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

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MAY 9 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Diflubenzuron.** Response to Solvay-Duphar/Uniroyal Estimation of the Potential Lifetime Cancer Risk to the US Population from Dietary Exposure to Diflubenzuron-derived Para-Chloroaniline and Related Products dated April, 1994. Reregistration Case No. 0144 Chemical No. 108201 No MRID #. DP Barcode D202763 CBRS #13,595

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THRU: Edward Zager, Chief
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TO: The HED Metabolism Committee

and

Albin Kocialski, Section Head
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Solvay-Duphar/Uniroyal Chemical Company have responded to a the decision of the HED Metabolism Committee concerning the risk analysis for diflubenzuron and metabolites (S.Knizner, 3/22/94, memo entitled "Outcome of the 3/17/94 Meeting of the HED Metabolism Committee"). The registrant has submitted a document entitled "Estimation of the Potential Lifetime Cancer Risk to the US Population from Dietary Exposure to Diflubenzuron-derived Para-Chloroaniline and Related Products", dated April, 1994.

The points raised in this response concerning levels of diflubenzuron (DFB), para-chloroaniline (PCA), and/or chlorophenylurea (CPU) found in raw and processed agricultural commodities (found in pages 6-11 of the registrant's response) are addressed below.

Conclusions

In general, the residue values for DFB, PCA, and CPU in/on raw and processed agricultural commodities and meat/poultry/milk/eggs calculated by CBRS and the registrant are in agreement.

The registrant and CBRS differ in percent crop treated for some commodities. Whenever available, CBRS used percent crop treated data as supplied by the Biological and Economical Analysis Division (BEAD) of OPP, and if this information was not available, a worst case estimate of 100% crop treated was used, as per Branch policy. Since writing the 3/22/94 memo, CBRS has received additional information from BEAD concerning percent crop treated for mushrooms and citrus. New risk calculations (see below) have been conducted reflecting this additional information.

The primary reason risk calculations performed by the registrant are lower than those calculated by the Agency is that the registrant assumed that only 20% of CPU residues would be converted to PCA. In its meeting on 11/5/93, **the HED Metabolism Committee concluded that the sum total of PCA, CPU and PCAA (para-chloroacetaniline) should be used for all risk calculations** (A.Rathman, 11/15/93, memo entitled "Outcome of the HED Metabolism Committee meeting of 11/5/93"). CBRS abided by this decision in all calculations. A memo from R. Engler, dated 2/14/94, entitled "Risk Assessment for 'Chloroanilines', and Other Carcinogenic Metabolites" contains further discussion concerning the Metabolism Committee's decision. Additionally, CBRS used 2% for the in vivo conversion of DFB to PCA based on a memo from TOX (H.Spencer, 3/21/94). CBRS defers to the HED Metabolism Committee and TOX for a response to these matters.

Based on the new information received from BEAD concerning mushroom and citrus percent crop treated, and following the instructions of the Metabolism Committee noted in the previous paragraph, CBRS revises its risk estimates as follows: For the "Low Animal Dietary Burden" the risk estimate is 1.00×10^{-6} (previously it was 1.13×10^{-6}); and for the "High Animal Dietary Burden the risk estimate is 1.53×10^{-6} (previously it was 1.66×10^{-6}).

Detailed Considerations

Mushrooms

1) The registrant agreed that using the data from a mushroom metabolism study (Accession No. 265703), residues of DFB were determined to be 0.18 ppm, PCA was found at 0.02 ppm and CPU was found at 0.6 ppm. The registrant also agrees that extrapolating to the 0.2 ppm tolerance for DFB, residue levels would be 0.022 ppm for PCA and 0.667 ppm for CPU.

The registrant states that 20% of the amount of CPU could be converted to PCA, yielding a total PCA level of 0.155 ppm. CBRS calculated that the total residues of concern (PCA and CPU) would be 0.689 ppm.

CBRS Response: In its meeting on 11/5/93, the HED Metabolism Committee concluded that the sum of PCA, CPU and PCAA (para-chloroacetaniline) should be used for all risk calculations (A.Rathman, 11/15/93, memo entitled "Outcome of the HED Metabolism Committee meeting of 11/5/93"). CBRS abided by this decision in all calculations.

