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

AUG 9 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: 6(a)(2) data on contamination of **benomyl** [methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate] products. CB#'s 8204, 8273. DP Barcode 165858, 166182. (No MRID #)

FROM: Richard Loranger, Ph.D., Chemist
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R. Loranger

THRU: Richard D. Schmitt, Ph.D., Chief
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Health Effects Division (H7509C)
Richard D. Schmitt

TO: Susan Lewis/Carl Grable, PM Team 21
Herbicide Fungicide Branch
Registration Division (H7505C)

We have been requested to review packages from E.I. du Pont de Nemours & Co., Inc. that are submitted under Section 6(a)(2) of FIFRA (according to note from Product Manager). The packages address contamination of certain benomyl (Benlate) formulations with the herbicide atrazine and the fungicides chlorothalonil and flusilazole (Nustar).

The first package (barcode 165858; received by EPA on 6/21/91) consists of the following:
(1) A 6/21/91 article from the Orlando Sentinel entitled "Tainted fungicide withers plant industry in Florida".
(2) A 6/19/91 letter from the Florida Commissioner of Agriculture to the DuPont Agricultural Products Dept.
(3) A 5/22/91 letter from DuPont to the Florida Dept of Agriculture & Consumer Services.
(4) A 6/21/91 Benlate Information Bulletin from DuPont External Affairs.

The second package (barcode 166182; received 7/3/91) contains the following (numbered for ease of referral):
(5) A 7/3/91 letter from John Gardiner, DuPont, to Frank Sanders, EPA.
(6) Feb. 1977 "CONTAMINANT SCREENING GUIDELINES" from the Enforcement Division of Pesticides and Toxic Substances.
(7) A transcript of a 6/26/91 Florida TV news report.

1

Each of the above documents is summarized below followed by conclusions that can be drawn regarding contamination levels in the benomyl formulations or possible residues in food crops from use of such formulations.

The Orlando newspaper article (document 1) provides background on the crop damage being observed in Florida. It states that hundreds of farmers have reported yellowing crops and undersized plants with misshapen leaves after using Benlate.

The article goes on to explain that DuPont recalled the fungicide in March due to contamination with herbicides and has discontinued production of Benlate 50DF, Benlate 1991 DF, and Tersan DF. Contamination of these "pellet" forms of Benlate with the herbicide atrazine was found in 1989 and again this year. A powdered form of Benlate is still available.

The 6/19/91 letter (document 2) from Bob Crawford, Florida Commissioner of Agriculture, to DuPont contains a request for a meeting with his staff, the U.S. EPA, and the University of Florida Institute of Food and Agricultural Sciences.

Neither of the above two documents provides data on actual levels of contaminants in the Benlate products or in food crops.

The 5/22/91 letter from DuPont (document 3) gives results of the analysis of a "Benlate" 50 DF sample (lot# 40190) for various pesticidal contaminants. The results were as follows.

Analyte	Field sample U 40190 Fuzzell	Retain sample U 40190-0267
atrazine	ND*	ND
cyanazine	ND	ND
simazine	ND	ND
chlorothalonil	39 ppm	30 ppm
flusilazole	42 ppm	35 ppm

*ND is less than 2 ppm

Analyses for the above pesticides were done by GC-MS with single ion monitoring. Chlorothalonil is a registered fungicide with tolerances on a variety of fruits and vegetables. Flusilazole is a DuPont fungicide registered in Europe and undergoing experimental use in the U.S.

Document #4 in the package is the 6/21/91 "Benlate Information Bulletin". As background it states that DuPont initiated a stop sale and recall of the three DF products mentioned above on March 22 due to trace levels of atrazine herbicide in some batches. (EPA formally issued its own stop sale about one week later.) A recall of Benlate DF was carried out in

1989 for the same reason. It is noted that atrazine was produced at the same contract formulation plant sites as Benlate DF. Only the dry flowable (DF) formulation has been recalled. No problems have been found with the wettable powder (WP) formulation, which is produced at a DuPont facility under strict quality control procedures and is "completely free of traces of atrazine".

The information bulletin also contains the following section on food safety.

