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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

TXR No.

MEMORANDUM

Date: June 5, 2003

Subject: **Oryzalin; Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Decision Document.** DP Barcode D289755. Chemical 104201. Case 0186.

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To: Yan Donovan, HED MARC Executive Secretary (7509C)

Introduction
The MARC reviewed electronically distributed material 5/8/03 to determine the oryzalin residues of concern in water.

Question to the Committee

Does the Committee agree oryzalin, per se, is the sole residue of concern in water?

Comments Received From: John Doherty, Norman Birchfield, Christine Olinger, Yan Donovan, Rick Loranger, and Alberto Protzel, Leonard Keifer.

Memorandum was also circulated to: Abdallah Khasawinah, Sheila Piper, Leung Cheng, William Wassell, PV Shah, Steve Knizner.

MARC Decision Table
The recommendation for degradates and metabolites to be included in the risk assessment is summarized in Table 1.

Table 1. Summary of MARC Decision for Oryzalin

Matrix	For Risk Assessment	For Tolerance Expression
Water	Parent only	Not applicable

Note that the chemical names and structures for these metabolites and degradates may be found in Table 2.

MARC Decision Rationale

<u>Water</u>

No major degradates were observed in the aerobic soil metabolism study

The only major degradates (not greater than 15 % of the applied dose) were observed in the anaerobic soil and the aqueous photolysis studies.

Due to the use pattern of oryzalin (application of oryzalin to orchard floor or turf), anaerobic metabolism and aqueous photolysis are not expected to be major routes of degradation. Aqueous photolysis is limited to clear shallow water and anaerobic metabolism is also only likely to be relevant for the fraction of material that reaches anaerobic environments.

Based on the structures of the degradates; OR-2, OR-20, OR-21 (nitroanilines or potential nitroanilines) HED suspects that these compounds will share in the properties of the parent Oryzalin. The parent produces hematologic effects and thyroid tumors. HED considers that the three compounds mentioned above will also have these effects based on their nitroaniline structure This contention is suppported by the finding of thyroid tumors in trifluralin and pendimethalin, compounds also possessing a nitroaniline structure. Based on the environmental fate data presented, suggesting that there will not be significant exposure to nitroaniline degradates in drinking water, HED does not have specific concerns at this time.

Some benzimidazole compounds are of toxicological concern but exposure to the benzimidazole compounds formed is likely to be minimal since relatively minor amounts (~10 % or less) were formed in the environmental fate studies.

The major route of degradation is likely to be aerobic soil metabolism only due to the use pattern of oryzalin (application of oryzalin to orchard floor or turf). Degradates found in this study are all <10% (OR-20 at 4.7%, UN-2 at 2.4%, and UN-1 at 1.4%), and none of these degradates are considered to be significantly more toxic than the parent.

MATERIAL REVIEWED: The following information was provided to the HED Metabolism Assessment Review Committee.

1. TEAM PROPOSAL

Table 1.1. Proposed Residues of Concern in Water

Matrix	Tolerance Expression	Residues for Risk Assessment
Water	**Not Applicable**	**Oryzalin**

2. QUESTIONS FOR THE METABOLISM ASSESSMENT REVIEW COMMITTEE

1. Does the committee agree that for purposes of risk assessment, the residue of concern in water is oryzalin, per se?

3. BACKGROUND INFORMATION

Oryzalin [3,5-dinitro-N^4,N^4-dipropylsulfanilamide] is a selective preemergence herbicide registered for use on a variety of bearing and nonbearing fruit and nut crops and vineyards**.** Granular (G), wettable powder (WP), emulsifiable concentrate (EC), flowable concentrate (FlC) and dry flowable (DF) are the oryzalin formulation classes registered for food/feed uses. The DF and G formulations may contain multiple active ingredients. Oryzalin is typically applied on these crops as a band treatment, directed spray, over-the-top broadcast application (nonbearing crops only), or soil broadcast application. Ground, aerial, or irrigation equipment may be used to apply oryzalin. Tolerances for residues of oryzalin in/on plant commodities are expressed in terms of residues of oryzalin *per se* at 0.05 ppm for pome fruits, stone fruits, small fruits/berries, tree nuts, and a variety of tropical fruits [40 CFR §180.304(a)]. Tolerances with regional registration are expressed in terms of residues of oryzalin *per se* at 0.05 ppm for guavas and papayas [40 CFR §180.304(b)]. Neither tolerances for animal commodities nor food/feed tolerances for processed commodities have been established. Adequate enforcement methods are available for the determination of oryzalin residues of concern in/on plant commodities.

