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

3

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Human Health Assessment of Propazine, PC Code 080808, D22149, D224185

FROM: Kathryn Boyle, Chemist Kathryn Boyle 3/7/96
Risk Characterization and Analysis Branch
Health Effects Division

THROUGH: Michael Metzger, Chief
Risk Characterization and Analysis Branch
Health Effects Division

TO: Robert Taylor, PM Team 25
Fungicide-Herbicide Branch
Registration Division
and
Joseph Bailey
Special Review Branch
Special Review and Reregistration Branch

In response to the Agency's letter (Grassley-Allen notification) of August 18, 1995, notifying Griffin Corporation that the Agency was considering including propazine in the ongoing triazines special review, Griffin Corporation submitted on September 27, 1995, a Propazine Health Hazard Assessment. As a chemical, propazine is unusual in that it is going through the registration process as a new chemical and is also being considered for inclusion in the triazines special review. Thus, Health Effects Division (HED) was tasked by both Registration Division and Special Review and Reregistration Division to review the human health portions of the Griffin Assessment.

The registration for propazine was previously held by Ciba-Geigy Corporation. Thus, Ciba has ownership of the propazine database. However, the registration was voluntarily cancelled in 1990. Presently, the only uses of propazine are under the Section 18 emergency exemption. In reviewing a Section 18, the Agency can use all available data to make the best possible decision. However, for a new chemical registration, Griffin must either perform or purchase all studies used by the Agency to make the registration decision. HED has attempted to

obtain information on exactly which of the Ciba studies were purchased by Griffin. However, the information provided has been conflicting, such as study titles being cited in one list, but the MRID number of the cited study is not in another list. HED requests that Registration Division obtain a listing of the studies purchased by Griffin with complete titles, MRID numbers and a statement specifying which guideline number each study is expected to fulfill. Please note that HED has attempted, as best possible, considering the conflicting information, to ascertain the data gaps that could exist in the Griffin propazine database. (Farwell memo July 2, 1996)

Without a complete toxicology database, HED was unable to have propazine reviewed by the RfD Committee and the Toxicology Endpoint Selection Committee (TESC). Therefore, HED cannot comment on the endpoints selected by Griffin in its assessment. Since it is not possible to complete the Hazard Identification /Dose Response Assessment portion of the review, this review can only be considered to partially fulfill HED's original tasking from RD and SRRD.

HED's Chemistry Branch Reregistration Support (CBRS) reviewed the dietary exposure section of the Assessment. Propazine is used on sorghum, which is used as livestock feed. Overall, Griffin's approach was similar to the approach that would be used by HED. The major comments from CBRS's review are that (1) it is not possible for HED to comment on the residue values in the Assessment since the metabolism studies on sorghum, lactating goats, and laying hens used in the assessment have not been submitted to or reviewed by HED, (2) data from the April 1994 version of Table II was used instead of the more recent Table II (September 95), and (3) a value of 7 percent crop treated (CT) was used. (Abbotts memo May 14, 1996)

HED's Occupational and Residential Exposure Branch (OREB) reviewed the worker exposure section of the Assessment. The RfD is not the traditionally selected endpoint for estimating occupational exposures. TESC would select appropriate endpoints for the short-term, intermediate-term and chronic scenarios. Also, in the absence of a TESC determination, 100% dermal absorption is assumed. OREB noted problems/deficiencies in the methodology used to derive unit exposure values from PHED, and used to extrapolate estimated doses from unit exposures. The exposures were recalculated. (Carleton memo May 20, 1996)

There are differences in the assumptions used in the drinking water assessment. HED uses the following equation:

Exposure (mg/kg/day) = (ppb in the water consumed)(10^{-6})(22.6)

The 22.6 mg/kg-body wt/day used in this calculation was derived using water consumption values and self-reported body weights obtained from USDA's 1977-1978 Nationwide Food Consumption Survey. 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.

The following must occur before HED can properly complete it's review of the human health portion of the Griffin Assessment:

1) HED must be given a complete listing of studies purchased by Griffin from Ciba, with subsequent HED/TOX rereview of the studies using the current guidelines (See Farwell memo),
2) Submission by Griffin of the sorghum, goat, and hen metabolism studies with subsequent HED/CBRS review of the studies,
3) Confirmation by BEAD (Biological and Economic Analysis Division) of the 7% CT,
4) Submission of the Griffin-performed toxicological studies with subsequent HED/TOX review of the studies,
5) Review of propazine by RfD Committee,
6) Review of propazine by TESC,
7) Review of propazine by CPRC (Cancer Peer Review Committee),
8) Possible review of propazine by HED Metabolism Committee,
9) Performance of DRES (Dietary Risk Evaluation System),
10) Calculation of occupational MOEs for short-term, intermediate-term and chronic scenarios,
11) Consultation with EFED (Environmental Fate and Effects Division) on the available data on propazine in groundwater and surface water.

HED would be willing to meet or to hold a conference call with Griffin to discuss these issues.

cc: Kit Farwell
Jim Carleton
John Abbotts
Bill Hazel
Debbie McCall
Mike Metzger
Terri Stowe (RD)
Andrea Medici (OGC - 2333)
RCAB files

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

MAY 14 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: Propazine (080808), Reregistration Case No. 0230.
Registrant Griffin Corporation.
Dietary and Drinking Water Health Hazard Assessment.
CBRS No. 16780, DPBarcode No. D222623 (SRRD);
CBRS No. 17099, DPBarcode No. D224749 (RD); No MRID No.

FROM: John Abbotts, Chemist
Special Review Section I
Chemistry Branch II - Reregistration Support
Health Effects Division [7509C]

THRU: Andrew R. Rathman, Section Head
Special Review Section I
Chemistry Branch II - Reregistration Support
Health Effects Division [7509C]

TO: Kathryn Boyle
Special Review Section
Risk Characterization and Analysis Branch
Health Effects Division [7509C]

and Joseph Bailey
Special Review Branch
Special Review and Reregistration Division [7508W]

and Terri Stowe, PM Team 25
Fungicide-Herbicide Branch
Registration Division [7505C]

In support of a proposed registration on sorghum, Registrant Griffin Corporation has submitted a health hazard assessment of propazine. Assignment instructions are to review the dietary and drinking water portions of this assessment. Please be specific about the differences such as assumptions and methodology from how CBRS/HED would perform the assessment. Conclusions and Recommendations below pertain only to this assignment.

Tolerances are established for residues of the herbicide propazine, 2-chloro-4,6-bis(isopropylamino)-*s*-triazine, in or on sorghum commodities at negligible levels (0.25 ppm) (40 CFR 180.243); see Figure 1 for structure. Propazine is a List A Chemical. The Residue Chemistry Chapter was issued 5/19/87; the

Registration Standard (Guidance Document) was issued 12/88. Reregistration was not supported, and the Registrant plans to petition for a new use on sorghum.

Conclusions

1. Conclusions here will be limited to the present submission, a health assessment of propazine. However, the Agency has initiated special review of the chloro triazines atrazine and simazine, and has taken the position that risk estimates for these chemicals should be combined across several exposure pathways (59 FR 60412, 11/23/94). Propazine is also a chloro triazine with obvious structural similarity to atrazine and simazine (Figure 1).

2. Comments in this review pertain to residue chemistry matters. We defer to other branches for review pertaining to their applicable disciplines.

3. Dietary exposure assessment in the present submission was conducted using data from "draft reports" for metabolism studies on sorghum, goat, and hen. These studies have not been submitted to either Chemistry Branch for review, and may not yet have been submitted to the Agency. CBRS therefore cannot comment on the precise residue values used, but can comment on the methodology used in the present submission.

