



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Maneb Comprehensive Data Call-In Notice dated April 1, 1987: Registrants response (RD I.D. No. 014505; No Accession No.; Record No. 199296; RCB No. 2532)

FROM: William J. Hazel, Ph.D., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769) *W. J. Hazel*

THRU: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769) *[Signature]*

TO: Susan Lewis (PMT 50)
Data Call-In Program
Registration Division (TS-767)

Introduction

BASF Corp., Griffin Corp., and Pennwalt Corp. have submitted their 90-day responses to the April 1, 1987 Maneb Comprehensive Data Call-In Notice (DCI). All three of these registrants are members of the Maneb Data Task Force and their responses, for the most part, are identical. Note that a Storage Stability DCI was issued March 31, 1987.

Discussion

General Issues

RCB will respond to several comments made in all three cover memos dated July 6, 1987. We feel that other registrant comments/questions are best dealt with by the Registration Division.

1. Registrant comment. The registrants feel that they should have access to all EPA reviews so that they are able to determine reasons for deficiencies in the existing data and, hence, avoid problems in generating data in the future.

RCB response. RCB agrees with the registrants and, further, we feel that the Product and Residue Chemistry "Chapters" of what will eventually become the Maneb Registration Standard should be made available to the registrants (or at least the discussion of the data portions).

2. Registrant comment. The registrants claim that, since the DCI arrived too late to begin field studies in the 1987 crop season, they will need additional time to comply with the DCI due dates for data on bulb onions, lima beans, apricots, peaches, and almonds (refer to footnotes R10, R14, and R19). The registrants also state that, in the case of apples (footnote R18), they plan to treat late variety apples in 1987 to obtain the best data possible given the time restraint.

RCB response. In the case of the crops listed above, the first applications are made between February and April. The data required under this DCI will be used for purposes of reregistration and tolerance reassessment and, therefore, must represent actual, typical cultural practices. In all of the above cases, satisfaction of the DCI requirements within the 18-month timeframe should be achievable by conducting trials in 1987 and/or 1988.

3. Registrant comment. The registrants state that the comprehensive DCI is internally inconsistent in that residue data on maneb, ETU, and "other metabolites of toxicological concern" are due within 11 months whereas plant metabolism data are due within 18 months. They question how they can conduct and report residue studies on "other metabolites of toxicological concern" when they will not yet have determined what these metabolites are from the metabolism studies.

RCB response. This would be a valid argument if the 11-month figure was correct. However, the comprehensive DCI "90-Day Data Call-In Summary Sheets" clearly provide deadlines of 18 months for both metabolism and all field residue studies.

Specific Issues

Product chemistry

Registrant comment. A response from Griffin Corp. concerning the product chemistry portion of the DCI was not submitted and is not required because they have registered only end-use products. Pennwalt intends to generate the data. BASF responded that all product chemistry data are being submitted with their response (none were provided to RCB), that all data will be generated, but that they consider the requirements inapplicable. Further, BASF refers to their footnote A1 which cannot be located in their submission; this footnote may help to explain the position of BASF regarding product chemistry.

RCB response. If BASF footnote A1 to the Metiram Comprehensive DCI can be assumed to be identical to that cited here, then it requests a meeting with EPA scientists to discuss reasons for inadequacies of the existing data. This was suggested in the DCI.

Residue Chemistry

Registrant footnote R1. The registrants claim that, contrary to the Agency view the available plant metabolism data are adequate and that EPA's position should be reconsidered. They state that the objective of metabolism studies is to qualitatively characterize residues. In the case of maneb, characterization of residues in plants is complex and difficult due to extensive degradation and metabolism and eventual incorporation into the carbon pool. As a result, most unidentified residues are claimed to be bound such that not even SnCl_2 in refluxing acid will release them. Unidentified polar products usually comprised <10% of the residue, similar metabolites occurred in all crops, hydantoin was always the major identified metabolite (up to 11% in lettuce), and other identified metabolites (ETU and EBIS) were generally <5% of the total residue. The registrants believe that the Agency should consider metabolism data for all EBDCs as a whole and, if done, this will adequately delineate plant metabolism of maneb. The registrants state that they cannot adequately perform crop residue studies [i.e., ascertain any additional residues of concern] within 11 months (required by the March 31, 1987 Storage Stability DCI) since they will not have completed The metabolism studies sufficiently early.

