control], and (3) food consumption in both sexes [males 79-91%/females 75-93% of control], which are likely to be related to the poor palatability of propachlor. None of the neurotoxicity parameters examined was affected by treatment in either sex. **The NOEL in males is 55.8 mg/kg/day and in females is 66.3 mg/kg/day. The LOEL in males is 120.6mg/kg/day and in females is 316.4 mg/kg/day based on decreased body weight/gain and food consumption. Propachlor does not appear to be a neurotoxin.** This guideline [§82-5] subchronic neurotoxicity study in rats is classified Acceptable.

2. Dose/Response Assessment

a. Consideration of FQPA Issues for Propachlor

Under the Food Quality Protection Act (FQPA), P.L. 104-170, which was promulgated in 1996 as an amendment to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug and Cosmetic Act (FFDCA), the Agency was directed to "ensure that there is a reasonable certainty that no harm will result to infants and children" from aggregate exposure to a pesticide chemical residue. The law further states that in the case of threshold effects, for purposes of providing this reasonable certainty of no harm, "an additional tenfold margin of safety for the pesticide chemical residue and other sources of exposure shall be applied for infants and children to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children. Notwithstanding such requirement for an additional margin of safety, the Administrator may use a different margin of safety for the pesticide residue only if, on the basis of reliable data, such margin will be safe for infants and children."

OPP's Health Effects Division RfD Committee met on May 7, 1997, (1) to evaluate the reproductive, developmental, and neurotoxicity data for propachlor, and (2) to address the sensitivity of infants and children from exposure to propachlor as required by FQPA.

Adequacy of data: An acceptable two-generation reproduction study in rats and acceptable prenatal developmental toxicity studies in rats and rabbits have been submitted to the Agency, meeting basic data requirements, as defined for a food-use chemical by 40 CFR Part 158. Based upon a weight-of-the-evidence evaluation, the Committee determined that a developmental neurotoxicity study would not be required for Propachlor. The following information was utilized in the decision. No structural anomalies of the developing central nervous system were observed in the prenatal developmental toxicity studies in rats and rabbits. No structural anomalies of the central nervous system were reported in the two-generation reproduction study in rats. There were no effects of propachlor administration on the organ weight and/or histopathology data of the nervous system in any of the long term studies in rats, mice, or dogs. Although relative brain weight was increased (due to body

weight losses) in the subchronic toxicity studies in rats and mice, the subchronic neurotoxicity study in rats was negative for neurotoxic effects. In the acute neurotoxicity study in rats, an increase in landing foot splay was noted for females at 7 hours posttreatment; this was the only indication of neurotoxic potential. Therefore, based upon consideration of the toxicity profile for propachlor, a developmental neurotoxicity study in rats was not recommended. The Committee concluded that there are no data gaps for the assessment of the effects of propachlor following *in utero* or early postnatal exposure.

Susceptibility issues: The data demonstrated no indication of increased sensitivity of rats to *in utero* and/or postnatal exposure to propachlor. In the two-generation reproduction study in rats (MRID 43862901), the parental and offspring systemic NOELs and LOELs were equivalent at 100 ppm (7.1/8.2 mg/kg/day in M/F) and 1000 ppm (69.6/80.1 mg/kg/day in M/F), respectively. In the prenatal developmental toxicity study in rats with propachlor (MRID 00115136), no maternal or developmental toxicity was noted up to the highest dose tested of 200 mg/kg/day. However, data from the 2-generation reproduction study indicates that the developmental NOEL in rats is estimated to be within the range of 200 to 315 mg/kg/day, with the caveat that this is an extrapolation from two separately conducted studies in the same strain of rats, with different routes (gavage vs. dietary) and different durations of *in utero* exposure.

The data demonstrated no indication of increased sensitivity of rabbits to *in utero* exposure to propachlor. In the prenatal developmental toxicity study in rabbits, the maternal and developmental NOELs and LOELs were equivalent at 58.3 mg/kg/day and 116.7 mg/kg/day, respectively.

Uncertainty factor: The RfD Committee determined that for propachlor, the 10-fold uncertainty factor required by FQPA for the protection of infants and children could be removed, based upon the following information: (1) The data base was complete for the evaluation of potential hazard to perinatal animals following pre- and/or postnatal exposure to propachlor. (2) Based upon a weight of the evidence determination, as described previously in this document, there was no concern regarding the potential for effects on functional development following in utero exposure to propachlor, and a developmental neurotoxicity study was not required. (3) The studies demonstrated no indication of increased sensitivity of rats to *in utero* and/or postnatal exposure to propachlor and rabbits to *in utero* exposure to propachlor.

Therefore, an uncertainty factor of 100 (10 for interspecies extrapolation and 10 for intraspecies variability) is appropriate, and will adequately protect infants and children.

b. Reference Dose [RfD]

A Reference Dose (RfD) represents the quantity of a substance which if absorbed on a daily basis over a lifetime, is not expected to pose significant risk of adverse health effects.

The RfD for propachlor was first established in 1986 based on a 90 day feeding study in

rats that was conducted with the 65% wettable powder. The NOEL was 13.3 mg/kg/day. The LOEL was 133.3 mg/kg/day based on decreased weight gain, food consumption, and increased relative liver weights. An uncertainty factor of 1000 (10 x 10 x 10) was used to account for inter- and intraspecies differences, and the insufficient duration of the study to fully assess chronic effects. The Agency's Integrated Risk Information System (IRIS) gave the 1986 propachlor data base a low confidence rating. Therefore, there was low confidence in the 1986 RfD of 0.013 mg/kg/day.

On May 7, 1997, after reviewing chronic studies in rats, mice, and dogs, the RfD for propachlor was determined to be 0.054 mg/kg/day, based on the rat chronic toxicity study [MRID 44168301] with a NOEL of 5.4 mg/kg/day. (The LOEL was 16.1 mg/kg/day, based on stomach lesions in males and liver lesions in both sexes.) An uncertainty factor of 100 (previously determined appropriate by the HED RfD Committee) was applied to account for both inter-species extrapolation and intra-species variability.

c. FAO/WHO

Propachlor has not been reviewed by the FAO/WHO Joint Committee Meeting on Pesticide Residues [JMPR] or the International Agency for Research on Cancer [IARC].

d. Carcinogenicity Classification and Risk Quantification

Lifetime feeding studies in two species of laboratory animals are conducted to screen pesticides for cancer effects. When evidence of increased tumor incidence is noted in these studies, the Agency conducts a weight of the evidence review of all relevant toxicological data including short-term and mutagenicity studies and structure activity relationship.

The carcinogenic potential of propachlor was evaluated by the HED Cancer Assessment Review Committee on July 30, 1997. The Committee recommended that propachlor be classified as a "**Likely**" human carcinogen, based on (a) the observance of multiple tumors at multiple sites, including the rare stomach tumor in a male Fischer 344 rat, thyroid tumors in male and ovarian granulosa/theca cell tumors in female Sprague-Dawley rats, and hepatocellular tumors in CD-1 mice; (b) in vitro clastogenic activity; (c) tumors observed at one or more of the same sites with three structurally-related chloroacetanilide compounds (alachlor, acetochlor, and butachlor); (d) lack of data on mode of action; and (e) the relevance of the observed tumors to human exposure.

The Committee also recommended a linear low-dose approach for human risk assessment with extrapolation being based on both the neoplastic [ovarian tumors in rats and liver tumors in male mice] and non-neoplastic [liver hypertrophy in mice] lesions. The "points of departure" for extrapolations (which refers to that estimate of dose-response information in the observable range from which low-dose extrapolation occurs) are 2.4 mg/kg/day for neoplastic lesions [ovarian tumors] and 75 mg/kg/day for non-neoplastic lesions [liver hypertrophy].

Since a linear low-dose approach for human risk assessment was recommended, cancer potency factors for propachlor were calculated for 2 tumor types and a combined tumor/ hyperplasia finding. These cancer potency factors were calculated using the Tox_Risk 4.0_K. Crump model and converted from animals to humans by the use of the 3/4's scaling factor.

For male mouse liver tumors the Q_1^* was estimated to be 5.0×10^{-3} $(mg/kg/day)^{-1}$ in human equivalents.

For male mouse liver tumors and liver hyperplasia the Q_1^* was estimated to be 1.4×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents.

For female rat ovarian tumors the Q_1^* was estimated to be 3.2×10^{-2} $(mg/kg/day)^{-1}$ in human equivalents.

For risk assessment, the largest Q_1^* (based on female rat ovarian tumors) of 3.2×10^{-2} $(mg/kg/day)^{-1}$ will be used. Note that this Q_1^* will also be used for the adult male population even though the Q_1^* is based on female rat ovarian tumors.

e. Assessment of Reproductive/Developmental Toxicity

The database for developmental toxicity and reproductive toxicity is considered to be complete at this time. There was no indication of reproductive or developmental effects. The data demonstrated no indication of increased sensitivity of rats to in utero and/or postnatal exposure to propachlor. The data demonstrated no indication of increased sensitivity of rabbits to in utero exposure to propachlor. Therefore, the RfD Committee did not refer propachlor to the Developmental/Reproductive SARC.

f. Dermal Absorption Factor

Two dermal studies were reviewed to determine if either study was appropriate for use in this assessment. One of the studies is an IBT study [Accession No. 30649], which was performed using a combination of propachlor and atrazine. This study was classified INVALID.

Another study [Accession No. 93269/104299], performed using a 65% wettable powder formulation of propachlor, was determined to be inadequate for use in estimating the dermal absorption of propachlor. This was a 1963 study that was performed using only two dose levels. The percent of the body surface area exposed was not provided, no stability/ homogeneity/dose preparation data were provided, no hematology or clinical chemistry parameters were monitored, eye examinations were not performed, and the age of the rabbits at study initiation was not provided. Only 5 rabbits/sex/group were tested [although 10/sex were exposed to the high-dose level, 5/sex of these were held for two weeks after exposure ended before they were sacrificed and examined histologically]. No toxic effects were produced at either dose level; however, the limit dose was not tested, and there was no discussion as to

how the dose levels were chosen.

There are inadequate data available on technical propachlor with which to estimate dermal exposure. There is a lack of acute data in the same species of animal for comparison, since the acute oral study was performed on rats and the acute dermal study was performed on rabbits.

Given the deficiencies in the repeated dose dermal study on the 65% wettable powder and the lack of acute data in the same species with which to estimate dermal absorption, the default estimate of 100% must be utilized pending submission of a 21-day dermal toxicity study and/or a dermal absorption study.

g. Toxicological Endpoints of Concern for Use in Human Risk Assessment

The toxicological effects of a pesticide can vary with different exposure durations. HED considers the entire toxicity data base, and based on the effects seen for different durations and routes of exposure, determines which risk assessments should be done to assure that the public is adequately protected from any pesticide exposure scenario. Exposure scenarios can be dietary or non-dietary. Both short and long durations of exposure as well as routes of exposure are always considered. Typically, risk assessments include "acute", "short-term", "intermediate-term", and "chronic" risks. These assessments are defined as follows:

> Acute risk results from a one day or single event consumption of food and water, and reflects toxicity which could be expressed following oral exposure to the pesticide residues. High-end exposure to food and water residues are assumed.
>
> Short-term risk results from exposure to the pesticide for a period of 1-7 days, and therefore overlaps with the acute risk assessment. Historically, this risk assessment was intended to address primarily dermal and inhalation exposure which could result, for example, from occupational pesticide applications. Since enaction of FQPA, this assessment has been expanded. The assessment will be performed when there are primary dermal and inhalation exposures that result from residential or occupational exposures lasting from 1-7 days. However, the analysis for residential exposures will now address both dietary and non-dietary sources of exposure, and will typically consider exposure from food, water, and residential uses when reliable data are available. In a short term assessment, risks from average food and water exposure, and high-end residential exposure, are aggregated. High-end exposures from all three sources are not typically added because of the very low probability of this occurring in most cases, and because the other assumptions built into the assessment assure adequate protection of public health.
>
> Intermediate-term risk results from exposure for 7 days to several months. This assessment is handled in a manner similar to the short-term risk assessment.

Chronic risk assessment describes risk which could result from several months to a lifetime of exposure. For this assessment, risks are aggregated considering average exposure from all sources for representative population subgroups including infants and children.

HED's Toxicity Endpoint Selection Committee met on May 7, 1997 and the Hazard Identification Committee (HIARC) on December 5, 1997, determine the endpoints for use in the propachlor risk assessment.

Acute Dietary Risk Assessment

An acute dietary risk assessment is required. The NOEL of 175 mg/kg from a single dose acute neurotoxicity study in rats will be used in estimating the MOE. The LOEL was 350 mg/kg, based on an increase in landing foot splay at 7 hours [peak effect time] in female rats. An acute neurotoxicity study is pertinent for an acute dietary assessment because the test animals receive a single oral administration of the pesticide, and therefore all toxicological effects can be attributed to that one dose. This effect, landing foot splay, is appropriate for all population sub-groups, including infants and children. An MOE of 100 will adequately protect all population sub-groups including infants and children.

Chronic (non-cancer) Dietary Risk Assessment

The RfD is the traditionally accepted endpoint for a chronic (non-cancer) dietary risk assessment. The RfD of 0.054 mg/kg/day will be used for estimating chronic (non-cancer) dietary risk for all population sub-groups from exposure through both food and water. A percent RfD of less than 100 is considered protective.

Carcinogenic Dietary Risk Assessment

The Q_1^* of 3.2×10^{-2} $(mg/kg/day)^{-1}$ based on female rat ovarian tumors will be used for estimating carcinogenic dietary risk from exposure through both food and water. Carcinogenic risk is estimated for adults only. A risk of less than 1×10^{-6} is considered protective for dietary exposures.

Dermal Absorption

A dermal penetration study has not been submitted. (See discussion on dermal absorption factor.) The available data cannot be used to estimate a dermal absorption factor. Therefore, 100% dermal absorption is assumed.

Residential

Propachlor is a restricted use pesticide; therefore, propachlor can be used only by certified applicators and cannot be purchased or used by the general public. HED has not

identified any propachlor products that are intended for home use, or uses in/around schools, parks, or other public areas. Therefore, residential assessments are not appropriate.

