R.F

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

MAY 1 1986

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP #6G3353 1,3-Dichloropropene (Telone II™) in or on various raw agricultural commodities. Evaluation of the analytical method and residue data. Accession No. 261117 and RCB #512.

FROM: John M. Worthington, Chemist
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TO: Henry M. Jacoby, PM. No. 21
Registration Division (TS-767)
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THRU: Charles L. Trichilo, Chief
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The Dow Chemical Company, Agricultural Products Department, proposes that a temporary tolerance be established for residues of the insecticide/nematocide, 1,3-dichloropropene (Trade name Telone II) and its metabolite, 3-chloroallyl alcohol, in or on almonds, cherries, citrus fruits, grapes, peaches, plums and walnuts at 0.01 ppm.

No permanent tolerances have been established for 1,3-dichloropropene. Telone II is currently registered for use on a variety of agricultural crops as non-food uses. Temporary tolerances for residues of 1,3-dichloropropene and its metabolite, 3-chloroallyl alcohol, in or on various raw agricultural commodities were granted and extended pursuant to PP #0G2392. PP #6G3352 proposing temporary tolerances for residues of Telone II in or on cottonseed and soybeans is also currently pending.

The proposed three year experimental program involves the treatment of 1310 acres of almonds, cherries, citrus fruits, grapes, peaches, plums and walnuts in ten states with a maximum of 393,055 lbs. a.i.

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Conclusions

1. The fate of 1,3-dichloropropene in plants and animals has been adequately delineated for the purpose of the proposed temporary tolerance. 1,3-dichloropropene, per se, and its metabolite, 3-chloroallyl alcohol are considered the principal residues of concern.

2. The proposed analytical methods are adequate to enforce the proposed temporary tolerance.

3a. For the purpose of the proposed temporary tolerance only, RCB can conclude that no detectable residues will result in treated crops soybeans from the proposed use.

3b. RCB also concludes that no processing fraction studies are needed for the purpose of the proposed temporary tolerance.

4. The proposed use falls under Category 3 of Section 180.6(a), for the purpose of the proposed temporary tolerance

5. The currently available description of the manufacturing process does not provide adequate detail. Further, additional analyses of the technical product will be required for a favorable recommendation. (See the attached Confidential Appendix for a list of ingredients and the specific requirements for a favorable recommendation.)

Recommendations

1. Residue Chemistry Branch recommends against the establishment of the proposed temporary tolerance for the reasons cited in Conclusion #5.

2. For a favorable recommendation, the submission of information specified in the the attached Confidential Appendix will be required.

3. The following will be required for future permanent tolerance:

   a) The submission of additional residue data reflecting the maximum application rates for each type of treatment. The additional data should determine the highest expected residue level for at least one crop from each crop grouping to be treated. Care should be taken so that samples are analyzed as soon as possible after harvest. The additional data must include interval between harvest and analysis for each sample.

   b) If any real residues of any additional toxicologically significant metabolites are found in the additional metabolism study required in connection with PP #6G3352 (See

the memo dated 5/1/86 by J. Worthington), or if it is determined that the new formulation results in detectable residues of 1,3-dichloropropene, per se, or its metabolite, 3-chloroallyl alcohol, ruminant and poultry metabolism data, additional analytical methodology and corresponding residue data, and appropriate conventional cattle and poultry feeding studies will be required for the additional metabolites.

Detailed Considerations

Formulation

Technical 1,3-dichloropropene is approximately 94% pure. The petition does not specifically state the nature of the formulated product. RCB is assuming that technical 1,3-dichloropropene is the agricultural product to be applied.

The currently available description of the manufacturing process does not provide adequate detail. Further, additional analyses of the technical product will be required for a favorable recommendation. (See the attached Confidential Appendix for a list of ingredients and the specific requirements for a favorable recommendation.)

Proposed Use

A single post plant injection of 1,3-dichloropropene at rates ranging from 9.9 to 303 lbs a.i. per acre, or one or two post plant irrigation water treatments at rates ranging from 50.5 to 151.5 lbs. a.i. per acre are recommended for the control of various nematodes and soil pests in almonds, cherries, citrus fruits, grapes, peaches, plums and walnut orchards. A maximum of 151.5 lbs. a.i. per acre per year may applied by water irrigation treatments. No additional use restrictions regarding residues in treated crops have been imposed.

Nature of the Residue

The fate of 1,3-dichloropropene applied to the soil has been investigated in several previously submitted radiotracer studies. No new metabolism studies have been submitted in support of this petition. A study with uniformly labeled ^{14}C-1,3-dichloropropene was conducted on sugar beets grown in California. The plants were treated at a rate equivalent to 250 lbs. a.i./acre 10 to 14 days before planting. The mature beets were harvested 159 days after planting. Radioactivity was detected through out the treated plants. Concentrations in the beets averaged 0.6 ppm while the levels in the tops ranged between 0.94 and 7.61 ppm. Sucrose was isolated from the treated beets, subjected to yeast fermentation, and the released carbon dioxide analyzed to determine the concen-

tration of labeled vs unlabeled carbon. Approximately 0.68 ppm of the sucrose carbon was shown to be derived from the applied 1,3-dichloropropene.

