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GAO

United States
General Accounting Office
Washington, D.C. 20548

Resources, Community, and
Economic Development Division

B-256727

June 21, 1994

The Honorable John Glenn
Chairman, Committee on Governmental Affairs
United States Senate

Dear Mr. Chairman:

This correspondence responds to your September 28, 1992, request that we review the Environmental Protection Agency's (EPA) February 1992 decision to retain 45 crop uses for a group of fungicides known as EBDCs (ethylene bisdithiocarbamates), while canceling 11 uses. This decision was almost the reverse of an initial proposal made about 2 years earlier. In your letter, you asked that we determine whether there were deficiencies in the way human health concerns about EBDCs were handled. We recently briefed your staff on the results of our data collection.

In summary, we did not find any significant weaknesses in EPA's review of the health effects of EBDCs. EPA's decision to retain most of the crop uses for EBDCs was based on lower estimates of the carcinogenic risk from dietary exposure to EBDCs. The risk estimates EPA used in its February 1992 decision were lower than those used in its initial proposal and resulted primarily from two factors--a reduction in the estimates of EBDC residue on food crops and a reduction in the cancer potency factor.

We reviewed the basis for EPA's decision and determined that EPA's market basket survey and the reevaluation of, and subsequent reduction in, the cancer potency factor had the greatest effect on overall reductions in risk estimates. Our review focused primarily on these two efforts. The market basket survey, which involved a sampling of food items from grocery store shelves, essentially confirmed EPA's belief that EBDC residues on food crops at the marketplace were much lower than the estimates used in its preliminary decision. The earlier estimates were based on food samples taken at the farm gate immediately after harvest.

In addition, the reevaluation of the cancer potency factor --a measure of a chemical's ability to cause or induce cancer--resulted in about a sixfold reduction in the potency factor. The cancer potency factor is a numerical value determined from evaluating tumor data taken from test animals. The larger the number, the greater the chemical's comparative ability to induce cancer. The cancer potency factor is a key element in determining dietary risk.

Although we found no significant weaknesses in the process leading to EPA's decision to retain 45 crop uses, we did find some minor discrepancies in its calculations of average EBDC residue estimates. We discussed the discrepancies with EPA staff and asked the agency to recalculate risk estimates using corrected residue estimates. We reviewed the recalculated risk estimates with EPA and we subsequently determined that the discrepancies did not have a significant impact on the overall risk estimates. However, because of the extensive number of computations and the potential for errors that could possibly have a significant effect on risk estimates for other pesticides, we are sending a letter to EPA's Assistant Administrator for Prevention, Pesticides and Toxic Substances, recommending that procedures be instituted to strengthen internal controls to prevent these types of discrepancies.

BACKGROUND

EBDCs are a group of fungicides intended to protect a wide variety of fruit and vegetable crops against diseases. Dietary exposure to EBDCs, however, has been linked to potential carcinogenic, developmental, and thyroid effects in humans. The EBDC fungicides break down into ETU (ethylenethiourea), a metabolite product common to all EBDCs. ETU has been classified by EPA as a probable human carcinogen. Because of concerns over the possible risks associated with EBDCs, EPA in 1987 initiated a special review of the risks and benefits of EBDCs.

On the basis of information obtained through the special review, EPA concluded that the cumulative carcinogenic dietary risk of all EBDC uses was unreasonable (about 300 additional cancer cases per million people over a lifetime of exposure). In December 1989, EPA announced its preliminary decision to cancel EBDC use on 45 crops and to retain the use on 10 crops, thus reducing the dietary risk

to about 3 cancer cases in a million.[1]

EPA's preliminary decision was based on testing for EBDC residue levels before, or shortly after, harvesting.[2] However, EPA believed that the dietary risk from EBDC residue on food items by the time they are sold to consumers at the marketplace could be substantially lower because the residues would dissipate over time. In this connection, EPA required EBDC manufacturers to collect data on the amount of EBDC residue on representative crops at the marketplace. EBDC manufacturers subsequently conducted an extensive market basket study estimated to cost about $10 million. The survey data demonstrated that, in general, EBDC residues in foods on the grocery shelves are much lower than residue estimates from field trial data.

In addition to obtaining the results of the manufacturers' market basket survey during the special review, EPA reevaluated the cancer potency of EBDCs on the basis of further analysis of existing tumor data. As a result, EPA concluded that the cancer risk from EBDCs was also significantly less than estimated in the preliminary decision.

With the reduced residue estimates and reduced cancer potency factor, EPA determined that, for 45 crop uses, the dietary risk would be reduced to 1.6 additional cancer cases per million. In March of 1992, EPA published its intention to retain EBDC use on 45 crops and cancel the

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[1]EPA's target for a negligible risk is 1 additional cancer case per million people. However, there is considerable uncertainty associated with risk assessment, and EPA may decide that benefits outweigh risks to the extent that the agency will accept a risk that is in the range of 1 additional cancer for every 1 million persons, i.e., 2 in a million, 3 in a million.

