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PM 520992



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

JUL 1 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP #6G3398. Metsulfuron methyl on range and pasture
grasses. Comments on the analytical method and
residue data. Accession Nos. 262110 and 262324.
RCB #874 and #875.

FROM: John M. Worthington, Chemist
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*Linda S. Propst
for*

TO: Robert Taylor, PM. No. 25
Registration Division (TS-767)
and
Toxicology Branch
Hazard Evaluation Division (TS-769)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

NO

E.I. du Pont de Nemours and Company proposes the establishment of temporary tolerances for residues of the herbicide, metsulfuron methyl, (methyl 2-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-amino]-carbonyl]-amino]sulfonyl]benzoate in or on grass forage and fodder at 15 ppm, grass hay at 60 ppm and in milk at 0.3 ppm metsulfuron methyl is structurally related to chlorsulfuron.

Permanent tolerances have been established for residues metsulfuron methyl in barley and wheat grain at 0.05 ppm, in their forage at 5.0 ppm, in their hay at 20 ppm in their straws at 0.1 ppm, in milk at 0.05 ppm and in meat, fat, and meat by-products of cattle, goats, hogs, horses and sheep at 0.10 ppm pursuant to PP #4F3127.

The proposed one year experimental program for grasses involves the application of approximately 132 lbs. a.i. to 3500 acres of grasses in Texas and New Mexico.

Conclusions

1. The fate of metsulfuron methyl in plants has been adequately delineated for the purpose of the proposed temporary tolerance.
2. Adequate methodology is available to enforce the proposed temporary tolerances.
3. For the purpose of the proposed temporary tolerance, the available residue data are adequate to demonstrate that residues of metsulfuron methyl will not exceed the proposed tolerance levels for grass forage and fodder and grass hay.
- 4a. The available feeding data are adequate to demonstrate that secondary residues in milk from the proposed use will not exceed 0.2 ppm. Therefore, a 0.2 ppm tolerance level for milk would be more appropriate rather than the 0.3 level currently proposed.
- 4b. The available feeding data are adequate to demonstrate that secondary residues in meat and meat by-products from the feeding of treated grass hay will not exceed the existing 0.1 ppm tolerance in all tissues except kidney. In the case of kidney, a level of 0.5 ppm will be needed to cover residues from the use requested here.

Recommendations

1. Contingent upon the revision of the proposed tolerance for milk to 0.2 ppm and the request of a 0.5 ppm tolerance for residues in the kidney of cattle, goats, hogs, horses, and sheep, RCB recommends that the proposed tolerances be granted.
2. For a future permanent the following will be required:
 - a) Additional residue for grasses reflecting the maximum proposed rate.
 - b) Residue data determining the actual level of metsulfuron methyl resulting in treated hay from the proposed use.

Detailed Considerations

Formulation

Technical metsulfuron methyl is at least 93% pure. RCB does not anticipate any residue problems resulting from the technical impurities. (See the attached Confidential Appendix for a discus-

sion of the manufacturing process and a list of the technical impurities.)

Metsulfuron methyl is to be formulated as Escort Herbicide which is a 60% a.i. dry flowable. The composition of the product is

[REDACTED] The inert ingredients of the proposed formulation are exempt from the requirement of a tolerance under Section 180.1001.

Proposed Use

Metsulfuron methyl is proposed for use to control of a variety of weeds in rangeland and pasture grasses at rates ranging from 0.3 oz. to 1.6 lbs. active ingredient per acre. Both aerial and ground applications are permitted. A minimum spray volume of 10 gallons is required for aerial applications.

A label restriction prohibiting grazing livestock in treated areas within one day of treatment has been imposed.

Nature of the Residue

Plant Metabolism: The fate of metsulfuron methyl in wheat and barley has been discussed in detail in the review of PP #4F3127. (See the memos of 6-12-85 by Philip Errico, 11-4-85 and 1-27-86 by Karl Arne). In summary, metsulfuron methyl is catabolized to methyl 2-[[[[[4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]-carbonyl]-amino]-sulfonyl] 4-hydroxybenzoate and its glucose conjugate, methyl 2-[[[[[4-methoxy-6-methyl-1,3,5-triazin-2-yl)-amino]-carbonyl]-amino]-sulfonyl] 4-glucopyranosyl benzoate.

RCB considers the fate of metsulfuron methyl in grasses adequately delineated for the purpose of the proposed temporary tolerance. Metsulfuron methyl, per se, is the principal residue of concern.

Animal Metabolism: The fate of metsulfuron methyl in rats and goats is also discussed in detail in the above memos. Again, metsulfuron methyl, per se, was shown to to be the principal residue of concern.

Analytical Methods

The proposed analytical method for the determination residues of metsulfuron methyl in grasses involves an 80% acetone and 20% aqueous sodium acetate buffer extraction. After centrifugation of the extract, a 25 ml aliquot is diluted with 100 mls of a sodium bicarbonate buffer and washed with methylene chloride. The extract is then acidified and partitioned against toluene. After centrifugation, the toluene layer is evaporated to dryness and metsulfuron methyl determined by HPLC using a photo-conductivity detector.

Information which may reveal the manufacturing process is not included.

