



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

September 10, 2001

SUBJECT: **Propanil** Magnitude of the Residue in/on Wheat Forage and Dairy Cattle Feeding Study; PC code 028201; Rereg. Case 0226; DP Barcode D276424; MRID No. 44550101 and 44768801.

FROM: Sherrie L. Kinard, Chemist *Sherrie L. Kinard*
Reregistration Branch II
Health Effects Division (7509C)

THROUGH: Alan Nielsen, Branch Senior Scientist *Alan Nielsen 9/10/01*
Reregistration Branch II
Health Effects Division (7509C)

TO: Tom Meyers, Chemical Review Manager
Reregistration Branch II
Special Review and Reregistration Division (7508W)

INTRODUCTION

In response to the Propanil Reregistration Standard Guidance Document dated 12/23/87, the Propanil Task Force (PTF; with members consisting of Cedar Chemical Corporation, Westrade USA, Retzloff Delta Company, and Rohm and Haas Company) has submitted a dairy cattle feeding study (1998; MRID 44550101). In addition, Rohm and Haas Company has submitted a study (1999; MRID 44768801) depicting the magnitude of propanil residues in/on wheat forage. These submissions are evaluated herein for their adequacy in fulfilling residue chemistry data requirements for the reregistration of propanil.

Attached is the residue chemistry reviews of the Task Force submitted data dairy cattle feeding study (1998; MRID 44550101) and the Rohm and Haas Company submitted study (1999; MRID 44768801) depicting the magnitude of propanil residues in/on wheat forage. This information was compiled by Dynamac Corporation under supervision of RRB2. This review has undergone secondary review by RRB2 and has been revised to reflect current HED and Office of Pesticide Programs (OPP) policies.

EXECUTIVE SUMMARY OF CHEMISTRY DEFICIENCIES

- The registrant is required to amend propanil labels with registered uses on wheat to specify a pregrazing/preharvest interval of "Feekes Growth Stage 7 to 9 (typically 24-25 days, stem elongation stage to flag leaf stage)" for wheat forage.
- The product labels for the 3 lb/gal EC (EPA Reg. Nos. 707-75 and 707-182) and the 81% DF (EPA Reg. No. 707-226) formulations must be modified to remove the feeding restriction for the grazing of treated crop or cutting for green chop.
- Residue data for wheat hay are required.

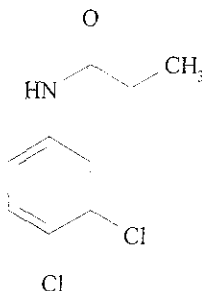
RECOMMENDATIONS

Based on the available data, the Agency concludes that: (i) the established milk tolerance of 0.05 ppm is appropriate; (ii) the established fat tolerance of 0.1 ppm is also appropriate; (iii) the established meat tolerance of 0.1 ppm may be lowered to 0.05 ppm; and (iv) the established meat byproducts tolerance of 0.1 ppm should be increased to 1.0 ppm.

cc: Sherrie L. Kinard (RRB2), Propanil Reg. Std. File, Propanil Subject File, RF, LAN. RD/I: Propanil Team Review (9/5/2001).

7509C: RRB2: S. Kinard: CM#2:Rm 722B: 703-305-0563: 9/10/2001.

PROPANIL



PC Code 028201; Case 0226

(DP Barcode D276424)

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

BACKGROUND

In response to the Propanil Reregistration Standard Guidance Document dated 12/23/87, the Propanil Task Force (PTF; with members consisting of Cedar Chemical Corporation, Westrade USA, Retzlöff Delta Company, and Rohm and Haas Company) has submitted a dairy cattle feeding study (1998; MRID 44550101). In addition, Rohm and Haas Company has submitted a study (1999; MRID 44768801) depicting the magnitude of propanil residues in/on wheat forage. These submissions are evaluated herein for their adequacy in fulfilling residue chemistry data requirements for the reregistration of propanil.

The qualitative nature of the residue in plants and animals is adequately understood. The results of acceptable metabolism studies conducted on rice, wheat, poultry, ruminants, and crayfish were presented at the 1/16/96 meeting of the HED Metabolism Committee. The Metabolism Committee concluded that propanil and residues convertible to 3,4-dichloroaniline (3,4-DCA) are the residues to be regulated in plants and animals; there is no need for individual quantitation of propanil metabolites.

Tolerances for residues of propanil in/on the grain and straw of barley, oats, rice, and wheat, in eggs and milk, in the fat, meat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep, and in processed rice commodities (bran, hulls, mill fractions, and polishings) are established under 40 CFR §180.274(a)(1) and (a)(2). Propanil tolerances are currently expressed in terms of propanil (3',4'-dichloropropionanilide) and its metabolites (calculated as propanil). The tolerance expression should be revised to include propanil and residues convertible to 3,4-DCA.

