12-20-88

DATA EVALUATION RECORD

CHEM 101101 Metribuzin §165-1

FORMULATION--00--ACTIVE INGREDIENT

Naidu, M.V. 1988. Metribuzin confined accumulation study on peanuts. Laboratory Project ID AMR-563-86. Unpublished study prepared and submitted by E.I. du Pont de Nemours and Company, Inc., Wilmington, DE.
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DIRECT REVIEW TIME = 16

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This study was provided by the registrant as support data for reducing the rotational interval for metribuzin on peanuts from 12 months to 8 months.

CONCLUSIONS:

Confined Accumulation - Rotational Crops

This study provides supplemental information towards the registration of metribuzin. This study does not fulfill EPA Data Requirements for Registering Pesticides because peanuts are not a standard crop. More importantly, it does not support the requested reduction in rotational interval for peanuts because storage stability data were not provided and the residues found in peanut foliage may be of concern.

SUMMARY OF DATA BY REVIEWER:

[^{14}C]Metribuzin residues accumulated in peanuts (mature foliage, nut shells, and nut meats) that were planted in sandy loam soil 125 and 246 days after 5-[^{14}C]metribuzin (radiochemical purity >98%) was applied to the soil at 1 lb ai/A (1.8x the maximum application rate). Total [^{14}C]residues were 1.7-3.3x higher in nut meats, nut shells, and foliage

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from the 125-day rotation compared to the 246-day rotation. In both the 125- and 246-day rotations, the majority (>80%) of [^{14}C]residues were either polar compounds or unextractable; no organosoluble [^{14}C]residues were present in quantities sufficient to identify.

The concentrations of total [^{14}C]metribuzin residues in peanuts from the 125-day rotation were: 0.047 ppm in the nut meats; 0.221 ppm in the nut shells; and 1.811 ppm in the foliage. In the nut meats, organosoluble [^{14}C]residues totaled 0.008 ppm, water-soluble [^{14}C]residues totaled 0.018 ppm, and unextractable [^{14}C]residues totaled 0.017 ppm. In the nut shells, organosoluble [^{14}C]residues totaled 0.012 ppm, water-soluble [^{14}C]residues totaled 0.081 ppm, and unextractable [^{14}C]residues totaled 0.097 ppm. In the foliage, organosoluble [^{14}C]residues totaled 0.034 ppm, water-soluble [^{14}C]residues totaled 1.580 ppm, and unextractable [^{14}C]residues totaled 0.158 ppm. The aqueous extract from the foliage contained 14 compounds, two of which were "major". Polar Metabolite I, detected at 0.624 ppm, was tentatively identified as

N-glucoside of 6-tert-butyl-1,2,4-traizin-3,5(2H,4H)-dione;

Polar Metabolite II, detected at 0.521 ppm, was highly unstable and could not be identified. Acid hydrolysis or enzyme hydrolysis with ß-glucosidase or cellulase of the extracted crop fractions did not release any significant organosoluble [^{14}C]residues.

The concentrations of total [^{14}C]metribuzin residues in peanuts from the 246-day rotation were: 0.027 ppm in the nut meats; 0.066 ppm in the nut shells, and 0.628 ppm in the foliage. In the nut meats, organosoluble [^{14}C]residues totaled 0.005 ppm, water-soluble [^{14}C]residues totaled 0.017 ppm, and unextractable [^{14}C]residues totaled 0.009 ppm. In the nut shells, organosoluble [^{14}C]residues totaled 0.004 ppm, water-soluble [^{14}C]residues totaled 0.035 ppm, and unextractable [^{14}C]residues totaled 0.028 ppm. In the foliage, organosoluble [^{14}C]residues totaled 0.009 ppm, water-soluble [^{14}C]residues totaled 0.502 ppm, and unextractable [^{14}C]residues totaled 0.061 ppm. The aqueous extract from the foliage contained "several" compounds; polar Metabolites I and II were detected at 0.139 and 0.238 ppm, respectively.

