K7-

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

MAR 8 1991

MAR 8 1991

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: SAN-582H Herbicide in/on Soybeans. Metabolism Study. DEB # 7657.

Memorandum of Conference 2/21/91.

FROM: Michael T. Flood, Ph.D., Chemist
Tolerance Petition Section II
Chemistry Branch I -- Tolerance Support
Health Effects Division (H7509C)

THROUGH: Elizabeth T. Haeberer, Section Chief
Tolerance Petition Section II
Chemistry Branch I -- Tolerance Support
Health Effects Division (H7509C)

TO: Joanne Miller/Sangeeta Khattar, PM 23
Fungicide-Herbicide Branch
Registration Division H7505C

Representatives of Sandoz Crop Protection Corporation met with Mike Flood and Betty Haeberer to discuss the preliminary report of the soybean metabolism study on the herbicide SAN-582H. Sandoz intends to submit an.d EUP application very soon. PP#0G3892, which would permit use in/on corn, was recently reviewed by CBTS (Mike Flood, memo of 1/24/91).

The metabolism of SAN-582H in soybeans is similar to that in corn. Parent is extensively metabolized to at least 40 metabolites and not present in any rac from forage through mature soybeans. In an attempt to characterize the metabolites, Sandoz synthesized numerous likely metabolites for co-chromatography and spectroscopic comparison. Three significant metabolites were identified: oxalamide, which probably is a soil metabolite; the sulfonate conjugate of SAN-582H and the sulfoxide of thiolactic acid. However, these three metabolites constituted less than 30% of the total radioactive residue in forage, hay or seed. A major problem in identification was the presence of coextractives which resulted in broad TLC bands and made characterization by spectroscopic methods impossible.

Because the problems in the soybean metabolism study are likely to be quite similar to those encountered in the already reviewed corn metabolism study, we discussed the deficiencies in that study. CBTS admitted that complete characterization of all

metabolites resulting from use of preemergence herbicides was not a realistic possibility in most cases. In the absence of complete characterization, registrants should proceed as follows:

1. Those compounds that have been identified must be identified by more than one method, or if only TLC is possible, the metabolite should co-chromatograph with the standard in more than one solvent system. In the corn metabolism study, a common deficiency was that only one solvent system was used in characterization. In the case of SAN-582H, characterization in two solvent systems is especially important because the TLC bands were very broad.

2. When concentrations of metabolites are reported, data (chromatographs, standard curves) from which the concentrations were obtained should also be reported so that we can verify these concentrations. For example, in the corn metabolism study we were unable to verify the reported concentrations of oxalamide because supporting data were incomplete.

3. If an elaborate solvent fractionation scheme is used, such as in the corn metabolism study, the registrant should try to demonstrate that metabolites isolated but not identified in one fraction are not identical to those in other fractions. This becomes important when the registrant argues that no one metabolite is present at concentrations greater than 0.05 ppm or 10% of the total radioactive residue.

We recommended that the numerous polar metabolites be subjected to more rigorous hydrolysis conditions, such as reflux in 3N HCl for several hours, to release more easily identifiable organosoluble species.

CBTS did not recommend for the proposed temporary tolerance for corn because of an inadequate analytical method. We told Sandoz that percent recoveries and standard deviations of the method were too high. Our evaluation of an analytical method includes examination of relevant chromatograms as well as numerical recoveries. Hence supporting chromatograms -- especially the chromagrams of samples fortified at the limit of quantitation -- should be submitted in the future. The company is revising its analytical method.

cc: SF, RF, Circu., Reviewer(M.Flood), C.Furlow(PIB/FOD), E. Haeberer, PP#0G3892, PP#0F3918.

RDI:SectionHead:E.T.Haeberer:3/6/91:BranchSeniorScientist: R.A.Loranger:3/6/91
H7509C:CBTS:Reviewer(MTF):CM#2:Rm810:557-4362:typist(mtf):3/7/91.