2) The registrant cited MRID #40870501 which described results from diflubenzuron field trials on mushrooms. In this study, the average CPU residue was 0.006 ppm, with a maximum of 0.015 ppm. The registrant then states that 20% of this CPU level should be converted to PCA.

CBRS Response: This study was not used for CBRS calculations because a review by the Agency (S.Malak, CBTS #4608, 3/31/89) found the study to be deficient for the following reasons: (i) data indicating that residues of DFB per se in/on mushrooms treated at 1 x were <0.01 (non-detectable) - 0.049 ppm were not supported by sample chromatograms of treated vs. fortified mushrooms, nor were standard curves for DFB, CPU or DFBA provided; and (ii)no data were submitted depicting residues of PCA or PCAA. The Registration Standard Update (6/21/92) required additional data depicting PCA and PCAA (and any other residues of concern that might be identified in required metabolism studies) in mushrooms reflecting label rates and directions as required by the Guidance Document. Residues must be determined in/on the first, second, third, fourth, and fifth flush mushrooms treated at spawning. The residue analytical method used for PCA and PCAA should be sensitive to the 1 ppb level.

Concerning the 20% conversion of CPU to PCA, see response to Point 1 above.

3) The registrant estimates that the DFB market share for use on mushrooms is about 51% based on total US production.

CBRS Response: When CBRS estimated levels of DFB and PCA to be used for the risk assessment dated 3/22/94, BEAD was unable to provide data depicting percent crop treated. In the 3/22/94 memo, CBRS noted that when this information becomes available, it should be used to refine the risk estimate. BEAD has now obtained mushroom percent crop treated data. BEAD estimates that approximately 90% of all mushrooms grown on the East Coast of the US are treated with DFB and 70% of total US production is treated with DFB. The difference between CBRS' original assumption of 100% crop treated versus 90% crop treated does not significantly alter the risk calculations, that is the total risk remains above 1.0×10^{-6}. Specifically, the mushroom contribution to risk changes from 8.7×10^{-7} to 7.8×10^{-7} when going from

100% crop treated to 90% crop treated, and the total risk changes from 1.13×10^{-6} to 1.05×10^{-6} for the "Low Animal Dietary Burden" and from 1.66×10^{-6} to 1.58×10^{-6} for the "High Animal Dietary Burden"

Citrus

4) The registrant stated that "The pending use of diflubenzuron on citrus is limited to the state of Florida...", and FL represents 63.59% of the total US citrus production. The registrant then assumed a 33% market share for DFB, resulting in an estimate of 21% crop treated.

The registrant also noted that although no PCA residues were detected (less than 1 ppb) in citrus, PCA levels were estimated using a 2% conversion of DFB residues to PCA.

CBRS Response: CBRS notes that a Section 3 registration is being sought for DFB use on citrus, and based upon this pending national registration, CBRS assumed 100% crop treated for all citrus calculations in its 3/22/94 memo.

Since this time, BEAD has informed CBRS that DFB use on citrus, to control the citrus rust mite, would be necessary only in FL. CBRS therefore has recalculated risk based on 64% citrus crop treated. The citrus (grapefruit and oranges) contribution to risk changes from 1.4×10^{-7} to 0.90×10^{-7} when going from 100% crop treated to 60% crop treated.

Additionally, the difference between CBRS' original assumption of 100% crop treated versus 64% crop treated results in a difference to livestock dietary burden, changing the "Low Animal Dietary Burden" from 0.65 ppm to 0.50 ppm and the "High Animal Dietary Burden" from 4.45 ppm to 4.30 ppm. The result of these changes on the risk contribution from red meat and milk is as follows: High Animal Dietary Burden risk contribution changes from 1.53×10^{-8} to 1.48×10^{-8} and Low Animal Dietary Burden risk contribution changes from 2.6×10^{-9} to 2.0×10^{-9}.

Therefore, the total risk changes from 1.13×10^{-6} to 1.08×10^{-6} for the "Low Animal Dietary Burden" and from 1.66×10^{-6} to 1.61×10^{-6} for the "High Animal Dietary Burden"

CBRS used 2% for the in vivo conversion of DFB to PCA based on a memo from TOX (H.Spencer, 3/21/94).