Short-Term (1 - 7 days) Occupational Risk Assessment

A short-term occupational risk assessment is required. Generally end-point selection should be made using toxicity generated by the same route as the likely exposure - in this case dermal. However, no dermal study was available for selecting a NOEL. Therefore, the NOEL of 175 mg/kg from a single dose acute neurotoxicity study in rats will be used in estimating the MOE. The LOEL was 350 mg/kg, based on an increase in landing foot splay at 7 hours [peak effect time] in female rats. This effect is appropriate for all population sub-groups. An MOE of 100 will adequately protect adult workers. Since the NOEL is from an oral study and dermal absorption data are not available, a dermal absorption factor of 100% must be used in estimating the risk.

Intermediate-Term (1 week to several months) Occupational Risk Assessment

An intermediate term occupational risk assessment is required. Generally end-point selection should be made using toxicity generated by the same route as the likely exposure - in this case dermal. However, no dermal study was available for selecting a NOEL. The subchronic (90 day) feeding study in the dog, the subchronic neurotoxicity study in rats, and the 2-generation reproduction study in rats were considered. All of these studies exhibit decreased body weight gain and food consumption. As noted previously there are palatibility problem with propachlor; therefore, the HIARC concluded that the decreased body weight gain and food consumption should not be used for regulatory purposes.

In the 2-generation reproduction study liver lesions, characterized as contrilobular hepatocellular hypertrophy were observed in both the F_o and F_{1a} generation in both sexes at 69.6 mg/kg/day. The NOEL for this effect was 7.1 mg/kg/day. This was supported by the 2 year rat study at the interim (1 year) sacrifice in which liver lesions, characterized as hepatocellular hypertropy were observed. The observance of liver lesions in both studies at approximately the same time period (i.e., after several months of exposure) and therefore was deemed appropriate for the intermediate-term exposure (i.e., 7 days to several months). Therefore, the maternal/paternal NOEL of 7.1 mg/kg/day from the 2-generation reproduction study in rats will be used in estimating the MOE. The effect (liver lesions) is appropriate for all population sub-groups. An MOE of 100 will adequately protect adult workers. Since the NOEL is from an oral study and dermal absorption data are not available, a dermal absorption factor of 100% must be used in estimating the risk.

Chronic (non-cancer)(several months to lifetime) Occupational Risk Assessment:

As part of the hazard assessment process, an endpoint of concern was determined for the chronic occupational assessment. However, during the exposure assessment process, the exposures which would result from the use of propachlor were determined to be of an

intermittent nature. The frequency and duration of these exposures do not exhibit a chronic exposure pattern. The exposures do not occur often enough to be considered a chronic exposure, i.e. a continuous exposure that occurs for at least several months. Therefore, performing a chronic occupational assessment is not appropriate.

If a chronic scenario can be identified, then this assessment is required. No chronic dermal toxicity studies are available. The NOEL of 5.4 mg/kg/day from the combined oral chronic toxicity/carcinogenicity study in rats will be used in estimating the MOE. (Note that this study was used to establish the RfD.) The LOEL is 16.1 mg/kg/day, based on stomach lesions in males and liver lesions in both sexes. This effect is appropriate for all population sub-groups. An MOE of 100 will adequately protect adult workers. Since the NOEL is from an oral study and dermal absorption data are not available, a dermal absorption factor of 100% must be used in estimating the risk.

Carcinogenic Occupational Risk Assessment

Since a linear low-dose approach for carcinogenic risk assessment was recommended, the assumption is made that any exposure to propachlor during a 70 year lifetime leads to an increase in the carcinogenic risk that is linearly proportional to the exposure level, regardless of the pattern (frequency and level of dosing). All exposures even those of an intermittent nature should be assessed. Therefore, a carcinogenic risk assessment for workers is appropriate. The Q_1^* of 3.2×10^{-2} $(mg/kg/day)^{-1}$ will be used for estimating carcinogenic occupational risk. A risk within the ranges of 10^{-4} to 10^{-6} (or lower) per the Non-Dietary Cancer Risk Policy (8/14/96) is considered protective for adult workers.

Inhalation

A separate inhalation risk assessment is not required since propachlor was classified as toxicity category III based on an acute inhalation study. The inhalation exposure will be added to the dermal exposure for all occupational risk assessments.

Table 5: Summary of Toxicological Endpoints for Propachlor

Exposure Duration	Exposure Route	Dose (mg/kg/day)	Endpoint	Level of Concern
Acute	Dietary (food and water)	NOEL =175	Increase in landing foot splay at 7 hours post treatment	MOE equal to or greater than 100 is protective
Chronic	Dietary (food and water)	RfD = 0.054 (calculated from NOEL = 5.4 using UF = 100)	Stomach lesions and liver lesions	less than 100% of the RfD is protective

Carcinogenic	Dietary (food and water)	$Q_1^* = 3.2 \times 10^{-2}$	Based on female rat ovarian tumors	Less than 1×10^{-6} is protective
Short-Term Occupational	Dermal and Inhalation	NOEL = 175	Increase in landing foot splay at 7 hours post treatment	MOE equal to or greater than 100 is protective
Intermediate-Term Occupational	Dermal and Inhalation	NOEL = 7.1	Liver lesions in F_o and F_{1a} generations supported by liver lesions at the interim sacrifice in the 2-year rat study	MOE equal to or greater than 100 is protective
Chronic-Term Occupational (only if scenario identified)	Dermal and Inhalation	NOEL = 5.4	Based on the use pattern (pre-plant) chronic exposure is not anticipated, therefore, this risk assessment will not be performed	
Carcinogenic Occupational (adult only)	Dermal and Inhalation	$Q_1^* = 3.2 \times 10^{-2}$	Based on female rat ovarian tumors	Within the ranges of 10^{-4} to 10^{-6} (or lower) is protective

3. Dietary Exposure and Risk Assessment/Characterization

Propachlor [2-chloro-N-isopropylacetanilide] is a selective herbicide manufactured by Monsanto Agricultural Company under the trade name Ramrod®. A search of the Reference Files System (REFS) conducted on 02/27/97 indicated that propachlor is federally registered for uses on corn and sorghum. The granular (G), flowable concentrate (FlC), and dry flowable (DF) are the propachlor formulation classes registered for use on these crops. These formulations are applied preemergence to the soil using ground equipment.

There are also SLNs (Special Local Needs) for the use of propachlor on onions grown for seed (non-food use) in Oregon and Washington.

Propachlor was the subject of a Reregistration Standard Guidance Document dated

12/84. The Residue Chemistry Chapter Update of the Propachlor Reregistration Standard was issued on 4/10/90. These documents summarized the regulatory conclusions based on available residue chemistry data, and specified the additional data required for reregistration purposes. Data submitted and evaluated following the Update are incorporated into this document, which outlines the Residue Chemistry Science Assessments with respect to the reregistration of propachlor. The conclusions are based on the use patterns supported by the basic producer, Monsanto Agricultural Company.

a. Dietary Exposure (Food Source)

The residue chemistry database includes information on the pesticide residues found in plants and animals, the levels of the detected pesticide residues, and a description of the analytical methods used. Residue chemistry data are used by HED to determine the residues of concern and to establish tolerances in food and feed. Tolerances are pesticide residue levels that should not be exceeded in or on a raw agricultural commodity in the channels of interstate commerce when the pesticide is applied according to label directions.

The residue chemistry database for propachlor is adequate and will support reregistration eligibility, provided the necessary label changes are made.

GLN 860.1200: Directions for Use

Four propachlor end-use products (EPs) are registered under FIFRA Section 3 to Monsanto. These EPs, including the associated Special Local Need (SLN) registrations under FIFRA Section 24 (c), are listed in Table 6.

Table 6: Propachlor EPs with Food/Feed Uses Registered to Monsanto.

EPA Reg. No.	Label Acceptance Date	Formulation	Product Name
524-152	11/16/94	20% G	Granular Ramrod® 20 Selective Herbicide
524-328	4/26/94	3 lb/gal FlC	Ramrod® and Atrazine Flowable Herbicide Mixture
524-331 [1]	10/2/96	4 lb/gal FlC	Ramrod® Flowable Herbicide
524-423	6/16/96	48.1% DF [2]	Ramrod® + Atrazine Dry Flowable Herbicide

[1] Including SLN Nos. OR950022 and WA950031.

[2] REFs lists EPA Reg. No. 524-423 as an FlC formulation; however, upon examination of the product label, it was determined that the formulation is more correctly described as a DF.

GLN 860.1300: Nature of the Residue - Plants

The qualitative nature of the residue in plants is adequately understood, based on an acceptable [^{14}C]propachlor metabolism study in sorghum. The sorghum study results have shown that propachlor was not detectable in any edible sorghum commodity. The principal

metabolite in sorghum grain and foliage was propachlor oxanilic acid; in addition, all of the propachlor metabolites identified in sorghum commodities contained the N-isopropylaniline (NIPA) moiety.

Radiotracer studies on corn, sorghum, soybeans, and sugar beets conducted using [^{3}H]propachlor, indicated that degradation of propachlor was rapid. In these studies, no intact propachlor was observed 5-7 days following application. Based on the available metabolism data, HED has determined that the residues of concern (i.e. those to be regulated in the tolerance expression) in plant commodities are propachlor and all metabolites containing the N-isopropylaniline (NIPA) moiety.

GLN 860.1300: Nature of the Residue - Livestock

The qualitative nature of the residue in livestock is adequately understood. HED has determined that ruminant, swine, and poultry metabolism studies in which animals were fed a mixture of radiolabeled metabolites (rather than radiolabeled propachlor) are acceptable since no radiolabeled propachlor was detected in the sorghum metabolism study. (See Meat, Milk, Poultry, Eggs Section for a description of the studies) The residues of concern in livestock commodities are propachlor and its metabolites containing the NIPA moiety.

GLN 860.1340: Residue Analytical Methods

Adequate methods are available for data collection and tolerance enforcement in plant and livestock commodities. The Pesticide Analytical Manual (PAM) Vol. II lists two GC methods, using flame ionization detection, for the determination of propachlor and its metabolites containing the N-isopropylaniline moiety in animal tissues and milk (Method I) and in plant commodities and eggs (Method A). The registrant has proposed a GC method using thermionic specific detection for tolerance enforcement in plant and livestock commodities. This method is a modification of current enforcement methods and has successfully undergone Agency method validation. HED has concluded that the proposed method is adequate for tolerance enforcement provided the registrant incorporates the comments made by BEAD/ACB. The methods used for data collection were GC methods similar to the enforcement methods.

GLN 860.1360: Multiresidue Methods

The 1/94 FDA PESTDATA database (PAM Volume I, Appendix I) indicates that propachlor is completely recovered (>80%) using Multiresidue Method Section 302 (Luke method; Protocol D) but is not recovered using Multiresidue Methods Section 303 (Mills, Onley, Gaither method; Protocol E, non-fatty foods) and Section 304 (Mills method; Protocol E, fatty foods). The registrant has submitted the results of multiresidue methods testing of the acid metabolites of propachlor (propachlor oxanilic acid, propachlor sulfinyl lactic acid, propachlor sulfonic acid, and propachlor acetic acid) which have been forwarded to FDA for review; the acid metabolites of propachlor were not adequately recovered by any

of the multiresidue method protocols.

GLN 860.1380: Storage Stability Data

Adequate storage stability data are available to support reregistration. Storage stability data indicate that residues of propachlor oxanilic acid are stable in corn and sorghum matrices for up to 29-32 months of frozen storage, and residues of propachlor oxanilic acid, propachlor sulfinyl lactic acid, and propachlor sulfonic acid are stable for up to ~28 months of frozen storage in eggs and the kidney, liver, muscle, and fat of swine, poultry, and cattle. Residues of propachlor oxanilic acid, propachlor sulfinyl lactic acid, and propachlor sulfonic acid are stable for up to ~18 months of frozen storage in milk and residues of 4-hydroxyacetanilide are stable for up to 26 months in milk. Storage stability data for propachlor *per se* were not required because propachlor was not detected in the sorghum metabolism study.

GLN 860.1500: Crop Field Trials

Crop field trials are used to assess the magnitude of the pesticide residue in/on a commodity at the time of harvest. These studies usually involve application of the pesticide to a crop in accordance with label directions in a manner which would expose the crop to the maximum legal amount of the pesticide. This information is used to set pesticide tolerances.

The Agency has received adequate field trial data depicting propachlor residues of concern in field corn and sorghum commodities following applications made in accordance with the maximum registered use patterns.

Corn: Following treatment at 1X, residues were < 0.02 - 0.04 ppm in grain and < 0.02 - 0.52 in forage except for one grain sample in which residues were 0.19 ppm, and three forage samples in which residues were 1.53 - 2.12 ppm (One sample was from the same trial that yielded the 0.19 ppm grain sample.).

Sorghum: Following at 0.8X or 1.2 X, residues were 0.08 - 3.77 ppm in forage and 0.05 - 2.78 ppm in fodder except for one forage sample at 7.67 ppm, and one fodder sample at 10.59 ppm.

Label revisions are required for sorghum in order to reflect current Agency policies.

Requirements for residue data in aspirated grain fractions were waived because propachlor applications are made preemergence; thus, there is little likelihood that grain will contain surface residues of this chemical.

Although tolerances are listed at 40 CFR §180.211, there are no registered uses on cotton, flax, peas, pumpkins, sweet corn, and sugar beets. Therefore, no field trial data are required for these crops.

GLN 860.1520: Processed Food/Feed

Adequate corn and sorghum processing studies have been submitted. Residues of propachlor and its NIPA-containing metabolites, calculated as propachlor, did not concentrate in starch, crude oil(dry- and wet-milled), refined oil (dry- and wet-milled), and concentrated insignificantly in flour (1.1x), grits (1.2x), and meal (1.3x) processed from field corn grain bearing detectable propachlor residues following treatment with a single preemergence application of the 4 lb./gal FlC formulation at 3.3x.

No tolerances are required for residues in the processed commodities of field corn or sorghum. There are no federally registered uses on crops grown for seed; therefore, no processing study data are required for these crops.

GLN 860.1480: Meat, Milk, Poultry, Eggs

Acceptable ruminant and swine feeding studies are available to reassess the established tolerances for residues in milk and in the fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep. An acceptable poultry feeding study is available to determine the need for tolerances for residues in eggs and the fat, meat, and meat byproducts of poultry. A summary of the required tolerances for residues in livestock commodities is presented below.