4. The present submission ignored human consumption of sorghum commodities, although recent DRES runs have included a contribution from these commodities as human food. However, the relative contribution to dietary risk from direct human consumption of sorghum commodities may be small.

5. The present submission included no analysis of residues on rotational crops. Depending on the results of rotational crop studies, dietary exposure to propazine may increase from rotational use.

6. The HED Metabolism Committee recently decided for atrazine and simazine that separate dietary exposure assessments should be conducted with three different residue subsets for different toxicological endpoints (Memo, 9/29/95 and Memo, 11/28/95, J. Abbotts). Depending on the results of metabolism studies and toxicology studies, similar considerations may be relevant to designating propazine residues of concern. The present submission based its dietary exposure assessment on total radioactive residue (TRR) data. Use of TRR with each toxicological endpoint of concern would represent a conservative approach to risk assessment.

7. The present submission used data that differ somewhat from Pesticide Assessment Guidelines, Subdivision O, Residue

Chemistry, Table II (September 1995). Using Table II data and performing sample calculations with the residue values in the present submission, we determined anticipated residues in eggs that were identical to those in the present submission, and anticipated residues in milk 50% higher than those in the present submission.

8. CBRS generally determines anticipated residues in meat byproducts for cattle and poultry, translates anticipated residues in cattle commodities to goat and sheep, and determines anticipated residues in swine commodities, as appropriate. The present submission did not include these commodities.

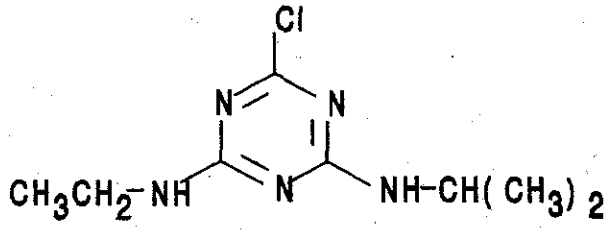
9. The present submission determined anticipated residues for "beef" and "poultry" by apportioning residues from muscle and fat of each animal category. We defer to DRES on whether the proportions used are appropriate based on consumption data.

10. The present submission includes an adjustment for percent crop treated of 7%. For its risk assessments, HED generally uses percent treated data that have been confirmed by BEAD. For a proposed new use, percent treated data may not be appropriate. Even if the proposed use is restricted to a designated five state target area, those states represent 66% of U.S. sorghum production. However, if propazine risks are to be assessed as part of special review with other triazines, then percent treated data may be appropriate.

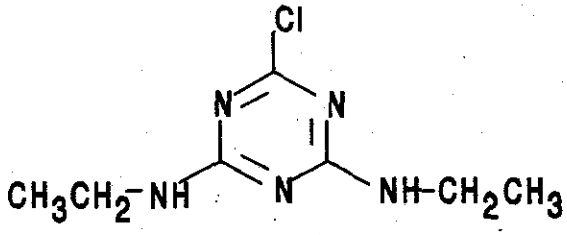
11. We expect that EFED will have detailed comments on the drinking water section of the present submission, but assignment instructions to CBRS specifically requested review of this section. We note that the present submission based its assessment on residues of parent propazine in drinking water. Consistent with the decisions of the HED Metabolism Committee (see Conclusion 6), the presence of propazine metabolites in drinking water could also be of toxicological concern.

Recommendations

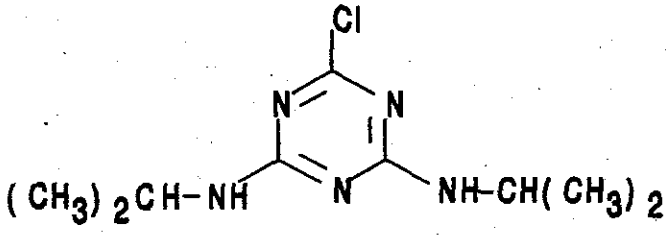
The present submission followed an approach similar to that which CBRS would take in conducting exposure assessment. However, that approach differed from CBRS procedures in both general and specific features. In some cases, such as Conclusion 6, these differences could result in a higher dietary risk than HED might estimate. In other cases, such as Conclusion 7, these differences could result in a lower dietary risk than HED might estimate. In the absence of the bases for the residue data (Conclusion 3), it is difficult to estimate what the results of HED risk assessment might be. In addition, consistent with Conclusion 1, even if the dietary risk for propazine on sorghum alone were negligible, this might have to be considered in conjunction with total risks from triazine chemicals.



Atrazine



Simazine



Propazine

Figure 1. Three chloro triazines with similar structures.

DETAILED CONSIDERATIONS

Present Submission

The following document was provided with the review instructions:

Propazine Health Hazard Assessment, ... Dietary and Drinking Water Health Hazard Assessment prepared by: Risk Communication International, Rockville MD; undated (No MRID No. provided).

We note at the outset that special review was initiated on the chloro triazine herbicides atrazine, simazine, and cyanazine; the Agency position was that risk estimates for all these chemicals should be combined across several exposure pathways (59 FR 60412, 11/23/94). The Agency subsequently proposed termination of special review of cyanazine due to voluntary cancellation (61 FR 8186, 3/1/96). Special review of atrazine and simazine continue, and they are structurally similar to propazine. These considerations lead to the following comment:

Conclusion 1: Conclusions here will be limited to the present submission, a health assessment of propazine. However, the Agency has initiated special review of the chloro triazines atrazine and simazine, and has taken the position that risk estimates for these chemicals should be combined across several exposure pathways (59 FR 60412, 11/23/94). Propazine is also a chloro triazine with obvious structural similarity to atrazine and simazine (Figure 1).

We further note that the Agency's dietary risk assessments depend on contributions from several scientific branches. This consideration leads to the following comment:

Conclusion 2: Comments in this review pertain to residue chemistry matters. We defer to other branches for review pertaining to their applicable disciplines.

Dietary Exposure Assessment

Information pertaining to dietary exposure is contained in pages 11-17 of the present submission. Direct exposure to humans from sorghum was ignored, on the grounds that sorghum and its processed products are not consumed by humans. Exposure from secondary residues in livestock commodities was evaluated.

Anticipated residues in feed items are based on total radioactive residues from the sorghum metabolism study; TRR was 0.126 ppm in forage, 0.133 ppm in grain, and 2.34 ppm in fodder. Transfer of residues from feed to livestock commodities was based on data from goat and hen metabolism studies, comparing TRRs in tissues with TRRs in feed in the daily diet.

Anticipated residues in livestock commodities were determined assuming that sorghum fodder represents 20% of the daily diet of beef cattle and 10% of the daily diet of dairy cattle, and sorghum grain represents 80% of poultry diets.

An extrapolation factor was calculated based on maximum residues in the appropriate feed item, compared to residues in the feed for the applicable animal metabolism study. For cattle commodities, this factor is
2.34 ppm TRR in fodder/10 ppm propazine fed to goat = 0.234.
For poultry commodities, the factor is
0.133 ppm TRR in grain/20 ppm propazine fed to hen = 0.007.

Anticipated residues in livestock commodities were calculated based on TRR in tissues from the ruminant or poultry metabolism study, multiplied by the feed extrapolation factor, multiplied by the percentage in the feed for a sorghum commodity. For milk as an example, the calculation was:
0.238 ppm TRR in milk x 0.234 x 0.10 of diet = 0.006 ppm.
For eggs as an example, the calculation was:
1.041 ppm TRR in eggs x 0.007 x 0.80 of diet = 0.006 ppm.