Adequate methods are available for tolerance enforcement. For the enforcement of plant commodity tolerances, the Propanil Task Force has proposed a GC/NPD method (EN-CAS Method No. ENC-9/90) which uses a base hydrolysis step resulting in the conversion of propanil and metabolites containing the 3,4-DCA moiety to 3,4-DCA. EN-CAS Method No. ENC-9/90 has undergone a successful independent laboratory validation (ILV) trial and will be forwarded to the Analytical Chemistry Branch for Agency validation. For the enforcement of animal commodity tolerances, the preferred method is Method I of the Pesticide Analytical Manual (PAM) Vol. II. Method I also uses base hydrolysis to convert propanil and its metabolites to 3,4-DCA; residues are then detected using GC/ECD and are reported as propanil. There are no Codex MRLs in effect for residues of propanil; therefore, there is no question with respect to Codex/U.S. tolerance compatibility.

CONCLUSIONS AND RECOMMENDATIONS

OPPTS GLN 860.1340: Residue Analytical Methods

1. A GC/NPD method (EN-CAS Method No. ENC-9/90) was used to analyze samples of wheat forage, collected from the current wheat field study, for propanil residues of concern. A slightly modified version of the above GC/NPD was the method used in the analyses of milk and cattle tissue samples collected from the storage stability and ruminant feeding studies. The data-collection methods are adequate for the purpose of data collection based on acceptable method recoveries.

OPPTS GLN 860.1380: Storage Stability Data

- 2a. Samples of wheat forage were stored frozen for 123-126 days prior to residue analysis. Previously reviewed storage stability data (DP Barcode D200811, 10/3/95, C. Swartz and DP Barcode D178275, 9/14/92, R. Perfetti) are available to support the storage intervals and conditions of wheat forage samples. These data indicate that residues of propanil are stable during frozen storage in/on rice bran and polished rice for up to 10 months, rice straw for up to 18 months, and rough rice grain and rice hulls for up to 20 months.
- 2b. Samples of milk were stored frozen for 2-126 days prior to residue analysis. Samples of fat, muscle, liver, and kidney were stored frozen for 60-92 days prior to residue analysis. The registrant conducted a storage stability study to validate the above storage conditions and intervals. These data indicate that residues of propanil are relatively stable in frozen cattle liver, kidney, muscle, and fat for at least 127 days and in milk for at least 132 days.

OPPTS GLN 860.1500: Crop Field Trials

- 3a. The wheat forage data are adequate and may be used for tolerance establishment. Residues, determined as 3,4-DCA and calculated as propanil, ranged from 0.02 to 0.16 ppm in/on six

treated samples of wheat forage harvested 24 or 25 days (when plants were at the Feekes Growth Stage 7 to 9, stem elongation stage to flag leaf stage) following a single postemergence broadcast application of the 81% DF formulation at 1.14-1.19 lb ai/A (~1x the maximum registered rate). TOX and ORE considerations permitting, the registrant must propose a propanil tolerance for wheat forage at 0.20 ppm.

- 3b. Based on the submitted data, the registrant is required to amend propanil labels with registered uses on wheat to specify a pregrazing/preharvest interval of "Feekes Growth Stage 7 to 9 (typically 24-25 days)" for wheat forage. Finally, the product labels for the 3 lb/gal EC (EPA Reg. Nos. 707-75 and 707-182) and the 81% DF (EPA Reg. No. 707-226) formulations must be modified to remove the feeding restriction for the grazing of treated crop or cutting for green chop.
- 3c. Table 1 of OPPTS GLN 860.1000 recognizes hay as a raw agricultural commodity (RAC) of wheat. Therefore, residue data for wheat hay are required for reregistration. The required data should be generated using representative EC and DF formulations of propanil applied according to the maximum registered use patterns. The number and locations of wheat hay field trials should be in compliance with the current applicable OPPTS guideline.

OPPTS GLN 860.1480: Meat, Milk, Poultry, and Eggs

- 4a. The submitted ruminant feeding study is acceptable. Four groups of Holstein dairy cows were dosed orally once daily following the morning milking for 28 days with either rice-based rations containing field-aged residues at 3.9 ppm (propanil equivalents) or gelatin capsules fortified with propanil at dose levels equivalent to 15, 45, and 150 ppm (mg/kg diet on a dry weight basis). The feeding levels depicted in the study are approximately equivalent to 0.2x (rice-fed), 0.75x, 2.2x, and 7.5x, respectively, the anticipated maximum dietary burden of 19.9 ppm for dairy cattle.
- 4b. Milk samples were collected on Days 0, 1, 3, 7, 11, 14, 18, 21, 24, and 27. Dairy cows were sacrificed within 4-10 hours of the final dose administration. At sacrifice, samples of fat (composite omental and perirenal), muscle (round and loin), liver, and kidney (both) were collected.
- 4c. Maximum residues, determined as 3,4-DCA and calculated as propanil, that were obtained from dairy cattle fed at the 15-ppm dosing level (1.1x) were: 0.035 ppm in milk, 0.31 ppm in liver, 0.77 ppm in kidney, <0.05 ppm (nondetectable) in muscle, and 0.10 ppm in fat.
- 4d. Based on the available data, The Agency concludes that: (i) the established milk tolerance of 0.05 ppm is appropriate; (ii) the established fat tolerance of 0.10 ppm is also appropriate; (iii) the established meat tolerance of 0.1 ppm may be lowered to 0.05 ppm; and (iv) the established meat byproducts tolerance of 0.1 ppm should be increased to 1.0 ppm.