Soybeans

5) The registrant again noted that CBRS assumed 2% conversion of DFB to PCA for all calculations. Based on the DFB soybean tolerance of 0.05 ppm, this results in 0.001 ppm PCA.

CBRS Response: CBRS used 2% for the in vivo conversion of DFB to PCA based on a memo from TOX (H.Spencer, 3/21/94). CBRS and the registrant agree that the percent crop treated (less than 1%). CBRS obtained this information from BEAD.

Walnuts

6) The registrant again noted that CBRS assumed 2% conversion of DFB to PCA for all calculations. Based on the DFB walnut tolerance of 0.05 ppm, this results in 0.001 ppm PCA.

CBRS Response: CBRS used 2% for the in vivo conversion of DFB to PCA based on a memo from TOX (H.Spencer, 3/21/94). Because BEAD had no information concerning percent crop treated, 100% was assumed. The registrant also assumed 100% crop treated.

Cottonseed

7) The registrant again noted that CBRS assumed 2% conversion of DFB to PCA for all calculations. Based on the DFB walnut tolerance of 0.2 ppm, this results in 0.004 ppm PCA.

CBRS Response: CBRS used 2% for the in vivo conversion of DFB to PCA based on a memo from TOX (H.Spencer, 3/21/94). BEAD estimated percent crop treated as less than 10%. The registrant also assumed 10% crop treated.

Livestock

Calculation of Livestock Dietary Burden

8) For grass, cottonseed, soybean seed, soybean hulls, and soybean soapstock the livestock dietary burden calculated by the registrant is the same as that calculated by CBRS. For dehydrated orange pulp, the registrant generated a lower dietary burden than CBRS because of the assumption of 21% crop treated versus CBRS' assumption of 100% crop treated.

The registrant agreed with CBRS that the bolus use in cattle results in a dietary burden of 4.0 ppm, however, the registrant estimated that less than 1% (specifically 0.3%) of cattle are treated with the bolus, resulting in a dietary burden from this use of 0.04 ppm.

The net result of the registrant's calculations was a dietary burden of 0.21 ppm for beef/dairy cattle, and 0.0013 ppm for poultry.

CBRS Response: The effect of changing the percent crop treated from 100% to 64% is discussed under "Citrus" above. Concerning the bolus use of DFB, CBRS in its original risk assessment calculated a dietary burden assuming 100% of cattle receive

the bolus ("High Animal Dietary Burden" representing 4.00 ppm DFB in the livestock diet) or 5% of cattle receive the bolus ("Low Animal Dietary Burden", representing 0.20 ppm DFB in the livestock diet). The 5% cattle treated estimate was based on information supplied by BEAD.

Cattle

9) The registrant's calculation for levels of PCA in cattle liver, milk, kidney, fat, and muscle are all based on: 1) an anticipated dietary burden of 0.21 ppm; 2) 20% conversion rate of CPU to PCA; and 3) in some cases (kidney, fat, and muscle) a 2% conversion of DFB to PCA.

Poultry

10) For poultry fat, muscle, kidney, liver and eggs the registrant's calculations result in lower risk than those of CBRS because although there is agreement on the dietary burden (0.0013 ppm DFB in the poultry diet), the registrant assumes 20% conversion of CPU to PCA whereas CBRS calculations add all residues of these metabolites. Additionally, using data available from MRID #00070186, CBRS extrapolated residues of DFB, PCA and CPU from the 5 ppm dosing level whereas the registrant extrapolated values from the 0.05 ppm dosing level.

CBRS Response: The assumptions made by the registrant result in a lower risk than calculated by CBRS. The basis for CBRS' summation of CPU and PCA metabolites and in vivo conversion of DFB to PCA have been discussed above.

CBRS also notes that the registrant seems to have assumed that DFBA was used in the summation of "PCA and related compounds". On page 2 of its 3/22/94 memo, CBRS notes that only CPU and PCAA were considered "PCA related" compounds, not DFBA.

cc: S.F., circ., R.F., Reg Stnd File, S.Knizner
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