[2]Residue data obtained by testing crops collected at the farm gate are referred to as field trial data.

EBDC registration for use on 11 crops--almost the reverse of its initial proposal made 2 years earlier.[3]

MARKET BASKET SURVEY

In March 1989, EPA required EBDC manufacturers to generate market basket data for representative crops, which could then be translated to other crops. In response to EPA's request, EBDC manufacturers established the ETU Task Force to conduct a market survey of selected crops in the United States to determine the levels of EBDC residues on foods as they are purchased for consumption. Using a probability sample, the task force selected grocery stores across the 48 contiguous states and purchased various "food forms" (canned, frozen, raw, juice) of 12 representative crops: almonds, apples, bananas, broccoli, cucumbers, dry beans, grapes, head lettuce, onions, potatoes, sweet corn, and tomatoes. The survey provided data on 5,784 food samples.

The final market basket survey, however, produced residue data for only 8 out of the 12 crops. Because industry detected test problems with one of the laboratories, the market basket data collected for 4 of the 12 crops--bananas, almonds, apples, and grapes--were not used in the survey.

Residue levels for 20 crops were based on translation[4] from the 8 crops surveyed, while residue estimates for the remaining 28 crops, including bananas, almonds, apples, and grapes, were based on field trial data. These data were adjusted for updated information on the percentage of the crops treated with EBDCs, some limited industry surveys, and food processing data.

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[3]While EPA's initial proposal affected 55 crop uses for EBDCs, EPA's final decision affected 56 crop uses. In the initial proposal, the use on dry and succulent beans was listed as one use. While in the final determination, the use on dry and succulent beans was considered two separate uses, for a total of 56 crop uses for EBDCs.

[4]Generally, residue data from a particular crop may be translated to other crops within the same crop group. For example, using the market basket residue estimates for tomatoes, EBDC/ETU residues for eggplants and peppers, which are in the same crop group, can be estimated.

Industry Planned for and Collected Data; EPA Reviewed and Verified

EPA relied on EBDC manufacturers to plan for and carry out the market basket survey. Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the burden of proof that the pesticide does not cause unreasonable risk to humans or the environment (taking into account the economic, environmental, and social costs and benefits of the use of the pesticide) rests with the registrant--the company that holds the pesticide registration. The registrants are responsible for providing all test data necessary to satisfy EPA's requirements. The time and cost involved in conducting the studies of health or environmental effects of pesticides generally preclude EPA from independently conducting these studies. EPA, however, did review the data submitted by the EBDC manufacturers, including data opposed to EBDCs' continued use, and data relating to the health effects or economic costs and benefits of pesticides.

Although the survey was sponsored by the industry-backed ETU Task Force, we noted that EPA reviewed and modified the survey design, reviewed the residue data, and independently computed the national averages for the residues in the crops and found them to correspond closely to the averages computed by the industry. We reviewed EPA's actions to independently validate the task force's survey results and determined that there was essentially no difference between the survey results and the residue estimates calculated by EPA.

Quality Assurance Problems Found at One of Four Laboratories Performing EBDC Analyses

EPA relied on the industry task force to ensure adequate monitoring and control of the actual collection of the sample food items for laboratory analyses. In this regard, the industry task force, in August 1990, informed EPA of potential quality assurance problems with the work being performed at one of the four laboratories conducting EBDC analyses. EPA subsequently performed a Good Laboratory Practices inspection of this laboratory--Craven Laboratories, Inc. On the basis of the September 1990 inspection, the inspection team turned the matter over to EPA's criminal enforcement personnel for further

investigation.[5]

Following a 3-year EPA/Department of Justice investigation, the Craven Laboratory and its owner were subsequently tried and convicted of conspiracy and falsely certifying that food was tested for the presence of pesticide residues or metabolites.

None of the EBDC market basket survey data analyzed by Craven was used. In addition, EPA took action to determine whether any other pesticide chemicals were supported in any way by Craven's data. As a result, EPA is currently requiring the submission of new studies/data to replace data generated by the Craven Laboratory to support other chemicals.

Minor Discrepancies Found in EPA's Average Residue Calculations

Before using the market basket survey's crop residue estimates to calculate dietary risk, EPA adjusted them to reflect the current estimates of the percentage of the crops treated with EBDCs. In reviewing these adjustments, we noted that many of EPA's calculations were made manually, and many computations were not independently verified. Because of the numerous calculations and the high potential for error, we conducted a spot check of the residue calculations.

We tested EPA's computation of the mean residue estimates for 17 foods and/or food forms (raw, frozen, paste, puree, etc.) and found 15 discrepancies in 34 residue estimates.[6] These discrepancies, which were discussed with EPA, appeared to be fairly minor in that they generally involved decimal numbers that differed by one or more digits at the fourth decimal place. For example, we calculated a mean ETU residue estimate of 0.0013 parts per million for frozen broccoli, while EPA used 0.0021, and we calculated a mean of 0.0074 parts per million for tomato paste, while EPA used 0.0073. Eight discrepancies were due to using an incorrect figure (for, for example, the percentage of the

[5]No significant problems were found during EPA's audits and/or inspections carried out at the three other laboratories involved in the market basket survey.

