SEP - 5 1986

BASF Wyandotte Corporation
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Attention: Donald M. Yoder

Gentlemen:

Subject: Poast Herbicide (Alfalfa and Soybeans)
EPA Registration No. 7969-58
EPA Pesticide Petition No. 3F2904
Your Submission Dated December 5, 1985

This refers to Pesticide Petition No. 3F2904 proposing the establishment of tolerances for the combined residues of the herbicide sethoxydim [2-[(1-ethoxyimino)butyl]-5-(ethythio)propyl]-3-hydroxy-2-cyclohexen-1-one and its metabolites containing the 2-cyclohexen-1-one moiety (calculated as the herbicide) in or on the raw agricultural commodities soybean hay at 10 parts per million (ppm), alfalfa hay and forage at 40 ppm and milk at 0.05 ppm.

The scientific review and evaluation of the information submitted above have been completed. The following are our conclusions/comments.

Residue Chemistry

1. Sethoxydim residues detectable in ruminant milk consist of MSO, accounting for 25% of the total radioactivity; nor-MSO, accounting 5% of total radioactivity; MSO_2, accounting for 10% of the total radioactivity; and nor-MSO_2, accounting for < 3% of the total radioactivity.

2. Sethoxydim residues detectable in ruminant liver consist of MS, accounting for 12% of the total radioactivity; nor-MS, accounting for 7% of the total radioactivity; MSO accounting for 8% of the

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CONCURRENCES								
SYMBOL ▶	TS-767C							
SURNAME ▶	VKWells							
DATE ▶	9/5/86							

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total activity; nor-MSO, accounting for 3% of the total radioactivity; MSO_2, accounting for 21% of the total radioactivity; and nor-MSO_2, accounting for 55% of identified activity. It was shown that MSO_2 and MSO are the two major metabolites in the goat liver accounting for a total of 73% identified activity.

3. Sethoxydim residues detectable in rumaniant kidney consist of MS, accounting for 2.5% of total radioactivity; nor-MS, accounting for < 2% of the total radioactivity; MSO, accounting for 21% of the total radioactivity; nor-MSO, accounting for 12% of the total activity; MSO_2, accounting for 16% of the total radioactivity; and nor-MSO_2 accounting for 5% of the total radioactivity, for a total of 58% identified activity.

4. Sethoxydim residues in ruminant meat and fat were too low to permit characterization of their nature.

5. Since known metabolites contain the 2-cyclohexene-1-one moiety, the nature of the residues in ruminants is adequately defined. The residue of concern in ruminants consists of the parent and its metabolites containing the 2-cyclohexene-1-one moiety which are: MSO, MSO_2, nor-MSO; and nor-MSO_2.

6. When the parent compound is used in the poultry metabolism study, the following occurs.

   a. Sethoxydim residues in poultry muscle consist of parent compound sethoxydim, per se, MS, accounting for 4% of the total radioactivity; MSO, accounting for 60% of the total radioactivity; MSO_2 accounting for 30% of the total radioactivity, for a total of 94% identified activity.

   b. Sethoxydim residues in poultry fat consist of the parent compound sethoxydim, per se, MS, accounting for 69% of the total radioactivity; MSO, accounting for 16% of the total radioactivity; and MSO_2, accounting for 7% of the total radioactivity, for a total of 92% identified activity.

   c. Sethoxydim residues in poultry liver consist of parent compound sethoxydim, per se, MS, accounting for 3% of the total radioactivity; MSO, accounting for 58% of the total radioactivity; MSO_2 accounting for 21% of the total radioactivity, for a total of 82% identified activity.

7. When the sulfoxide metabolite is used in the metabolism study, the following occurs.

   a. Sethoxydim residues in poultry fat consist of MSO, accounting for 50% of the total radioactivity; MSO_2, accounting for 27% of the total radioactivity; and MISO accounting for 5% of the total radioactivity, for a total of 82% of the identified activity.

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b. Sethoxydim residues in poultry fat consist of MSO, accounting for 39% of the total radioactivity; MSO_2, accounting for 23% of the total radioactivity; and $MISO_2$, accounting for 6% of the total radioactivity, for a total of 68% identified activity.

c. Sethoxydim residues in poultry liver consist of MSO, accounting for 37% of the total radioactivity; MSO_2, accounting for 35% of the total radioactivity; and MISO, accounting of 14% of the total radioactivity, for a total of 86% identified activity plus 6% unidentified polar compounds.

d. Neither metabolism of the compounds to the corresponding nor-series, nor reduction of the sulfoxide to the parent compound occurred in poultry as it did in the goat. Note, too, that both BWC-30 and the Direct Oxidation Methods are capable of determining the nor-series uncovered in ruminants milk and tissues.

e. Since known sethoxydim metabolites contain the 2-cyclohexene-1-one moiety, our conclusion regarding the terminal residues in poultry is consistent with that for ruminant animals. It is our judgment that sethoxydim metabolism in poultry is adequately delineated. The residues of concern in poultry consist of the parent compound, sethoxydim, and its metabolites containing the 2-cyclohexene-1-one moiety which are MSO, MSO_2, and MISO.

8. Adequate analytical methodologies are available for enforcement of the proposed tolerances. A method trial will be initiated for the nor-metabolites. You must agree to submit the following standards to EPA, RTP, and COB, Beltsville laboratory: MISO, nor-MSO, and nor-MSO_2.

9. The grazing restriction should include the term "green succulent" to read "Do not graze treated soybean fields and do not feed treated soybean forage (green succulent) or ensilage to livestock." A revised Section B is needed to reflect this.

10. The available comparability data between ground and aerial applications indicate that no significant differences are expected in sethoxydim residues in/on plant commodities from either ground or aerial applications from the proposed use.

11. Additional feeding studies are not needed.

12. The proposed tolerances of 10 ppm for soybean hay and 40 ppm of alfalfa hay and forage for residues of sethoxydim are adequate.

13. The proposed 0.05 ppm tolerance for milk is adequate and consistent with currently established tolerance for milk.

14. The present tolerances for residues of sethoxydim in/on the meat, milk, poultry and eggs will not be exceeded as a result of this use as well as registered and currently pending uses.

Toxicology

The submitted Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay of 5-OH-MSO_2 has been reviewed and is unacceptable.

1. A description of the procedures used in performing the study was lacking.

2. No mention of the vehicle used in dosing the negative controls was made.

3. The SOP stated that the positive controls were to be dosed at a concentration at 0.05 ug/mL, but the table reported a concentration of 0.10 ug/mL.

4. Mean cultures for each concentration/control were reported, but there were no individual culture data.

5. The assay should have been repeated using hepatocytes from a female rat to confirm the reported negative results.

Summary

The following items are needed.

1. A label revising the soybean grazing restriction as discussed in comment 9 under Residue Chemistry.

2. Agreement to submit the following standards to EPA, RTP, and COB, Beltsville laboratory: MISO, nor-MSO, and nor-MSO_2

3. Agreement to repeat the above toxicology study.

Sincerely yours,

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Fungicide-Herbicide Branch
Registration Division (TS-767C)