The proposed procedure is reportedly sensitive to 0.05 ppm metsulfuron methyl in grasses. Recoveries of metsulfuron methyl from grass samples fortified at levels ranging from 0.05 to 5 ppm averaged 79.5%. Control values are reported as <0.05 ppm.

The proposed analytical method is considered adequate to enforce the proposed 15 ppm temporary tolerance in grasses and 60 ppm level for the hogs.

The analytical method for the determination of metsulfuron methyl residues in milk is reportedly sensitive to 0.01 ppm metsulfuron methyl in milk. The procedure involves extraction with water, 10% HCL and toluene mixture, centrifugation and removal of the toluene layer. The aqueous portion is reextracted with toluene and the combined toluene fractions chromatographed in a Bond Elut cartridge. Metsulfuron methyl is eluted from the cartridge and determined by an HPLC equipped with photo-conductivity detector. (Milk fat samples, after the cartridge chromatography, were also partitioned between acetonitrile and hexane for additional clean-up.)

The analytical method for the determination of metsulfuron methyl residues in meat is also reportedly sensitive to 0.01 ppm. The method involves grinding the meat sample, extraction with a mixture of acetone, water, sodium acetate and glacial acetic acid, partitioning between sodium carbonate and methylene chloride, acidification and extraction with toluene. The toluene extract is then passed through the Bond Elut cartridge and the metsulfuron methyl residues determined as described above.

Recoveries of metsulfuron methyl from samples of milk, cream, skim milk, kidney, lean meat and liver fortified 0.01-0.10 ppm 69 to 118% and averaged 86%. RCB considers the available methodology for the determination of residues in meat and milk adequate to enforce the proposed temporary tolerances.

Residue Data

Residue data have been submitted from 11 experiments conducted in six different states. Samples of grass were analyzed for residues of metsulfuron methyl 0 to 82 days after treatment. Each study was set up as a residue decline experiment. Application rates ranged up to 2.5 times the maximum proposed rate. Although residues appeared to decline rapidly after treatment, they do not show a typical log-linear decline pattern. The highest reported residue level, 14 ppm, was found 1 day after the application of 1.2 times the maximum proposed rate. Considering the label restriction, prohibiting livestock in treated areas for one day after application the proposed 15 ppm tolerance is adequate to cover residues of metsulfuron methyl resulting in treated grass from the proposed use. Additional residue data reflecting the residue levels resulting from the maximum propose rate will be required for a future permanent tolerance

In lieu of residue data for grass hay the petitioner has proposed a tolerance level adequate to cover the maximum possible concentration of metsulfuron methyl residues in hay from treated grass. The maximum concentrate rate is 4X; and therefore, the petitioner has proposed a 60 ppm tolerance for residues in grass hay.

The proposal of a 60 ppm tolerance is acceptable for the purpose of the proposed temporary tolerance; however, for a future permanent tolerance the residue data determining the level of metsulfuron methyl expected in treated hay will be required.

Storage stability data have been submitted demonstrating that residues of metsulfuron methyl are stable in frozen storage.

Meat, Milk, Poultry and Eggs

The propose use on grasses could theoretically result in a dietary burden of 60 ppm from the feeding of treated grass hay as 100% of the diet. Although we concur with the petitioner that this is extremely unlikely, tolerances to cover any secondary residues from the ingestion of grass hay are required.

Pursuant to PP #4F3127, permanent tolerances have been established for residues metsulfuron methyl in in milk at 0.05 ppm and in meat, fat, and meat by-products of cattle, goats, hogs, horses and sheep at 0.1 ppm to cover the secondary residues resulting from the use on wheat and barley.

The available feeding study shows that milk from cows feed up to 20 ppm metsulfuron methyl contained less than 0.05 ppm and that residues in milk from the highest dose level (100 ppm) could approach 0.217 ppm. Therefore, a 0.2 ppm tolerance level for residues of metsulfuron methyl in milk would be adequate, rather than the 0.3 ppm level proposed.

The available feeding study indicates that the highest concentration of metsulfuron methyl in meat or meat by-products from the ingestion of 100 ppm in the diet was 0.67 ppm in kidney. Maximum kidney residues from the 20 ppm feeding level were 0.32 ppm. Maximum liver residues from the 100 ppm feeding level were 0.07 ppm. All other tissues contained 0.02 ppm or less from all feeding levels. The currently established 0.1 ppm meat tolerance will cover residues from this use on grass with the exception of kidney residues. We believe a level of 0.5 ppm is needed to cover residues in kidney of cattle, goats, hogs, horses and sheep.

cc: S.F., Circu., FDA, PP #6G3398, R.F., PM-25, TOX, Reviewer,
PMSD/ISB, EEB, EAB, and R. Thompson (RTP)

Attachment 1: Confidential Appendix
(attached copy to: PP #6G3398, R.F., PM-25, TOX, Reviewer and
PMSD/ISB only)

TS-769:Reviewer:JMWORTHINGTON>Date:6/30/86
RDI:Section Head:ARR>Date:6/30/86:RDS>Date:6/30/86

METSULFURON METHYL REVIEWS

Page 7 contains the confidential statement of formula.
This page is not included.