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

MAY 1 1986

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP #6G3352 1,3-Dichloropropene (Telone II™) in or on cottonseed and soybeans. Evaluation of the analytical method and residue data. Accession No. 261122 and RCB #515.

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TO: Henry M. Jacoby, PM. No. 21
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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) in or on cottonseed and soybeans 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 #6G3353 proposing temporary tolerances for residues of 1,3-dichloropropene in or on almonds, cherries, citrus, grapes, peaches, plums, and walnuts is also currently pending.

The proposed two year experimental program involves the treatment of 1810 acres of cotton and soybeans in seven states with a maximum of 6806 lbs. a.i. in the first year. A second Experimental Use permit will be be submitted for the second year.

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 cottonseed and soybeans from the proposed use.

3b. RCB also concludes that no soybean or cottonseed 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) Additional metabolism data delineating the distribution and fate of 1,3-dichloropropene residues in soybeans or cotton will be required. The additional study should reflect a single preplant soil injection application, and sampling at regular intervals encompassing seedling and mature growth stages. The experiments should also reflect the current formulated product.

   b) The submission of additional residue data reflecting the residue levels that will result from the application of any new formulation of 1,3-dichloropropene. Care should be taken so that samples are analyzed as soon as possible after harvest. The additional data must include the interval between harvest and analysis for each sample.

c) If any real residues of any additional toxicologically significant metabolites are found in the required plant metabolism study 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 at-planting injection of 1,3-dichloropropene at rates ranging from 25.3 to 40.4 lbs. a.i. per acre is recommended for the control of various nematodes in cotton and soybeans.

No additional use restrictions regarding residues in the treated cotton and soybeans 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 lbs. 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 concentration 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 metabolite 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 the 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.

However, for a future permanent tolerance additional metabolism data delineating the distribution and fate of 1,3-dichloropropene residues in soybeans or cottonseed will be required. The additional study should reflect a single preplant soil injection application, and sampling at regular intervals encompassing seedling and mature growth stages. The experiments should also reflect the current formulated product.

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 treated cottonseed or soybeans 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 above, metabolism data delineating the fate of 1,3-dichloropropene in ruminants and poultry will also be required.

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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. Recoveries from samples of cottonseed and soybeans fortified with 0.01 to 0.05 ppm 1,3-dichloropropene ranged between 85 and 102%. 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 cottonseed and soybeans fortified with 0.01 to 0.05 ppm 1,3-dichloropropene ranged between 80 and 94%. Control values were reported as less than 0.01 ppm. RCB considers the proposed procedures adequate to enforce the proposed temporary tolerance.

However, if any real residues of any additional toxicologically significant metabolites are found in additional the plant metabolism study required above, additional analytical methodology to determine the additional residues will be required for a future permanent tolerance.

Residue Data

Two cotton and two soybean residue studies have been submitted in support of the proposed temporary tolerance. Cotton and soybean fields were treated with 1,3-dichloropropene at rates of 20 to 120 lbs. a.i. per acre (approximately 0.5 to 3 times the maximum proposed rate). The Telone II was injected into the soil, immediately before planting, to a depth of 6 to 8 inches.

Samples of soybeans, soybean forage and straw as well as cottonseeds, field trash and gin trash were collected from the treated fields. Harvest intervals ranged between 127 to 200 days for the cotton samples and from 67 to 154 days for the soybean samples.

No detectable residues (<0.01 ppm) were found in any of the samples. For the purpose of the proposed temporary tolerance only, RCB can conclude that no detectable residues will result in cottonseed and soybeans from the proposed use. RCB can also conclude that no soybean or cottonseed fraction study is needed for the purpose of the proposed temporary tolerance, because no detectable residues are expected in cottonseed or soybeans.

However, if any real residues of toxicologically significant metabolites are found in the additional plant metabolism study required above, additional residue data determining the levels of any additional toxicologically significant metabolites will 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 be also required for a future permanent tolerance. Care should be taken so that samples are analyzed as soon as possible after harvest. The additional data must include the interval between harvest and analysis for each sample.

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. 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 above or if the additional residue data reflecting the new formulation 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 #6G3352, R.F., PM-21, TOX, Reviewer, PMSD/ISB, EEB, EAB, and R. Thompson (RTP)

Attachment 1: Confidential Appendix
(attached copy to: PP #6G3352, 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.