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

8/7/1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Atrazine (080803), Reregistration Case No. 0062.
Special Review. Ciba-Geigy Comments on the
Triazine PD1; Dietary Risk Assessment.
CBRS No. 15630, DPBarcode No. D215553, MRID 43598633.

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

THRU: Francis B. Suhre, Section Head
Special Review Section II
Chemistry Branch II - Reregistration Support
Health Effects Division [7509C]

TO: Joseph Bailey, PM Team 63
Special Review Branch
Special Review and Reregistration Division [7508W]

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

Special Review of triazine herbicides, including atrazine, has been initiated (59 FR 60412, 11/23/94, PD1). Ciba-Geigy Corporation has submitted comments in response, including a dietary risk assessment for atrazine; the present submission represents Volume 38 of the Registrant's comments. Assignment instructions are to review the present submission in response to the PD1 and provide evaluation for PD2/3. The conclusions below pertain to the present submission, and its relation to the Agency position in the PD1.

Tolerances are established for residues of the herbicide atrazine, 2-chloro-4-ethylamino-6-isopropylamino-s-triazine, in or on various raw agricultural commodities (40 CFR 180.220(a)), and for combined residues of atrazine and its metabolites 2-amino-4-chloro-6-ethylamino-s-triazine,

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2-amino-4-chloro-6-isopropylamino-*s*-triazine, and
2-chloro-4,6-diamino-*s*-triazine, in or on specified plant
commodities (40 CFR 180.220(b)). Designations for the

metabolites in the tolerance expression are G-28279, G-30033, and G-28273, respectively; structures are indicated in Figure 1. Atrazine is a List A Chemical. The Residue Chemistry Chapter was issued 7/25/83; the Registration Standard (Guidance Document) was issued 9/85; a Second Round Review (SRR) Residue Chemistry Chapter was issued 10/18/88.

Conclusions on This Submission

1. Assignment instructions indicate that a copy of this document was also provided to DRES. CBRS defers to DRES with regard to matters relevant to the model used to estimate dietary risk.
2. The present submission contains combined anticipated residues for parent and chloro metabolites, based on residue data submitted as separate volumes of the Registrant's comments on the PD1. CBRS has separately examined those comments on the magnitude of the residues in corn and sorghum, and concluded that a detailed review was not needed at this time since the present Agency position is that exposure assessment should be based on the best available data for total triazine ring residues (CBRS 15629, 15635, 15636, 8/1/95, J. Abbotts).
3. The present submission estimates dietary risk based on a reference dose (RfD) as the relevant toxicological concern. This is inconsistent with the Agency position that cancer risk for dietary assessment should be quantified based on a cancer potency factor, or Q_1^* , assigned by the Agency (59 FR 60417, 11/23/94).

Conclusion with Regard to the PD1

The present submission reports dietary risk assessment for atrazine based on assumptions that are not consistent with the Agency position, as described in Conclusions 2 and 3 above. In addition, CBRS has previously determined anticipated residues for atrazine and its three chloro metabolites (DEB 5783, 5/3/90, M.S. Metzger). CBRS does not believe that detailed review of the present submission is necessary at this time. The Agency does not preclude the possibility that the assumptions underlying exposure assessment may ultimately be altered. Should the Agency position on the residues of concern change in such a way that the data in the present submission would be appropriate, then CBRS will consider the submission in determining anticipated residues for dietary risk assessment for preparation of a PD2/3.