RCB response. A complete understanding of the metabolism of maneb is of primary and paramount importance to risk assessment, reregistration, and tolerance reassessment. The registrants are correct in stating that the major objective of metabolism studies is to qualitatively characterize residues. However, they must not overlook the fact that the failure to identify 49-99% of the residues represents not only a failure in quantitation, but also a failure to adequately qualify the major portion of the residue. Since these apparently "bound" residues are not extracted by the same means as the identified residues, we must assume they are either different residues or conjugated forms of already-characterized residues. If degradation is so extensive that incorporation into the plant carbon pool occurs, the registrants must assure us that this is the case. In addition to acid refluxing and separate extraction with a polar solvent system, numerous other techniques should be applied alone or in combination to release the "bound" residues. Such techniques include, but are not limited to: (i) alkaline hydrolysis; (ii) enzymatic hydrolysis using enzymes such as glycosidases, proteases, esterases; (iii) sonication; and (iv) extraction with organic solvent systems. If the major portion of the "bound" residues cannot be released by the above techniques and subsequently identified and/or if it cannot be demonstrated that the residues have been incorporated into natural plant constituents, then the registrants must subject the "bound" residues to biological testing such as feeding these residues to rats. Monitoring the form (whether still

"bound" or whether identified, released metabolites) of the residues in excreta will help determine the bioavailability of "bound" residues. In any event, known or potential metabolites (particularly ETU) must be determined in excreta. An additional study that may help reduce concern for the "bound" residues would be to treat "bound" residues in such a way as to generate ETU from any ETU-generating residues that may be present. Note that recoveries of maneb and ETU were poor to moderate from spiked tomatoes (27-70%) and lettuce (50-76%); we would expect recoveries to be lower from these and other crops if extraction was attempted 7 days after the last of three applications of [¹⁴C] maneb, as was the case in the recently conducted maneb metabolism studies. It is possible, therefore, to increase the percentage of residues identified by simply improving the extraction efficiencies. We do not feel that metabolism studies conducted on other EBDCs are acceptable to elucidate the metabolism of maneb because: (i) the available studies on other EBDCs are all deficient except for one; (ii) it is an RCB policy not to translate data from one pesticide to another particularly if data compensation is an issue; and (iii) different free or "bound" residues/conjugates may form from different EBDCs and in different plant parts at different rates. Regarding the generation of metabolism and residue data within 11 months, the registrants are reminded that the March 31, 1987 Storage Stability DCI requires that residue data on only maneb and ETU be submitted within 11 months, i.e. no metabolism data or residue data on other metabolites for purposes of generating a dietary exposure assessment. The April 1, 1987 Comprehensive DCI requires that, within 18 months, metabolism data as well as residue data on maneb, ETU, and "other metabolites of toxicological concern" must be submitted. We realize that this presents a logistical problem and that the registrants do not want to conduct two sets of studies on each commodity. It is possible that, while metabolism studies are being conducted, residue field trials can be initiated. For many commodities, harvest from field trials can occur after the completion of metabolism studies such that all residues of concern can now be determined. If not, analysis of frozen stored samples for any new residues of concern can be performed as soon as possible after their identification in metabolism studies and storage stability studies can be initiated. Of course, method development and validation must be conducted on each new metabolite of concern.

Residue Trials

Registrant footnote R2. EPA must identify which residues are of concern other than maneb and ETU before the Maneb Data Task Force can conduct complete residue trials using validated methods. Multiresidue Protocols I, II, III, and IV will be performed.

RCB response. RCB agrees. Upon complete characterization of plant residues (refer to RCB response to registrant footnote R1) in the required metabolism studies, RCB, in conjunction with the Toxicology Branch, will identify the residues of concern. At such time, method development, validation, and residue analysis of crops can begin if not already initiated. Metabolism data will be

given priority status with the associated rapid Agency turnaround.

Registrant footnote R3. Due to the conflicting due dates associated with the 3/31/87 Storage Stability DCI and 4/1/87 Comprehensive DCI, particularly since the Agency requests in the Comprehensive DCI that residue trials be delayed until plant metabolism studies are submitted, the Task Force may be forced to repeat residue trials-at great cost. The Task Force is proceeding with a 1987-88 residue trial program in response to the two DCIs.

RCB response. We will cooperate as much as possible to help the Task Force avoid repeating field trials. Assuming that all required field trials are to be conducted in the 1987-88 program, we approve of the schedule for purposes of the Comprehensive DCI. This review will not address timeframes of the 3/31/87 Storage Stability DCI.

Registrant footnote R4. The Task Force is performing storage stability studies to validate existing residue data and is performing concurrent storage stability studies with new residue trials. Chain of custody information is being tabulated. Storage stability data may reflect >12 months of storage and, therefore, an 11-month deadline is unreasonable. Contrary to earlier discussions between Agency scientists and the Task Force, the Special Review Branch has rejected the option of validating existing residue data with newly-generated storage stability data; the Task Force takes exception to this position.