Milk and the fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep: The maximum theoretical dietary burdens of propachlor to beef and dairy cattle are 11.99 and 12.91 ppm, respectively (see Table 7). The maximum theoretical dietary burden of propachlor to swine is 0.25 ppm based on a diet consisting of 90% sorghum grain and 10% corn milled byproducts.

Table 7: Calculation of Maximum Ruminant Dietary Burden for Propachlor.

Feed Commodity	Reassessed Tolerance (ppm)	% Dry Matter	Beef Cattle		Dairy Cattle	
			% of Diet	Burden[1] (ppm)	% of Diet	Burden[1] (ppm)
Sorghum grain	0.25	86	40	0.116	40	0.116
Sorghum forage	8.0	35	40	9.143	50	11.429
Sorghum stover	12.0	88	20	2.727	10	1.364
		TOTAL	100	11.986	100	12.909

1 Burden (ppm) = (% of diet)(reassessed tolerance)/(%dry matter)

An adequate dairy cattle feeding study was reviewed in the Propachlor Reregistration Standard Update; this study reflected dosing with a mixture of propachlor metabolites

(oxanilic acid, sulfinyl lactic acid, and sulfonic acid at a 6:3:1 ratio) at ~0.4X, 1.3X, and 4X (5, 15, and 50 ppm, respectively) for 28 days. The 15 ppm (1.3X) most closely approximates the estimated total dietary burden. Propachlor metabolite residues were <0.02-0.02 ppm in milk samples from both the 1.3X and 4X dosing levels. In tissues, residues were <0.02-0.04 ppm in liver, 0.09-0.12 ppm in kidney, <0.02 ppm in muscle, and <0.02-0.04 ppm in fat at the 1.3X dosing level.

Based on the maximum theoretical dietary burden, and based on residues in milk and ruminant tissues, the following revised tolerances must be proposed: 0.05 ppm for residues in the meat byproducts (except kidney) and fat and 0.2 ppm for residues in the kidney of cattle, horses, goats and sheep. Existing tolerances for residues in milk and in the meat of cattle, horses, goats and sheep are adequate.

An adequate swine feeding study was reviewed in the Propachlor Reregistration Standard Update; this study reflected dosing with a mixture of propachlor metabolites at ~20X, 60X, and 200X (5, 15, and 50 ppm, respectively) for 28 days. At the 20X dosing level, propachlor metabolite residues were 0.02-0.04 ppm in liver, 0.04-0.06 ppm in kidney, <0.02 ppm in muscle, and <0.02 ppm in fat. Based on these data, the existing tolerances of 0.02 ppm for propachlor residues in hog meat, fat, and meat by-products are adequate.

Eggs and the fat, meat, and meat byproducts of poultry: The maximum theoretical dietary burden of propachlor to poultry is 0.24 ppm (see Table 8).

Table 8: Calculation of Maximum Poultry Dietary Burden for Propachlor

Poultry Feed Commodity	Reassessed Tolerance (ppm)	% of Diet	Burden[1] (ppm)
Field corn grain	0.20	20	0.040
Sorghum grain	0.25	80	0.200
	TOTAL	100	0.240

1 Burden (ppm) = (%of diet) (reassessed tolerance)

An adequate poultry feeding study was reviewed in the Propachlor Reregistration Standard Update; the study reflected dosing with a mixture of propachlor metabolites at ~20X, 60X, and 200X (5, 15, and 50 ppm, respectively) for 28 days. At the 20X and 60X dosing levels, propachlor metabolite residues were <0.02 ppm in eggs, and <0.02-0.02 ppm in fat, kidney, liver, and muscle. Based on this study, HED concludes residues in poultry commodities can be classified under Category 3 of 40 CFR §180.6(a), i.e. there is no reasonable expectation of detectable residues; therefore, no tolerances are needed for residues in poultry commodities.

GLN 860.1400: Water, Fish, and Irrigated Crops

Propachlor is not registered for direct use on water and aquatic food and feed crops; therefore, no residue chemistry data are required under this guideline topic.

GLN 860.1460: Food Handling

Propachlor is not registered for use in food-handling establishments; therefore, no residue chemistry data are required under this guideline topic.

GLN 860.1850: Confined Accumulation in Rotational Crops

The nature of the residue in rotational crops is adequately understood, based on an adequate confined rotational crop study. Following application of [^{14}C]propachlor to sandy loam soil at 6.0 lb ai/A (1X the maximum rate), lettuce, radishes, and wheat planted were planted at 30-, 120-, and 365- day plantback intervals (PBIs). Lettuce, and radishes (roots and tops), as well as immature and mature wheat, were harvested and analyzed for total radioactive residues (TRR). Accumulation of radioactive residues was highest in samples planted 30 and 120 days after treatment (DAT) and decreased at the 365-DAT planting interval. Radioactive residues (expressed as [^{14}C]propachlor equivalents) were highest in wheat straw at 9.630, 5.281, and 1.704 ppm at the 30-, and 120-, and 365-DAT intervals, respectively, and lowest in lettuce at 0.124, 0.161, and 0.049 ppm, respectively. Propachlor residues of concern were present in rotational crops at 30-, 120-, and 365-day plantback intervals (PBIs). Parent propachlor was not detected in any rotational crop commodity at any rotational interval. The major metabolite identified in all matrices at all three plantback intervals was oxanilic acid.

The confined rotational crop study indicates that the metabolism of propachlor in rotational crops is similar to that in primary plants; metabolites containing the NIPA moiety were observed in both studies. Because propachlor metabolites of concern (those containing the NIPA moiety) were detected in all rotational crop commodities at all plantback intervals at greater than 0.01 ppm, limited field rotational crop studies must be conducted.

GLN 860.1900: Field Accumulation in Rotational Crops

The reregistration requirement for data pertaining to field accumulation in rotational crops is not fulfilled. The confined rotational crop data indicate that limited field rotational crop studies must be conducted. The limited field trials should be conducted on representative crops of the root and tuber vegetables, leafy vegetables, and small grains at two sites per crop for a total of six trials

This requirement should not affect the reregistration eligibility decision for propachlor; however, the registrant must amend the product labels to add a rotational crop restriction stating that only crops for which there are registered propachlor uses may be

rotated to treated fields.

Tolerance Reassessment Summary

Tolerances for propachlor residues (40 CFR §180.211) are presently expressed in terms of residues of propachlor and its metabolites, calculated as propachlor. Based on metabolism data, HED has determined that the propachlor residues to be regulated in plant and livestock commodities are those which contain the NIPA moiety. Therefore, the tolerances should be expressed in terms of the combined residues of propachlor and its metabolites containing the N-isopropylaniline moiety, calculated as propachlor.

The Agency has recently updated the list of raw agricultural and processed commodities and feedstuffs derived from crops (Table 1, OPPTS GLN 860.1000). Due to these changes, some commodity definitions must be corrected. In addition, tolerances for commodities for which there are currently no registered uses of propachlor need to be revoked, and the "N" notation next to some tolerance levels designating negligible residues should be deleted. A summary of reassessed tolerances is presented in Table 9.

Table 9: Tolerance Reassessment Summary for Propachlor.

Commodity	Current Tolerance, ppm	Tolerance Reassessment, ppm	Comment/ *[Correct Commodity Definition]*
Tolerances Listed Under 40 CFR §180.211			
Beets, sugar, roots	0.2	Revoke	There are currently no registered uses of propachlor on this commodity.
Beets, sugar, tops	1.0		
Cattle, fat	0.02 (N)	0.05	The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Cattle, mbyp	0.02 (N)	0.05	*[Cattle, mbyp (except kidney)]* The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Cattle, meat	0.02 (N)	0.02	
Corn, forage	1.5	3.0	*[Corn, field, forage]* Highest residue detected in corn forage in a 1X field trial is 2.12 ppm.
Corn, grain	0.1 (N)	0.2	*[Corn, field, grain]* Highest residue detected in corn grain in a 1X field trial is 0.19 ppm.

Corn, sweet (K + CWHR)	0.1 (N)	Revoke	There are currently no registered uses of propachlor on this commodity.
Cotton seed	0.1 (N)	Revoke	There are currently no registered uses of propachlor on this commodity.
Flax, seed	3.0	Revoke	There are currently no registered uses of propachlor on this commodity.
Flax, straw	10.0	Revoke	There are currently no registered uses of propachlor on this commodity.
Goats, fat	0.02 (N)	0.05	The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Goats, mbyp	0.02 (N)	0.05	*[Goats, mbyp (except kidney)]* The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Goats, meat	0.02 (N)	0.02	
Hogs, fat	0.02 (N)	0.02	
Hogs, mbyp	0.02 (N)	0.02	*[Hogs, mbyp (except kidney)]*
Hogs, meat	0.02 (N)	0.02	
Horses, fat	0.02 (N)	0.05	The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Horses, mbyp	0.02 (N)	0.05	*[Horses, mbyp (except kidney)]* The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Horses, meat	0.02 (N)	0.02	
Milk	0.02 (N)	0.02	
Peas (with pods)	0.2	Revoke	There are currently no registered uses of propachlor on this commodity.
Peas, forage	1.5	Revoke	There are currently no registered uses of propachlor on this commodity.
Pumpkins	0.1	Revoke	There are currently no registered uses of propachlor on this commodity.

Sheep, fat	0.02 (N)	0.05	The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Sheep, mbyp	0.02 (N)	0.05	*[Sheep, mbyp (except kidney)]* The tolerance increase is based on residues detected in a dairy cattle feeding study and an estimation of maximum ruminant dietary burden.
Sheep, meat	0.02 (N)	0.02	
Sorghum, fodder	5.0	12.0	*[Sorghum, stover]* Highest residue detected in sorghum fodder in a .8X or 1.2X field trial is 10.59 ppm.
Sorghum, forage	5.0	8.0	Highest residue detected in sorghum forage in a .8X or 1.2X field trial is 7.67 ppm.
Sorghum, grain	0.25	0.25	
Eggs	0.02 (N)	Revoke	Based on the available data, residues in poultry commodities can be classified under Category 3 of 40 CFR §180.6(a); therefore, tolerances for residues in poultry commodities are not required.
Poultry, fat	0.02 (N)		
Poultry, mbyp	0.02 (N)		
Poultry, meat	0.02 (N)		
Tolerances to be Proposed:			
Cattle, kidney	0.02(N)	0.2	Feeding study data indicate that separate tolerances for residues in kidney are required.
Goats, kidney	0.02(N)	0.2	
Hogs, kidney	0.02(N)	0.02	
Horses, kidney	0.02(N)	0.2	
Sheep, kidney	0.02(N)	0.2	
Corn, field, stover	--	1.0	

Codex Harmonization

There are no Codex MRLs established for propachlor; therefore, issues of compatibility with U.S. tolerances do not exist.

b. Dietary Risk Assessment (Food Source)

DRES analyses were performed to estimate acute and chronic dietary risk for propachlor. HED uses the Dietary Risk Evaluation System (DRES) to combine the pesticide residue data with food consumption data. Thus, dietary (food source) exposure is equal to pesticide residues present in food multiplied by consumption data for the food item.

The consumption information used in this analysis is derived from USDA's 1977-78 Nationwide Food Consumption Survey (NFCS). Over 30,000 respondents were surveyed over three days as to what foods they ate, with each individual's consumption information being associated with their body weight, sex, age, ethnicity and other sociodemographic information. Individual consumption estimates were weighted to be nationally representative. From these data single day and 3 day average consumption estimates were derived for the U.S. population and select population subgroups. Three day average information is used in the DRES chronic exposure analyses.

HED acknowledges that the data from this survey are nearly 20 years old. However, at this time, the data are the best information available to the Agency. USDA did conduct another NFCS in 1987-1988. However, the representativeness of these consumption data were called into question per a GAO Report due to the low response rate of certain groups. Therefore, the data are not used for routine risk assessment purposes. Surveys were conducted in 1989-1991 and 1994-1996. The 1994-1996 data are currently undergoing translation, which involves taking the consumed foods such as apple pie; breaking this into raw agricultural commodities such as sugar, apples, and flour; and then using standard recipes to reaggregate the amounts of sugar, apples and flour with all of the other foods consumed.

Note that a tiered approach is used for dietary risk assessment. The pesticide residue component is progressively refined proceeding from worst-case assumptions (such as tolerance level residues) to more realistic assumptions (such as use of monitoring data). Refinement of pesticide residues continues until no risk concern is indicated or a determination is made that mitigation is required. This tiering approach conserves Agency resources.

Acute - Tier 1 - Point Estimates

A Tier 1 acute assessment was performed to estimate the risk of consuming a large amount of propachlor residues in the food consumed on a single day. The assessment uses a single high-end residue estimate, which is usually the tolerance, together with a distribution of individual food consumption values as reported by respondents in the USDA 1977-78 Nationwide Food Consumption Survey. Thus, exposure to the chemical is accumulated for each commodity to estimate a single-day's exposure. It is assumed that propachlor is uniformly distributed in the food supply at the tolerance level. Note that a Tier 1 acute dietary asessment does not account for blended commodities or percent crop treated data.

As previously discussed the appropriate endpoint for an acute dietary assessment is 175 mg/kg/day.

Acute Dietary Risk = 175 mg/kg/day/ high-end exposure = MOE

The Margin of Exposure (MOE) is a measure of how close the high-end exposure comes to the NOEL. An MOE greater than 100 will adequately protect all population sub-groups including infants and children. The acute dietary MOEs (rounded to two significant

figures) for food source exposure to propachlor for various population sub-groups are given in Table 10.

Table 10: Acute MOEs

Population Sub-Groups	High-End Exposure (mg/kg/day)	MOE
Infants < 1 year	0.01	18,000
Child (1 - 6 years)	0.004	44,000
Females (13+ years)	0.0012	150,000
Males (13+ years)	0.001	180,000
General Population	0.003	58,000

All population sub-groups greatly exceed 100. Therefore, HED has no concerns for acute dietary (food) exposure for all population sub-groups.

Chronic Dietary (food source)

A chronic (non-carcinogenic) dietary assessment is performed to estimate the lifetime risk of consuming an average amount of propachlor residues. The assessment uses 3 day average consumption values from USDA's 1977-1978 Nationwide Food Consumption Survey. Chronic dietary risk is calculated for the U.S. population and 22 population sub-groups using DRES (Dietary Risk Evaluation System). As previously discussed, the appropriate endpoint for the chronic assessment is the RfD, 0.054 mg/kg/day. Chronic risk is reported as the percent of the RfD that is taken up by the estimated exposure.