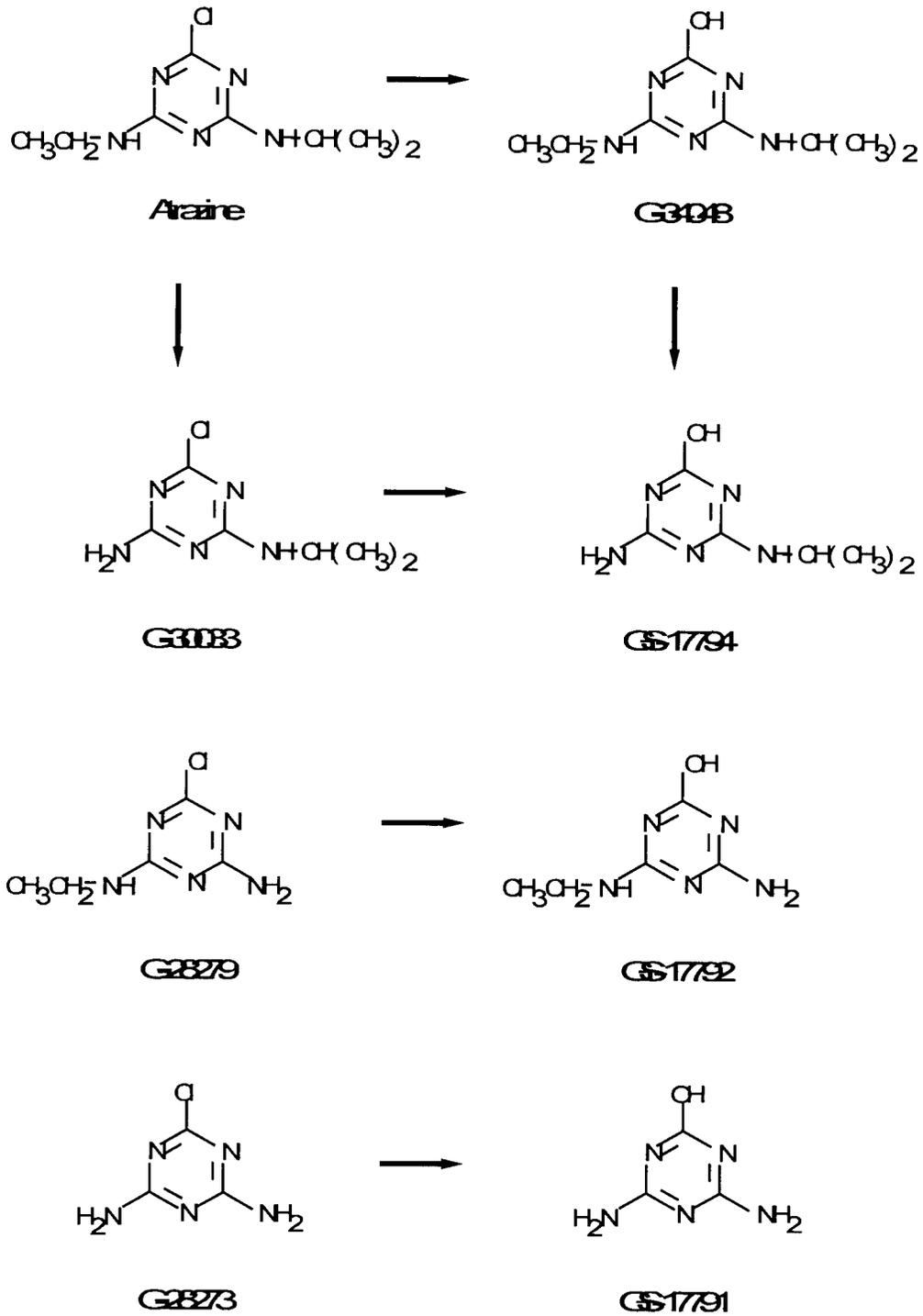


Figure 1. Atrazine, chloro (left), and hydroxy metabolites

Background

As part of its response (Volume 38 of 54) to the FR notice initiating special review, the Registrant submitted the following document:

Dietary Risk Exposure Assessment for Atrazine, Report ABR-94021, Ciba-Geigy Corporation, Greensboro, NC, March 7, 1995 (MRID 43598633).

This submission provides combined anticipated residues for atrazine and its chloro metabolites G-30033, G-28279, and G-28273 in plant and animal commodities. These anticipated residues are then used to calculate dietary risk, based on a reference dose (RfD) for chronic risk.

CBRS Comments

The first conclusion pertains to assignment instructions:

Conclusion 1: Assignment instructions indicate that a copy of this document was also provided to DRES. CBRS defers to DRES with regard to matters relevant to the model used to estimate dietary risk.

