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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

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.

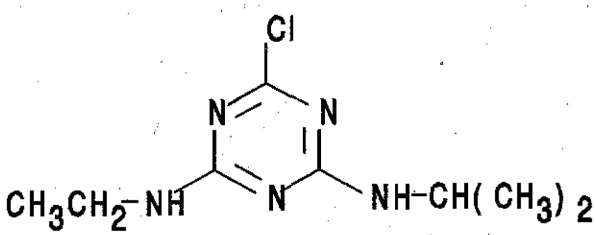
9. The present submission determined anticipated residues for "beef" and "poultry" by apportioning residues from muscle and fat of each animal category. We defer to DRES on whether the proportions used are appropriate based on consumption data.

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.

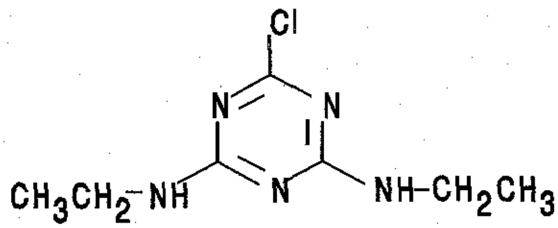
11. We expect that EFED will have detailed comments on the drinking water section of the present submission, but assignment instructions to CBRS specifically requested review of this section. We note that the present submission based its assessment on residues of parent propazine in drinking water. Consistent 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

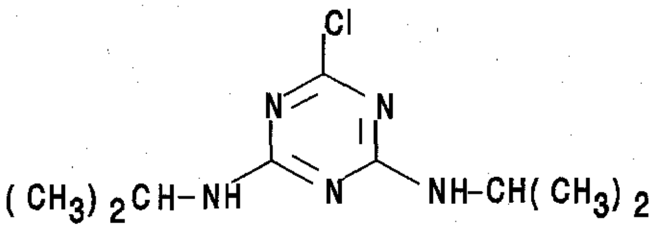
The present submission followed an approach similar to that which CBRS would take in conducting exposure assessment. However, that approach differed from CBRS procedures in both general and specific features. In some cases, such as Conclusion 6, these differences could result in a higher dietary risk 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 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 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 <u>Agricultural Statistics, 1993</u>, 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

13544

057122

Chemical:	Propazine
PC Code:	080808
HED File Code	16000 Water Assessment Reviews
Memo Date:	05/14/96
File ID:	DPD222623; DPD224749
Accession Number:	412-03-0019

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