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

MAR 18 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No. 100-587. Metolachlor (CGA-24705).

Evaluation of a Protocol for a Frozen Storage Stability Study in Animal Products.

RCB No.: 2028. Accession No.: None.

FROM: Maxie Jo Nelson, Chemist
Tolerance Petition Section I
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

mjn

THRU: Robert S. Quick, Section Head
Tolerance Petition Section I
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

RSQ

TO: Richard F. Mountfort, PM Team 23
Herbicide-Fungicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

By letter dated 2/20/87, Ciba-Geigy Corporation has submitted a draft protocol for a "Residue Stability Study for Metolachlor Residues Determined as CGA-37913 and CGA-49751 in Animal Samples Under Freezer Storage Conditions", Project No. 130925, to the Agency for review. Ciba plans to initiate this study in late March.

The study is required under the Metolachlor Registration Standard. [See Metolachlor Final Registration Standard and Tolerance Reassessment (FRSTR), 6/11/86.]

Specifically, the FRSTR (Residue Chemistry Chapter, p. 25) indicates the following storage stability data for animal products are required:

- Data delineating the stability of metolachlor in animal products (tissues, milk, and eggs). Spiked samples should be stored at sub-freezing temperatures for intervals approximating the storage intervals associated with treated samples used to determine the magnitude of the residue.

Tolerances in animal products are established [40 CFR 180.368(a)] for combined residues of metolachlor and its metabolites, all determined as the derivatives CGA-37913 and CGA-49751, each expressed as the parent compound, at levels of:

0.02 ppm - milk; eggs; fat, meat, and meat by-products (except liver and kidney) of cattle, goats, hogs, horses, poultry, and sheep;

0.05 ppm - liver of aforecited animals; and,

0.2 ppm - kidney of aforecited animals, except poultry for which there is no kidney tolerance.

Protocol Proposal

Study Objective

The objective of this study is to determine the stability of metolachlor residues, determined as CGA-37913 and CGA-49751, in dairy tissues (muscle, liver, milk) and eggs under freezer storage conditions for a period of one year. These results will be used to support the re-registration of metolachlor.

Test Substances

CGA-37913: 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol

CGA-49751: 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone

PETITIONER'S REMARKS: The analytical method (AG-338) used for the determination of metolachlor residues employs an acid hydrolysis to transform the residues to two moieties, CGA-37913 and CGA-49751, which are then assayed by GLC. Therefore, test substrates will be fortified with CGA-47913 and CGA-49751 rather than parent metolachlor.

OUR COMMENTS: No objections. The enforcement methodology in PAM II is based on the derivatization of "combined residues of metolachlor and its metabolites" to CGA-37913 and CGA-49751 for analysis by GLC. Since metolachlor per se has not been reported in animal products (see FRSTR, Residue Chemistry Chapter, pages 16-17), fortification with these two compounds is appropriate.

Test Substrates

Dairy (muscle, liver, milk)

Poultry (eggs)

PETITIONER'S REMARKS: The four substrates chosen are representative of dairy and poultry studies. Samples will be obtained from Ciba's existing freezer inventory, or purchased commercially.

OUR COMMENTS: No objections to the choice of test substrates. We would prefer, however, that fresh samples be used.

Fortification Level

0.5 ppm each of CGA-37913 and CGA-49751

PETITIONER'S REMARKS: None.

OUR COMMENTS: No objections, assuming: (1) this level is well above the limits of detection of each of these two compounds by the analytical procedure which will be employed; and, (2) the analytical methodology used gives adequate recovery of these two compounds at this fortification level.

Sampling Intervals

0-day, 3-month, 6-month, and 12-month.

PETITIONER'S REMARKS: Residue stability will be monitored for a period of one year since previous tissue residue analyses were performed within one year of sample collection.

OUR COMMENTS: We suggest samples also be collected/analyzed at the 1-month interval. The duration of the study should be of sufficient length to validate past feeding study data, and to cover any future needs the petitioner anticipates. If sufficient sample permits, we suggest either an 18-month or 24-month interval be added.

Conduct of Study

Typically, for each test substrate at each sampling interval, five samples will be collected and analyzed:

(1) Control;

(2) Replicate A of a control sample freshly fortified at 0.5 ppm each of CGA-37913 and CGA-49751 (to provide method recovery validation data);

(3) Replicate B of (2);

(4) Replicate A of sample previously fortified (at 0-day) with 0.5 ppm each of CGA-37913 and CGA-49751 and maintained under freezer storage conditions (to provide frozen storage stability validation data); and,

(5) Replicate B of (4).

PETITIONER'S REMARKS: None.

OUR COMMENTS: This experimental design appears adequate to provide the required information. No objections.

Analytical Method

Analytical Method AG-338, "Analytical Method for Residues of Metolachlor Plant Metabolites Determined as CGA-37913 and CGA-47951 After Acid Hydrolysis", by N. L. Cargile and J. A. Ross, will be used to determine residues of CGA-37913 and CGA-47951 in dairy and poultry substrates.

PETITIONER'S REMARKS: Any necessary method modifications will be documented in protocol addenda and the final study report.

OUR COMMENTS: No objections, assuming this analytical procedure is properly validated for use with animal substrates. We note with approval that the petitioner plans to run recovery studies with each test substrate at each sampling interval for method validation purposes.

Records To Be Maintained

All necessary to conform with Good Laboratory Practices.

PETITIONER'S REMARKS: A summary of the type records to be kept and their storage/disposition is provided.

OUR COMMENTS: It appears the petitioner is making adequate provision for record-keeping in conjunction with the proposed study.

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Recommendation

This review should be sent to the petitioner as soon as possible so that our comments may be incorporated into the final protocol for the frozen storage stability study in animal products.

cc: RF, Circ, Reviewer (M. Nelson), Metolachlor Registration Standard File, TOX, PM#23, ISB/PMSD (Eldridge).

TS-769C:RCB:Reviewer(MJN):CM#2:Rm804:557-7484:typist(mjn):3/16/87.

RDI:SectionHead:RSQuick:3/16/87:DeputyChief:RDSchmitt:3/16/87.