[6]Each food form has a residue estimate for both EBDC and ETU.

crop treated), four were transcription errors (all for the same crop, tomatoes), while three were due to truncating a digit instead of rounding. In eight of the cases where a discrepancy was found, the actual residue estimate was higher than that used by EPA, while in seven cases, the residue estimate was lower than that used by EPA.

EPA officials reviewed our recalculated residue estimates and told us that the differences were insignificant and would not significantly change the ultimate risk assessment numbers. We subsequently asked EPA to recalculate the risk estimates for the food forms for which we found differences in residue estimates. Our recalculated residue estimates resulted in some minor changes in the carcinogenic risk estimates; however, we agree that the changes in the estimates are insignificant. For example, EPA had estimated that the risk for cucumbers was about 3.4 additional cancer cases per 100 million people, while our calculation resulted in a risk of about 3.5 additional cancer cases per 100 million people.

EPA officials said that the calculations for EBDCs were substantially more complicated than those for most pesticide chemicals, with two interdependent residues (EBDC as parent compound and the ETU metabolite) that had to be calculated. Although the discrepancies we found had no significant effect on EPA's risk estimates or EPA's subsequent decision to retain 45 crop uses for EBDCs, the number, or significance, of discrepancies in residue calculations for other pesticides is unknown. Because the types of discrepancies found in the calculations of EBDC residues could also be occurring in residue calculations for other pesticide chemicals, we will be recommending that procedures to strengthen internal controls be instituted to prevent these types of discrepancies.

CANCER POTENCY FACTOR

EPA based its conclusions on the health effects of EBDCs primarily on a study by the National Toxicology Program (NTP), which includes four agencies of the U.S. Department of Health and Human Services. The cancer potency factor, which is one of the key elements of the formula[7] used to

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[7]The basic formula for estimating dietary risk is: dietary risk = exposure (pesticide residues X food consumption) X the cancer potency factor. The food consumption portion of

(continued...)

calculate the dietary risk of a chemical, was also determined using data from the NTP study.

The potency factor is expressed as a numerical value and is based on a mathematical extrapolation of tumor incidence observed at the high doses used in animal tests. The cancer potency represents the estimated tumor incidence expected to occur at the relatively low doses of pesticides in the human diet. At the time EPA announced its decision to cancel 45 uses for EBDCs, EPA had calculated a preliminary cancer potency factor of 0.6 $[mg/kg/day]^{-1}$.

Responding to industry comments that the 0.6 potency factor was statistically unacceptable, EPA's Health Effects Division Carcinogenicity Peer Review Committee met to review and discuss the NTP study and the rationale for determining the potency factor. EPA also reanalyzed the animal laboratory data in the NTP study and recalculated a cancer potency factor of 0.11, representing almost a sixfold decrease in the potency factor.

EPA's reassessment of the study's laboratory data resulted in including an additional group of animals (mice), which had liver cancer, in the calculations of the potency factor. In this connection, EPA's Peer Review Committee voted to include the group as a new data point in the determination of the potency factor.

However, because there were questions within the committee regarding the statistical appropriateness of including the additional group of animals in the calculations, EPA asked for a meeting of the FIFRA Science Advisory Panel.[8] In September 1991, the panel reviewed and unanimously approved the methodology for calculating a potency factor of 0.11.

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[7](...continued)
the formula is based on the 1977-78 Nationwide Food Consumption Survey by the U.S. Department of Agriculture.

[8]A panel of scientists established by FIFRA to provide independent scientific advice on pesticides and pesticide-related issues as to the impact on health and the environment of various regulatory actions.

SCOPE AND METHODOLOGY

To determine whether there were deficiencies in the way human health concerns about EBDCs were handled, we interviewed officials and staff from EPA's Office of Prevention, Pesticides and Toxic Substances and its Health Effects Division, Special Review and Reregistration Division, Biological and Economic Analysis Division, and Compliance Division. We reviewed numerous EBDC special review documents and records associated with the market basket survey and cancer potency evaluation, as well as records relating to benefit analyses, dietary risk assessment, and other factors/rationale leading to EPA's final decision to retain 45 uses for EBDCs.

We also performed a limited review of the market basket survey's approach and methodology and the statistical sampling issues involved. To determine how EPA arrived at final residue estimates for the market basket survey, we reviewed EPA's methodology, selecting 17 foods and/or food forms for a detailed review.

We conducted our review between June 1993 and May 1994 in accordance with generally accepted government auditing standards.

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As arranged with your office, unless you publicly announce its contents earlier, we plan no further distribution of this correspondence until 15 days after the date of this letter. If you or your staff have any questions about the data contained in this correspondence, please contact me at (202) 512-6111.

Sincerely yours,

Peter F. Guerrero
Director, Environmental Protection Issues

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