DETAILED CONSIDERATIONS

OPPTS GLN 860.1340: Residue Analytical Methods

Data-collection method - wheat forage

Samples of wheat forage, collected from the subject wheat field study, were analyzed using EN-CAS Method No. ENC-9/90 (also referred to as Method TR 34-93-99). The method has been previously described and deemed adequate for data collection on rice and wheat (DP Barcode D205676, C. Swartz, 9/8/94 and DP Barcode D203514, C. Swartz, 9/22/94). The method has also undergone an acceptable ILV trial (DP Barcodes D253336 and D253337, S. Kinard, 9/10/01) and was successfully radiovalidated using ¹⁴C-labeled samples from the confined rotational crop study (DP Barcode D196301, C. Swartz, 10/23/95).

Briefly, residues are hydrolyzed with sodium hydroxide which results in the conversion of propanil and metabolites containing the 3,4-DCA moiety to 3,4-DCA. The hydrolysate is steam distilled for 16 hours using a Nielsen-Kryger apparatus, and the hexane and water fractions separated. The hexane fraction is then cleaned up on a silica gel column which has been pre-conditioned with hexane. The aqueous phase is washed with hexane, and the hexane wash added to the column. Residues are eluted from the column using hexane:ethyl acetate (75:25, v:v). Residues are quantitated using a GC equipped with a DB-17 or DB-1701 column and a nitrogen/phosphorous (N/P) detector. Residues are determined as 3,4-DCA, and calculated as the parent, propanil. This method has a limit of quantitation (LOQ) of 0.01 ppm, with a limit of detection of 0.003 ppm.

The performing laboratory, EN-CAS Labs (Winston-Salem, NC), validated the method prior to analysis of the field trial samples. In addition, concurrent method recovery data were provided using untreated samples of wheat forage collected from the field trials. The results of the method validation and concurrent method recovery analyses are presented in Table 1. The Agency concludes that the analytical method used to measure residues of propanil in/on rice and wheat is adequate for data collection based on overall average recoveries.

Table 1. Recoveries of propanil from fortified control samples using GC/NPD method ENC-9/90.

Crop	Fortification levels (ppm)	No. of Samples	Recovery % ^a
Method validation recoveries			
Wheat, forage	0.010	2	80, 88
	0.050	2	77, 80
	0.20	1	106
	1.00	2	102; 127 ^b
	mean ± s.d.		88.8 ± 12.4
Concurrent recoveries			
Wheat forage	0.010	1	101
	1.00	1	72
	overall mean ± s.d.		88.3 ± 13.1

^a Recovery values outside the acceptable 70-120% range are listed separately.

^b This data point was eliminated, more than 3 sigma from average for evaluation data.

Data-collection methods - milk and tissues of ruminants

In conjunction with the ruminant feeding study (1998; MRID 44550101), the registrant provided descriptions and validation data for a GC/NPD method used to analyze propanil residues of concern in cattle commodities. The method is based on EN-CAS Method No. ENC-9/90, described above for crop matrices, with some modifications.

Briefly, residues of propanil in fat samples were hydrolyzed with a 40% NaOH solution under reflux (overnight), cooled, and partitioned into hexane. Residues were partitioned into 2 N HCl, adjusted to pH 11, re-partitioned into hexane, and concentrated prior to analysis. Residues in milk, muscle, kidney, and liver were base hydrolyzed, steam distilled (overnight) into iso-octane, and cleaned-up on a silica gel SPE column eluted with hexane:ethyl acetate (1:1, v:v). Residues are determined as 3,4-DCA using a GC/NPD equipped with a DB-17 or DB-1701 column, and calculated as the parent compound. The LOQ for residues of propanil are 0.05 ppm in tissues (liver, kidney, muscle, and fat) and 0.005 ppm in milk.

Method validation and concurrent recovery data are presented in Table 2. For method validation, control samples of fat, liver, kidney, and muscle were fortified with propanil at 0.05-0.20 ppm, and milk samples were fortified with propanil at 0.005-0.10 ppm. Overall, method validation recoveries were 72-103% (n=9) in milk and 63-120% (n=54) in tissue samples; only two recoveries, one each from samples of liver and kidney, were unacceptable. Overall concurrent recoveries were 65-120% (n=30) in milk and 72-119% (n=15) in tissue samples. Adequate sample calculations, raw data, and representative chromatograms were provided. Sample analyses were conducted by PTRL East, Richmond, KY.

The Agency concludes that the GC/NPD method (slightly modified version of EN-CAS Method No. ENC-9/90) is adequate for collecting data on propanil residues of concern in milk and tissues of dairy cattle. Acceptable method validation data were provided with the current submission.

Table 2. Method recoveries of propanil from fortified control samples of cattle tissues and milk using the GC/NPD data collection method (EN-CAS Method No. ENC-9/90, modified).

Matrix	Fortification level (ppm)	Number of samples	% Recovery	
			Range ^a	Mean (±SD)
Method Validation Recoveries				
Milk	0.005-0.100	9	72.0-103.2	85.0 ± 11.9
Liver	0.05-0.20	14	63.2; 73.2-113.7	90.7 ± 16.2
Kidney	0.05-0.20	12	67.7; 70.0-116.9	89.7 ± 15.6
Muscle	0.05-0.20	14	72.7-117.6	85.0 ± 14.8
Fat	0.05-0.20	14	75.3-119.8	97.8 ± 15.1
Concurrent Method Recoveries				
Milk	0.01-0.10	30	64.6; 70.4-119.9	91.4 ± 16.3
Liver	0.20, 0.50	4	73.0-107.8	
Kidney	0.05, 0.20	5	71.8-119.3	
Muscle	0.05, 0.20	3	90.7-118.0	
Fat	0.05, 0.20	3	101.2-115.4	

^a Recovery values outside the acceptable 70-120% range are listed separately.