Anticipated residues for "beef" were calculated assuming beef intake consists of 20% fat and 80% muscle, and anticipated residues for "poultry" were calculated assuming poultry intake consists of 4% fat and 96% muscle.

A correction for percent crop treated of 7% was applied, but at the point of determining consumption rates for livestock commodities (see Table 8 of the present submission).

<u>CBRS Comments, Dietary Exposure</u>

The present submission cites as references for metabolism data "draft reports" on each of sorghum, goat, and hen (present submission, p. 20). There is no record of these studies being submitted to either Chemistry Branch for review. These considerations lead to the following comment:

Conclusion 3: Dietary exposure assessment in the present submission was conducted using data from "draft reports" for metabolism studies on sorghum, goat, and hen. These studies have not been submitted to either Chemistry Branch for review, and may not yet have been submitted to the Agency. CBRS therefore cannot comment on the precise residue values used, but can comment on the methodology used in the present submission.

The present submission ignored human consumption of sorghum commodities. Although such consumption is limited, the Agency dietary risk assessments for atrazine and cyanazine did include estimates for sorghum (59 FR 60412, 11/23/94). The Agency's

Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Table II, Raw Agricultural and Processed Commodities and Feedstuffs Derived from Field Crops (September 1995) has recently been updated. Sorghum flour is not used either as human food or animal feed, but residue data are required on syrup from sweet sorghum; this syrup is a food item.

In addition, sorghum is rotated to other crops, and Registrant Griffin Corporation plans to submit residue data on rotational crops. These considerations lead to the following comments:

Conclusion 4: The present submission ignored human consumption of sorghum commodities, although recent DRES runs have included a contribution from these commodities as human food. However, the relative contribution to dietary risk from direct human consumption of sorghum commodities may be small.

Conclusion 5: The present submission included no analysis of residues on rotational crops. Depending on the results of rotational crop studies, dietary exposure to propazine may increase from rotational use.

The HED Metabolism Committee recently issued decisions pertaining to dietary exposure assessment of atrazine and simazine. The residues of concern for cancer dietary risk are parent and chloro metabolites (Memo, 9/29/95, J. Abbotts). For chronic non-cancer dietary risk, exposure assessment should be performed on two different sets of residues. One assessment should be based on anticipated residues of combined free hydroxy metabolites, using an RfD assigned for hydroxyatrazine. The second evaluation should be based on anticipated residues for all other metabolites (total radioactive residues minus free hydroxy metabolites), using the RfD for parent atrazine. (Memo, 11/28/95, J. Abbotts). These considerations, when applied to propazine, lead to the following comment:

Conclusion 6: The HED Metabolism Committee recently decided for atrazine and simazine that separate dietary exposure assessments should be conducted with three different residue subsets for different toxicological endpoints (Memo, 9/29/95 and Memo, 11/28/95, J. Abbotts). Depending on the results of metabolism studies and toxicology studies, similar considerations may be relevant to designating propazine residues of concern. The present submission based its dietary exposure assessment on total radioactive residue (TRR) data. Use of TRR with each toxicological endpoint of concern would represent a conservative approach to risk assessment.

Discounting the more general considerations described in the Conclusions above, the approach used in the present submission is

similar, but not identical, to the approach that CBRS would use in determining anticipated residues in livestock commodities. CBRS would determine anticipated residues in hypothetical animal diets, assuming a reasonable diet and using anticipated residues determined for each potential feed item. This analysis is simplified when use is on a single crop, as is the case with the proposed use of propazine on sorghum only.

As noted above, Table II, which designates animal feed items and their maximum expected proportions in animal diets, was updated in September 1995. The values used in the present submission should therefore be changed moderately. Under Table II (September 1995), sorghum grain can represent 40% of the diet for each of beef and dairy cattle, 80% for poultry, and 90% for swine. Sorghum forage can represent 40% of the diet for beef cattle and 50% for dairy cattle. Sorghum fodder can represent 25% of the diet for beef cattle, and 15% for dairy cattle. Aspirated grain fractions (grain dust) is also a potential animal feed item, but the present submission provided no data on this commodity, and residue data would not be required until field trials are conducted. Dietary burdens are determined on a dry weight basis for cattle, and on an "as-fed" basis for poultry and swine.

Once anticipated residues are determined for animal diets, anticipated residues in livestock commodities are calculated using transfer ratios from the best available data. The preferred source of transfer data is from animal feeding studies. In the absence of acceptable feeding studies, or in cases such as the triazines where TRR would be of concern, the best available data from metabolism studies would be used.

Using current data from Table II (September 1995), sorghum forage is the single commodity likely to provide the highest residues in cattle feed, and sorghum grain is the only poultry feed item. These are the same feed commodities as those used in the present submission. Performing sample calculations for milk and eggs, using the residue data in the present submission, gives the following results:

$$2.34 \text{ ppm in fodder} \times \frac{0.15 \text{ diet proportion}}{0.88 \text{ dry matter}} \times \frac{0.238 \text{ TRR in milk}}{10 \text{ ppm in feed}}$$

$$= 0.009 \text{ ppm in milk}$$

$$0.133 \text{ ppm in grain} \times 0.80 \text{ diet proportion} \times \frac{1.041 \text{ TRR in eggs}}{20 \text{ ppm in feed}}$$

$$= 0.006 \text{ ppm in eggs}$$

These values are 50% higher than determined in the present submission for milk, and identical to the value for eggs. CBRS would also determine anticipated residues for meat byproducts for both cattle and poultry, using the best available data for

residues in commodities other than meat and fat. Anticipated residues in cattle would also be translated to goats and sheep (although tolerances are set on horse commodities, human consumption of these is negligible). A hypothetical diet and anticipated residues would also be determined for swine commodities, using transfer data from cattle unless separate data on swine were available. These considerations lead to the following comments:

Conclusion 7: The present submission used data that differ somewhat from Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry, Table II (September 1995). Using Table II data and performing sample calculations with the residue values in the present submission, we determined anticipated residues in eggs that were identical to those in the present submission, and anticipated residues in milk 50% higher than those in the present submission.

Conclusion 8: CBRS generally determines anticipated residues in meat byproducts for cattle and poultry, translates anticipated residues in cattle commodities to goat and sheep, and determines anticipated residues in swine commodities, as appropriate. The present submission did not include these commodities.

Conclusion 9: The present submission determined anticipated residues for "beef" and "poultry" by apportioning residues from muscle and fat of each animal category. We defer to DRES on whether the proportions used are appropriate based on consumption data.

As noted above, a percent crop treated adjustment was applied to the dietary assessment, but at the point of determining consumption rates. Within HED, percent treated data for food commodities are applied during the DRES run, if anticipated residues were based on field trial data. For animal feed items, CBRS uses percent crop treated data in determining residues in animal diets. This approach would be required if multiple crops with different percent treated factors represent animal feed items. In the present case, where only one crop contributes to the risk, the percent treated adjustment could be made at later points in the assessment.

We note that CBRS generally uses percent crop treated data that have been confirmed by BEAD. In the case of a proposed new use, percent treated data may not be appropriate for risk assessment. The present submission notes that propazine use on sorghum is expected to fill a niche use in CO, KS, NM, OK, and TX. According to Agricultural Statistics, 1993, U.S. Department of Agriculture, KS and TX together account for 60% of U.S. sorghum production (data for 1991), and CO, NM, and OK together account for 6.4% more. Even if registration were restricted to the

designated five state region, the ultimate market for this new use could be considerable.

