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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

October 29, 1998

MEMORANDUM

SUBJECT: Diflufenzopyr. PC Code 005107. Outcome of the HED Metabolism Assessment Review Committee Held on September 28, 1998.

FROM: Leung Cheng, Chemist
Chemistry & Exposure Branch 1
Health Effects Division (7509C)

THROUGH: Francis Suhre, Branch Senior Scientist
Chemistry & Exposure Branch 1
and
Richard Loranger, Chair
Metabolism Assessment Review Committee
Health Effects Division (7509C)

TO: George Kramer, Executive Secretary
Metabolism Assessment Review Committee
Health Effects Division (7509C)

The metabolism of diflufenzopyr in field corn, livestock, and rotated crops was discussed at the 9/28/98 HED Metabolism Assessment Review Committee meeting. Details of the metabolites found in corn and livestock or taken up in the rotated plants were described in a briefing memorandum (L. Cheng, 9/16/98).

Diflufenzopyr was not detected in corn. Major metabolites found in corn forage and stover include M1 (8-methylpyrido(2,3-d)-pyridazin-5(6H)-one), M10 (8-hydroxymethyl-5(6H)-pyrido(2,3-d)pyridazone), its glucose conjugate, and M9 (8-methylpyrido(2,3-d)pyridazine-2,5(1H,6H)-dione). Corn grain contained 3-4 discrete unknowns, all at <10% TRR or <0.05 ppm. Diflufenzopyr and M5 (6-((3,5-difluorophenylcarbamoyl-8-methylpyrido(2,3-d)-5-pyridazinone) were found in >10% total radioactive residue in milk, kidney and liver of goats, but not in fat. M1 and M19 (8-hydroxymethylpyrido(2,3-d)-2,5(1H,6H)-dione) were also found

in significant levels (10% or greater) in milk. Diflufenzopyr was not detected in poultry, and M1 was the only significant metabolite identified, and in egg white. The HIARC expressed a concern that if 3,5-difluoroaniline (M2), a rat urinary metabolite, were found in significant levels in meat and milk, this metabolite would be regulated based on the carcinogenicity of dichloroaniline. In both field corn and livestock, no metabolite matched chromatographically with 3,5-difluoroaniline. In any future radiolabeled studies, the registrant should be advised to look for free 3,5-difluoroaniline.

The Committee concluded that the tolerance for diflufenzopyr in field corn includes parent and metabolites convertible to M1. However, M10 needs to be included in the assessment of dietary exposure because of its structural similarity to M1. It also commented that because of the exaggerated dose administered in the livestock metabolism studies and the metabolism results, tolerances on meat and milk are not needed. If any livestock feeding studies are conducted in the future, analyses should be done for parent, metabolites convertible to M1, and free and acid released M19.

According to the information presented at the 10/5/98 FQPA Safety Factor Committee meeting, movement of diflufenzopyr into surface water through runoff may occur under limited conditions when sufficient rainfall occurs close to the time of application. In laboratory studies, SAN 835H hydrolyzed in sterile buffer solutions at 25 C with half-lives of 12.9 days, 23.9 days, and 25.6 days in pH 5, 7, and 9 buffer solutions, respectively. Major degradates at all pH's were M1 and M6 (2-acetylnicotinic acid). M1 was 12% of applied (1 ppm - treatment rate) at pH 5 from days 21-31 and 27-29% of applied at pH's 7-9 at day 31. At pH 5, M8 (methyl N-(3,5-difluorophenyl)-carbamate) was also a major degradate and accounted for 9% of the applied at day 31. M2 (3,5-difluoroaniline), M3 (N,N-bis(3,5-difluorophenyl)-urea), M5 (6-((3,5-difluorophenyl)carbamoyl)-8-methyl-pyrido(2,3-d)-5-pyridazinone), and an unidentified product were minor hydrolysis products. At pH's 7 and 9, M8 was also present as a minor product.

The Committee concluded that diflufenzopyr, metabolites convertible to M1, and difluoroaniline need to be included when conducting acute and chronic risk assessments in drinking water.

The Committee commented that in the confined rotational crop study diflufenzopyr was not sprayed directly to the soil, and the total radioactivity in the rotated crops were fractionated among several organic solvents without attempts for structural identification. As a result, the Committee concluded that the study was not conducted according to 860 guidelines.

2

Attendees
Richard Loranger
Leung Cheng
Kit Farwell
George Kramer
Chris Olinger
William Dykstra

cc:RF, Cheng, Dykstra (RAB1), Stanton (RD)
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