OPPTS GLN 860.1380: Storage Stability Data

Sample storage intervals and conditions

Wheat forage: Untreated and treated samples of wheat forage were collected from the fields, placed in coolers with blue ice, and frozen within 0.5-1.5 hours of sampling. Samples were first shipped by ACDS freezer truck to Rohm and Haas Company (Springhouse, PA) for processing prior to shipment to EN-CAS Analytical Laboratories (Winston-Salem, NC) for analysis. The total storage interval (between harvest and analysis) of treated wheat forage samples was 123-126 days.

Milk: Milk samples were collected on Days 0, 1, 3, 7, 11, 14, 18, 21, 24, and 27 for each dose group and stored frozen. For each designated collection day, a proportional daily milk composite was prepared for each animal based on the relative amounts of milk produced in the morning and evening milkings. The combined milk samples were stored frozen prior to analysis. The storage interval from sample collection to residues analysis was 2-126 days.

Cattle fat, muscle, liver, and kidney: Control and treated cows were sacrificed within 4-10 hours of the final dose administration. At sacrifice, samples of fat (composite omental and perirenal), muscle (round and loin), liver, and kidney (both) were collected, placed in insulated coolers with

crushed ice, and transported to the livestock facility at PTRL East, Inc. for sample preparation. At the facility, tissue samples were rinsed with water, cut into small chunks, placed in storage bags, and frozen (within 9.5 hours) until processing. Tissue samples were then processed by homogenization with dry ice and stored frozen until analysis. The frozen tissue samples were processed within 1-11 days of collection and stored frozen (temperature not specified) for 60-92 days prior to analysis.

Storage stability data

Wheat forage: No supporting storage stability data were included in the study submission for wheat forage; however, the registrant cited (DP Barcode D200811, 10/3/95, C. Swartz and DP Barcode D178275, 9/14/92, R. Perfetti) previously reviewed storage stability data for rice commodities. These data indicate that residues of propanil are stable during frozen storage in/on rice bran and polished rice for up to 10 months, rice straw for up to 18 months, and rough rice grain and rice hulls for up to 20 months.

Dairy cattle milk and tissues: Supporting storage stability data were included in the ruminant feeding study (MRID 44550101). Control samples were fortified with propanil at 0.2 ppm (milk, liver, kidney, muscle, and fat) and stored frozen. At three sampling intervals ranging from 0-127 days for tissues and 0-132 days for milk, a control sample, two freshly-fortified samples and two stored fortified samples were analyzed for each matrix using the analytical method described above. Adequate representative chromatograms, raw data, and sample calculations were provided. The results of the storage stability study are presented in Table 3. These data indicate that residues of propanil are relatively stable in frozen cattle liver, kidney, muscle, and fat for at least 127 days and in milk for at least 132 days.

Table 3. Stability of propanil fortified in cattle liver, kidney, muscle, fat and milk and stored frozen for up to 4 months.

Matrix	Storage Interval (days)	Fortification Level (ppm)	Fresh Fortification Recovery (%) ^a	Stored Sample Recovery (%)	Stored Sample ^b Corrected Recovery %
Liver	0	0.2	85.1, 89.5, 105.2, 115.4	--	--
	69		89.5, 105.2 (97.4)	100.5, 117.9	103.2, 121.1
	127		105.7, 114.2 (110.0)	94.6, 102.2	94.6, 102.2
Kidney	0	0.2	44.6, 107.0, 108.9, 105.5	--	--
	51		107.0, 108.9	114.8, 119.4	106.3, 110.6
	126		95.8, 96.8 (96.3)	86.9, 86.9	90.2, 90.2
Muscle	0	0.2	78.0, 79.4, 107.4, 119.5	--	--
	48		107.4, 119.5 (113.5)	101.6, 105.2	89.6, 92.7
	125		110.3, 112.7 (111.5)	101.4, 119.2	90.9, 106.9
Fat	0	0.2	80.4, 82.1, 105.7, 113.9	--	--
	22		80.4, 105.7 (93.1)	84.8, 104.5	91.1, 112.3
	124		111.8, 119.4 (115.6)	113.0, 116.2	97.8, 100.5
Milk	0	0.2	63.1, 73.0, 81.5, 85.8	--	--
	47		73.0, 85.8 (79.4)	77.7, 83.2	97.9, 104.8
	132		75.0, 83.9 (79.5)	88.3, 89.0	111.1, 112.0

^a Average recovery reported in parentheses.

^b Apparent recoveries in stored samples were corrected by dividing by average recovery in fresh fortification samples.

Conclusions

The animal storage stability data are adequate and indicate that residues of propanil are stable frozen in cattle liver, kidney, muscle, and fat for at least 127 days, in milk for at least 132 days. These data support the frozen storage intervals (maximum of 92 days for cattle tissues and 126 days for milk, from sampling to analysis) depicted in the current ruminant feeding study.