However, if propazine risks are to be assessed as part of special review with other triazines, then percent crop treated data may be appropriate. Dietary risks for atrazine, for example, were assessed assuming use on 70% of sorghum (Memo, 6/7/93, J. Abbotts). The considerations above lead to the following comment:

Conclusion 10: The present submission includes an adjustment for percent crop treated of 7%. For its risk assessments, HED generally uses percent treated data that have been confirmed by BEAD. For a proposed new use, percent treated data may not be appropriate. Even if the proposed use is restricted to a designated five state target area, those states represent 66% of U.S. sorghum production. However, if propazine risks are to be assessed as part of special review with other triazines, then percent treated data may be appropriate.

We believe that the above comments address the major components of dietary exposure assessment in the present submission.

Drinking Water

We have one comment on this topic:

Conclusion 11: We expect that EFED will have detailed comments on the drinking water section of the present submission, but assignment instructions to CBRS specifically requested review of this section. We note that the present submission based its assessment on residues of parent propazine in drinking water. Consistent with the decisions of the HED Metabolism Committee (see Conclusion 6), the presence of propazine metabolites in drinking water could also be of toxicological concern.

Our overall evaluation is provided in the Recommendations section above.

cc:Abbotts, RF, Propazine List A File, SF
RDI:ARRathman:5/6/96:RBPerfetti:5/13/96:EZager:5/13/96
7509C:CBII-RS:JAbbotts:CM-2:Rm805A:305-6230:5/14/96
■JA17\propazin.3

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

MAY 20 1996

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of handler exposure assessment submitted in response to the Propazine Grassley-Allen letter.

TO: Kathryn Boyle
Risk Characterization and Analysis Branch (7509C)

FROM: Jim Carleton, Chemist

THRU: Francis B. Suhre, Section Head
Special Review and Reregistration Section

Larry C. Dorsey, Chief
Occupational and Residential Exposure Branch
Health Effects Division (7509C)

DP Barcode:	D222622, D224748
Pesticide Chemical Codes:	080808 Propazine
EPA Reg. Nos.:	N/A
EPA MRID Nos.:	N/A
Review Time:	10 days
PHED:	yes

I. BACKGROUND

OREB has reviewed the worker exposure portions of a human health hazard assessment for Propazine, submitted by Griffin Corp. in response to the Propazine Grassley-Allen letter. The report employs data from the Pesticide Handlers Exposure Database (PHED) to estimate unit exposures, then extrapolates these values into estimated doses based upon label application rates, and usage data obtained from the 1992 Census of Agriculture.

II. DETAILED CONSIDERATIONS

The following problems/deficiencies were noted in the methodology used to derive unit exposure values from PHED:

- In estimating exposure to handlers who both mix/load and apply pesticides, it is inappropriate to average data obtained from the MLAP file (mixer/loader/applicator) with data obtained from the MIXLD (mixer/loader) and APPL (applicator) files. For propazine use on ornamentals, mixer/loader/applicator (M/L/A) exposures should be modeled using only the MLAP file. This results in an estimated total unit exposure (dermal + inhalation) of 899.4748 μg/lb active ingredient.

- In estimating exposure to mixer/loaders for sorghum application, it is inappropriate to exclude data from studies with tank/hoppers less than 100 gallons. The report's authors quote a figure of 124 acres per farm average for sorghum in the state of Kansas. Based on the a.i. concentration of 4 lb/gal, and assuming an application rate of 1.2 lb a.i./A, this results in an estimate of only 37 gallons of Propazine 4L used per farm per treatment, *on average*. When data are not subsetted by tank/hopper size, the estimated total unit exposure is 43.7331 μg/lb active ingredient.

- In estimating exposure to open cab groundboom applicators, subsetting should include closed cabs with windows open, in addition to open cab studies. Subsetting for application methods should include groundboom truck, as well as groundboom tractor. When the data are subsetted this way, the estimated total unit exposure is 15.6808 μg/lb active ingredient.

- Data from open and closed cab applications should not be combined. In estimating exposure to aerial applicators, there are sufficient data only to model a closed cab scenario. It is also inappropriate to subset in such a fashion as to remove the low application rate data. When dermal grades A,B, and C are selected (in order to generate a sufficient number of replicates), the estimated total unit exposure for closed cab application is 5.3091 μg/lb active ingredient.

The following problems/deficiencies were noted in the methodology used to extrapolate estimated doses from unit exposures:

- The report's authors made an assumption of 2 percent dermal absorption, based on comparison with other triazines. However, as EPA has not defined a chemical specific

absorption factor for propazine, it is inappropriate at this time to assume that dermal absorption is less than 100 percent (K. Boyle, personal communication, 5/96).

The authors estimated amortized annual average daily doses, and lifetime average daily doses, but did not calculate short or intermediate term doses. EPA has not yet established a toxicological end point for propazine, therefore it is inappropriate to exclude short and intermediate term doses, especially as these will tend to be substantially higher than average long term doses. This review corrects that omission by including estimates of short term, average daily doses (ADDs).

III. CONCLUSIONS

The following table summarizes the correct unit exposures and estimated doses as determined by OREB. In order to extrapolate the doses, OREB employed the assumption that the usage and farm size data presented in the report are correct. However these values have not been verified by BEAD, therefore the doses presented here are subject to change based upon updated use/usage information. For ornamental handlers, the maximum label rate of 1.5 lb/A/day is assumed, and a total of 4.5 lb/A/yr, for one acre treated in one day. For sorghum groundboom application, the maximum label rate of 2.4 lb/A is assumed, along with 290 A/day, and 2 days/yr, for a total of 590 A/yr treated by a commercial applicator. For sorghum aerial application (pilots and flaggers) and mixing/loading, 2.4 lb/A is again assumed, along with 1000 A treated in one day, one time per year. All scenarios assume a 70 Kg body weight, and a 40 year career in a 70 year lifetime.

Job Function	Total Unit Exposure (μg/lb a.i.)	Absorbed Daily Dose (ADD) (mg/Kg/day)	Annual Average ADD (mg/Kg/day)	Lifetime Annual Average ADD (mg/Kg/day)
Ornamental M/L/A	899.4748	1.93 E-02	1.58 E-04	9.05 E-05
Sorghum M/L, open pour, for aerial application	43.7331	1.50	4.11 E-03	2.35 E-03
Sorghum Groundboom Commercial App., open cab	15.6808	1.56 E-01	8.54 E-04	4.88 E-04
Sorghum Aerial Appl. (pilot), closed cab	5.3091	1.82 E-01	4.99 E-04	2.85 E-04
Sorghum Flagger	11.7122	4.02 E-01	1.10 E-03	6.29 E-04

cc: J. Carleton, OREB
J. Bailey, SRRD
Chemical file - Propazine

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

JUL - 2 1996

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PROPAZINE; Required Studies for Non-food Greenhouse Use by Griffin Corporation.

Barcode No.: D227218
Submission No.: S493480
PC Code: 080808
Tox Chem No.: 184

TO: Kathryn Boyle
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

FROM: Kit Farwell
Section 3, Toxicology Branch I
Health Effects Division (7509C)

Kit Farwell 6.24.96

THRU: Edwin Budd, Acting Section Head
Section 3, Toxicology Branch I
Health Effects Division (7509C)

Budd 6/25/96
KB 6/25/96

ACTION REQUESTED:

Risk Characterization and Analysis Branch (RCAB) requested Toxicology Branch I to identify which required studies have not been submitted by Griffin Corporation in support of non-food greenhouse use of propazine. Propazine is being treated as a new chemical for purposes of registration and only studies sponsored by or owned by Griffin Corporation are to be considered for this registration.