> "The food safety question has been thoroughly considered, and there is no reason to believe there is a food safety concern.
>
> The recall was initiated because trace levels of atrazine herbicide were found, by routine analysis, in some production batches. Through our investigations of reports of plant damage, we detected effects that we do not fully understand.
>
> From the plant symptoms we have seen and our extensive analytical investigations, we believe the cause must be a herbicide at extremely low levels.
>
> The plants show reduced vigor or stunted growth. If the herbicide was present at higher levels, it would be easily detectable and the plants would show more severe symptoms. Based on this information and calculations assuming highest EPA-registered use rates of Benlate, we believe the material is present at extremely low levels and would not present a food safety concern. We cannot find it in the undiluted material straight from the package using highly sensitive analytical techniques. Certainly it would be far below detectable levels after dilution and spraying."

The 7/3/91 letter (document 5) contains the results of analyses of Benlate DF for the contaminants chlorothalonil (see 2 left columns below) and flusilazole (see 2 right columns).

# OF LOTS	CHLOROTHAL. PPM RANGE	# OF LOTS	FLUSILAZOLE PPM RANGE
27	200-300	1	422
114	100-200	0	300-400
395	10-100	1	261
199	<10	0	100-200
		9	10-100
		28	2-10
		37	<2

An additional 28 lots had higher levels of chlorothalonil, but were not released. No information is provided as to the analytical method. Chromatograms and raw data are also not submitted.

DuPont states that the "CONTAMINANT SCREENING GUIDELINES" (document 6) were given to them by EPA Region III in 1989 as the current EPA internal enforcement guidance. These guidelines basically define contamination as the presence of other pesticides. It does not include impurities that arise from reactions that occur during the manufacture of a product. With respect to the levels of contaminants for which further analyses should be done to identify and quantify such pesticides, the Guidelines state the following:

> "The presence of any pesticide other than what is declared on the label and present in quantities equal to or greater than .05%; however, highly toxic material (e.g., endrin or sulfotepp) if present in an amount equal to or greater than .01%, and undeclared herbicides which may cause plant damage at a level greater than .001% would be considered contamination."

DuPont states "We believe we are in compliance with this guidance." Assuming that chlorothalonil and flusilazole are not in Toxicity Category I, the levels reported in this submission would not be considered contamination by the above guidelines as they are below 0.05% (500 ppm). Also, the atrazine levels (<2 ppm) in the one lot reported in document 3 are below the 0.001% (10 ppm) cutoff for undeclared herbicides.

The TV news transcript (document 7) provides no information on contamination levels or residues in crops. It merely reports that Benlate treated crops have been damaged in Florida.

CONCLUSIONS AND RECOMMENDATIONS

1. With regard to the levels of contaminants in the Benlate formulations, we can draw no firm conclusions as only a summary of the results of analyses of Benlate 50 DF is reported. We recommend that DuPont be requested to submit a detailed description of the analytical method(s) and representative chromatograms and raw data to allow our verification of reported levels of atrazine, chlorothalonil, and flusilazole. More analyses for atrazine and other triazine herbicides should be reported for the DF formulations since the analysis of only one batch is reported in the present submission.

2. We also request that analyses and representative chromatograms be submitted for recent production of Benlate **WP**. These analyses at a minimum should include atrazine, chlorothalonil, and flusilazole.

3. We are also unable to draw a firm conclusion as to the levels of atrazine, chlorothalonil, and flusilazole residues in food crops from use of the contaminated Benlate products as no such analyses have been reported. However, if the data requested in

Conclusions 1-2 confirm that typical atrazine contamination is low (i.e., earlier this year we were informed verbally that 2-5 ppm are present in Benlate DF), we could conclude that the presence of detectable residues of atrazine in crops is very unlikely. See the attached 7/11/91 note by Richard Schmitt for an explanation of how these residues were estimated. This note also states that detectable residues of chlorothalonil and flusilazole could be found on those crops with benomyl tolerances on the order of 10 ppm or higher.

4. At this time we recommend that a decision as to the need for actual residue data on crops be delayed until the product analyses described in Conclusions 1-2 are submitted. We are attaching to this memo a preliminary dietary risk assessment by William Burnam for the chlorothalonil and flusilazole (Nustar) contaminants in Benlate. This assessment assumes 100% crop treated with benomyl having the maximum contaminant levels of the other two fungicides.

Attachments
7/11/91 R.D. Schmitt note
7/12/91 W. Burnam note

cc: Loranger, RF, Benomyl SF, Circu
Disk 03:File ATRAZIN4.BEN

July 11, 1991

Subject: Contamination of Benomyl Formulations

Benlate DF (50% benomyl) has been reported to have been contaminated with atrazine, chlorothalonil and Nustar. The atrazine contamination of benlate was reported as 100 ppm in 1989 and 2-5 ppm this year. The chlorothalonil contamination of benlate was reported as ranging from < 10 ppm to 300 ppm. The Nustar (flusilazole) contamination of benlate ranged from < 2 ppm to 422 ppm.