OPPTS GLN 860.1500: Crop Field Trials

Wheat forage

Established tolerances: Tolerances have been established for the residues of propanil and its metabolites, calculated as propanil, in/on wheat grain at 0.2 ppm and wheat straw at 0.75 ppm [40 CFR §180.274(a)(1)]. No propanil tolerances have been established for wheat forage or hay.

Registered use pattern: The 81% DF (EPA Reg. No. 707-226) and the 3 lb/gal EC (EPA Reg. Nos. 707-75 and 707-182) formulations are registered for use limited to Durum and hard, red spring wheat grown in the states of MN, MT, ND, and SD as a single postemergence broadcast application at 1.13 lb ai/A using ground or aerial equipment. The 3 lb/gal EC (EPA Reg. No. 707-75) formulation is registered for use limited to hard, red spring wheat grown in MN, MT, ND, and SD as a single postemergence broadcast application at 1.5 lb ai/A using ground or aerial equipment. Applications are to be made using ground equipment (minimum of 10 gal/A of water) or aerial (5 gal/A of water) equipment. A preharvest interval is not specified. Treatment of wheat beyond the four- or five-leaf stage and the grazing of treated crop or cutting for green chop feed are prohibited.

Discussion of data: The Agency (DP Barcode D203514, 9/22/94, C. Swartz) no longer considers restrictions against the feeding of wheat forage to livestock to be practical and required the registrant to generate propanil residue data for wheat forage. In response, Rohm and Haas has submitted data (1999; MRID 44768801) depicting the magnitude of propanil residues of concern in/on wheat forage. Three field trials were conducted during the 1996 growing season in the state of North Dakota. Spring wheat plants were treated with a single postemergence broadcast application of the 81% DF formulation (EPA Reg. No. 707-226) at 1.14-1.19 lb ai/A (~1x the maximum registered single application rate). The test formulation was applied using ground equipment (tractor mounted sprayer) in 19.8-20.9 gal/A of water. Wheat forage was harvested 24-25 days following treatment when plants were at the Feekes Growth Stage 7 to 9 (stem elongation stage to flag leaf stage).

A single untreated and duplicate treated samples of wheat forage were collected, placed in coolers with blue ice, and frozen within 0.5-1.5 hours of sampling. Samples were first shipped by ACDS freezer truck to Rohm and Haas Company (Springhouse, PA) for processing prior to shipment to EN-CAS Analytical Laboratories (Winston-Salem, NC) for analysis. The total storage interval (between harvest and analysis) of samples was 123-126 days. Wheat forage samples were analyzed for propanil residues (determined as base-releasable 3,4-DCA) using the method described in "Residue Analytical Methods" section. The reported method LOQ is 0.010 ppm, with an LOD of 0.003 ppm. Apparent residues were less than the LOD (<0.003 ppm) in/on three samples of untreated wheat forage. Propanil residues in/on treated wheat forage samples are presented in Table 4.

Table 4. Residues of propanil (determined as base-releasable 3,4-DCA) in/on **wheat forage** harvested 24-25 days following a single postemergence broadcast application of the 81% DF formulation at 1.14-1.119 lb ai/A (~1x the maximum registered single application rate).

Trial location (County)	PHI (days)	Propanil residues (ppm)
Velva, ND (Ward)	25	0.020, 0.030
Velva, ND (Ward)	25	0.020, 0.030
Velva, ND (McHenry)	24	0.14, 0.16

Geographic representation of data: The registered use of propanil on wheat is limited to the states of MN, MT, ND, and SD. Prior to initiation of the wheat field trials, the registrant submitted a letter to the Agency (6/15/95) requesting a reduction in the number of field trials required for wheat forage based on limited uses. The registrant's proposal was to conduct three field trials based on OPPTS 860.1500, Attachment 11, "Number of Field Trials Required for Tolerances With Geographically Restricted Registration...." According to this guideline, the required number of field trials is equal to the number of field trials required for the commodity for a national tolerance or registration, multiplied by the proportion (by acres) of the crop grown in that region. The registrant indicated that given the small use area bordering Regions 5 and 7, one could reasonably consider this as one region which following calculation resulted in 1.2 field trials. The guideline require either a minimum of two trials at 1x and 2x or three trials at 1x. Because of the availability of cooperators and test sites, it was necessary for the registrant to conduct all three trials in ND. In consideration of the fact that propanil formulations registered for use on wheat are limited, the Agency considers the geographic representation of residue data to be adequate.

Conclusions:

The wheat forage data are adequate and may be used for tolerance establishment. Residues of propanil, determined as 3,4-DCA, ranged from 0.02 to 0.16 ppm in/on six treated samples of wheat forage harvested 24 or 25 days (when plants were at the Feekes Growth Stage 7 to 9, (stem elongation stage to flag leaf stage) following a single postemergence broadcast application of the 81% DF formulation at 1.14-1.19 lb ai/A (~1x the maximum registered rate). TOX and ORE considerations permitting, the registrant must propose a tolerance for wheat forage at 0.2 ppm.