The qualitative nature of the residue in vine and orchard crops is adequately understood. The existing grape metabolism study provides sufficient data to conclude that the terminal residues of concern in vine and orchard crops consists of unchanged oryzalin. The study with grapes indicated that there was little uptake or translocation of oryzalin from the soil; no oryzalin or oryzalin-related compounds were identified in grapes. HED considers grapes representative of the crops (vine and orchard) on which oryzalin is currently registered for use; therefore, only one plant metabolism study, with grapes, was required to satisfy plant metabolism data requirements. In the event an interested party wishes to obtain registration for use of oryzalin on crops other than vine or orchard crops, additional plant metabolism data will be required. The residue of concern in plants is oryzalin, which is the residue presently included in the tolerance expression

4. TOXICOLOGY SECTION

Summary of Toxicological Dose and Endpoints for Oryzalin

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (Females 13-50 years of age)	NOAEL = 25 mg/kg/day UF = 1000 Acute RfD = 0.025 mg/kg/day	FQPA SF = 1x aPAD = acute RfD / FQPA SF = 0.025 mg/kg/day	Rabbit Developmental Study LOAEL = 55 mg/kg/day based on decreased live fetuses, increased resorptions, and increased postimplantation loss
Chronic Dietary (All populations)	NOAEL= 13.82 mg/kg/day UF = 1000 Chronic RfD = 0.014 mg/kg/day	FQPA SF = 1x cPAD = chronic RfD / FQPA SF = 0.014 mg/kg/day	2-year rat feeding study LOAEL = 42.89 mg/kg/day based on decreased body weight gain, decreased hematology parameters, and increased microscopic findings in the thyroid
Short-Term Incidental Oral (1-30 days)	NOAEL= 25 mg/kg/day	Residential LOC for MOE = 1000 Occupational = 100	Rabbit Developmental Study LOAEL = 55 mg/kg/day based on decreased body weight gain and food consumption in does
Intermediate-Term Incidental Oral (1- 6 months)	NOAEL= 13.82 mg/kg/day	Residential LOC for MOE = 1000 Occupational = 100	2-year rat feeding study LOAEL = 42.89 mg/kg/day based on decreased body weight gain, decreased hematology parameters, and increased microscopic findings in the thyroid
Short-Term Dermal (1 to 30 days), Intermediate-Term Dermal (1 to 6 months) and Long-Term Dermal (>6 months)	Dermal study LOAEL= 1000 mg/kg/day	Residential LOC for MOE = 3000 Occupational LOC for MOE = 300	21-Day Dermal Toxicity Study LOAEL = 1000 mg/kg/day based on increased thyroid weights in males and increased bilirubin in both sexes.
Short-Term Inhalation (1 to 30 days)	Inhalation (oral) study NOAEL= 25 mg/kg/day (inhalation absorption rate = 100%)	Residential LOC for MOE = 1000 Occupational LOC for MOE = 100	Rabbit Developmental Study LOAEL = 55 mg/kg/day based on decreased body weight gain and food consumption in does

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Intermediate-Term Inhalation (1 to 6 months) and Long-Term Inhalation (>6 months)	**Inhalation (or oral) study NOAEL = 13.82 mg/kg/day (inhalation absorption rate = 100%)**	**Residential LOC for MOE = 1000** **Occupational LOC for MOE = 100**	**2-year rat feeding study LOAEL = 42.89 mg/kg/day based on decreased body weight gain, decreased hematology parameters, and increased microscopic findings in the thyroid**
Cancer (oral, dermal, inhalation)	**skin, mammary gland (females), and thyroid tumors in rats**		**scheduled to be reevaluated**

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

5. Residues in Water Section

Environmental Persistence

The major route of oryzalin disappearance is aqueous photolysis (half-life is 1.4 hours), photodegradation on soil surface (half-life of 3.8 days), and reduction under anaerobic condition (half-life of 10 days). Oryzalin appears to degrade slowly under aerobic soil conditions (half-life of 63 days) and is stable to hydrolysis. Under field conditions oryzalin appeared to be moderately persistent, with a half-life of about two months.

The aerobic and anaerobic aquatic metabolism studies for oryzalin were not submitted. Oryzalin persistence in water is not well known. If oryzalin reaches ground water, it probably will readily undergo reduction to more polar compounds. Oryzalin appears to be susceptible to rapid direct photolysis in water, therefore, oryzalin is not expected to persist in clear shallow surface waters exposed to sunlight.

Expected Mobility

According to the McCall classification (McCall et al., 1980), oryzalin appears to be mobile in sand and sandy loam, relatively mobile in loam, and immobile in clay loam. Oryzalin K_d values are 2.1, 4.9, 8.4, and 12.9 L kg o.c.$^{-1}$ (MRID 41479802). Parent oryzalin would be most mobile in coarse, wet, alkaline soils with little organic matter. Over time soil binding of oryzalin residues (i.e., parent and metabolites) appears to be an important route of dissipation. In an aerobic soil metabolism study, oryzalin non-extractible residues (i.e., parent and metabolites) increased to 63.1% of time zero radioactivity at six months posttreatment (PTT) and to 70.6% of time zero radioactivity at 60 days PTT in an anaerobic study. Formation of CO_2 and/or volatile degradation products was not a major route of dissipation for oryzalin in both aerobic and anaerobic metabolism studies. The pesticide is not expected to be volatile.