Tolerance level residues (Table 9) were used for corn and sorghum. However, HED refined its assessment by using percent crop treated (%CT) information for these two commodities. OPP's Biological and Economic Analysis Division supplied the %CT information, which was obtained from various public and proprietary sources. The following values were used: corn 2%, and sorghum 8%. This analysis assumes that propachlor is uniformly distributed in the food supply at the tolerance level adjusted for the percent crop treated.

Section 408(b)(2)(F) requires that if a tolerance relies on percent crop-treated data, that the Agency make a determination as to the reliability of the data. Percent crop-treated estimates are derived from federal and private market survey data. Typically, a range is assumed for the exposure assessment. By using this upper end estimate of percent crop treated, the Agency is reasonably certain that exposure is not understated for any significant

population sub-group. Additionally, the DRES (Dietary Risk Evaluation System) modeling used in estimating chronic dietary risk uses regional consumption information to estimate exposure for four population sub-groups that are geographically based regions of the United States. To provide for the periodic evaluation of these estimates of percent crop treated, the Agency will require under Section 408(b)(2)(F) for periodic re-evaluation of the percent crop treated data as long as the tolerances remain in force.

Anticipated residues were estimated for meat and milk by re-estimating the dietary burden using the percent crop treated data. (See Table 11)

Table 11: Re-Estimation of Ruminant Dietary Burden for Propachlor Using Percent Crop Treated Data

Feed Item	Reassessed Tolerance (mg/kg)	% Dry Matter	% Crop Treated	Beef Cattle		Dairy Cattle	
				% of Diet	Burden[1] (mg/kg)	% of Diet	Burden[1] (mg/kg)
Sorghum grain	0.25	86	8	40	0.0093	40	0.0093
Sorghum forage	8.0	35	8	40	0.731	50	0.914
Sorghum stover	12.0	88	8	20	0.218	10	0.109
TOTAL				100	0.958	100	1.03

1 Burden (ppm) = (%of diet)(reassessed tolerance)(%CT) / % dry matter

The dietary burden for ruminants is now 1.0 mg/kg, as compared to the previous estimation of 13 mg/kg. In the previously described feeding studies, at the mg/kg feeding level (5X), residues were not detected (<0.02 mg/kg) in milk, muscle, fat, and liver. Residues were 0.03 - 0.05 mg/kg in kidney. At the 15X feeding level, residues were detected in kidney (0.12 mg/kg), fat (0.04 mg/kg), and liver (0.04 mg/kg), but not in milk or muscle (<0.02 mg/kg). Thus, the anticipated residues are for use in dietary risk estimation are: milk 0.001 mg/kg, meat 0.001 mg/kg, fat 0.003 mg/kg, liver 0.003 mg/kg, and kidney 0.01 mg/kg. These anticipated residues are based on the finite residues or limits of quantitation found at the exaggerated feeding levels. Note that the residues in kidney, the only commodity with finite residues at three feeding concentrations, were approximately linear with feeding level: 0.05 mg/kg at 5X; 0.12 mg/kg at 15X; and 0.53 mg/kg at 50X.

Section 408(b)(2)(E) requires that if a tolerance relies on anticipated or actual residue levels, that the Agency make a determination every five years as to the reliability of the data, i.e. that the current residue levels are not above the levels relied on. For anticipated residues for meat and milk, instead of using tolerances as the level of propachlor present in the feed items, anticipated residues as estimated for food /feed crops were used in the calculation. To provide for the periodic evaluation of these anticipated residues, the Agency will require

under Section 408(b)(2)(E) residue data to be submitted every 5 years as long as the tolerances remain in force.

Chronic (Non-Carcinogenic Dietary Risk) is reported in Table 12 to one significant figure.

Table 12: Chronic (Non-Carcinogenic) Dietary Risk

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.000018	0.03
Children (1-6 years)	0.000045	0.08
Non-nursing infants	0.000073	0.1
Adult Females (20+ years)	0.000009	0.02
Adult Males (20+ years)	0.000011	0.02

The %RfDs for all population sub-groups are less than 1%, which is much less than HED's level of concern of 100%.

Carcinogenic Dietary (Food Source)

A carcinogenic dietary assessment is performed to estimate the additional lifetime carcinogenic risk of consuming an average amount of propachlor residues. The assessment uses 3 day average consumption values from USDA's 1977-1978 Nationwide Food Consumption Survey. The exposure (mg/kg/day) is the same as that estimated by DRES for the chronic dietary assessment. Carcinogenic dietary risk is calculated for the adult U.S. population. As previously discussed, the appropriate endpoint for the carcinogenic assessment is the Q_1^*, 0.032 $(mg/kg/day)^{-1}$. This analysis also assumes that propachlor is uniformly distributed in the food supply.

Carcinogenic dietary risk is estimated by:

Exposure (mg/kg/day) x Q_1^* (0.032 $(mg/kg/day)^{-1}$) = Risk

For propachlor, carcinogenic risk for adult females is:

(0.000009 mg/kg/day)((0.032 $(mg/kg/day)^{-1}$) = 2.9×10^{-7}

For propachlor, carcinogenic risk for adult males is:

(0.000011 mg/kg/day)((0.032 $(mg/kg/day)^{-1}$) = 3.5×10^{-7}

These estimates of carcinogenic dietary risk are less than 1×10^{-6}.

c. Dietary (Drinking Water) Exposure

The environmental chemistry database for propachlor is largely complete. The major routes of dissipation is via aerobic soil metabolism. The overall result of this mechanism of dissipation appears to indicate that propachlor would have low to moderate persistence in the environment.

Hydrolysis: Propachlor is stable to hydrolysis at pH's 5,7,. Therefore, no consideration for this process was factored into the analysis.

Photolysis: Propachlor did not photodegrade significantly in water and was observed to degrade very slowly in a soil system. Therefore, no consideration for this process was factored into the analysis.

Soil and Aquatic metabolism: The aerobic soil metabolism of propachlor had an observed half-life of 2.7 days in an aerobic sandy loam soil. No anaerobic soil metabolism study was provided.

The anaerobic aquatic metabolism half-life was not an important route of dissipation for propachlor. A half-life from 146 days was observed.

Soil-Water Partition Coefficient: Adsorption/desorption studies of propachlor indicated that it is very mobile in the four soils tested.

Groundwater (Modeling)

SCI-GROW (Screening Concentration in Groundwater) is a prototype model for estimating "high-end" ground water concentrations of pesticides considering the maximum allowable use-rate in an area where the ground water is exceptionally vulnerable to contamination. The model uses existing environmental fate properties of the pesticide being examined, the application rate from the label, and the existing body of data from Agency-required small-scale prospective and two large-scale prospective groundwater monitoring studies for all pesticides. It should be noted that SCI-GROW is biased in the sense that negative data were ignored, i.e., studies where the pesticide was not detected in ground water were not included in the data set. Thus, it is not expected that SCI-GROW estimates would be exceeded.

With most groundwater sources there are no known predictable seasonal or longer term trends in concentration of pesticide contaminants. Therefore, only one concentration is estimated which should be used for both acute and chronic scenarios. The concentration estimated for propachlor using SCI-GROW is 0.027 ppb (ug/L).

Groundwater (Monitoring)

Propachlor has been reported in numerous small scale studies in areas of the U.S. where it is or is suspected of being used. The Pesticide In Ground Water Database (*EPA,*

1992) reported studies covering 11 states from 1985 to 1990 in which 2718 wells were sampled. No samples reported finding propachlor above the maximum contaminant level (MCL)(90 ug/L). For those studies with measurable results (33 total wells), the range of concentrations are 0.02-3.5 ppb.

Readily available sources of ground water monitoring data was reviewed for the presence of propachlor. Monitoring data was extracted from the U.S. EPA's Office of Water STORET Database maintained on the IBM mainframe at Research Triangle park, North Carolina. (See Table 13)

Table 13. Ground Water Monitoring Data From STORET

Source	Dates	# Samples <LOD[1]	# Samples >LOD <LOQ[2]	# Samples >LOQ	
				Num.	Results (ppb)
Wells	1980-1997	1671[3]	5950[4]	10	0.004-0.17

[1]LOD: Level of Detection, below which the substance cannot be detected.
[2]LOQ: Level of Quantification, below which the substance can be detected but not quantified with certainty.
[3]For this dataset ranged from 0.004-0.4 ppb (0.4 applied to one sample, otherwise maximum would be 0.012 ppb).
[4]For this dataset ranged from 0.004-0.012 ppb.

Impact to ground water source drinking water is expected to be minimal based on the known environmental fate of the substance. However, monitoring data does indicated that propachlor has reached surficial groundwater resources in several studies above the LOQ and in many above the LOD. Therefore, impact to drinking water source ground water may be likely.

Consistency between the modeled results (SCI-GROW) and the range in monitoring data suggests that the estimated value can be used for assessing an upper bound risk for ground water source drinking water, although the fate properties of propachlor would indicate a low probability of contaminating groundwater. The following may help explain why detections were reported in the various studies when the fate properties might suggest otherwise.

Interpretation of STORET ground water monitoring data and perhaps the Pesticide in Ground Water Database data may be complicated by the presence of closely related parent metabolites. Degradates such as hydroxypropachlor, propachlor oxanilic acid, and propachlor sulfonic acid may have been detected and reported as propachlor due to the limitations of the analytical methods or, in the case of STORET data, a lack of an appropriate input parameter value for data storage. Additionally, metabolites of propachlor tend to be more persistent and mobile which may explain the presence of propachlor in ground water if the method or lack of parameter values results in the metabolite being reported as the parent.

Finally, the presence of propachlor in surficial ground water, if not the metabolites, may be the result of conditions after application and prior to measurement which favored migration to groundwater. Such events as surface tillage, major rain storm, and/or irrigation may contribute to rapid migration before significant aerobic degradation could occur. Additionally, improper sample collection and pesticide application techniques or poorly installed wells may contribute to ground water contamination.

Surface Water (Modeling)

For Tier 2, two models, PRZM2.3 and EXAMS2, are used to estimate concentrations of pesticide contaminants in surface water. PRZM2.3 (Pesticide Root Zone Model) can be linked to EXAMS2 (EXposure Analysis Modeling System) for a direct transfer of data.

PRZM2.3 is a runoff model, which can estimate the off-site movement of synthetic organic chemicals from agricultural fields over a period of up to 36 years. PRZM2.3 was developed to simulate the transport and transformation of field-applied pesticides in the crop root zone and the vadose zone taking into account the effects of agricultural management practices. It is considered to be appropriate for modeling most agricultural field crops on mineral soils in the US. Using input variables such as pesticide fate properties, soil characteristics, soil/crop management practices, and daily weather, PRZM2.3 can simulate a pesticide's fate and transport in/on soil and plants, leaching to the bottom of the root zone, water runoff and soil erosion. The output that is linked to EXAMS2 includes estimated runoff volume, sediment yield, and associated edge of the field pesticide losses (which constitute pesticide loadings to edge of the field surface water).

Surface water models such as EXAMS2 simulate pesticide fate and transport in surface water and sediment. Input includes runoff volume, and pesticide losses dissolved in runoff water and adsorbed to eroding soil (from PRZM2.3) as well as pesticide fate properties, and receiving water characteristics. Output includes estimated peak and various average pesticide concentrations dissolved in the water column, adsorbed to suspended sediment, and adsorbed to bottom sediment as a function of time and location.

It should be noted that PRZM2.3/EXAMS2 were designed for use in ecological risk assessment. They are not ideal tools for use in drinking water risk assessment. Drinking water taken from surface water tends to come from bodies of water that are substantially larger than a 1 hectare by 2 meters deep pond. As in the case of the Tier 1 screen, PRZM2.3/EXAMS2 assumes that the entire basin (a 10 hectare field) receives an application of the chemical. In virtually all cases, basins large enough to support a drinking water facility will contain a substantial fraction of area which does not receive the chemical. Furthermore, there is always at least some flow (in a river) or turn over in a reservoir or lake. Pesticide concentrations modeled using PRZM2.3/EXAMS2 represent upper-bound concentrations that may actually occur at the edge of a pond, but not the concentrations that could occur in flowing water. Therefore, PRZM2.3/EXAMS2 should be considered as a screen. PRZM2.3/EXAMS2 could over-estimate the actual drinking water concentrations.

There are large uncertainties in extrapolating fate data from laboratory to field, and from field to field. Additionally, several important environmental processes are not adequately simulated such as pesticide uses on turf, and orchards. Screening models such as PRZM2.3/EXAMS2 are best used to determine that a chemical poses little or no exposure. If, a risk assessment performed using an high-end/upper-bound exposure modeled by PRZM2.3/EXAMS2 does not exceed HED's level of concern, then there would be no reason to refine the assessment.

The scenarios chosen for propachlor were a corn field in Pattawattamie County, Iowa and a sorghum field in Neosho County, Kansas. Scenarios were chosen to represent sites that were expected to produce runoff greater than 90% of the sites where the appropriate crop is grown. Model simulations were made with the maximum application rates, maximum number of yearly applications, and the shortest recommended application interval.

Since, label application rates are one of the input parameters for PRZM2.3/EXAMS2, different concentrations are generated for different commodities. Using PRZM2.3/EXAMS2 the peak concentration appropriate for use in an acute assessment is 44 ppb (corn) and 64 ppb (sorghum). The concentration appropriate for use in the chronic and carcinogenic assessments is 0.5 ppb (corn) and 0.6 ppb (grain sorghum).

Surface Water (Monitoring)

Readily available sources of surface water monitoring data was reviewed for the presence of propachlor. Surface water monitoring data was extracted from the U.S. EPA's Office of Water STORET Database maintained on the IBM mainframe at Research Triangle park, North Carolina. Propachlor was monitored in numerous surface water features throughout the U.S. during the past 20 years. It is known that propachlor was applied in the watershed of several of the monitored sites according to the data owners. The remaining sites have not had the use of propachlor ascertained. Table 14 provides a gross summary of the data for surface water sources.