SUMMARY:

1. This memo only addresses the non-food greenhouse use of propazine. Risk Characterization and Analysis Branch will be requesting information about datagaps for food use at a later date. The datagaps for food use will be addressed in a separate memo.

2. Studies required to support the non-food greenhouse use of propazine are listed in Tables 1 and 2. Requirements tentatively satisfied by Griffin Corporation and outstanding

datagaps are also presented in Tables 1 and 2. Studies sponsored by Griffin Corporation are presently under review and studies purchased by Griffin Corporation will be re-reviewed, so the acceptability of submitted studies may change upon review or re-review.

3. Present datagaps for the non-food greenhouse use are listed below by guideline number. Requirements for several of the listed studies are reserved at this time or are contingent on the results of other studies. Certain other studies need not be submitted at this time. See the comments in Tables 1 and 2 for specific information on each of the datagaps listed below.

81-8	Acute Neurotoxicity - rat
82-3	90-day Dermal Toxicity
82-4	90-day Inhalation Toxicity
82-7	90-day Neurotoxicity - rat
83-2(a)	Carcinogenicity - mouse
83-3(a)	Developmental Toxicity - species A
83-3(b)	Developmental Toxicity - species B
84-2	Bacterial Cell Mutation
84-2	Additional Mutagenicity Studies
85-7	Immunotoxicity

4. The Reference Dose (RfD) Peer Review Committee and the Toxic Endpoint Selection (TES) Committee were scheduled to discuss propazine on 8/15/96 and 8/20/96 respectively. These meetings have been postponed until the complete toxicology database has been submitted by Griffin Corporation. Only studies sponsored by or owned by Griffin Corporation are to be used in support of registration when the RfD and TES Committees meet.

5. The Cancer Peer Review (CPR) Committee will meet as scheduled on 8/28/96 to consider the carcinogenic potential of propazine.

6. Risk Characterization and Analysis Branch also has requested copies of memos which addressed previous datagaps for propazine. Attached is a copy of a Section 18 memo from Toxicology Branch, document date 1/19/96, which referred to gaps in the toxicology database other than Griffin Corporation's datagaps.

DISCUSSION:

Propazine is being treated by Registration Division as a new chemical and only studies sponsored by or owned by Griffin Corporation are to be considered for this registration. Tables 1 and 2 show which guideline studies are required for non-food

greenhouse use of propazine and which requirements have been tentatively satisfied. Notes on the acceptability of submitted studies and comments on toxicity requirements follow the tables. The studies included in Tables 1 and 2 are only those studies sponsored or purchased by Griffin Corporation according to the attached note from Risk Characterization and Analysis Branch (RCAB) dated 6/12/96.

According to the RCAB note, Griffin Corporation has performed and submitted the following acute toxicity studies with both technical and end-use products: acute oral, acute dermal, acute inhalation, primary eye irritation, primary dermal irritation, and dermal sensitization. A metabolism study with technical propazine has also been submitted. The submitted studies are presently being reviewed and may or may not meet guideline requirements for acceptability. Any study found to be unacceptable will have to be replaced with an acceptable study.

The RCAB note also reports that Griffin Corporation has purchased the following studies: 2 year chronic/carcinogenic rat study, rat reproduction study, nucleus anomaly test in nuclei of Chinese hamster, and a V79 Chinese hamster point mutation test.

The 2 year chronic/carcinogenic rat study is undergoing re-review because a re-read of histology slides may have changed the conclusions of the study report. Other studies purchased by Griffin will undergo re-review and may or may not meet current guideline requirements for acceptability. Any study found to be unacceptable will have to be replaced with an acceptable study.

The Reference Dose (RfD) Peer Review Committee and the Toxic Endpoint Selection (TES) Committee were scheduled to discuss propazine on 8/15/96 and 8/20/96, respectively. Datagaps for propazine were discussed, however, in a Health Effects Division management meeting on June 17, 1996, and it was decided to postpone the RfD and TES meetings until the complete toxicology database has been submitted by Griffin Corporation.

The Cancer Peer Review (CPR) Committee will meet as scheduled on 8/28/96. Propazine has been found to cause mammary tumors in Sprague-Dawley rats. Further testing of propazine and/or its metabolites may be required by the Cancer Peer Review committee.

At this time, it is not certain exactly which studies Griffin Corporation purchased. Toxicology Branch I has requested Registration Division to contact Griffin to obtain a listing of specifically which studies have been purchased, their identifying MRID numbers, and a statement detailing which guideline number each study is expected to fulfill. If the listing of purchased studies changes, then the datagaps will also change.

TABLE 1 PROPAZINE TECHNICAL: TOXICOLOGY
STUDIES REQUIRED FOR NON-FOOD GREENHOUSE USE[a]

GUIDE-LINE	STUDY IDENTIFICATION	REQUIRED	TENTATIVELY SATISFIED	COMMENT
81-1	Acute oral toxicity	Yes	Yes (b)	
81-2	Acute dermal toxicity	Yes	Yes (b)	
81-3	Acute inhalation toxicity	Yes	Yes (b)	
81-4	Primary eye irritation	Yes	Yes (b)	
81-5	Primary dermal irritation	Yes	Yes (b)	
81-6	Dermal sensitization	Yes	Yes (b)	
81-7	Delayed neurotoxicity - hen	No	---	
81-8	Acute neurotoxicity - rat	Yes	No	1
82-1(a)	90-day oral, rodent	No	---	
82-1(b)	90-day oral, non-rodent	No	---	
82-2	21-day dermal	No	---	
82-3	90-day dermal	Yes	No	2
82-4	90-day inhalation	Yes	No	3
82-6	28-day delayed neurotox. - hen	No	---	
82-7	90-day neurotoxicity - rat	Yes	No	1
83-1(a)	Chronic feeding - rodent	No	---	
83-1(b)	Chronic feeding - nonrodent	No	---	
83-2(a)	Carcinogenicity - rat	Reserved	Yes (c)	4
83-2(b)	Carcinogenicity - mouse	Reserved	No	4
83-3(a)	Developmental tox. - species A	Yes	No	5
83-3(b)	Developmental tox. - species B	Reserved	No	5
83-4	Reproductive toxicity	No	---	
83-6	Postnatal developmental tox.	No	---	
84-2	Mammalian Cell Mutation	Yes	Yes (c)	6
84-2	Bacterial Cell Mutation	Yes	No	6
84-2	Structural Chromosomal Aberr.	Yes	Yes (c)	6
84-2	Additional Mutagenicity Studies	Reserved	No	7
85-1	Metabolism	Reserved	Yes (b)	8
85-2	Domestic animal safety	No	---	
85-3	Dermal penetration	No	---	
85-4	Visual system studies	No	---	
85-7	Immunotoxicity	Yes	No	1

NOTES ON ACCEPTABILITY OF STUDIES FOR NON-FOOD GREENHOUSE USE OF PROPAZINE TECHNICAL:

(a) Only studies sponsored or owned by Griffin Corporation (according to Risk Characterization and Analysis Branch) are included in this table. See attached note from Kathryn Boyle of RCAB, dated 6/12/96.

(b) This requirement is tentatively satisfied by a study sponsored by Griffin Corporation. Study is being reviewed in accordance with current criteria for acceptability.

(c) This requirement is tentatively satisfied by a study owned by Griffin Corporation. Study is being re-evaluated in accordance with current criteria for acceptability.