In the soil, [^{14}C]residues were 0.326 ppm immediately posttreatment, 0.181 ppm at 125 days, 0.125 ppm at 246 days, 0.082 ppm at 267 days, and 0.064 ppm at 393 days posttreatment. [^{14}C]Metribuzin decreased from 0.278 ppm immediately posttreatment to 0.12 ppm at 125 days and <0.004 ppm at 246-393 days. Organosoluble metribuzin [^{14}C]degradates identified in the soil were:

6-tert-butyl-1,2,4,triazin-3,5(2H,4H)-dione (0.047 ppm);

6-tert-butyl-3(methylthio)-1,2,4-triazin-5(4H)-one (0.014 ppm); and

4-amino-6-tert-butyl-1,2,4-triazin-3,5(2H,4H)-dione (0.005 ppm).

During the 393-day study, organosoluble [^{14}C]residues in the soil decreased from 97.2 to 26.6% of the recovered, water-soluble [^{14}C]residues increased from 1.8 to a maximum 28.6% (246 days), and unextractable [^{14}C]residues increased from 0.9 to 50.0%.

DISCUSSION:

1. The concentration of metribuzin residues in the soil was 0.326 ppm at day 0 for a 14-inch deep segment; this is equivalent to 1.3 lb ai/A and confirms that the stated application rate was achieved and actually reflected a slightly greater rate. The registrant stated that 1 lb ai/A was equivalent to 1.8x the maximum registered application rate.

2. The following items are missing from this study:

   a. Storage stability data were not provided to confirm that the [^{14}C]-residues in the crops and soil did not degrade between sampling and analysis.

   b. Recovery efficiencies from soil and plant samples fortified with metribuzin and its degradates were not provided.

   c. The CEC of the soil was not provided.

2. The registrant stated that Polar Metabolite II may be a polysaccharide conjugate or a mixture of several sugar conjugates, but because a small amount of sample was available and the MS analysis was complex, further analysis could not be carried out.

3. The levels in the nut meat and shell were only 0.027 ppm and 0.066 ppm, respectively, and would be expected to be even lower if the label (vs. exaggerated) rate were used. However, approximately 0.6 ppm levels of incompletely characterized radiolabeled material were found in the foliage portions of peanuts after an 8 month rotational interval. this study does not support the requested reduction from 12 months.

4. Soil residues of radiolabeled metribuzin were not detectable (<0.004 ppm) for either the 4 or 8 month rotational intervals at exaggerated (1.8X) rates. Likewise, there was no significant difference between the total ^{14}C residues for either interval (0.08 or 0.06 ppm, respectively). These levels would be expected to be below 0.04 ppm at the maximum label rate, and thus support the request for the reduction to an 8 month crop rotation interval for peanuts. Finally, from the increase in total recovered unextracted residues (0.9 to 50%, day 0 to 393) and from the decrease in the organosoluble residues (97 to 27%), it is suggested that the radiolabeled carbon is progressing into the general carbon pool.

MATERIALS AND METHODS

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MATERIALS AND METHODS:

Sassafras sandy loam soil (76% sand, 16% silt, 8% clay, 0.7% organic matter, pH 6.5) was used to fill eight pots (15-inch diameter, 14-inch depth), which were then buried at ground level in the field. The soil in each pot was surface-treated with an aqueous solution of 5-[^{14}C]metribuzin (radiochemical purity >98%, specific activity of 7.54 Ci/mg, Mobay Chemical Corporation) at 12.8 mg ai/pot (1 lb ai/A). The treated soils were kept in the field for 125 days, and then were transferred into a greenhouse maintained at 27-30°C. Four of the pots were planted to peanuts immediately (125 days); the remaining four were aged in the greenhouse until 246 days posttreatment, at which time the pots were planted to peanuts. During the aging period, the treated soil was kept moist and any weeds that sprouted were pulled and left on top of the soil surface to dry and decompose. During the crop growth period, the plants were watered "as necessary" and a 14-hour photoperiod was maintained (light source unspecified).

The peanuts were harvested at maturity (142-147 days postplanting), which was 267 days posttreatment for the 125-day rotation and 393 days posttreatment for the 246-day rotation. Plant samples were divided into foliage and nuts. All plant tissues were washed with water and air-dried; the nuts were separated into shells and meats; and the foliage, nuts and meats were freeze-dried and frozen (-20°C) until analysis. Soil samples (0- to 14-inch depth) were taken at the times of treatment, planting, and harvest (0, 125, 246, 267, and 393 days posttreatment). Soil samples were air-dried overnight, homogenized, and frozen (-20°C) until analysis.