Table 14: Surface Water Monitoring Data From STORET

Source	Dates	# Samples <LOD[1]	# Samples >LOD <LOQ[2]	# Samples >LOQ	
				Num.	Results (ppb)
Streams	1978-1997	423[3]	13667[3]	270	0.001-9.9
Reservoirs	1986-1996	0[4]	51[5]	0	NA
Lakes	1979-1997	84[6]	1761[7]	25	0.002-10.0

Springs	1991-1997	0	161[8]	0	NA
Estuary	1993-1994	0	7[8]	0	NA
Canals	1989&1992	0	6[9]	0	NA

[1]LOD: Level of Detection, below which the substance cannot be detected.
[2]LOQ: Level of Quantification, below which the substance can be detected but not quantified with certainty.
[3]For this dataset ranged from 0.001-0.5 ppb.
[4]For this dataset no value was reported.
[5]For this dataset ranged from 0.03-0.1 ppb.
[6]For this dataset ranged from 0.002-0.5 ppb.
[7]For this dataset ranged from 0.002-1.3 ppb.
[8]For this dataset ranged from 0.007-0.1 ppb.
[9]For this dataset ranged from 0.05-0.1 ppb.

Final note, a small percentage of the STORET surface water monitoring data did not report a minimum detection (LOD) or quantification limit (LOQ) for the analytical technique. Although this artifact would lessen the quality of these data relative to all datasets that did report an LOD or LOQ, there were no measured values reported below the lowest detection limit for all data sets (0.001 ug/L). Additionally, none of the values from the datasets that did report an LOD or LOQ were among the highest found in surface waters.

Propachlor has been detected in surface waters of the U.S. in numerous monitoring studies. The potential for source drinking water contamination is therefore highly likely. The Office of Water has established an MCL of 90 ug/L for propachlor. No surface water sample exceeded the MCL and, with the exception of a few, all were more than an order of magnitude less. Additionally, considering the rate of microbial degradation, propachlor is not likely to be found in drinking water source water or drinking water after treatment and distribution to the consumer tap for any appreciable length of time. Therefore, the impact on surface water drinking water quality and drinking water at the consumer tap may be considered minimal**.**

Data for Use in Risk Assessment

As previously stated, there are limitations when Tier 2 EECs as estimated by PRZM2.3/EXAMS2 are used for drinking water exposure estimates. A single 10 hectare drainage basin with a 1 hectare pond does not accurately reflect the dynamics in a watershed which is large enough to support a drinking water utility. A basin of adequate size to support a drinking water facility would not be planted completely in a single crop or, for that matter, entirely of crops nor would it be treated entirely with the pesticide being modeled. Additionally, the pesticide would more than likely be applied over several days to weeks rather than on a single day. This would reduce the magnitude of the conservative concentration peaks, but also make them broader, reducing the acute exposure but perhaps increasing the chronic exposure. The final overriding concern with estimates derived from

PRZM2.3/EXAMS2 is the fact that the simulated pond has no outlets which any water body capable of supporting a drinking water facility would at least have some flow through (rivers) or turnover (reservoirs).

Surface water monitoring data is primarily limited by the lack of correlation between sampling date and the use patterns of the pesticide within the study's drainage basin. Additionally, the sample locations were not associated with actual drinking water intakes for surface water.

The monitored wells were not associated with known groundwater drinking water sources.

The monitoring data presented in this document provides verification that propachlor is found in surface and ground waters of the U.S. However, the lack of correlation between use and sampling and sampling and mitigation measures that may have occurred over time make it difficult to rely on the data for quantitative risk assessment purposes without further analysis. Review of the data did not provide evidence as to whether the data were representative of vulnerable areas, peaks, long term means, or other important factor in determining the extent of impact on an aquatic environment.

As such, it was recommended by the Environmental Fate and Effects Division that the monitoring data be used only for illustrative purposes although the monitoring data and estimated values were within the same order of magnitude. For quantifying risks to the general population, including infants and children, SCI-GROW and PRZM2.3/EXAM2 estimated EECs are recommended.

Since all surface water numbers exceed the groundwater estimate of 0.027 ppb, only the surface water estimates will be used in the risk assessment. For propachlor, the acute exposure will be estimated using the highest of the estimated values which is 64 ppb estimated by PRZM2.3/EXAMS2 for grain sorghum. The chronic and carcinogenic exposure will be estimated using the highest of the estimated values which is 0.6 ppb estimated by PRZM2.3/EXAMS2 for grain sorghum.

d. Dietary Exposure (Drinking Water)

Adult Female

The exposure estimate for an adult female (13+ years) is calculated by the following equation:

Exposure = (chemical concentration in µg/L in consumed water) X (10^{-3} mg/µg) ÷ (60 kg body weight) X (2L water consumed/day)

The 2 Liters of water is a default assumption used by the Office of Water. The 60

kilograms is the Agency's default female body weight.

Adult Male

The exposure estimate for an adult male is calculated by the following equation:

Exposure = (chemical concentration in µg/L in consumed water) X (10^{-3} mg/µg) ÷ (70 kg body weight) X (2L water consumed/day)

The 2 Liters of water is a default assumption used by the Office of Water. The 70 kilograms is the Agency's default male body weight.

Child (1 - 6 years)

The exposure estimate for a child (1- 6 years) is calculated by the following equation:

Exposure = (chemical concentration in µg/L in consumed water) X (10^{-3} mg/µg) ÷ (10 kg body weight) X (1L water consumed/day)

The 1 Liter of water is a default assumption used by the Office of Water. The 10 kilograms is an assumption per memo of D. Edwards.

The other assumption used is assuming that water from the same source containing the same contaminant level is consumed throughout a 70 year lifetime. Most of the US population moves at some time during their life and does not live in the same area, drinking from the same water source for a 70 year lifetime. It could be considered as either an over-estimation or an under-estimation of risk depending on the contaminant levels in the other sources of drinking water.

Acute Exposures

For propachlor, acute exposure for adult females is:

(64 ug/L)(0.001)(2 L) / 60 kg = 0.002133 mg/kg/day

For propachlor, acute exposure for adult males is:

(64 ug/L)(0.001)(2 L) / 70 kg = 0.001829 mg/kg/day

For propachlor, acute exposure for children (1 - 6 years) is:

(64 ug/L)(0.001)(1 L) / 10 kg = 0.0064 mg/kg/day

Chronic/Carcinogenic Exposures

For propachlor, chronic/carcinogenic exposure for adult females is:

(0.6 ug/L)(0.001)(2 L) / 60 kg = 0.00002 mg/kg/day

For propachlor, chronic/carcinogenic exposure for adult males is:

(0.6 ug/L)(0.001)(2 L) / 70 kg = 0.000017 mg/kg/day

For propachlor, chronic/carcinogenic exposure for children (1 - 6 years) is:

(0.6 ug/L)(0.001)(1 L) / 10 kg = 0.00006 mg/kg/day

e. Dietary Drinking Water Risk

Note that all MOEs and carcinogenic risk estimates have been rounded to two significant figures. All RfD risk estimates are reported to 1 significant figure.

Acute Risk

As previously stated, the NOEL for use in estimating acute dietary risk is 175 mg/kg/day.

MOE = NOEL/exposure

For propachlor, acute risk for adult females is:

175 mg/kg/day / 0.002133 mg/kg/day = 82,000

For propachlor, acute risk for adult males is:

175 mg/kg/day / 0.001829 mg/kg/day = 96,000

For propachlor, acute risk for children (1 - 6 years) is:

175 mg/kg/day / 0.0064 mg/kg/day = 27,000

All MOEs greatly exceed 100. Therefore, HED has no concerns for acute drinking water dietary exposure.

Chronic Risk

As previously stated, the RfD of 0.054 mg/kg/day will be used in estimating chronic (non-cancer) dietary risk.

Exposure/RfD x 100 = % RfD

For propachlor, chronic risk for adult females is:

0.00002 mg/kg/day / 0.054 mg/kg/day x 100 = 0.04%

For propachlor, chronic risk for adult males is:

0.000017 mg/kg/day / 0.054 mg/kg/day x 100 = 0.03%

For propachlor, chronic risk for children (1 - 6 years) is:

0.00006 mg/kg/day / 0.054 mg/kg/day x 100 = 0.1%

All %RfDs are less than 1%, which is much less than HED's level of concern of 100%.

Carcinogenic Risk

As previously stated, the Q_1^* of 0.032 $(mg/kg/day)^{-1}$ will be used in estimating carcinogenic dietary risk. Note that carcinogenic risk is estimated for the adult population only.

(Exposure)(Q_1^*) = risk

For propachlor, carcinogenic risk for adult females is:

(0.00002 mg/kg/day)(0.032 $(mg/kg/day)^{-1}$) = 6.3×10^{-7}

For propachlor, carcinogenic risk for adult males is:

(0.000017 mg/kg/day)(0.032 $(mg/kg/day)^{-1}$) = 5.4×10^{-7}

These carcinogenic risks are less than 1×10^{-6} .

f. Total Dietary (Food and Water) Assessment

Propachlor can be consumed in both food and drinking water. Therefore, a total dietary assessment must account for both. Estimates of acute dietary risk, chronic dietary risk, and carcinogenic dietary risk from consumption of propachlor residues in food and in water were estimated previously in this document.

Per current HED policy, dietary drinking water risk can be estimated only for adult females, adult males, and child (1 - 6 years). Therefore, only these population sub-groups can be carried forth in this assessment. MOEs and carcinogenic risk are rounded to two significant

figures. Chronic risk is rounded to one significant figure.

Table 15: Total Dietary Acute MOEs

Population Sub-Group	Food Exposure (mg/kg/day)	Water Exposure (mg/kg/day)	Total Dietary Exposure (mg/kg/day)	Total Dietary Acute MOEs
adult female	0.0012	0.002133	0.003333	53,000
adult male	0.001	0.001829	0.002829	62,000
child (1 - 6 years)	0.004	0.0064	0.0104	17,000

All total dietary MOEs greatly exceed 100. Therefore, HED has no concerns for total acute dietary exposure.

Table 16: Total Chronic (non-carcinogenic) Dietary %RfD

Population Sub-Group	Food Exposure (mg/kg/day)	Water Exposure (mg/kg/day)	Total Dietary Exposure (mg/kg/day)	Total Dietary RfD
adult female	0.000009	0.00002	0.000029	0.05
adult male	0.000011	0.000017	0.000028	0.05
child (1 - 6 years)	0.000045	0.00006	0.000105	0.2

All total dietary RfDs are much less than HED's level of concern of 100%.

Table 17: Total Dietary Carcinogenic Risk

Population Sub-Group	Food Exposure (mg/kg/day)	Water Exposure (mg/kg/day)	Total Dietary Exposure (mg/kg/day)	Total Dietary Carcinogenic Risk
adult female	0.000009	0.00002	0.000029	9.3×10^{-7}
adult male	0.000011	0.000017	0.000028	9.0×10^{-7}

The carcinogenic risk is less than HED's level of concern of 1×10^{-6}.

Note that there are no residential uses of propachlor. Therefore, an aggregate assessment due to exposure from residues of propachlor in food and water, and from residential uses is not possible. Therefore, these total dietary (food and water) assessments are the aggregate assessments for the purposes of FQPA.

g. Dietary Risk Characterization

The acute dietary food source assessment was performed at tolerance level and did not consider any blended commodities, anticipated residues, or percent crop treated data. Therefore, actual residues are likely to be lower, which would correspondingly increase the MOEs (decreasing risk).

The chronic/carcinogenic food source assessments were performed at tolerance level with percent crop treated data for corn and sorghum. Anticipated residues were estimated for meat and milk. These assessments are more refined than Tier 1 (tolerance level assessments), and therefore are a more realistic assessment.

The drinking water assessments are considered to be over-estimates since surface water modeling numbers are from PRZM2.3/EXAMs2 which is an ecological model. It does not necessarily represent drinking water that would be obtained from a treatment plant.

HED considers that the data used to perform these assessments was adequate. Overall, HED does not consider any of these estimates to under-represent residue levels and corresponding risk estimates.

4. Occupational Exposure and Risk Assessment/Characterization

a. Occupational Exposure Assessment

An occupational and/or residential exposure assessment is required for an active ingredient if (1) certain toxicological criteria are triggered and (2) there is potential exposure to handlers (mixers, loaders, applicators) during use or to persons entering treated sites after application is complete. For propachlor the toxicological criteria are triggered by the determination that propachlor is a "likely" human carcinogen. The potential for exposure does exist.

Use Patterns

Propachlor, 2-chloro-N-isopropylacetanilide, is a selective herbicide used in commercial settings for the preemergence weed control of annual grasses and broadleaf weeds in grain sorghum (milo), field corn, hybrid seed corn, and silage corn, and for weed control "in the first season, growth-establishment phase" for onion seed use in Washington and Oregon. Propachlor is formulated as a manufacturing product (93 and 96.5 percent active ingredient), a flowable concentrate liquid (31.5 and 42 percent active ingredient), a dry flowable (48.1 percent active

ingredient formulated with atrazine), and as a granular (20 percent active ingredient).

Propachlor can be applied with groundboom sprayers, tractor drawn granular broadcast spreaders, and granular row planters. Application rates vary from 3.0 to 6.0 pounds active ingredient per acre depending upon the application scenario. Propachlor can be applied to the following crops/areas: field corn, hybrid seed corn, silage corn, grain sorghum (milo), and onion seed.

Occupational-use Products and Homeowner Use Products

At this time, products containing propachlor are intended for occupational uses. Propachlor is a restricted use pesticide and is only available for retail sale to and use by certified applicators (or persons under their direct supervision) and only for those uses covered by the certified applicator's certification.

Due to the lack of residential uses, a residential assessment has not been performed.

Acute Toxicology Categories

Guideline studies for acute toxicity indicate that the technical grade of propachlor is classified as category I for primary eye irritation, category IV for primary skin irritation.

Under the Worker Protection Standard (WPS) interim restricted entry intervals (REI) for all uses within the scope of the WPS are based on the acute toxicity of the active ingredient. A 48 hour REI is required under WPS based on toxicity category I for primary eye irritation.