If the contamination level is 100 ppm, the contaminant/benomyl ratio is:

$$100 \text{ ppm}/500{,}000 \text{ ppm} = 0.0002 \ (2 \times 10^{-4})$$

Other contaminate ratios can be estimated in a similar manner.

If one assumes similar deposition and dissipation for the contaminants and benomyl residues, the maximum residues of the contaminant on crops can be estimated by multiplying the contaminant/benomyl ratio times the tolerance levels for benomyl.

For example, if the atrazine/benomyl ratio is 0.00001 (i. e., 5 ppm atrazine in Benlate) and the grape tolerance for benomyl is 10 ppm, maximum atrazine residues in grapes are estimated to be 0.00001 times 10 ppm = 0.0001 ppm. The following table shows estimated contaminant residues in some representative crops assuming 5 or 100 ppm atrazine contamination, 300 ppm chlorothalonil contamination and 400 ppm Nustar contamination.

CONTAMINANT RESIDUE LEVELS

CROP	BENOMYL TOLERANCE(ppm)	5 ppm ATRAZINE (ppm)	100 ppm ATRAZINE (ppm)	300 ppm Chlorothalonil (ppm)	400 ppm Nustar (ppm)
BEAN FORAGE	50	0.0005	0.01	0.03	0.04
PINEAPPLES	35	0.00035	0.007	0.021	0.028
GRAPES	10	0.0001	0.002	0.006	0.008
CUCUMBERS	1	0.000001	0.0002	0.0006	0.0008

Considering that the detection limit for atrazine is in the 0.02-0.05 ppm range, it is very unlikely that detectable residues of atrazine will be found on crops treated with Benlate containing 5 ppm of atrazine (the contamination level found this year). If the contamination level rises to 100 ppm, it is possible that atrazine residues could approach the detection limit in those crops having the highest benomyl tolerances..

For chlorothalonil, the detection limit is 0.01 ppm. It is possible that detectable residues of chlorothalonil will be found on crops such as bean forage or pineapple treated with Benlate containing 300 ppm chlorothalonil. In fact, any crop with a benomyl tolerance of 15 ppm or greater could have detectable residues of chlorothalonil if treated with benlate containing 300 ppm chlorothalonil.

For Nustar, the detection limit is 0.005 to 0.01 ppm. Crops having benomyl tolerances at 10 ppm or higher that are treated with Benlate containing 400 ppm Nustar contaminant may show detectable residues of Nustar. In the above table, bean forage and pineapples could all show detectable residues of Nustar.

R D Schmitt

Note to Frank Sanders, FHB, RD

Subject: Chlorothalonil and Nustar (flusilazole) Contamination of Benomyl Formulations

I'm attaching Dr. Schmitt's memo regarding Chem Branch's opinion of the significance of benomyl's contamination. Using Schmitt's worst-case ratio of contamination and similar deposition and dissipation rates rough estimates of exposure and thus risk can be made for chlorothalonil and Nustar residues appearing on benomyl treated crops.

Estimates of exposure can be made by multiplying the TMRC for benomyl (0.056 mg/kg/day) times the contamination ratio of 6×10^{-4} for chlorothalonil or 8×10^{-4} for Nustar. The resulting dietary lifetime exposure for 100% of crops treated are 3.4×10^{-5} mg/kg/day for chlorothalonil and 4.5×10^{-5} mg/kg/day for Nustar. For chlorothalonil (a B_2 carcinogen with a Q_1^* potency factor of 0.011) the most sensitive indicator of risk is its cancer potential. The lifetime cancer risk (100% crop treated) is $(3.4 \times 10^{-5}) \times (0.011)$ or 4×10^{-7} for chlorothalonil.

Nustar, due to the lack of an MTD, is being retested for cancer. One year interim data for female rats showed an increase in urinary bladder transitional cell carcinomas in the high dose group. The complete study has not been sent in nor reviewed but is likely that a Peer Review will be needed. Currently there is an ADI (RfD) available for Nustar based on a NOEL of 0.2 mg/kg/day in a dog study and a safety factor of 300. When the exposure estimate of 4.5×10^{-5} is compared to the RfD of 7×10^{-4}, only 6.5% of the RfD is used by Nustar contamination of benomyl.

Attachment
cc: Caswell file (Benonyl)
Penelope Fenner-Crisp
Richard Schmitt

7/12/91