Based on the submitted data, the registrant is required to amend propanil labels with registered uses on wheat to specify a pregrazing/preharvest interval of "Feekes Growth Stage 7 to 9 (typically 24-25 days (stem elongation stage to flag leaf stage))" for wheat forage. Finally, the product labels for the 3 lb/gal EC (EPA Reg. Nos. 707-75 and 707-182) and the 81% DF (EPA Reg. No. 707-226) formulations must be modified to remove the feeding restriction for the grazing of treated crop or cutting for green chop.

Table 1 of OPPTS GLN 860.1000 recognizes hay as a raw agricultural commodity (RAC) of wheat; therefore, residue data for wheat hay are required for reregistration. The required data should be generated using representative EC and DF formulations of propanil applied according to the maximum registered use patterns. The number and locations of wheat hay field trials should be in compliance with the current applicable OPPTS guideline.

OPPTS GLN 860.1480: Meat/Milk/Poultry/Eggs

Ruminant Feeding Study

Established tolerances: Tolerances have been established for the combined residues of propanil (3', 4'-dichloropropionanilide) and its metabolites (calculated as propanil) in livestock commodities at 0.05 ppm for milk and at 0.1 ppm for the meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep [40 CFR §180.274(a)(1)].

Discussion of the data: The Propanil Task Force has submitted a ruminant feeding study (1998; MRID 44550101) conducted by PTRL East, Inc. (Richmond, KY). Four groups of Holstein dairy cows (3 cows in the rice-fed rations dose group and 2 cows each in the low, mid, and high dose groups) were dosed orally once daily following the morning milking for 28 days with either rice-based rations containing field-aged residues at 3.9 ppm (propanil equivalents) or gelatin capsules fortified with propanil at dose levels equivalent to 15, 45, and 150 ppm (mg/kg diet on a dry weight basis). One additional cow was not treated and served as a control animal. The feeding levels depicted in the study approximate 0.17x (rice-fed), 0.65x, 2.0x, and 6.5x, respectively, the anticipated maximum dietary burden for beef cattle of 23.0 ppm and 0.30x (rice-fed), 1.1x, 3.4x, and 11.4x, respectively the anticipated maximum dietary burden for dairy cattle of 13.2 ppm. The calculation of maximum dietary burdens is presented below in Table 5.

Table 5. Calculation of maximum dietary burdens of propanil to livestock.

Feed Commodity	% Dry Matter ^a	% Diet ^a	Reassessed Tolerance Level (ppm) ^b	Dietary Contribution (ppm) ^c
Beef Cattle				
Rice grain	88	40	10	4.5
Rice straw	90	10	75	8.3
Rice hulls	90	10	30	3.3
Rice bran	90	15	40	6.7
Wheat forage	25	25	0.2	0.2
TOTAL BURDEN		100		23.0
Dairy Cattle				
Rice grain	88	40	10	4.5
Rice straw	90	10	75	8.3
Wheat forage	25	50	0.2	0.4
TOTAL BURDEN		100		13.2

^a Table 1 (OPPTS Guideline 860.1000).

^b Reassessed level based on data from field trials.

^c Contribution = [tolerance ÷ %DM] X %diet).

The rice-based ration was prepared using rough rice treated postemergence at the maximum label rate (6 lb ai/A) and harvested 63 days posttreatment. The registrant stated that as cows are fed field-aged residues in their diets and metabolism data show that propanil *per se* is not expected to be a residue in rice commodities at harvest, feeding of propanil treated rice grain and straw containing field-aged residues to cows is the appropriate route of exposure. In its review of the ruminant feeding study protocol (DP Barcode D224402, C. Swartz, 4/10/96), the Agency indicated that data from a study conducted using field-aged residues in the diet will be taken into consideration during risk assessment, but may not enable the determination of appropriate tolerance levels for livestock commodities. In the subject ruminant feeding study, maximum residues were lowest in tissues and milk from the rice-fed group compared to the propanil-fed groups.

Cows in the rice-based rations group were fed specially formulated rice-based rations containing rough rice and other ingredients needed for a complete ration. Before study start, these cows were fed untreated (control) rice diet. Cows in the control and capsule groups were fed a commercially available dairy concentrate throughout the study.

The treated and control animals were observed throughout the study for clinical abnormalities. Feed consumption and milk production were recorded daily. Animals were weighed prior to acclimation, during the acclimation period, and at sacrifice. There was no apparent effect of propanil dosing on overall animal health and feed consumption at any dose level. There was a slight increase in milk production in the control cow and cows treated with capsules compared with production levels during acclimation, but milk production in cows in the rice-based ration dose groups were slightly lower when compared with the production levels during acclimation. These minor changes were not considered biologically significant and therefore there was no apparent effect of propanil dosing on milk production.

The animals were milked twice daily (a.m. and p.m.). Milk samples were collected on Days 0, 1, 3, 7, 11, 14, 18, 21, 24, and 27 for each dose group and stored frozen. For each designated collection day a proportional daily milk composite was prepared for each animal based on the relative amounts of milk produced in the morning and evening milkings. The combined milk samples were stored frozen prior to analysis. The sampling-to-analysis interval for milk samples was 2-126 days.

