PP# 0F3948

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

DEC 16 1992

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

SUBJECT: SAN-582H (Dimethenamide/Frontier®). Determination of the Sulfonate Metabolite in Goat Excreta.

DP Barcode: D181807. CBTS # 10447.
MRID # 424395-02.

FROM: Michael T. Flood, Ph.D., Chemist
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Health Effects Division (H7509C)

THROUGH: Debra F. Edwards, Ph.D., Acting Chief
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TO: C. Giles-Parker/J. Stone, PM 22
Fungicide-Herbicide Branch
Registration Division (H7505C)

and

Toxicology Branch II
Health Effects Division (H7509C)

This submission consists of two parts. The first part consists of one volume dated 7/29/92 and contains a discussion of the toxicology of SAN-582H corn metabolites and a response to the 6/8/92 meeting held with TB II. CBTS will not comment on this volume, which should be forwarded to TB; but we observe that issues discussed have probably been already resolved. Results of the Metabolism Committee meeting of 11/3/92 have rendered much of this submission moot.

The second part, with accompanying letter dated 8/5/92, consists of sulfonate analyses in mouse and goat excreta. We have already forwarded the mouse metabolism results (MRID # 424395-01) to TB II for review.

Conclusions (pertaining to this memo only)

1. The sulfonate conjugate of SAN-582H is probably present in the urine and feces of ruminants administered SAN-

582H. Absolute identification, if ever necessary, would have to consist of matching spectra (MS, IR and/or NMR) with those of standards.

2. The HED Metabolism Committee, in its meeting of 11/3/92, concluded that the sulfonate metabolite need not appear in the tolerance expression for corn. This conclusion was based in part on the preliminary evaluation of residue data showing the absence of this metabolite at a level of 0.05 ppm in corn RACS. Therefore, until the submitted residue data are reviewed, this conclusion is provisional.

Recommendation

CBTS continues to recommend against the proposed tolerances for reasons listed in our 7/29/92 memo.

Detailed Considerations

Sandoz has submitted the following report:

"SAN 582 H: Determination of the Presence of Sulfonate Metabolite in Goat Excreta;" A.S. Guiguis, C.C. Yu; 6/10/92; Lab. Project ID 414105-24; Performing Lab.: Sandoz Agro, Inc., Des Plaines, IL. (MRID # 424395-02)

Urine from the goat metabolism study discussed in our 1/24/91 memo was fractionated using a C18 cartridge. The residue, dissolved in a small amount of methanol, was subjected to TLC. The band corresponding to the sulfonate standard was scraped, shaken for one hour with methanol. The methanol solution was filtered, reduced to a small volume and again subjected to TLC but with a different solvent system. A total of 6 different solvent systems were used sequentially. The sulfonate was further confirmed by two-dimensional TLC with two additional solvent systems and by HPLC. The sulfonate metabolite accounted for 0.01% of urinary radiocarbon, although because of the multiple purification steps more was probably lost.

Feces were extracted with acetone and methanol and then subjected to four successive TLC's. Confirmation was by two-dimensional chromatography with two different solvent systems. FAB-MS and NMR spectra are also given. The corresponding MS of the standard is not given. The NMR spectrum, when compared to a standard spectrum, showed that the isolated compound was still not pure, but peaks corresponding to those from the sulfonate standard are present. Sandoz reports that the sulfonate metabolite accounted for 0.31% of the total radiocarbon.

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Comment

If it were absolutely essential that the sulfonate metabolite be identified in ruminant excreta, further characterization would be necessary. Sandoz would have to show that the isolated material has an identical spectrum to the NMR, IR or MS of the standard. It is noteworthy that adequate separation could only be attained after chromatography in many solvent systems -- six for urine extracts, four for feces extracts. In its first submission, Sandoz identified metabolites on the basis of co-chromatography with standards in one solvent system.

The HED Metabolism Committee, in its meeting of 11/3/92, concluded that the sulfonate metabolite need not appear in the tolerance expression for the SAN-582H residue in/on corn. The conclusion was based on the absence of this metabolite in residue field trials at levels greater than 0.05 ppm. The conclusion concerning sulfonate residue levels, in turn, was based on preliminary evaluation of residue data and is therefore provisional until the data are formally reviewed.

cc: RF, SF(SAN-582H), Circu., PP#0G3980, PP#0F3918, Mike Flood, E. Haeberer.
H7509C:CBTS:Reviewer(MTF):CM#2:Rm800A:305-6362:typist(mtf):12/16/92.
RDI:SectionHead:ETHaeberer:12/16/92:BranchSeniorScientist:RALoranger: 12/16/92.