COMMENTS ON TOXICITY TESTING REQUIREMENTS FOR NON-FOOD GREENHOUSE USE OF PROPAZINE TECHNICAL:

1. Although required, the lack of this study at this time should not delay registration for this use.

2. When the 21-day dermal study is submitted and evaluated, a judgement will be made as to whether an additional 90-day dermal study will be required.

3. The 90-day inhalation study is required unless Griffin Corporation can demonstrate that use of the end-use-product in greenhouses will not result in respirable droplets and/or use will not result in repeated inhalation exposure at a concentration likely to be toxic.

4. The requirement for carcinogenicity studies in rats and/or mice to support this non-food use is reserved pending assessment of the carcinogenic potential of propazine by the HED Carcinogenicity Peer Review Committee.

5. The requirement for developmental toxicity testing in a second species to support non-food greenhouse use is reserved pending a full evaluation by Occupational and Residential Exposure Branch of the potential exposure to greenhouse workers from this use. Developmental toxicity testing in a second species will be required if significant exposure to human females of child-bearing age may reasonably be expected to occur, or if significant developmental toxicity occurs in the first species.

6. Since propazine is considered a new chemical, the <u>new</u> guidelines for mutagenicity testing are applicable.

7. Additional mutagenicity studies may be required by the HED Carcinogenicity Peer Review Committee to assist in the assessment of the mutagenic and carcinogenic potential of propazine.

8. The requirement for a general metabolism study in rats is reserved pending the decision as to whether carcinogenic studies in rats and/or mice will be required to support this non-food use. If a carcinogenicity study in either species is required, then the metabolism study will also be required.

TABLE 2 PROPAZINE END-USE PRODUCT (PROPAZINE 4L)
TOXICOLOGY STUDIES REQUIRED FOR NON-FOOD GREENHOUSE USE[a]

GUIDE-LINE	STUDY IDENTIFICATION	REQUIRED	TENTATIVELY SATISFIED	COMMENT
81-1	Acute oral toxicity	Yes	Yes (b)	
81-2	Acute dermal toxicity	Yes	Yes (b)	
81-3	Acute inhalation toxicity	Yes	Yes (b)	
81-4	Primary eye irritation	Yes	Yes (b)	
81-5	Primary dermal irritation	Yes	Yes (b)	
81-6	Dermal sensitization	Yes	Yes (b)	

NOTES ON ACCEPTABILITY OF STUDIES FOR NON-FOOD GREENHOUSE USE OF PROPAZINE END-USE-PRODUCT:

(a) Only studies sponsored or owned by Griffin Corporation (according to Risk Characterization and Analysis Branch) are included in this table. See attached note from Kathryn Boyle of RCAB, dated 6/12/96.

(b) This requirement is tentatively satisfied by a study sponsored by Griffin Corporation. Study is being reviewed in accordance with current criteria for acceptability.

Attachment

From: Kathryn Boyle at DCOPP3 6/12/96 11:57AM (1753 bytes: 1 ln)
To: Kit Farwell at DCOPP5, Ed Budd at DCOPP5, Terri Stowe at DCOPP2, JOSEPH BAILEY at DCOPP6, Deborah McCall
Subject: propazine database
---------- Message Contents----------

Kit - This is my understanding of the status of the propazine tox database.

Since this is a registration action only those studies that have been performed by Griffin or purchased by Griffin can be considered in evaluating whether or not there are any data gaps.

Griffin has performed and submitted the following studies:

acute oral
acute dermal
acute inhalation
primary eye irritation
primary dermal irritation
dermal sensitization
metabolism

Griffin has purchased and submitted the following studies:

2 year chronic/carcinogenic rat
reproduction study (rat)
nucleus anomaly test in nuclei of Chinese hamster
V79 Chinese hamster point mutation test

Based on these two lists only (no other studies exist) what data gaps exist for which a study has not even been submitted based on

1) non-food greenhouse use

2) food use (sorghum)

Terri, please realize that the list of data gaps that will be generated is preliminary. If any of these submitted studies are determined to be unacceptable, that will be another/additional data gap.

Kathryn

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

CASWELL FILE

JAN 19 1996

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: **Section 18: PROPAZINE. ID# 96TX0002.** Specific Exemption Request by the State of Texas for Use of Propazine to Control Weeds in Sorghum.

Tox.Chem. No.: 184
PC No.: 080808
Barcode No.: D220613
Submission No.: S495360

FROM: William Dykstra, Ph.D. William Dykstra 11/27/95
Section I, Tox. Branch I
Health Effects Division (7509C)

TO: Teung Chin, Ph.D., Manager, PM Team 41
Andrea Beard, Reviewer, PM Team 41
Emergency Response and Minor Use Section/Registration Support Branch
Registration Division (7505W)

THRU: Roger Gardner, Section Head, Toxicologist
Section I, Tox. Branch I
Health Effects Division (7509C) Roger Gardner for RA 12/15/95
11-27-95

I. CONCLUSIONS

The current toxicology database for propazine is incomplete and does not support the proposed specific exemption to control weeds in approximately 1.82 million acres of grain sorghum in the State of Texas.

Propazine was evaluated by the HED Carcinogenicity Peer Review Committee and has been classified as a C carcinogen without quantitation based on increased incidence of mammary gland adenomas in female rats at high dose in the 2-year feeding study. However, discrepancies in interpretation of the mammary gland histopathology were required to be resolved and the classification is subject to change pending results of currently available independent assessments by the Registrant, Griffin Corporation. It has been learned from oral communication by personnel of the Griffin Corporation that a significant number of female mammary gland tumors in the 2-year rat feeding study with propazine have been reclassified from BENIGN TO MALIGNANT.

THESE DATA HAVE NOT BEEN SUBMITTED TO THE AGENCY AND MUST BE EVALUATED BY THE CPRC BEFORE THE SECTION 18 CAN BE CONSIDERED.

Although no serious developmental or maternal toxicity concerns were identified in the rat developmental toxicity study, TB-I considers developmental toxicity studies in both species (rabbit developmental is a data gap) necessary for evaluation of risk to female farm workers, as well as the general public, from the proposed use pattern, particularly given the unprecedented number of acres involved in this Section 18.

II. ACTION REQUESTED

The Texas Department of Agriculture submitted an application for a specific exemption to use propazine to control weeds in grain sorghum (letter from Donnie Dippel dated 10-13-95). The specific product to be used is Milo-Pro® 4L (43% a.i.; not currently registered with the EPA).

The proposed use involves treatment of up to 1,823,000 acres in the Northern and Southern High Plains, Northern and Southern Low Plains, Cross Timbers, Blacklands, East Texas and Edwards Plateau at a rate of 1.2 lbs a.i. per acre (total maximum of 2,187,600 lbs. a.i.). A single application per growing season would be permitted. It was estimated that about 80% of the application would be with ground equipment and the rest by air. Timing of application would be based on State Agriculture Extension Service specific recommendations for the indicated areas. A 24 hr re-entry period must be observed following application.

III. TOX. BRANCH I COMMENTS

Registration of propazine was voluntarily canceled in 1988 by the Registrant (Ciba-Geigy). The following data gaps remain for propazine: rabbit developmental toxicity (83-3b), 21-day dermal (82-2), general metabolism (85-1) and dermal sensitization (81-6). In addition, mammary gland histopathology slides from the rat 2 yr study must be reread if propazine is to be reregistered again. No toxicology data was submitted since prior to issuance of the Reregistration Standard for propazine in 1987.

Tolerances of 0.25 ppm were established for sorghum commodities while the product was still registered for use by Ciba-Geigy and are still on record (40 CFR 180.243).