The initiation of special review on the triazines describes the Agency's position pertaining to triazine metabolism and residues of concern. The full FR notice contains more detail, but the following excerpts outline the Agency position (59 FR 60412, 11/23/94):

"In estimating triazine dietary risks, the Agency assumes that the total toxic residue of concern is the parent triazine compound plus all metabolites with a triazine ring, including among others, all chloro and hydroxy metabolites."

"Based on its assessment of the structure-activity relationship and potential carcinogenicity of all registered triazine compounds, EPA believes metabolites which have been dechlorinated may be less potent carcinogens than the parent compounds.... However, in the absence of completed laboratory studies of the hydroxy metabolites, the Agency has relied on its equivalency policy and has made the assumption that all metabolites containing the triazine ring are equipotent as carcinogens as the parent compound when conducting its risk assessment." (59 FR 60418-60419)

The Agency position is consistent with the most recent decision of the HED Metabolism Committee on triazine chemicals (Memo, 8/7/92, M.S. Metzger). The Committee noted that in the absence of data on the toxicity of triazine metabolites, all metabolites containing a triazine ring with a substituent would be assumed

toxicologically equivalent to the parent compound. Should data be reviewed and accepted which indicate that hydroxyatrazine is not carcinogenic, then the exposure assessment for atrazine will include only parent and chloro metabolites. No analytical methods were available to determine total residues of metabolites containing triazine rings with substituents. Field studies using ¹⁴C-atrazine would allow exposure assessment for total triazine ring residues as the total radioactive residue (TRR), because most of the radioactivity remains as triazine-ring containing metabolites; TRR will be assumed to represent all residues of concern.

The Agency therefore does not preclude the possibility that exposure assessment for cancer could be limited to combined residues of parent and chloro metabolites. However, at the present time, the Metabolism Committee has not altered its previous decision, and total triazine ring residues remain the appropriate value for exposure assessment.

Chemistry Branch has previously determined anticipated residues for atrazine, for combined residues of parent plus the three chloro metabolites, for agricultural commodities (DEB 3688-3703, 3756, 9/14/88, M.S. Metzger). Anticipated residues were revised to reflect total triazine residues for corn, sorghum, and animal commodities, based on metabolism data (DEB 5783, 5/3/90, M.S. Metzger). Modest revisions were subsequently made to anticipated residues for total triazine ring, based on data from field metabolism studies in corn and sorghum (Memo, 6/7/93, J. Abbotts).

These considerations lead to the following conclusion:

Conclusion 2: The present submission contains combined anticipated residues for parent and chloro metabolites, based on residue data submitted as separate volumes of the Registrant's comments on the PD1. CBRS has separately examined those comments on the magnitude of the residues in corn and sorghum, and concluded that a detailed review was not needed at this time since the present Agency position is that exposure assessment should be based on the best available data for total triazine ring residues (CBRS 15629, 15635, 15636, 8/1/95, J. Abbotts).

We note in addition that the present submission calculated dietary risk based on an RfD, which leads to the following conclusion:

Conclusion 3: The present submission estimates dietary risk based on a reference dose (RfD) as the relevant toxicological concern. This is inconsistent with the Agency position that cancer risk for dietary assessment should be quantified based on a cancer potency factor, or Q₁*, assigned by the Agency (59 FR 60417, 11/23/94).

These considerations lead to the following overall conclusion:

Conclusion with Regard to the PD1: The present submission reports dietary risk assessment for atrazine based on assumptions that are not consistent with the Agency position, as described in Conclusions 2 and 3 above. In addition, CBRS has previously determined anticipated residues for atrazine and its three chloro metabolites (DEB 5783, 5/3/90, M.S. Metzger). CBRS does not believe that a detailed review of the present submission is necessary at this time. The Agency does not preclude the possibility that the assumptions underlying exposure assessment may ultimately be altered. Should the Agency position on the residues of concern change in such a way that the data in the present submission would be appropriate, then CBRS will consider the submission in determining anticipated residues for dietary risk assessment for preparation of a PD2/3.

cc:Circ, Abbotts, RF, Atrazine List A File, SF
RDI:FBSuhre:7/17/95:RBPerfetti:7/26/95:EZager:8/1/95
H7509C:CBII-RS:JAbbotts:CM-2:Rm805A:305-6230:8/7/95
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