Samples of the raw beets were also exhaustively extracted with hot ethanol, the alcohol evaporated from the extract, and the residual aqueous solution washed with pentane and treated with Dowex 50W to remove cations and then Dowex 1 to remove anions. The residual solids were then extracted with hot sodium hydroxide. The solids remaining from that extraction were then extracted with hydrochloric acid. The material solubilized by the sodium hydroxide was treated with trichloroacetic acid to precipitate a crude protein fraction. An amino acid fraction was released from the Dowex 1 with sodium hydroxide. All of the various fractions contained labeled activity. However, only about 61% of the expected activity was recovered from the whole beet samples. The experiments were repeated in an all glass system to permit a material balance study on all fractions including any labeled volatile carbon. The recovery from these experiments was 74.5% with approximately 8, 6, and 12.5% absorbed by the Dowex 50W, the Dowex 1, and Norite filter medium, respectively.

A search for metabolites of 1,3-dichloropropene was also conducted. Any metabolite could be identified because it would have a much higher level of activity than any plant constituents with incorporated labeled carbon. Again a series of fractionations similar to those described above were completed. The eluate from the Dowex 1 resin was made basic and evaporated to dryness under vacuum. The residue was then taken up in hydrochloric acid and extracted with diethyl ether on a continuous liquid-liquid extractor for four days. The ether removed about 30% of the activity which was shown to be oxalic by infrared analysis. The aqueous portion was reduced to dryness, taken up in ether, methylated with diazomethane and various metabolites separated by gas chromatography. One fraction contained the equivalent of 400 ppm 1,3-dichloropropene, which was well above the highest level (16.6 ppm) found of incorporated activity. These and additional experiments confirmed the presence of an acidic metabolite that could be easily methylated. The unknown metabolite could not be solublized without an acid hydrolysis step and its methylated derivative had a retention time approximately five times longer than the common organic acids. Comparison of retention times with the methylated derivative of 3-chloroacrylic acid, a possible metabolite of 1,3-dichloropropene demonstrated that the metabolite was not 3-chloroacrylic acid. Attempts to isolate enough material for further analysis by additional techniques have not been successful. The unknown metabolite accounted for no more than 5% of the total residue or about 0.03 ppm.

Another study with ^{14}C labeled 1,3-dichloropropene and 3-chloroallyl alcohol was conducted with bush beans, tomatoes and carrots grown from solution culture or vermiculite. The beans, carrots and tomatoes were grown until they were well established and then

treated with labeled and unlabeled ^{14}C labeled 1,3-dichloropropene and 3-chloroallyl alcohol. Autoradiograms demonstrated detectable levels of activity throughout the plant 24 hours after treatment. Plant samples were extracted with 80% ethanol and acidic, basic and neutral ethers. The extracts which corresponded to 33%, 20%, 9% and 1% of the total activity detected in the plants, respectively, were partitioned against a variety of solvents and subjected to thin layer, paper, ion exchange, silica gel and Florosil column chromatography to isolate the various metabolites. Final determinations were made using a gas chromatograph equipped with an electron capture detector. The residual unextracted activity was reported to be only about 1% of the total; however, no explanation of the unaccounted 30-40% of the residue has been presented.

A wide variety of individual plant constituents, including sugars, organic acids, amino acids, lipids, cellulose, and pigments were isolated. Labeled carbon was shown to be incorporated into all of these natural plant constituents. The study indicates that within 48 hours 2/3 of the absorbed activity had been incorporated into natural plant components. No 1,3-dichloropropene, per se, was detected after 48 hours. Residues of 3-chloroallyl alcohol, 3-chloroacrylic acid and 3-chloro-1-propanol were detected after 48 hours. No specific statement is made as to the limit of detection, but the data reported indicate a sensitivity of about 1 ppb.

RCB concludes that for the purpose of proposed temporary tolerance, the fate of 1,3-dichloropropene (DCPE) in plants has been adequately delineated in plants. DCPE is rapidly absorbed and catabolized into natural plant constituents. Residues of the parent compound were no longer detectable after 48 hours. The principal residues of concern are 1,3-dichloropropene per se, and its metabolite, 3-chloroallyl alcohol.

No radiolabeled metabolism data investigating the fate of 1,3-dichloropropene in animals have been submitted to support the proposed temporary tolerance. For the purpose of the proposed temporary tolerance, Residue Chemistry Branch can conclude that no detectable residues 1,3-dichloropropene or its metabolite, 3-chloroallyl alcohol, will result in the treated crops from the proposed use. Therefore, for the purpose of the proposed temporary tolerance RCB can conclude that the proposed use falls under Category 3 of Section 180.6(a).