IV. RISK/EXPOSURE ASSESSMENT

Applicator exposures and risk were determined for the proposed use pattern by OREB (memo of 11/22/95 form T. Manville to W. Dykstra). The rat developmental study with a NOEL of 10 mg/kg/day for developmental and maternal effects was used to calculate short term MOEs for exposed workers. At the LEL of 100 mg/kg/day, there were decreases in food consumption and body weight in the dams and delayed ossification of skeletal structures in the fetuses.

Calculations were based on a dermal absorption of 100%, because no dermal absorption data is available for propazine. **Dermal penetration of atrazine, a related pesticide, is 20%.** The 21-day dermal toxicity study in rabbits is a data gap and the actual dermal penetration may be less than 100%. Therefore, the actual MOEs may be much greater than the TB-I estimates.

TB-I also calculated two different cancer risks to female farm workers from the Section 18. The Q^*1 cancer risk was determined by the following equation: cancer risk = AADE x 0.17 $(mg/kg/day)^{-1}$ x 2/70. Secondly, a cancer risk to farm workers was calculated using the RfD approach by the following equation: cancer risk = RfD ÷ AADE x 2/70. As stated previously, the dermal penetration of propazine is calculated to be 100%. Actual cancer risk may be significantly less than the calculated risk, based on actual dermal penetration. **Dermal penetration of atrazine, a related pesticide, is 20%.** The Q^*1 of the original malignant mammary gland tumors diagnosis was used as a possible "worst case" scenario, due to oral communication with Griffin Corporation personnel regarding the change in diagnosis from benign to malignant for a significant number of mammary gland tumors in female rats. The RfD approach to cancer risk is based on the latest peer review (1989).

Formulas used in calculations:

Short-term MOE = NOEL (10 mg/kg BW/d) ÷ Exposure (mg/kg BW/d) (Assumes 100% dermal penetration)

OPERATION*	DAILY EXPOSURE (mg/kg/d)	SHORT TERM MOE
Mixer/Loaders-Ground	0.084	119
Applicator-Ground	0.032	312
Mixer/Loaders-Aerial	0.263	38
Applicators-Aerial	0.027	370
Mixer/Loaders -Commercial Aerial	0.347	29
Applicators-Commercial Aerial	0.035	285

"Worst Case" CANCER RISK = AADE X Q^*1 X 2/70 (Assumes 100% dermal penetration)

$Q^*1 = 0.17\ (mg/kg/day)^{-1}$

CANCER RISK = RfD + AADE X 2/70 (Assumes 100% dermal penetration)

OPERATION*	AADE (mg/kg/d)	RfD CANCER RISK	Q^*1 CANCER RISK
Mixer/Loaders-Ground	0.00081	865	3.93×10^{-6}
Applicator-Ground	0.00031	2,257	1.51×10^{-6}
Mixer/Loaders-Aerial	0.00072	972	3.5×10^{-6}
Applicators-Aerial	0.000074	9,478	3.5×10^{-7}
Mixer/Loaders-Commercial Aerial	0.0072	97	3.5×10^{-5}
Applicators-Commercial Aerial	0.00073	972	3.5×10^{-6}

* Minimum clothing requirements are: long-sleeved shirt, long pants, shoes, socks, and chemically resistant gloves for each job function (Worker Protection Standard for Agricultural Pesticides).

Toxicity Data Base:

Series. Study Type	Status	Comments/Significant Findings	Doc.#
81-1. Acute Oral, rat	A	Tox. Category IV	1379 5823
81-2. Acute Dermal, rabbit	A	Tox. Category III (limit test)	1379 5823
81-3. Acute inhalation, rat	A	Tox. Category III	1379 5823
81-4. Primary eye, rabbit	A	Tox. Category III	1379 5823
81-5. Primary dermal, rabbit	A	Tox. Category IV	7419
81-6. Dermal sensitization, guinea pig	NA	DATA GAP	
82-1a. Subchronic, rat	NA		
82-1b. Subchronic, dog	NA		

82-2. 21-Day dermal, rabbit	NA	DATA GAP	
83-1a, 2a. Feeding/onco, rat	A	NOEL = 5 mg/kg/day. LEL = 50 mg/kg/day (decr. body wt.). Incr. incid. mammary tumors in females, 50 mg/kg/day (HDT).[1]	575 4542 5419 5508 5823
83-1b. Chronic feeding, dog	NA	WAIVED	
83-2. Oncogenicity, mouse	A	NOEL = 10 mg/kg/day (myocardial histopath.). No oncogenic effects.	575 4542 5823
83-3a. Developmental toxicity, rat	A	Maternal NOEL/LEL = 10/100 mg/kg/day (decr. food cons., decr. body wt.). Developmental NOEL/LEL = 10/100 mg/kg/day (incr. incid. incompl. skeletal ossific.).	5226 5823
83-3b. Dev. toxicity, rabbit	NA	DATA GAP	
83-4. 2-generation reproduction, rat	A	Reproductive NOEL/LEL = 5 mg/kg/day (decr. pup wt.).	575 4542 5823
84-2a. Gene mutation	A	CHO gene mutation: positive w/o activation; weak positive with activation.	5611 5823
84-2b. Chromosome aberration	A	CHO nucleus anomaly: negative	5226 5823
84-4. Genotoxicity, other mechanism	A	DNA repair, rat: negative	5226 5823
85-1. Metabolism, rat	NA	DATA GAP	
85-3. Dermal absorption	NA		

A Study Acceptable
NA Study Not Available
1 Rereading of mammary histopathology required if product reregistered

Special Toxicology Issues and Problems.

1. Labelling. Propazine is no longer registered for use as a pesticide; it was voluntarily canceled by the manufacturer.

2. Carcinogenicity. Propazine is classified as a C carcinogen with no quantitation based on increased incidence of mammary tumors in female rats (Peer Review Re-evaluation dated 1-10-89; previously assigned quantitation of 1.7×10^{-1} removed

based on single sex benign tumors without dose-response). However, due to discrepancies in mammary tumor counts in histopathology readings of different pathologists, all mammary histopathology slides must be reread if reregistration of this active ingredient is ever pursued. Propazine is a S-chloro-triazine and is related to other similar pesticides which induce malignant mammary gland tumors in female rats. These pesticides include atrazine, terbutryn, cyanazine (voluntarily canceled) and others.

3. RfD. An RfD of 0.02 mg/kg/day was established based on the NOEL of 5 mg/kg/day from the rat chronic feeding study and an uncertainty factor of 300 (extra 3 for data gaps). This value was verified by the Agency RfD Workgroup on 5-20-87.

4. Non-carcinogenic risk assessment. At this time there are no known non-carcinogenic risk assessment concerns for propazine other than the RfD; however, the toxicology database is not complete. Important missing studies needed to evaluate the risks to the public as well as farm workers are (a) rabbit developmental (b) re-read of mammary gland tumor slides in female rats in 2-year rat study (c) 21-day dermal study and (d) rat metabolism study.

5. Mutagenicity/genetic toxicity comments. Propazine produced a dose-related mutagenic response without activation and a weak response with activation in the Chinese hamster ovary point mutation assay but was negative in the other assays submitted to support reregistration.