Other Endpoints of Concern

The propachlor Toxicology Endpoint Selection (TES) document, dated May 7, 1997, indicates that there are toxicological endpoints of concern for propachlor. (See Dose-Response Section)

Epidemiological Information

The OPP Incident Data System, the Toxic Exposure Surveillance System (National Poison Control Centers), California Department of Food and Agriculture/Department of Pesticide Regulation Database, and the National Pesticide Telecommunications Network were searched for poisoning incident data on the active ingredient propachlor. In these databases, no serious illnesses have been reported due to exposure to propachlor, although there are reports of dermatitis and skin sensitivity.

The World Health Organization (1993) does have a report concerning a 29 year old agricultural worker who had been in contact with propachlor for 8 days and experienced contact eczema on the palms, wrists, and forearms. The skin lesions disappeared after contact ceased.

In another 1993 WHO report concerning a patch test of 17 farmers, there were seven cases that had a positive patch test reaction, and five cases that had an irritant reaction to propachlor. In a study of 79 workers manufacturing 65% propachlor, 19% of the workers showed contact dermatitis due to propachlor exposure.

Handler Exposure Assessment

HED has determined that there are potential exposures to mixers, loaders, applicators, and other handlers during usual use-patterns associated with propachlor. Based on the use patterns, 5 major exposure scenarios were identified for propachlor:
(1) mixing/loading liquids for groundboom application;
(2) mixing/loading dry flowables for groundboom application;
(3) loading granulars for tractor-drawn spreader application;
(4) applying sprays with groundboom equipment; and
(5) applying granulars with a tractor-drawn spreader.

Dermal and inhalation exposures are presented in Table 18. No chemical-specific data were submitted; therefore, Table 18 was developed using PHED Version 1.1 surrogate data. The Pesticide Handlers Exposure Database (PHED) was developed by Health Canada, the American Crop Protection Association, and EPA. PHED was initially released for public use in 1992. PHED is a generic/surrogate exposure database containing a large number of measured values of dermal and inhalation exposure for pesticide workers (e.g., mixers, loaders, and applicators) involved in the handling or application of pesticides in the field. The database currently contains data for over 2000 monitored exposure events. Use of surrogate or generic data is appropriate since it is generally believed that the physical parameters of the handling and application process (e.g. the type of formulations, the method of application, and the type of clothing), not the chemical properties of the pesticide, control the amount of dermal and inhalation exposure. Thus, PHED typically allows exposure and risk assessments to be conducted with a much larger number of observations than available from a single exposure study.

PHED also contains algorithms that allow the user to complete surrogate task-based exposure assessments beginning with one of the four main data files contained in the system (i.e., mixer/loader, applicator, flagger, and mixer/loader/applicator). Users select data from each file and construct exposure scenarios that are representative of the use of the chemical. HED, in conjunction with the PHED task force, has evaluated all

of the data currently in PHED, and developed a surrogate exposure table that contains a series of standard exposure estimates for various scenarios. These standard unit exposure values are the basis for this assessment. The standard exposure values (i.e., the unit exposure values included in the exposure and risk assessment tables) are based on the "best fit" values calculated by PHED. PHED calculates "best fit" exposure values by assessing the distributions of exposures for each body part included in datasets selected for the assessment (e.g., chest or forearm) and then calculating a composite exposure value representing the entire body. PHED categorizes distributions as normal, lognormal, or in an "other" category. Generally, most data contained in PHED are lognormally distributed or fall into the PHED "other" distribution category. If the distribution is lognormal, the geometric mean for the distribution is used in the calculation of the "best fit" exposure value. If the data are an "other" distribution, the median value of the dataset is used in the calculation of the "best fit" exposure value. As a result, the surrogate unit exposure values that serve as the basis for this assessment generally range from the geometric mean to the median of the selected dataset.

HED's first step in performing a handler exposure assessment is to complete a baseline exposure assessment. The baseline scenario generally represents a handler wearing long pants, a long-sleeved shirt, and no chemical-resistant gloves. If, there is a level of concern, then increasing levels of risk mitigation, such as PPE (personal protective equipment) and engineering controls, are used to achieve an appropriate margin of exposure or cancer risk. Table 18 exposure estimates are baseline estimates.

Table 19 summarizes the assumptions, specific to each exposure scenario, as well as describing the quality of the PHED data used in the assessment.

Note that the formulas for all calculations are given in the foot-notes in the various Tables.

Table 18: Dermal and Inhalation Exposures to Propachlor

Exposure Scenario (Scenario.#)	Baseline Dermal Unit Exposure (mg/lb ai)[a]	Baseline Inhalation Unit Exposure (µg/lb ai)[b]	Crop Applied[c]	Application Rate (lb ai/acre)[d]	Acres Treated (acres/day)[e]	Daily Dermal Exposure (mg/day)[f]	Daily Inhalation Exposure (mg/day)[g]
Mixer/Loader Exposure							
Mixing/Loading Liquids for Groundboom Application (1)	2.9	1.2	corn	6	80	1,392	0.6
			grain sorghum, onions	5		1,160	0.5
Mixing/Loading Dry Flowables for Groundboom Application (2)	0.07	0.8	corn, grain sorghum	4.8	80	27	0.3
Loading Granulars for a Tractor-Drawn Spreader Application (3)	0.008	1.7	corn	6	80	3.8	0.8
			grain sorghum	5		3.2	0.7
Applicator Exposure							
Applying Sprays with a Groundboom Sprayer (4)	0.014	0.7	corn	6	80	6.7	0.3
			grain sorghum, onions	5		5.6	0.3
Applying Granulars with a Tractor-Drawn Spreader (5)	0.01	1.2	corn	6	80	4.8	0.6
			grain sorghum	5		4.0	0.5

[a] Baseline dermal unit exposure represents long pants, long sleeved shirt, no gloves, open mixing/loading for M/Ls, and open cab tractor for applicators. It should be noted that labels 524-328, -152, and -331 require use of gloves and protective eyewear for mixer/loaders, which is more protective than baseline.

[b] Baseline inhalation unit exposure represents no respirator.

[c] Corn crops include field corn, hybrid seed corn, and silage corn; the onion uses are limited to the states of Washington and Oregon (EPA Reg 524-331).

[d] Application rates are maximum values found in the propachlor labels, which is available as a flowable liquid (EPA Regs. 524-331 and 524-328), a dry flowable (EPA Reg. 524-423), and granular (EPA Reg. 524-152).

[e] Daily acres treated values are from HED estimates of acreage that could be treated in a single day for each exposure scenario of concern.

[f] Daily dermal exposure (mg/day) = Exposure (mg/lb ai) * Appl. rate (lb ai/acre) * Acres treated (acres/day).

[g] Daily inhalation exposure (mg ai/day)= Exposure (µg/lb ai) x (1 mg/1000 µg) Conversion x Application Rate (lb ai/acre) x Acres treated (acres/day).

Table 19: Exposure Scenario Descriptions for the Use of Propachlor

Exposure Scenario (Number)	Data Source	Standard Assumptions (8-hr work day)	Comments
Mixer/Loader Descriptors			
Mixing/Loading Liquid Formulations (1)	PHED V1.1	80 acres for groundboom.	**Baseline:** Hands, dermal, and inhalation acceptable grades. Hands = 53 replicates; Dermal = 71 to 121 replicates; Inhalation = 85 replicates. High confidence in dermal and inhalation data. **PPE:** Hands and dermal acceptable grades. Hands = 59 replicates: Dermal = 71 to 121 replicates. High confidence in dermal and inhalation data. A 50% protection factor (PF) was applied on dermal, non-hand exposure to simulate coveralls - double layer clothing. **Engineering Controls:** Dermal = ABC, Hands and inhalation acceptable grades. Hands = 31 replicates; Dermal = 30 to 36 replicates; Inhalation = 27 replicates. High confidence in inhalation data. Medium confidence in dermal data. Gloves were worn during use of engineering controls.
Mixing/Loading Dry Flowable Formulations (2)	PHED V1.1	80 acres for groundboom.	**Baseline:** Hands, dermal, and inhalation acceptable grades. Hands = 7 replicates; Dermal = 16 to 26 replicates. Low Confidence in dermal data due to the small number of hand replicates. High confidence in inhalation data. **PPE:** Hands = ABC, Dermal and inhalation acceptable grades. Hands = 34 replicates; Dermal = 16 to 26 replicates. Medium Confidence in dermal data. High Confidence in inhalation data. A 50% protection factor (PF) was applied on dermal, non-hand exposure to simulate coveralls - double layer clothing. **Engineering Controls:** A 90% PF was applied on baseline dermal and inhalation exposure data to simulate a water soluble pack or closed mixing/loading system scenario.
Loading Granular Formulations (3)	PHED V1.1	80 acres for row planters and tractor drawn spreaders.	**Baseline:** Hands all grades; dermal = ABC; Inhalation acceptable grades. Hands = 10 replicates; dermal = 33 to 78 replicates; inhalation = 58 replicates. Low confidence in dermal data due to the poor quality of the hand replicates and low replicate numbers. High confidence for inhalation data. **PPE:** Hands and inhalation acceptable grades; Dermal = ABC. Hands = 45 replicates; dermal 12 to 59 replicates; inhalation = 58 replicates. High confidence in inhalation data. Low confidence in dermal data due to low number of replicates. **Engineering Controls:** A 90% PF was applied on dermal and inhalation exposure to simulate a closed loading system scenario.
Applicator Descriptors			

Applying Sprays with a Groundboom Sprayer (4)	PHED V1.1	80 acres.	**Baseline:** Hands, dermal, and inhalation acceptable grades. Hands = 29 replicates; dermal = 23 to 42 replicates; inhalation = 22 replicates. High confidence in dermal and inhalation data. **PPE:** Hands = ABC grades; dermal and inhalation acceptable grades. Hands= 21 replicates; dermal = 23 to 42 replicates; inhalation = 22 replicates. Medium confidence in dermal data, and high confidence in inhalation data. A 50% protection factor (PF) was applied on dermal, non-hand exposure to simulate coveralls - double layer clothing. **Engineering Controls:** Hands and dermal= ABC grades; inhalation acceptable grades. Hands= 16 replicates; dermal = 20 to 31 replicates; inhalation = 16 replicates. Medium confidence in dermal data, and high confidence in inhalation data.
Applying Granulars with a Tractor-Drawn Spreader (5)	PHED V1.1	80 acres.	**Baseline:** Hands, dermal, and inhalation = acceptable grades. Hands = 5 replicates; dermal = 1 to 5 replicates; inhalation = 5 replicates. Low confidence in dermal and inhalation replicates. **PPE:** Hands, dermal, and inhalation = acceptable grades. Hands = 5 replicates, dermal = 4 to 5 replicates, and inhalation = 5 replicates. Low confidence in hands, dermal, and inhalation. A 50% protection factor (PF) was applied on dermal, non-hand exposure to simulate coveralls - double layer clothing. A 90% PF was applied to hands to simulate gloves. **Engineering Controls:** Hands, dermal, and inhalation = acceptable grades. Hands = 24 replicates; dermal = 2 to 30 replicates; and inhalation = 37 replicates. High confidence in inhalation data. Low confidence in dermal and hands data.

[a] Standard Assumptions based on an 8-hour work day (i.e., how much a worker would handle in a single day).

[b] These grades are based on Quality Assurance/Quality Control data provided as part of the exposure studies. A replicate refers to data acquired during one complete work cycle. All handler exposure assessments in this document are based on the "Best Available" data as defined by HED SOP for meeting Subdivision U Guidelines (i.e., completing exposure assessments.) Best available grades are assigned as follows: matrices with grades A and B data (which is defined as acceptable grade data) and a minimum of 15 replicates; if not available, then grades A, B, and C data and a minimum of 15 replicates; if not available, then all data (all grades) regardless of the quality and number of replicates. High quality data with a protection factor take precedence over low quality data with no protection.

Data confidence as reported in the Table refers to both the quality and the quantity (number of replicates) of data for each PHED run. Each study in PHED has been graded from A to E. A high confidence run is grades A and B data and 15 or more replicates per body part. Any combination of A or B grade data are listed as AB grade data in the tables. A medium confidence run is grades A, B, and C data and 15 or more replicates per body part. Any combination of A, B, and C grade data are listed as ABC grade data in the tables. A low confidence run is all grades (any run that includes D or E grade data) or has less than 15 replicates per body part.

b. Occupational Risk Assessment

Handler Risk Assessment

All risks (MOEs and cancer estimates) are reported to 2 significant figures. Table 20 presents the dermal and inhalation risk assessment for the short-term exposures. The baseline daily exposures (from Table 18) were divided by 70 kg to estimate the baseline dose. It was necessary to use PPE (personal protective equipment) to achieve a MOE greater than 100 for scenario 1, mixing/loading liquid formulations.

Table 20: Short-Term Risks to Propachlor

Exposure Scenario (Scenario #)	Baseline Dose (mg/kg/day)[a]	Baseline MOE[b]	Risk Mitigation Measures			
			Additional PPE			
			PPE Dermal Unit Exposure. (mg/lb ai)[c]	PPE Inhalation Unit Exposure (ug/lb ai)[c]	PPE Daily Dose (mg/kg/day)[a]	PPE MOE[b]
Mixer/Loader Risk						
Mixing/ Loading Liquids for Groundboom Application (1)	20 (corn)	9	0.017	1.2	0.12	1,400
	17 (grain sorghum and onions)	10			0.10	1,700
Mixing/Loading Dry Flowables for Groundboom Application (2)	0.39 (corn and grain sorghum)	450	NA		NA	NA
Loading Granulars for Tractor-Drawn Spreader Application (3)	0.07 (corn)	2,750	NA		NA	NA
	0.06 (grain sorghum)	3,100				
Applicator Risk						
Applying Sprays with a Groundboom Sprayer (4)	0.1 (corn)	1,800	NA		NA	NA
	0.08 (grain sorghum and onions)	2,100				

Exposure Scenario (Scenario #)	Baseline Dose (mg/kg/day)[a]	Baseline MOE[b]	Risk Mitigation Measures			
			Additional PPE			
			PPE Dermal Unit Exposure. (mg/lb ai)[c]	PPE Inhalation Unit Exposure (ug/lb ai)[c]	PPE Daily Dose (mg/kg/day)[a]	PPE MOE[b]
Applying Granulars with a Tractor-Drawn Spreader (5)	0.08 (corn)	2,300	NA		NA	NA
	0.06 (grain sorghum)	2,800				

NA not applicable. MOE for the previous scenario is greater than 100; therefore, additional mitigation is not necessary.