The plant samples were homogenized, and portions of each sample were analyzed for total radioactivity by LSC following combustion. Additional material was extracted twice with hexane using "gentle refluxing and stirring", then four times with 20% aqueous acetonitrile using refluxing and stirring for one hour each time. The aqueous acetonitrile extracts were combined and concentrated using a rotary evaporator, and the residue was partitioned between water and chloroform. All fractions were analyzed for total radioactivity by LSC. The organosoluble extracts, along with nonradiolabeled reference standards, were analyzed by TLC on silica gel plates developed in benzene:chloroform:dioxane (80:60:60). Areas of radioactivity were visualized by autoradiography; nonradioactive standards were located by fluorescence quenching under UV light. Also, ^{14}C]-compounds were detected and quantified using a TLC linear analyzer, and were identified by comparison to [^{14}C]metribuzin reference standards and to the R_f of metribuzin. Radioactive zones were scraped from the TLC plates and quantified by LSC as a water gel. Additional organosoluble extracts were analyzed for degradates by reverse-phase HPLC. Unextractable [^{14}C]residues remaining in the plant tissues were quantified by LSC following combustion.

Subsamples of the extracted plant fractions or extracts were analyzed by enzyme hydrolysis, acid hydrolysis, or base hydrolysis. The organic and aqueous phases were analyzed by LSC and HPLC.

Total radioactivity in the soil was determined by LSC following combustion. The soil was refluxed sequentially once with hexane, once with acetonitrile, once with 10% aqueous acetonitrile, and once with 0.1 N hydrochloric acid:methanol. The aqueous acetonitrile and 0.1 N hydrochloric acid:methanol fractions were evaporated under vacuum, and the resulting residues were partitioned between water and chloroform. All fractions were analyzed for total radioactivity by LSC and analyzed by TLC or HPLC as described in the plant analysis section. Unextractable [^{14}C]residues in the soil were quantified by LSC following combustion.

METRIBUZIN

RIN: 3187-91

Page____ is not included in this copy.

Pages 7 through 33 are not included.

The material not included contains the following type of information:

____ Identity of product inert ingredients.

____ Identity of product impurities.

____ Description of the product manufacturing process.

____ Description of quality control procedures.

____ Identity of the source of product ingredients.

____ Sales or other commercial/financial information.

____ A draft product label.

____ The product confidential statement of formula.

____ Information about a pending registration action.

✓ FIFRA registration data.

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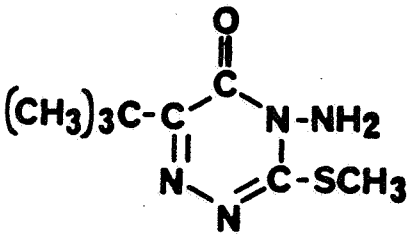
The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

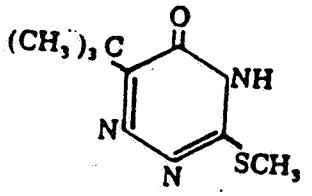
APPENDIX

METRIBUZIN AND ITS DEGRADATES



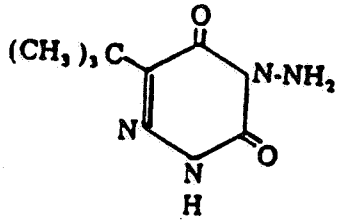
4-amino-6-tert-butyl-3(methylthio)-1,2,4-triazin-5(4H)-one

Metribuzin



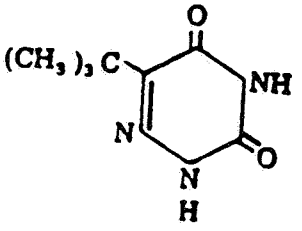
6-tert-butyl-3(methylthio)-1,2,4-triazin-5(4H)-one

Deamino Metribuzin (DA)



4-amino-6-tert-butyl-1,2,4-triazin-3,5(2H,4H)-dione

Dethiomethyl Metribuzin (DK)



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6-tert-butyl-1,2,4-triazin-3,5(2H,4H)-dione

Deamino Dethiomethyl Metribuzin (DADK)