Control and treated cows were sacrificed within 4-10 hours of receiving the final dose, and samples of fat (composite omental and perirenal), muscle (round and loin), liver, and kidney (both) were collected, placed in insulated coolers with crushed ice, and transported to the livestock facility at PTRL East, Inc. for sample preparation. At the facility, tissue samples were rinsed with water, cut into small chunks, placed in storage bags, and frozen (within 9.5 hours) until processing. Tissue samples were then processed by homogenization with dry ice and stored frozen until analysis. No significant conditions, gross abnormalities or gross pathological findings were noted at necropsy that was dose-related. The frozen tissue samples were processed within 1-11 days of collection and stored frozen (temperature not specified) for 60-92 days prior to analysis.

Residues of propanil were determined using the GC/NPD method described previously. Adequate concurrent recoveries of propanil were obtained from each ruminant commodity. Apparent residues of propanil were <LOQ (<0.005 ppm in milk; <0.05 ppm in tissue) for all control samples analyzed for milk, liver, kidney, muscle and fat. Sample analyses were performed by PTRL East, Inc. (Richmond, KY). Results from the analyses of milk and cattle tissues are presented in Tables 6 and 7, respectively.

Table 6. Residues of propanil in milk from cattle dosed daily for 28 days with either rice-based rations bearing field-incurred residues at 3.9 ppm (propanil equivalents) or gelatin capsules fortified with propanil equivalent to 15, 45 or 150 ppm in the diet [0.3x (rice-fed), 1.1x, 3.4x, and 11.4x, respectively the MTDB for dairy cattle of 13.2 ppm].

Sampling Day	Residues (ppm) ^a			
	Dose level			
	Rice-based Ration 3.9 ppm (0.3x)	15 ppm (1.1x)	45 ppm (3.4x)	150 ppm (11.4x)
0	<0.005, <0.005, <0.005	<0.005, <0.005	<0.005, <0.005	<0.005, <0.005
1	<0.005, 0.005, 0.005	0.019, 0.027	0.023, 0.050	0.082, 0.106
3	<0.005, 0.005, 0.006	0.011, 0.035	0.036, 0.050	0.086, 0.125
7	0.006, 0.007, 0.007	0.018, 0.029	0.025, 0.045	0.099, 0.099
11	0.007, 0.007, 0.009	0.017, 0.027	0.022, 0.042	0.089, 0.131
14	0.005, 0.005, 0.007	0.014, 0.025	0.024, 0.037	0.101, 0.116
18	0.006, 0.007, 0.008	<0.005 ^b , 0.023	0.028, 0.078 ^b	0.099, 0.144
21	0.009, 0.010, 0.013	0.016, 0.031	0.018, 0.045	0.119, 0.141
24	0.005, 0.007, 0.009	0.014, 0.030	0.038, 0.047	0.093, 0.123
27	0.007, 0.008, 0.010	0.014, 0.033	0.027, 0.045	0.091, 0.124

^a Each value represents a composite sample. **Bolded** values indicate the maximum residue for each dose group.

^b Value considered an outlier.

It is not apparent from Table 6 as to when residues of propanil in milk plateaued. Maximum propanil residues observed were 0.013 ppm in milk from cows dosed at 3.9 ppm (0.3x) with rice-based rations bearing aged residues of propanil, and 0.035, 0.050, and 0.144 ppm, respectively, in milk from cows dosed with propanil *per se* by capsule at 15 (1.1x), 45 (3.4x), and 150 ppm (11.4x).

Table 7. Residues of propanil in **edible tissues** from cattle dosed daily for 28 days with either rice-based rations bearing field-incurred residues at 3.9 ppm (propanil equivalents) or gelatin capsules fortified with propanil equivalent to 15, 45 or 150 ppm in the diet [0.3x (rice-fed), 1.1x, 3.4x, and 11.4x, respectively the MTDB for cattle of 23 ppm].

Matrix	Residues (ppm)			
	Rice-based Ration 3.9 ppm (0.17x)	15 ppm (0.65x)	45 ppm (2.0x)	150 ppm (6.5x)
Liver	0.07, 0.08, 0.08	0.26, 0.31	0.76, 0.82	1.92, 2.09
Kidney	0.12, 0.13, 0.14	0.50, 0.77	1.59, 6.50	4.51, 14.89
Muscle	<0.05, <0.05, <0.05	<0.05, <0.05	<0.05, 0.05	0.13, 0.13
Fat	<0.05, <0.05, <0.05	0.05, 0.10	0.10, 0.25	0.26, 0.37

Table 7 shows that residues of propanil in liver were 0.07-0.08 ppm in cows fed rice-based rations (0.3x). Residues in liver from cows in the 15 (1.1x), 45 (3.4x), and 150 ppm (11.4x) dose groups were 0.26-0.31, 0.76-0.82, and 1.92-2.09 ppm, respectively. Residues of propanil in kidney were 0.12-0.14 ppm in cows fed rice-based rations (0.17x). Residues in kidney from cows in the 0.65x, 2.0x, and 6.5x dose groups were 0.50-0.77, 1.59-6.50, and 4.51-14.89 ppm, respectively. Residues were <0.05 ppm (<LOQ) in muscle from the 0.17x (rice-fed) and 0.65x dose groups, and <0.05-0.05 and 0.13 ppm, respectively, from the 2.0x and 6.5x dose groups. In fat, propanil residues were <0.05 ppm (<LOQ) at the 0.17x (rice-fed), and 0.05-0.10, 0.10-0.25, and 0.26-0.37 ppm, respectively, from the 0.65x, 2.0x, and 6.5x dose groups.

