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

JUN 29 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Registration # 524-316. Feeding of radiolabeled alachlor metabolites to laying hens. Accession No. 252792.

FROM: Nancy Dodd, Chemist
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THRU: Charles L. Trichilo, Ph.D., Chief
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TO: Robert Taylor, PM #25
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and

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Monsanto submitted a study in which synthetic $^{13}C/^{14}C$ - radilabeled plant metabolites of alachlor (2-chloro-2',6'diethyl-N-(methoxymethyl)acetanilide) were fed to laying hens. The distribution of radioactivity in eggs, tissues and excreta was examined. Due to low levels of residues in tissues and eggs these were not identified. A summary of this study was reviewed previously (N. Dodd, memo of 4/10/84). This study is being submitted in lieu of conventional feeding studies which are apparently in progress in an effort to get EPA to use residue levels lower than the tolerance for risk assessment.

Tolerances are established for the herbicide alachlor [2-chloro-2',6'-diethyl-N-(methoxymethyl) acetanilide] and its metabolites (calculated as alachlor) in meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep and in milk and eggs at 0.02 ppm. The sensitivity of the analytical method accepted for enforcement (Method II, Pesticide Analytical Manual, Vol. II) ranges from 0.01-0.02 ppm for meat, milk, and eggs.

A laying hen metabolism study was conducted using $^{13}C/^{14}C$ labeled alachlor plant metabolites to determine residue levels in eggs, tissues, blood and exctreta. A mixture of five plant metabolites were administered by oral dose to 4 groups of 5 hens each for 6 days. The metabolites were labeled wih ^{14}C in the phenyl ring and with ^{13}C at the C-2 carbon of the acetamide moiety. The five metabolites are listed below:

I (40%)	N-[[2-ethyl-6-(1-hydroxyethyl)]-phenyl]-N-methoxymethyl-2-(methylsulfonyl)acetamide
II (15%)	N-[(2,6-diethyl)phenyl]-N-methoxymethyl-2-(hydroxy)acetamide
III (15%)	2',6'-diethyl-N-(methoxymethyl) oxanilic acid, sodium salt
IV (15%)	N-[(2,6-diethyl)phenyl]-N-methoxymethyl-2-amino-2-oxoethanesulfonic acid, sodium salt
V (15%)	3-[[N-(2,6-diethyl)phenyl-N-methoxymethyl]-2-amino-2-oxoethanesulfinyl]-2-hydroxypropanoic acid, sodium salt

Monsanto has not provided an explanation of why these particular metabolites were chosen. However, the composition of the mixture is consistent with the fact that as much as 40-50% of soybean residue consists of metabolites convertible to 2-ethylaniline upon strong acid hydrolysis.

The daily dose was a total of 1.066 mg/day calculated as alachlor equivalents or 1.24 mg/day calculated as component weight. Since the average daily diet intake is 0.116 kg of feed/day, a level of 9.2 ppm alachlor equivalents was fed in te diet for 6 days. Three treated groups of hens and the control group were killed approximately 24 hours after the final dose. The fourth treated group of hens was depurated for 10 days before being killed. Redioactivity in whole eggs increased rapidly by the second day of treatment. No plateau in the residue levels was evident. During depuration, activity in eggs declined rapidly by the second day after the last dose and declined slowly thereafter. Residues in excreta rose rapidly after the first dose. Elimination of residues from excreta was rapid during the depuration period. Recoveries of radioactivity in the hens ranged from 86.9-95.7% of the total dose, including 86.5-95.6% in excreta, 0.05-0.10% in eggs, less than 0.02% each in breast muscle, thigh muscle, kidney, fat, and blood, and less than 0.02 0.03% in liver. Residues in laying hens for a 9.2 ppm feeding level are below:

	Values (ppb) from Complete Data Submission	Values (ppb) from Report Summary Previously Reviewed on 4/10/84
Eggs	$\frac{560 \text{ dpm/g}^*}{1.84 \times 10^4 \text{ dpm/ug}} = 30.4$	30.4
Thigh muscle	$\frac{82 \text{ dpm/g}^*}{1.84 \times 10^4 \text{ dpm/ug}} = 4.5$	4.5
Breast muscle	$\frac{97 \text{ dpm/g}^*}{1.84 \times 10^4 \text{ dpm/ug}} = 5.3$	5.3
Kidney	$\frac{310 \text{ dpm/g}^*}{1.84 \times 10^4 \text{ dpm/ug}} = 17.0$	16.8
Liver	$\frac{1000 \text{ dpm/g}^*}{1.84 \times 10^4 \text{ dpm/ug}} = 54.0$	54.3
Fat	$\frac{<70 \text{ dpm/g}^*}{1.84 \times 10^4 \text{ dpm/ug}} = <3.8$	<3.8

* Highest value obtained as an average or rounded average of 3 replicate samples of a group.

Calculated residues assuming a 0.2 ppm dietary burden of alachlor and its metabolites and a linear relationship between feeding levels and residue concentration are below:

	Values (ppb) from Complete Data Submission	Values (ppb) from Report Summary Previously Reviewed on 4/10/84
Thigh muscle	0.10	0.09
Breast muscle	0.11	0.11
Kidney	0.37	0.35
Liver	1.2	1.1
Fat	<0.08	<0.08
Eggs	0.66	0.6

Approximately 90% of the administered dose was excreted by hens during the six-day treatment period. Residues in eggs and tissues were not identified because of the low levels found. In excreta of hens, some of the neutral compounds I and II are converted to acidic compounds. Conjugation of compounds I and II with glucuronic acid is assumed. Compounds III and IV are excreted unchanged.

Monsanto has indicated that complete results of this study will be submitted in the latter part of 1984.

Conclusions

1. The reliability of the study is questionable since the data reflected only one feeding level and a short (6 days) feeding study. (Since no plateau in the egg residue levels was observed the animals should have been kept on the test diet for at least 4 weeks).

2. The calculations of poultry and egg residues resulting from a 0.2 ppm feeding level are based on an assumption that a linear relationship for feeding levels vs residue concentration exists at low feeding levels. This may not be true.

3. No validated analytical method exists which would reliably determine alachlor residues below the 0.02 pm level in poultry and eggs.

In addition, recently reviewed soybean and corn metabolism data indicate that a significant portion of plant residues, particularly in soybeans, consists of metabolites convertible upon acid hydrolysis to 2-ethylaniline. These metabolites would not be detected by the present enforcement methodology.

We requested (M. Kovacs, PP#0F2448, 3F2832, 4/23/84) that Monsanto submit residue data for these metabolites. A reevaluation of the presently established crop tolerances will then be made. This may result in recalculation of livestock's dietary burden.

The submitted study is not an adequate response to the requirement of the registration standard that animal metabolism studies be conducted in order to determine if the residues of concern in animals do indeed contain only the 2,6-diethylaniline moiety; only residues containing this moiety were determined in the previously submitted animal residue studies.

Recommendation

Pending the receipt of additional information from Monsanto, RCB recommends that the established tolerance of 0.02 ppm in poultry and eggs be used to assess risk.

cc: R.F.
Circu.
Reviewer
Alachlor S.F.
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RDI:EZ:6/28/84:RDS:6/28/84
TS-769:RCB:N.Dodd:gmk:CM#2:RM800:X77484:Date:6/28/84