RCB response. For purposes of the Comprehensive DCI, storage stability data conducted for intervals >12 months are acceptable because of the 18-month deadline associated with this DCI. We will not comment in this memorandum whether data collected over <11-month storage intervals are adequate for purposes of the 3/31/87 Storage Stability DCI. The registrants must be reminded that the Agency currently will not accept validation of existing data; therefore, the Task Force is generating these data at its own risk i.e., the Agency may continue to reject validation of existing data with newly conducted storage stability studies.

Registrant footnote R5. The Task Force will not support the dust formulations. Application rates, locations, and formulations of current residue trials may not correspond exactly to the DCI. In many cases, this is because the registrants are amending their labels. Due to short time frame, the Task Force has changed geographical sites from those required in the DCI. An aerial vs. ground application bridging study will be submitted shortly: residues were not statistically different.

RCB response. As long as the dust formulations are cancelled or all food/feed crops are deleted from all dust labels, RCB has no objection to the Task Force not supporting these formulations. Regarding alteration of test parameters required in the DCI, we have no difficulty if label amendments account for the changes; alterations for other reasons (such as timeframe vs. geographical location of test sites) will be dealt with on a case by case basis.

The aerial vs. ground application bridging study is in support of a valid concept; we will reserve judgement on the adequacy of the data until it has been reviewed.

Registrant footnote R6. The Task Force is generating storage stability data to validate previously submitted residue data, apparently only for carrots, celery, spinach, peppers, apricots, peaches, and almonds.

RCB response. Refer to RCB response to Registrant footnote R4.

Registrant footnote R7. Potato residue trials will be conducted in CA, ID, ME, ND, and OR. The use of the 80% WP in CA at 4 lb ai/A will not be supported.

RCB response. RCB approves the minor change in test location from WA (as in the DCI) to OR. Note that the Intrastate label, EPA Reg. No. 5967-5138, must be cancelled concomitant with the failure to support the CA use of the 80% WP at 4 lb ai/A.

Registrant footnote R8. The Task Force will conduct potato processing studies if measurable residues are detected in the RAC following application at normal or exaggerated rates.

RCB response. We agree if residues of maneb, ETU, and any other residue that may be of concern (perhaps ones that may be degraded to ETU upon processing) are all nondetectable in the RAC following treatment at an exaggerated rate such as 10x.

Registrant footnote R9. Sugar beet residue trials will be conducted in CA, ID, MN, and ND. Dust formulations will not be supported.

RCB response. These are the test states cited in the DCI. As noted in RCB's responses to Registrant footnotes R5 and R7, if the registrant wishes not to support the dust uses, Section 3, Intrastate, and Section 24(c) labels must be amended/cancelled to eliminate use on food/feed crops.

Registrant footnote R10. Green onion residue trials will be conducted in CA, AZ, and TX. Bulb onion trials will be delayed until the 1988 growing season since the 1987 season was well underway by the time the Task Force received the DCI. Dust formulations will not be supported.

RCB response. Green onion test locations are as per the DCI. Bulb onion trials can await the 1988 growing season and still satisfy the 18-month timeframe of the 4/1/87 DCI. Refer to the RCB response to Registrant footnote R9 for our discussion of dust formulations.

Registrant footnote R11. Lettuce residue trials will be conducted in CA. Dust formulations will not be supported. Trimmed and untrimmed heads will be collected.

RCB response. The CA test location is as per the DCI. We definitely

recommend analyzing both trimmed and untrimmed heads as the Task Force intends. Refer to our response to Registrant footnote R9 for a discussion of dust formulations.

Registrant footnote R12. Broccoli trials will be conducted in CA. Dust formulations will not be supported.

RCB response. The CA test location is as per the DCI. Refer to our response to Registrant footnote R9 for a discussion of dust formulations.

Registrant footnote R13. Cabbage trials will be conducted in FL, TX, CA, MI, and NY. Trimmed and untrimmed heads will be collected.

RCB response. The planned test states are five of nine states required in the DCI. We approve of the Task Force plan because NJ, NC, OH, and WI are represented by NY, FL, and MI. We approve of the plan to analyze both trimmed and untrimmed heads.

Registrant footnote R14. Dry bean residue trials will be conducted in CA, CO, MI, ND, and NE. Snap bean trials will be conducted in MI, NY, OR, and WI. Lima bean trials will be conducted in CA and DE. The trials in IL will be conducted in 1988 due to late receipt of the DCI in relation to the normal growing season. Cannery waste residues will be determined. Dust formulations will not be supported.