Environmental Metabolites/Degradates

In the aerobic soil metabolism study, nine degradates have been identified. The major degradate is 4-hydroxy-3,5-dinitrobenzenesulfonamide (OR-20), which accounted for a maximum of 4.7% of radioactivity at 1 month posttreatment. Other three most abundant degradates 2-ethyl-7-nitro-1-propyl-1H-benzimidazole-5-sulfonamide 3-oxide (UN-2); 3,3'-azoxybis[4-(propylamino)-5-nitro]benzenesulfonamide (UN-1); and 3,5-dinitro-4-propylaminobenzenesulfonamide (OR-2) were formed at the maximum of 2.4, 1.4, and 1.2%, respectively, of time 0 radioactivity. Four other degradates were isolated, but all comprised #1.0% of the applied radioactivity.

In the anaerobic soil metabolism study, two major degradates were 7-amino-2-ethyl-1-propyl-1H-benzimidazole-5-sulfonamide (OR-14) and 7-amino-2-ethyl-1H-benzimidazole-5-sulfonamide (OR-16) which comprised up to 10.3 and 5.3%, respectively, of total time 0 radioactivity.

At least three oryzalin degradates, OR-20, UN-2 and UN-3, formed in aerobic soil metabolism (MRID 43433202), have the potential to leach into ground water. The major degradate (MRID 41322801), OR-20, is moderately persistent and has a very high potential for leaching. The degradate appears to be very mobile in sand, sandy loam, and loam soils, with Freundlich K_{ads} values ranging from 0.165 to 0.310 (MRID 43433201). Under aerobic conditions, in different soils, OR-20 appears to degrade with the average half-lives ($t_{1/2}$) of 58 days (based on a formation-decline curve; Tables IX through XII, 163-1, MRID 43433202) and 102 days (based on a formation-decline curve; 162-1, MRID 41323801). Apparent K_d values for UN-2 ranged from 0.89-4.52 L/kg and for UN-3 ranged from 1.50-4.85 L/kg with the exception of 12.19 L/kg in the sand soil (MRID 43433202). The OR-20 degradate and other degradates have not been monitored in the field. Their persistence in natural waters is not known.

Environmental Fate

Fate data on oryzalin behavior in aquatic environment were not submitted.

Terrestrial field dissipation studies were submitted but did not monitor for oryzalin degradates. The terrestrial field dissipation data provide no information about the dissipation route of oryzalin but merely indicate its rate of disappearance. Based on terrestrial field dissipation studies, oryzalin appeared to be moderately persistent under field conditions, its dissipation half-lives ranged from 58 to 77 days (1st t1/2).

Monitoring Data

Some information on measured concentrations of oryzalin in surface waters is available for California and the Pacific Northwest from USGS sources (Ebbert et al. 2000; Dubrovsky et al. 1998; Williamson et al. 1998; Wentz et al. 1998; Domagalski et al. 2000; Domagalski 2000). The monitoring shows that oryzalin has not been frequently detected and detected concentrations have been considerably less than modeled by PRZM/EXAMS from maximum applications to all modeled crop and non-crop uses. The maximum concentration of oryzalin was 1.5 : g/L in one of the surface water sites in Sacramento River Basin (Domagalski 2000). The second highest concentration was 1.2 : g/L in San Joaquin-Tulare and Willamette (Dubrovsky et al. 1998; Wentz et al. 1998). The frequency of oryzalin detection varied from no detected (Central Columbia; Williamson et al. 1998) to 50% detections (surface water Sites in Sacramento River Basin; Domagalski 2000) depending on the monitoring site.

Effects of Water Treatment

The effects of water treatment on the parent and its degradates are unknown.

Action Levels

No action levels for oryzalin have been established.