[a] Total Dose (mg/kg/day) = Dermal exposure (mg/day) + Inhalation exposure (mg/day) / Body weight (70 kg). There is no dermal absorption factor; therefore, 100% dermal absorption is assumed; 100% inhalation absorption is assumed.

[b] MOE = (NOEL (175 mg/kg/day) / Daily Dose (mg/kg/day)).

[c] Additional PPE: Double layer of clothing and chemical resistant gloves; no respirator.

Propachlor is used preemergence (corn and sorghum). Therefore, HED believes that the intermediate-term scenario is the most appropriate, since available information indicates that for pre-plant herbicide applications that a "window" of approximately 28 days is available once the weather and field conditions are right and the equipment can enter the fields. This is supported by information from the Biological and Economic Analysis Division (BEAD) that indicated that an early-season corn herbicide applied once per season would result in 20 days of exposure per year to commercial handlers. An early-season sorghum pesticide applied once per season would result in 14 days of exposure per year to commercial handlers.

Tables 21A and 21B present the risk assessment for the intermediate-term exposures. The baseline daily exposures (from Table 18) were divided by 70 kg to estimate the baseline dose.

Tables 22A and 22B present the cancer risk assessment for propachlor. Note that cancer risks were estimated beginning with the scenario for which intermediate term MOEs were greater than 100, since this level of mitigation would be required based on the risk assessment for the intermediate scenario. The Agency's default female body weight of 60 kg was used since the Q_1^* of 0.032 $(mg/kg/day)^{-1}$ was based on female rat ovarian tumors. No information on typical use rates are available; therefore, maximum use (label) rates were used.

Table 21A: Intermediate-Term Risks to Propachlor - Baseline and Personal Protective Equipment (PPE)

Exposure Scenario (Scenario #)	Baseline Dermal Dose (mg/kg/day)[a]	Baseline Inhalation Dose (mg/kg/day)[a]	Baseline Total Dose (mg/kg/day)[b]	Baseline MOE[c]	Risk Mitigation Measures					
					Additional PPE[d]					
					PPE Dermal Unit Exp. (mg/lb ai)	PPE Inhalation Unit Exposure (µg/lb ai)	PPE Daily Dermal Dose (mg/kg/d)[e f]	PPE Daily Inhalation Dose (mg/kg/d)[e]	PPE Total Daily Dose (mg/kg/d)[b]	PPE MOE [c]
Mixer/Loader Risk										
Mixing/Loading Liquids for Groundboom Application (1)	20 (corn)	0.008	20	< 1	0.025	1.2	0.17	0.008	0.18	40
	17 (grain sorghum and onions)	0.007	17	< 1			0.14	0.006	0.15	47
Mixing/Loading Dry Flowables for Groundboom Application (2)	0.39 (corn and grain sorghum)	0.004	0.39	18	0.04	0.8	0.22	0.004	0.22	32
Loading Granulars for Tractor-Drawn Spreader Application (3)	0.05 (corn)	0.01	0.07	110	NA	NA	NA	NA	NA	NA
	0.05 (grain sorghum)	0.01	0.05	130			NA	NA	NA	NA
Applicator Risk										
Applying Sprays with a Groundboom Sprayer (4)	0.1 (corn)	0.004	0.1	71	0.01	0.7	0.069	0.005	0.074	96
	0.08 (grain sorghum and onions)	0.004	0.08	84			0.057	0.004	0.061	120
Applying Granulars with a Tractor-Drawn Spreader (5)	0.07 (corn)	0.009	0.08	92	0.004	1.2	0.027	0.008	0.035	200
	0.06 (grain sorghum)	0.007	0.06	110	NA	NA	NA	NA	NA	NA

NA not applicable. MOE for the previous scenario is greater than 100; therefore. Additional mitigation is not necessary.

[a] Dose (mg/kg/day) = Exposure (mg/day) / Body weight (70 kg). There is no dermal absorption factor; therefore, 100% dermal absorption is assumed; 100% inhalation absorption is assumed. See Table 18 for baseline dermal and inhalation exposure estimates.

[b] Total Daily Dose = Dermal Daily Dose + Inhalation Daily Dose
[c] MOE = (NOEL (7.1 mg/kg/day) / Daily Total Dose (mg/kg/day)).
[d] Additional PPE for scenarios 1,2 and 4: Double layer of clothing and chemical resistant gloves; no respirator.
[e] PPE Daily Dose was estimated using application rate and acres treated per day from Table 18. See Table 18 footnotes for explanations and formulas.

Table 21B: Intermediate-Term Risks to Propachlor (Engineering Controls)

Exposure Scenario (Scenario #)	Risk Mitigation Measures					
	Engineering Controls[d]					
	Eng. Controls Dermal Unit Exp. (mg/lb ai)	Eng. Controls Inhalation Unit Exposure (µg/lb ai)	Eng. Controls Daily Dermal Dose (mg/kg/d) [a]	Eng. Controls Daily Inhalation Dose (mg/kg/d) [a]	Eng. Controls Total Daily Dose (mg/kg/d)[b]	Eng. Controls MOE [c]
Mixer/Loader Risk						
Mixing/Loading Liquids for Groundboom Application (1)	0.009 (gloves)	0.08	0.062	0.0005	0.062	110
			0.051	0.00045	0.052	140
Mixing/Loading Dry Flowables for Groundboom Application (2)	0.007	0.08	0.038	0.00045	0.039	180
Loading Granulars for Tractor-drawn Spreader Application (3)	NA	NA	NA	NA	NA	NA
			NA	NA	NA	NA
Applicator Risk						
Applying Sprays with a Groundboom Sprayer (4)	0.005	0.04	0.034	0.000027	0.034	210
			NA	NA	NA	NA
Applying Granulars with a Tractor-Drawn Spreader (5)	NA	NA	NA	NA	NA	NA
			NA	NA	NA	NA

[a] Engineering Control Daily Dose was estimated using application rate and acres treated per day from Table 18. See Table 18 footnotes for explanations and formulas.

[b] Total Daily Dose = Dermal Daily Dose + Inhalation Daily Dose

[c] MOE = (NOEL (7.1 mg/kg/day) / Daily Total Dose (mg/kg/day)).

[d] Engineering Controls are closed mixing/loading system and gloves for scenario 1; closed mixing/loading system for scenario 2

Table 22A: Combined Dermal and Inhalation Cancer Risk Assessment for Propachlor - Baseline and Personal Protective Equipment (PPE)

Exposure Scenario (Scenario #)	Baseline Dermal Dose (mg/kg/day)[a]	Baseline Inhalation Dose (mg/kg/day)[b]	Baseline Total Dose (mg/kg/day)[c]	Baseline LADD (mg/kg/day)[d]	Baseline Risk[e]	Risk Mitigation Measures						
						Additional PPE						
						PPE Dermal Unit Exp. (mg/lb ai)	PPE Inhalation Unit Exposure (µg/lb ai)	PPE Daily Dermal Dose (mg/kg/d) [f]	PPE Daily Inhalation Dose (mg/kg/d) [g]	PPE Total Daily Dose (mg/kg/d) [h]	PPE LADD (mg/kg/d)	PPE Risk [j]
Mixer/Loader Risk												
Mixing/Loading Liquids for Groundboom Application (1)	(corn)	---	---	---	NA	---	---	---	---	---	---	NA
	(grain sorghum and onions)	---	---	---	NA			---	---	---	---	NA
Mixing/Loading Dry Flowables for Groundboom Application (2)	(corn and grain sorghum)	---	---	---	NA	---	---	---	---	---	---	NA
Loading Granulars for Tractor-Drawn Spreader Application (3)	0.05 (corn)	0.013	0.06	0.001	4.5E-05	0.0034	1.7	0.027	0.014	0.041	0.001	3.6E-05
	0.04 (grain sorghum)	0.011	0.05	0.0014	4.4E-05			0.022	0.011	0.033	0.0012	3.9E-05
Applicator Risk												
Applying Sprays with a Groundboom Sprayer (4)	(corn)	---	---	---	NA	0.01	0.7	0.08	0.0056	0.09	0.0025	8.0E-05
	(grain sorghum and onions)	---	---	---	NA			0.07	0.0047	0.075	0.0021	6.7E-05
Applying Granulars with a Tractor-Drawn Spreader (5)	0.07 (corn)	0.010	0.08	0.0022	7.0E-05	0.004	1.2	0.032	0.01	0.042	0.0012	3.8E-05
	0.06 (grain sorghum)	0.008	0.07	0.0019	6.1E-05			0.027	0.008	0.035	0.001	3.2E-05

---/NA The intermediate term MOE for this scenario with PPE or at baseline is less than 100. Note that cancer risks were estimated beginning with the scenario for which intermediate term MOEs were greater than 100, since this level of mitigation would be required based on the risk assessment for the intermediate scenario.

[a] Dermal Dose (mg/kg/d) = Dermal exposure (mg/day) / Body weight (60 kg). See Table 18 for dermal exposure.
[b] Inhalation Dose (mg/kg/d) = Inhalation exposure (mg/day) / Body weight (60 kg). See Table 18 for inhalation exposure. (100% inhalation exposure is assumed)
[c] Baseline Daily Total Dose (mg/kg/d) = Baseline Dermal Dose (mg/kg/day) + Baseline Inhalation Dose (mg/kg/day).
[d] Baseline LADD (mg/kg/d) = Total Daily Dermal Dose (mg/kg/d) * (20 days per year worked/365 days per year) * (35 years worked/70 years lifetime).

[e] Baseline Risk = Baseline LADD (mg/kg/d) * (Q_1^*). Where Q_1^*= 0.032 $(mg/kg/d)^{-1}$.

[f] PPE Dermal Dose (mg/kg/d)= (PPE Dermal Unit Exp (mg/lb ai) * Max.Application Rate (lb ai/acre) * Daily Acres Treated (acres/day)) / 60 kg body weight. Note that Max Appl. Rate and Daily Acres Treated are provided in Table 18.

[g] PPE Inhalation Dose (mg/kg/d)= (PPE Inhalation Unit Exp (ug/lb ai) * Max. Appl. Rate (lb ai/acre) * Daily Acres Treated (acres/day) * CF (1,000 µg/mg)) / 60 kg body weight

[h] PPE Daily Total Dose (mg/kg/d)= PPE Dermal Dose (mg/kg/d) + PPE Inhalation Dose (mg/kg/d).

[I] PPE LADD (mg/kg/d) = PPE Dermal Dose (mg/kg/d) * (20 days per year worked/365 days per year) * (35 years worked/70 years lifetime).

[J] PPE Risk = PPE LADD (mg/kg/d) * (Q_1^*) Where Q_1^* = 0.032 $(mg/kg/d)^{-1}$.

Table 22B: Combined Dermal and Inhalation Cancer Risk Assessment for Propachlor (Engineering Controls)

Exposure Scenario (Scenario #)	Risk Mitigation Measures						
	Engineering Controls						
	Eng. Controls Dermal Unit Exp. (mg/lb ai)	Eng. Controls Inhalation Unit Exposure (µg/lb ai)	Eng. Controls Daily Dermal Dose (mg/kg/d) [a]	Eng. Controls Daily Inhalation Dose (mg/kg/d) [b]	Eng. Controls Total Daily Dose (mg/kg/d) [c]	Eng. Controls LADD (mg/kg/d) [d]	Eng. Controls Risk [e]
Mixer/Loader Risk							
Mixing/Loading Liquids for Groundboom Application (1)	0.009	0.08	0.072	0.00064	0.073	0.002	6.4E-05
			0.06	0.00053	0.061	0.0017	5.4E-05
Mixing/Loading Dry Flowables for Groundboom Application (2)	0.007	0.08	0.0448	0.00051	0.045312	0.00124	4.0E-05
Loading Granulars for Tractor-drawn Spreader Application (3)	0.0008	0.17	0.0064	0.0014	0.00536	0.0001468	4.67E-06
			0.0033	0.0011	0.00443	0.0001213	3.8E-06
Applicator Risk							
Applying Sprays with a Groundboom Sprayer (4)	0.005	0.04	0.040	0.00032	0.040	0.0011	3.5E-05
			0.033	0.00027	0.033	0.00091	2.9E-05
Applying Granulars with a Tractor-Drawn Spreader (5)	0.0021	0.22	0.017	0.00176	0.019	0.00051	1.6E-05
			0.014	0.00147	0.016	0.00042	1.4E-05

[a] Eng. Controls Dermal Dose (mg/kg/d)= (Eng. Controls Dermal Unit Exp (mg/lb ai) * Max.Application Rate (lb ai/acre) * Daily Acres Treated (acres/day))/60 kg body weight. Note that Max Appl. Rate and Daily Acres Treated are provided in Table 18.

[b] Eng. Controls Inhalation Dose (mg/kg/d)= (Eng. Controls Inhalation Unit Exp (ug/lb ai) * Max. Appl. Rate (lb ai/acre) * Daily Acres Treated/ 60 kg body weight * CF (1000 µg/mg).

[c] Eng. Controls Daily Total Dose (mg/kg/d)= Eng. Controls Dermal Dose (mg/kg/d) + Eng. Controls Inhalation Dose (mg/kg/d).

[d] Eng. Controls LADD (mg/kg/d) = Eng. Controls Dermal Dose (mg/kg/d) * (20 days per year worked/365 days per year) * (35 years worked/70 years lifetime).

[e] Eng. Controls Risk = Eng. Controls LADD (mg/kg/d) * (Q_1^*) Where Q_1^*= 0.032 $(mg/kg/d)^{-1}$.

Post-Application Exposure Assessment

No residue dissipation data (e.g., DFR (dislodgeable foliar residue)) or exposure monitoring data were submitted for propachlor. However, HED believes that the potential for post-application worker exposure is low, provided the 48 hour Restricted Entry Interval (REI - based on propachlor's classification as toxicity category I for primary eye irritation) is observed. There is low potential for exposure due to the timing of applications. Propachlor is applied to the soil and/or soil incorporated pre-emergent for corn and grain sorghum. This is well before the plants are mature, which likely mitigates the potential for post-application exposure due to contact with treated foliage. Additionally, most agricultural operations for corn and sorghum particularly early in the season are mechanical which minimizes the potential for contact. Significant exposure to propachlor during harvesting, or any other late season activities, is not likely since propachlor is applied pre-emergent. Therefore, HED does not require that any post-application exposure or residue dissipation monitoring data be generated to support the reregistration of propachlor.