RCB response. The dry bean and snap bean test locations are as per the DCI. Lima bean sites in CA and DE are as per the DCI; if the IL tests are to be conducted on lima beans, then we approve of the substitution of IL for WS (as required in the DCI). If conducted in the 1988 season, the 18-month timeframe of the 4/1/87 DCI can still be met. As required in the DCI, cannery waste will be analyzed. Refer to the RCB response to Registrant footnote R9 for a discussion of dust formulations.

Registrant footnote R15. Tomato residue trials will be conducted in CA, FL, MI, and TX. Dust formulations will not be supported. New processing studies will be conducted.

RCB response. The test states and processing studies are as per the DCI. Refer to the RCB response to Registrant footnote R9 for a discussion of dust formulations.

Registrant footnote R16. Cucumber trials will be conducted in CA, FL, MI, NC, and SC. Dust formulations will not be supported.

RCB response. Two test states cited in the DCI, TX and VA, are not among the proposed locations. We will allow NC to represent VA but tests must be conducted in TX due to its importance (11% of the cucumber crop) and because none of the proposed test states geographically represent TX. Refer to the RCB response to Registrant footnote R9 for a discussion of dust formulations.

Registrant footnote R17. Watermelon trials will be conducted in CA, GA, and TX. Dust formulations will not be supported.

RCB response. The Task Force has omitted FL as a test site; FL was required in the DCI in addition to CA, GA, and TX. We will accept GA as representing the entire southeastern U.S. melon-producing area. Refer to our response to Registrant footnote R9 for a discussion of dust formulations.

Registrant footnote R18. [Note that Griffin Corp. is the only Task Force member supporting the apple use.] Normal cultural practices dictate initiating treatments to apples prior to April 8 (date of receipt of the DCI). Griffin is attempting to locate late variety apples and provide the best residue data possible given the timing problems. Processing studies will be completed.

RCB response. We agree that the apple growing season in many parts of the country was well under way by the time Griffin received the DCI. We will not comment here whether the plan is acceptable for purposes of the 3/31/87 Storage Stability DCI. For purposes of the 4/1/87 Comprehensive DCI, however, we would not accept field studies unless they represented typical agricultural practices including parameters such as timing of first through final application, varieties of apple, and harvest time. This would most likely require testing in the 1987 season of late season varieties and testing in the 1988 season of early season varieties. We feel that the 18-month timeframe of the 4/1/87 DCI can be met by such a schedule. Unfortunately, this may be one case in which two separate sets of studies may need to be conducted to satisfy the 3/31/87 and 4/1/87 DCIs. As per the DCI, processing studies are to be conducted.

Registrant footnote R19. In the cases of apricots, peaches, and almonds, the DCI was received too late in the growing season to initiate 1987 trials; normal applications begin in February in the requested states. Trials will be conducted in 1988.

RCB response. We will not comment in this memo whether the proposal to test in 1988 is acceptable for purposes of the 3/31/87 Storage Stability DCI. We do find the proposal appropriate for purposes of the 4/1/87 Comprehensive DCI because we need full representation of the growing areas of these crops and because the 18-month timeframe is sufficient to allow testing in both the 1987 and 1988 growing seasons.

Registrant footnote R20. Grape trials will be conducted in CA. New processing studies will be conducted.

RCB response. Both the test location (CA) and the conduct of processing studies are as per the DCI.

Registrant footnote R21. Sweet corn trials will be conducted in GA, IL, MN, NY, WA, and WI. Dust formulations will not be supported. Forage samples will be collected.

RCB response. All test locations are as per the DCI except that GA was substituted for FL. Although less preferable, we will accept

the substitution. Refer to our response to Registrant footnote R9 for a discussion of dust formulations. As per the DCI, sweet corn forage will be analyzed.

Registrant footnote R22. Dust formulations will not be supported for use on corn forage.

RCB response. Refer to the RCB response to Registrant footnote R9 for a discussion of dust formulations.

Registrant footnote R23. Banana trials will be conducted in HI.

RCB response. The banana test state (HI) is as per the DCI.

Registrant footnote R24. Pennwalt and Griffin have entered into an agreement to generate residue data to support the use of maneb on seed, seed piece, planting stock, and propagation stock. BASF will delete these uses from its labels.

Label amendments. The following crops are to be deleted from the labels of all registered Task Force products and, concomitantly, uses will not be supported by residue data: asparagus, chinese cabbage, cranberries, figs, kale, papayas, rhubarb, and tobacco. All other uses will be supported.

Note to Product Manager: Tolerances for maneb residues (not applicable to tobacco) in or on the above crops to be deleted from labels must be revoked.

cc: L. Rossi (RD, HFB, PM #21), A. Rispin (SIS), PMSD/ISB