Environmental Degradates of Oryzalin

Degradate Name and Structure	Percent of Applied Dose	Study	Comments
Parent		Aqueous Photolysis (MRID 41 278701) Soil Photolysis (MRID 41050001)	Half Life = 1.4 hours Half Life = 3.8 days
		Aerobic Soil Metabolism (MRID 41322801) Anaerobic Soil Metabolism (MRID 4322802)	Half Life = 2.1 months Half Life = 10 days
		Field Dissipation	Half Life = 58- 77 days
OR-15	14.0	Aqueous Photolysis (MRID 41 278701)	Four radioactive peaks had relation times matching those of OR-6, OR-3, OR-15, and OR-5, and represented 2.9, 5.7, 14, and 4.0% of the time 0 radioactivity, respectively.
OR-21	4.6	Soil Photolysis (MRID 41050001)[1]	
OR-14 7-amino-2-ethyl-1-propyl-1H-benzimidazole-5-sulfonamide	10.3	Anaerobic Soil Metabolism (MRID 4322802)	10.3% of time 0 application at both 30 and 60 days after treatment
OR-20 4-hydroxy-3,5-dinitrobenzenesulfonamide	4.7	Aerobic Soil Metabolism (MRID 41322801)	Half Life = 58 days (based on a formation-decline curve; MRID 43433202) Half Life = 102 days (based on a formation-decline curve; MRID 41323801).
UN-2 2-ethyl-7-nitro-1-propyl-1H-benzimidazole-5-sulfonamide 3-oxide	2.4	Aerobic Soil Metabolism (MRID 41322801)	

Degradate Name and Structure	Percent of Applied Dose	Study	Comments
UN-1 3,3'-azoxybis[4-(propylamino)-5-nitro]benzenesulfonamde	1.4	Aerobic Soil Metabolism (MRID 41322801)	

[1] - in the soil photolysis study unknown 3 had the highest maximum formation rate of 6.8% of the applied at 34 hours

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Dubrovsky NM, Kratzer CR, Brown LR, Gronberg JM, Burow KR. 1998. Water Quality in the San Joaquin-Tulare Basins, California, 1992-95. U.S. Geological Survey Circular 1159.

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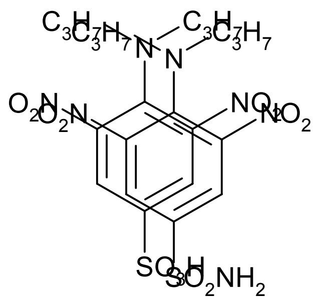
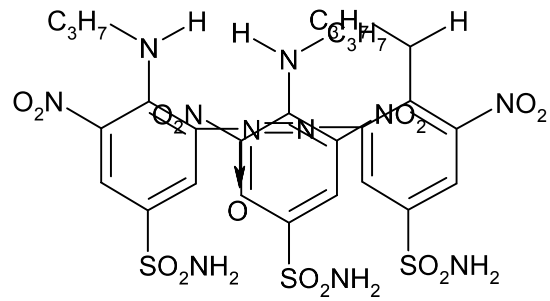
Williamson AK, Munn MD, Ryker SJ, Wagner RJ, Ebbert JC, Vanderpool AM. 1998. Water Quality in the Central Columbia Plateau, Washington and Idaho, 1992-95. U.S. Geological Survey Circular 1144.

cc:T. Morton (RRB4), HED Metabolism Committee file (C. Olinger)
RDI:SVH:6/5/03

Environmental Fate Study Degradates of Oryzalin



Oryzalin



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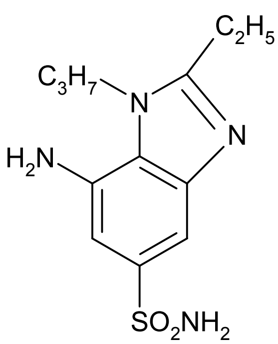

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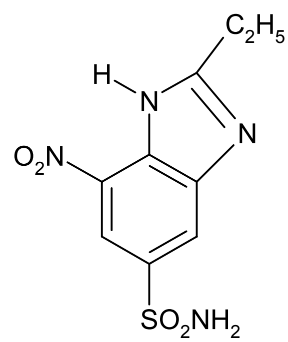

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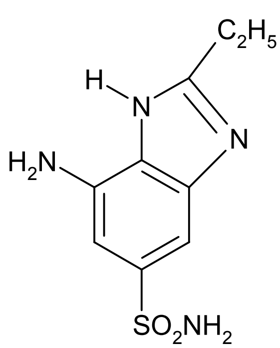

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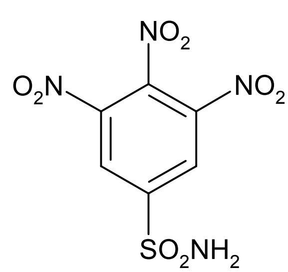
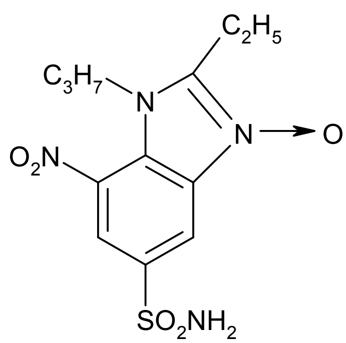


OR-20

OR-21

UN-1



UN-2