Conclusions

The submitted ruminant feeding study is acceptable. Four groups of Holstein dairy cows were dosed orally once daily following the morning milking for 28 days with either rice-based rations containing field-aged residues at 3.9 ppm (propanil equivalents) or gelatin capsules fortified with propanil at dose levels equivalent to 15, 45, and 150 ppm (mg/kg diet on a dry weight basis). The feeding levels depicted in the study are approximately equivalent to 0.3x (rice-fed), 1.1x, 3.4x, and 11.4x, respectively, the anticipated maximum dietary burden of 13.2 ppm for dairy cattle.

Milk samples were collected on Days 0, 1, 3, 7, 11, 14, 18, 21, 24, and 27. Dairy cows were sacrificed within 4-10 hours of the final dose administration. At sacrifice, samples of fat (composite omental and perirenal), muscle (round and loin), liver, and kidney (both) were collected.

Maximum residues, determined as 3,4-DCA and calculated as propanil, that were obtained from dairy cattle fed at the 15-ppm dosing level (1.1x) were: 0.035 ppm in milk, 0.31 ppm in liver, 0.77 ppm in kidney, <0.05 ppm (nondetectable) in muscle, and 0.10 ppm in fat.

Based on the available data, the Agency concludes that: (i) the established milk tolerance of 0.05 ppm is appropriate; (ii) the established fat tolerance of 0.1 ppm is also appropriate; (iii) the established meat tolerance of 0.1 ppm may be lowered to 0.05 ppm; and (iv) the established meat byproducts tolerance of 0.1 ppm should be increased to 1.0 ppm.

AGENCY MEMORANDA CITED IN THIS REVIEW

CB No.: 9876
DP Barcode: D178275
Subject: Response to the Propanil Reregistration Standard: Residue Chemistry.
From: R. Perfetti
To: L. Rossi and E. Saito
Dated: 9/14/92
MRID(s): 42301001

CB No.: 14030
DP Barcode: D205676
Subject: Propanil. List A Reregistration Case No. 0226/Chemical ID No. 028201.
Propanil Task Force Submission to Upgrade a Rice Metabolism Study [Guideline
Ref. No. 171-4(a)] and Rice Field Trials [Guideline Ref. No. 171-4(k)].
From: C. Swartz
To: E. Saito
Dated: 9/8/94
MRID(s): 43285401 and 43282801

CB No.: 13729
DP Barcode: D203514
SUBJECT: Propanil. List A Reregistration Case No. 0226/Chemical ID No. 028201. Rohm
and Haas Submission of Wheat Residue and Method Validation Data.
FROM: C. Swartz
TO: W. Waldrop
DATED: 9/22/94
MRID(s): 43196001 and 43196002

CB No.: 13433
DP Barcode: D200811
Subject: Propanil. List A Reregistration Case No. 0226/Chemical ID No. 028201.
Propanil Task Force Submission of Storage Stability Data in Rice [Guideline Ref.
No. 171-4(e)].
From: C. Swartz
To: W. Waldrop
Dated: 10/3/95
MRID(s): 43157001 and 43157002

CB Nos.: 12739 and 14594
DP Barcodes: D196301 and D208552
Subject: Propanil. List A Reregistration Case No. 0226/Chemical ID No. 028201.
Propanil Task Force Submission of a Confined Rotational Crop Study, and a
Method Radiovalidation Study for Rotational Crop Matrices [Guideline Ref. No.
165-1].
From: C. Swartz
To: W. Waldrop
Dated: 10/23/95
MRID(s): 42963001 and 43355201

CB No.: 17053
DP Barcode: D224402
SUBJECT: Propanil. List A Reregistration Case No. 0226/Chemical ID No. 028201.
Protocol: Propanil Task Force Proposal to Satisfy GLN 171-4(j), Magnitude of
the Residue in Meat and Milk.
FROM: C. Swartz
TO: K. Davis
DATED: 4/10/96
MRID(s): None

CB No.: None
DP Barcode: D253336 and D253337
Subject: Propanil. List A Reregistration Case No. 0226/Chemical ID No. 028201. Poultry
Feeding Study and Independent Laboratory Validation (ILV) Trial For a GC
Method Used to Determine Residues of Propanil in Rice.
From: S. Kinard
To: Tom Myers
Dated: 9/10/01
MRID(s): 44748201 and 44748202

MASTER RECORD IDENTIFICATION NUMBERS

Citations for the MRID documents referred to in this review are presented below.

44550101 Johnson, T.; Krautter, G.; Gibson, N. (1998) Magnitude of the Residue in Meat and Milk from Dairy Cows fed Propanil per se or Field-Aged Propanil Residues: Lab Project Number: 1006: 1961. Unpublished study prepared by PTRL East, Inc. 406 p.

44768801 Smith, S. (1999) Magnitude of the Residues of Propanil (Stampede) in or on Spring Wheat Forage Treated with Stampede 80EDF: Lab Project Number: 96395: 34P-96-91A: 34-98-11. Unpublished study prepared by EN-CAS Analytical Laboratories and Agro-Tech, Inc. 290 p.