However, for a future permanent tolerance, if any real residues are found in the additional plant metabolism study required in connection with PP #6G3352 (See the memo dated 5/1/86 by J. Worthington), metabolism data delineating the fate of 1,3-dichloropropene in ruminants and poultry also will be required.

Analytical Methods

The analytical method proposed for the determination of cis and trans 1,3-dichloropropene involves steam distillation of the sample, partitioning the distillate against hexane and determination of the isomers individually using a gas chromatograph equipped with an electron capture detector. Recovery data for almonds, cherries, citrus fruits, grapes, peaches, plums and walnuts fortified with 0.01 to 0.05 ppm 1,3-dichloropropene ranged between 82 and 108%. Control values were reported as less than 0.01 ppm. RCB considers the proposed procedure adequate to enforce the proposed temporary tolerance for residues of 1,3-dichloropropene, per se.

A similar procedure has been proposed for the determination of of cis and trans chloroallyl alcohols involving steam distillation of the sample, washing the distillate with hexane, extraction of the chloroallyl alcohols with diethyl ether and determination of the isomers individually using a gas chromatograph equipped with an electrolytic conductivity detector. Recoveries from samples of almonds, cherries, citrus fruits, grapes, peaches, plums and walnuts at fortified with 0.01 to 0.05 ppm 1,3-dichloropropene ranged between 78 and 100%. Control values were reported as less than 0.01 ppm. RCB considers the proposed procedures adequate to enforce the proposed temporary tolerance.

However, for a future permanent tolerance, if any real residues of toxicologically significant metabolites are found in additional the plant metabolism study required in connection with PP #6G3352 (See the memo dated 4/30/86 by J. Worthington), additional analytical methodology to determine the additional residues will be required for a future permanent tolerance.

Residue Data

Residue data reflecting the levels of 1,3-dichloropropene and its metabolite, 3-chloroallyl alcohol, in or on the subject crops has been submitted. Application rates are reported as 120-240 lbs. a.i. per acre for oranges, 60 to 303 lbs. a.i. per acre for peaches, and 202 lbs. a.i. per acre for grapes, almonds, plums, cherries and walnuts. Samples were collected after 1 to 334 days after treatment. The majority of samples were harvested after about a four months interval. No detectable residues (<0.01 ppm) were found in any sample. The available data do not report the interval between harvest and analysis.

The available storage stability data do not indicate that 1,3-dichloropropene residues are stable under frozen storage. Although the dissipation of residues did not show any consistent decline with time, all of the stored samples showed significantly lower residues (about 60% of the initial fortification level) after 75 days of frozen storage.

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The agricultural uses of Telone II have previously been considered non-food uses. The available residue data generally reflect the proposed use and showed no detectable residues in any sample regardless of application rate or harvest interval. Therefore, RCB can conclude that for the purpose of the proposed temporary tolerance residues will not exceed the proposed tolerance level. RCB can also conclude that no processing fraction study is needed for the purpose of the proposed temporary tolerance, because no detectable residues are expected in treated crops.

However, for a future permanent tolerance, additional residue data will be required. The additional data must reflect the maximum application rates for each type of treatment and determine the resulting level for at least one crop from each crop grouping to be treated. Care should be taken so that samples are analyzed as soon as possible after harvest. The additional data must include interval between harvest and analysis for each sample.

Further, if any real residues of toxicologically significant metabolites are found in the additional plant metabolism study required in connection with PP #6G3352, additional residue data determining the levels of any additional toxicologically significant metabolites will also be required for a future permanent tolerance. Further, as discussed in the attached Confidential Appendix, a new formulation for 1,3-dichloropropene is being proposed. Residue data reflecting the application of the modified formulation will also be required for a future permanent tolerance.

Meat, Milk, Poultry and Eggs

RCB can conclude that for the purpose of the proposed temporary tolerance no detectable residues of Telone II will result in any livestock feed items derived from treated crops. Therefore, for the purpose of the proposed temporary tolerance the proposed use can be categorized under Section 180.6(a)(3).

If any real residues of toxicologically significant metabolites are found in the additional plant metabolism study required in connection with PP #6G3352, or if the additional residue data required for a future permanent tolerance indicate that detectable residues may result from the use of the modified formulation appropriate cattle and poultry feeding studies may be be required for a future permanent tolerance.

cc: S.F., Circu., FDA, PP #6G3353, R.F., PM-21, TOX, Reviewer, PMSD/ISB, EEB, EAB, and R. Thompson (RTP)

Attachment 1: Confidential Appendix
(attached copy to: PP #6G3353, R.F., PM-21, TOX, Reviewer and PMSD/ISB only)
TS-769:Reviewer:JMWORTHINGTON:Date:4/18/86
RDI:Section Head:ARR:Date:4/30/86:RDS:Date:4/30/86

Telone

Page 8 is not included in this copy.

Pages _____ through _____ are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

____ FIFRA registration data.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

X CONFIDENTIAL BUSINESS INFORMATION APPENDIX

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.