Occupational Summary of Risks

Note that the PHED data confidence for dermal exposure is in parenthesis, and the use of any protection factors (PF).

Short-Term Risk

The estimations of short-term dermal and inhalation risk indicate that the MOEs are more than 100 at **baseline** for the following scenarios:

- (2) mixing/loading dry flowables for groundboom application
  (Based on low confidence data and no PF);
- (3) loading granulars for tractor drawn spreader application
  (Based on low confidence data and no PF);
- (4) applying sprays with groundboom sprayer
  (Based on high confidence data and no PF);
- (5) applying granulars with a tractor-drawn spreader
  (Based on low confidence data and no PF);

The estimations of short-term dermal and inhalation risk indicate that the MOEs are more than 100 with **additional PPE** for the remaining scenario:

- (1) mixing/loading liquids for groundboom application
  (Based on high confidence data and a 50% PF).

Intermediate-Term Risk

The estimations of intermediate-term dermal and inhalation risk indicate that the MOEs are more than 100 at **baseline** for the following scenarios:

- (3) loading granulars for tractor-drawn spreaders
  (Based on low confidence data and no PF);
- (5) applying granulars to sorghum with a tractor-drawn spreader
  (Based on low confidence data and no PF).

The estimations of intermediate-term dermal and inhalation risk indicate that the MOEs are more than 100 with **additional PPE** for:

- (4) applying sprays to sorghum and onions with a groundboom sprayer
  (Based on medium confidence data and no PF).

- (5) applying granulars to corn with a tractor-drawn spreader
  (Based on low confidence data and no PF).

The estimations of intermediate-term dermal and inhalation risk indicate that the MOEs are more than 100 with **engineering controls** for:

- (1) mixing/loading liquids for groundboom application
  (Based on medium confidence data and no PF).

- (2) mixing/loading dry flowables for groundboom application.
  (Based on low confidence data and a 90% PF)
- (4) applying sprays to corn with a groundboom sprayer
  (Based on medium confidence data and no PF).

Cancer Risks

The estimations of cancer risks are within the 10^{-5} or 10^{-6} risk range for the following scenarios:

- (1) mixing/loading liquids for groundboom application **with engineering controls (**Based on medium confidence data and no PF**)**;
- (2) mixing/loading dry flowables for groundboom application **with engineering controls** (Based on low confidence data and a 90% PF**);**
- (3) loading granulars for tractor-drawn spreader application at **baseline** (Based on low confidence data and no PF), **with additional PPE** (Based on low confidence data and no PF), and **with engineering controls** (Based on low confidence data and a 90% PF);
- (4) applying sprays with a groundboom sprayer with **additional PPE** (Based on medium confidence data and a 50% PF) and **with engineering controls** (Based on medium confidence data and no PF); and,
- (5) applying granulars with a tractor-drawn spreader at **baseline** (Based on low confidence data and no PF), **with additional PPE** (Based on low confidence data and two PFs - 90% and 50% PF), and **with engineering controls** (Based on low confidence data and no PF).

Although all risks are within the 10^{-5} risk range, going across Tables 22A and 22B, there is a steady reduction of the magnitude by an approximate factor of 2 with each progression from baseline to PPE to engineering controls.

Post-Application Risk

HED believes that, based on the current uses of propachlor, post-application exposure will be low and therefore is not requiring post-application exposure studies at this time.

Occupational Risk Characterization

Several issues must be considered when interpreting the occupational exposure and resultant risk assessment.

- No chemical-specific exposure data were submitted. As a result all risk estimates were performed using surrogate data in PHED.

- Several handler assessments were completed using "low quality " PHED data due to the lack of a more acceptable dataset.

- Several generic protection factors were used to calculate handler exposures. These protection factors are in general use, but have not been completely evaluated by HED.

- Acres treated per day for each application method are standard values used by HED, due to a lack of pertinent data. These values are based on the best professional judgement of HED staff and were arrived at after much internal discussion. The values are considered to represent typical values regardless of regional variability.

- A chemical-specific dermal absorption factor was not available. Therefore, 100% dermal absorption was assumed.

- A chemical-specific inhalation absorption factor was not available. Therefore, 100% inhalation absorption was assumed.

- Application rates are the maximum labeled rates for the sites and scenarios used in the assessment. However, it is acknowledged that actual application rates can vary. It is HED

policy that the maximum application rate be used for the short-term and intermediate-term scenarios, but that a typical application rate can be used for a carcinogenic assessment. HED has no information on typical application rates for propachlor.

If the registrant supplied any or all of the following information, then these propachlor risk estimations could probably be refined:
(1) a dermal absorption factor
(2) a 21 day dermal study
(3) additional information on number of days of exposure
(4) additional information on the systems/equipment typically used by M/L/As, especially the equipment used on large acreage farms
(5) additional information on typical use rates

There are two intermediate-risk scenarios for which MOEs of 92 and 96 were obtained. In all probability a dermal absorption factor or 21 day dermal study would allow HED to use less than 100%, thus achieving MOEs greater than 100. Another possibility would be to use the same label rate on corn as on sorghum, thus also achieving MOEs greater than 100.

However, in the absence of such information, for mixer/loaders to mitigate for both the dermal intermediate-term scenario and the carcinogenic scenario, the following is required:

- (1) mixing/loading liquids for groundboom application requires a closed mixing/loading system, and chemical resistant gloves.
- (2) mixing/loading dry flowables for groundboom requires the use of engineering controls. It will be necessary to investigate the possibility of developing a water-soluble pack (or similar mitigation) for dry flowables, or some type of closed mixing system, or reducing the application rate.
- (3) mixing/loading granulars for sorghum for tractor-drawn spreader application can be

performed at baseline; mixing/loading granulars for corn for tractor drawn spreader application requires use of PPE. HED notes that the label currently requires the use of gloves; therefore, it seems prudent to require the use of PPE for both corn and sorghum.

For applicators to mitigate for both the intermediate-term scenario and the carcinogenic scenario, the following is required:

- (4) applying sprays with a groundboom requires the use of mitigation: PPE for sorghum and engineering controls for corn.
- (5) applying granulars with a tractor-drawn spreader can be performed at baseline for sorghum and with PPE for corn

5. FQPA Considerations

a. Cumulative Effects

Propachlor is a member of the acetanilide class of herbicides. It is structurally similar to acetochlor, butachlor, metolachlor, and alachlor.

Section 408(b)(2)(D)(v) of FQPA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency believes that "available information" in this context might include not only toxicity, chemistry, and exposure data, but also policies and methodologies for conducting cumulative risk assessments. For most pesticides, the Agency has some information in its files that may turn out to be helpful in eventually determining whether a pesticide shares a common mechanism of toxicity with any other substances. However, at this time the Agency does not have the methodology to resolve the scientific issues concerning common mechanism of toxicity in a meaningful way. The Agency has begun a pilot process to study this issue further through the examination of particular classes of pesticides. Hopefully, the results of this pilot process will enable the Agency to develop and apply policies for evaluating the cumulative effects of chemicals having a common mechanism of toxicity. At present, however, the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments. Exceptions include pesticides that are toxicologically and structurally dissimilar to existing chemical substances (in which case the Agency can conclude that it is unlikely that a pesticide shares a common mechanism of activity with other substances) and pesticides that produce a common toxic metabolite (in which case the metabolite must be assessed as part of a common mechanism assessment).

In making individual tolerance decisions, the Agency will determine whether:

1) it has sufficient information to determine that a pesticide does not appear to share a common mechanism of toxicity with other substances;

2) it is unable to conclude that a pesticide does not share a common mechanism of toxicity with other substances; or

3) it is able to conclude that a pesticide does share a common mechanism of activity with other substances.

Due to the structural similarities with acetochlor, metolachlor, butachlor, and alachlor, propachlor may fall into the second category. However, at this time the Agency has not yet made a final decision concerning a possible common mechanism of toxicity for these five chemicals to scientifically apply that information to the tolerance decision. The process has begun, but is not yet completed. Therefore, for the purposes of this decision document, the tolerance decision will be reached based upon the best available and useful information for propachlor only. The risk assessment has been performed for propachlor only assuming that no common mechanism of toxicity exists. However, these decisions will be reexamined after methodologies and procedures for integrating information concerning common mechanism of toxicity into risk assessments are developed by the Agency.

Monsanto 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 propachlor shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for propachlor need to be modified or revoked.

b. Endocrine Disruptor Effects

The Agency is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect..." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1996) to implement this program. At that time, EPA may require testing of propachlor for endocrine disruptor effects.

c. Determination of Safety

FFDCA section 408(b)(2)(A)(I) allows EPA to establish a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is “safe”. FFDCA section 408(b)(2)(A)(ii) defines “safe” to mean that “there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all

anticipated dietary exposures and all other exposures for which there is reliable information." This includes exposure through drinking water and residential exposures, but does not include occupational exposure. Section 408(b)(2)(C) requires EPA to give special consideration to exposure of infants and children to pesticide chemical residue in establishing a tolerance and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue..."

Determination of safety includes consideration of special sensitivity to children, potential cumulative effects with pesticides that have a common mode of toxicity and aggregate risks resulting from exposure to dietary residues, residues in drinking water, and residential sources.

The database for developmental and reproductive toxicity of propachlor is considered to be complete at this time. A developmental neurotoxicity study was not required. There is no unique or special sensitivity for pre- or post-natal exposure. Based on these three factors, the Agency has concluded that the results of these data did not raise concerns regarding the use of 100 as the uncertainty factor. An uncertainty factor of 100 will adequately protect infants and children.

The Agency has determined that consideration of a common mode of toxicity with other chemicals such as acetochlor, butachlor, metolachlor, and alachlor is not appropriate at this time. Tolerance reassessments have occurred in the RED as a result of new data on the concentrations of propachlor residues present in food.

There are no residential uses of propachlor. The aggregate risk assessment from exposure to propachlor in food and water, does not result in aggregate risk that exceeds HED's level of concern.

Thus, HED concludes that there is a reasonable certainty of no harm to infants and children, and adults from residues of propachlor from aggregate exposure (food and water).

Residue Chemistry Science Assessments for Reregistration of Propachlor.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR §180.211]	Must Additional Data Be Submitted?	References
860.1200: Directions for Use	N/A = Not Applicable	Yes [1]	
860.1300: Plant Metabolism	N/A	No	40068601, 42140301
860.1300: Animal Metabolism	N/A	No	40123101, 40129301
860.1340: Residue Analytical Methods			
- Plant commodities	N/A	No [2]	40584004, 43028601, 43028602, 43251801
- Animal commodities	N/A	No	40584004, 43028602, 43251801
860.1360: Multiresidue Methods	N/A	No	43028501 [3]
860.1380: Storage Stability Data	N/A	No	40081701, 40085301, 40584005, 42121302, 42121303, 42140302
860.1500: Crop Field Trials			
Root and Tuber Vegetables Group			
- Sugar beet, roots	Revoke	No [4]	
Leaves of Root and Tuber Vegetables Group			
- Sugar beet, tops	Revoke	No [5]	
Legume Vegetables (Succulent or Dried) Group			
- Peas	Revoke	No [5]	
Foliage of Legume Vegetables Group			
- Peas vines and hay	Revoke	No [5]	
Cucurbit Vegetables Group			
- Pumpkins	Revoke	No [5]	
Cereal Grains Group			

GLN: Data Requirements	Current Tolerances, ppm [40 CFR §180.211]	Must Additional Data Be Submitted?	References
- Corn, field, grain	0.1	No	40085301
- Corn, sweet (K+CWHR)	Revoke	No [5]	
- Sorghum, grain	0.25	No	40081701
Forage, Fodder, and Straw of Cereal Grains			
- Corn, field, forage and stover	1.5, forage	No	40085301
- Corn, sweet, forage and stover	1.5, forage	No [5]	
- Sorghum forage and stover	5.0, forage 5.0, fodder	No	40081701
Miscellaneous Commodities			
- Cotton, seed and gin byproducts	Revoke	No [5]	
- Flax seed	Revoke	No [5]	
- Crops grown solely for seed	None established	No [6]	
860.1520: Processed Food/Feed			
- Corn, field	None established	No	40085302, 42962501
- Cottonseed	None established	No [6]	
- Flax seed	None established	No [6]	
- Sorghum	None established	No	40081702
- Sugar beet	None established	No [6]	
860.1480: Meat, Milk, Poultry, Eggs			
- Milk and the Fat, Meat, and Meat Byproducts of Cattle, Goats, Hogs, Horses, and Sheep	0.02	No	40584001, 40584003
- Eggs and the Fat, Meat, and Meat Byproducts of Poultry	0.02	No	40584002

GLN: Data Requirements	Current Tolerances, ppm [40 CFR §180.211]	Must Additional Data Be Submitted?	References
860.1400: Water, Fish, and Irrigated Crops	None established	N/A	
860.1460: Food Handling	None established	N/A	
860.1850: Confined Rotational Crops	N/A	No	43064501
860.1900: Field Rotational Crops	None established	Yes [7]	

2. Product labels with uses on sorghum must be amended to remove the restriction against the grazing or feeding of sorghum forage or silage from treated fields to dairy animals, since the Agency no longer considers such restrictions to be practical.

   Until adequate field rotational crop data have been submitted, product labels with uses on rotatable crops should be amended to specify that only crops that are listed on the label may be rotated to fields treated with propachlor.

3. Provided that the comments made by ACB are incorporated into the method, CBRS concluded that the proposed enforcement method (Monsanto Report No. MSL-12679) is suitable for the enforcement of tolerances for plant and animal commodities.

4. These data were forwarded to FDA for review (memo from L. Edwards to H. Hundley dated 5/18/94).

5. There are currently no registered uses on this crop. The established tolerance(s) should be revoked.

6. There are no registered uses on this crop.

7. Propachlor was previously registered for use on barley, oats, soybeans, and wheat grown for seed. Because these uses have been removed from product labels, data are no longer required to support these uses.

8. The available confined rotational crop data indicate that limited field rotational crop studies must be conducted.

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Blondell, and Spann - memo; Review of Propachlor Incident Reports; August 15, 1997

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Spencer, Henry - memo; RfD/Peer Review Report of Propachlor; September 30, 1997

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