6. Dermal Penetration. Data on dermal penetration is not available for propazine.

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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: TEXAS SECTION 18 REQUEST (96TX0002) TO USE PROPAZINE (MILO-PRO 4L HERBICIDE) ON GRAIN SORGHUM TO CONTROL WEEDS

FROM: Tina Manville, Biologist
Special Review and Registration Section II Tina Manville

TO: William Dykstra, Ph.D.
Toxicology Branch I
Health Effects Division (7509C)

THRU: Mark I. Dow, Ph.D., Section Head Carol E. Long for Mark Dow
Special Review and Registration Section II

Larry C. Dorsey, Chief
Occupational and Residential Exposure Branch
Health Effects Division (7509C)

Please find below, the OREB review of:

DP Barcode: D220614

Pesticide Chemical Code: 080808

EPA Reg. No.: _____

PHED: Yes, Version 1.1

TABLE ONE. SECTION 18 DETAILS	
Crop	Sorghum
Pest	weeds
Application method	ground boom (open cab) aerial (closed cab)
Max. application rate	1.2 lb ai/acre
Min. final spray volume	ground - 10 gal/acre air - 3 gal/acre
No. of applications	1 per crop growing season
Max acreage	1,823,000 acres
Manufacturer	Griffin Corp.
Use period	does not specify start date, ends August 1, 1996
Average sorghum farm size[1]	286 acres

1. 1992 Census of Agriculture, Vol. 1, part 43b, Ch. 2, Table 26. Grains: 1992.

OREB's exposure assessment is based on the following assumptions (Table Two. Assumptions):

TABLE THREE: PROPAZINE SECTION 18 WORKER EXPOSURE			
APPLICATION METHOD	WORKER	DAILY EXPOSURE µg/kg/day	Average Annual Daily Exposure µg/kg/day
Ground boom	Mixer/loader	84	0.81
	Applicator	32	0.31
Aerial	Mixer/loader	263	0.72
	Applicator	27	0.074
Commercial Aerial	Mixer/loader	347	7.2
	Applicator	35	0.73

For calculations please see appendix.

Mixer/loader and ground applicator exposures are based on an open pour and open cab scenario with the worker wearing long pants, long sleeved shirt, shoes and socks, and gloves. The aerial applicator exposure is based on a closed cockpit with the worker wearing long pants, long sleeved shirt, and shoes and socks. Aerial application to the average size sorghum farm can be accomplished in one day however OREB believes most aerial application is done by commercial applicators who can be reasonably assumed to treat 10 farms a year.

The Milo-Pro label states that the following personal protective equipment (PPE) are required: long pants and long-sleeved shirt, waterproof gloves, and shoes plus socks. This is in accordance with the Worker Protection Standard (WPS). The REI for Milo-Pro listed on the label is 24 hours, which is in agreement with WPS.

Attachments

cc: T. Manville
Chemical File: **PROPAZINE 080808**
Correspondence

Mixer/loader AADE:

347 µg/kg/day x 1 day/year ÷ 365 days/year = **0.72 µg/kg/day**

Applicator DE:

4.7 µg/lb a.i. x 343lb a.i./day ÷ 60 kg = **27 µg/kg/day**

Applicator AADE:

35 µg/kg/day x 1 day/year ÷ 365 days/year = **0.074 µg/kg/day**

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Commercial Aerial Application:

Total A.I. handled per day:

assume that worker will treat maximum possible number of acre/day = 377
1.2 lb a.i./acre x 377 acres/day = 452 lb a.i./day

Mixer/loader DE:

46 µg/lb a.i. x 452 lb a.i./day ÷ 60 kg = **347 µg/kg/day**

Mixer/loader AADE:

Assume that a commercial worker would treat 10 sorghum farms/year .
286 average farm size ÷ 377 acres applied/day = 0.76 day/farm
0.76 day/farm x 10 farms/year = 7.6 days/year

347 µg/kg/day x 7.6 day/year ÷ 365 days/year = **7.2 µg/kg/day**

Applicator DE:

4.7 µg/lb a.i. x 452lb a.i./day ÷ 60 kg = **35 µg/kg/day**

Applicator AADE:

35 µg/kg/day x 7.6 day/year ÷ 365 days/year = **0.73 µg/kg/day**

YSNG(BEAD) Estimate of Acres Treated by Various Application Methods

11/08/95

Site: SORGHUM Chem: PROPAZINE Hrs/day: 8.0 hr.
Appl. method: GROUND Speed: 4.0 (increment: 1) mph
Tank capacity(TC): 350 (Increment: 50) gal Length of run(LR): 2000 ft.
Swath width(SW): 26 (Increment: 6) ft. Water station(WS): 200 yd.
Finish spray(FS): 10 (Increment: 2) gal. Refill time(RT): 9.0 min
** Recommand: Ground -- RT = 2-3 mins. per 100 gal TC; LR = 1000 ft; **********
WS = varies; Ferry speed = speed * 2.0; Turning time = 0.25 min.

350 TC	4.0 mph				5.0 mph				6.0 mph				7.0 mph			
FS	10	12	14	16	10	12	14	16	A 10	12	14	16	10	12	14	16
26	81	78	76	73	96	93	89	86	C 111	106	102	98	124	118	113	108
SW 32	96	92	89	86	114	109	104	100	R 130	123	118	113	144	137	130	124
38	110	105	101	97	129	123	117	112	E 147	139	132	125	163	153	145	137

400 TC	4.0 mph				5.0 mph				6.0 mph				7.0 mph			
FS	10	12	14	16	10	12	14	16	A 10	12	14	16	10	12	14	16
26	81	78	76	73	96	93	90	86	C 111	106	102	98	124	118	113	108
SW 32	96	92	89	86	114	109	104	100	R 130	124	118	113	145	137	130	124
38	110	105	101	97	130	123	118	112	E 147	139	132	126	163	153	145	137

Make life easier, hit "PrtSc" to get a hard copy, than hit any key to continue

YSNG(BEAD) Estimate of Acres Treated by Various Application Methods

11/08/95

Site: SORGHUM Chem: PROPAZINE Hrs/day: 3.0 hr.
Appl. method: AERIAL Speed: 110.0 (increment: 10) mph
Tank capacity(TC): 400 (Increment: 50) gal Length of run(LR): 2000 ft.
Swath width(SW): 60 (Increment: 10) ft. Water station(WS): 8800 yd.
Finish spray(FS): 3 (Increment: 1) gal. Refill time(RT): 9.0 min
** Recommand: Aerial -- RT = 1-2 min. per 100 gal TC; LR = 2640 ft(.5 mile); ** Hrs/day=2-4; WS=8800 yd(5 miles), Ferry speed=speed; Turning time=0.25 mim.

400 TC	110.0mph				120.0mph				130.0mph				140.0mph			
FS	3	4	5	6	3	4	5	6	3	4	5	6	3	4	5	6
60	377	310	263	228	385	316	267	232	392	321	271	235	398	325	275	238
SW 70	397	323	272	235	405	329	277	239	412	334	281	242	418	338	284	245
80	413	334	280	241	421	339	284	245	428	344	288	248	434	349	292	251

450 TC	110.0mph				120.0mph				130.0mph				140.0mph			
FS	3	4	5	6	3	4	5	6	3	4	5	6	3	4	5	6
60	381	313	266	231	388	319	270	234	395	324	274	238	401	328	278	241
SW 70	401	326	275	238	409	332	280	242	415	337	284	245	421	341	287	248
80	417	337	283	244	425	343	287	247	432	348	291	250	438	352	295	253

Make life easier, hit "PrtSc" to get a hard copy, than hit any key to continue

13544

R058924

Chemical:	**Propazine**
PC Code:	**080808**
HED File Code	**14000 Risk Reviews**
Memo Date:	**08/07/96 12:00:00 AM**
File ID:	**DPD224149; DPD224185**
Accession Number:	**412-04-0046**

HED Records Reference Center
03/25/2004