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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Amended Frozen Storage Stability Study Protocol
for Maneb and ETU on Animal Commodities
(RCB No. 2847) - No Accession Number

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THRU: Charles L. Trichilo, Ph.D., Chief
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RCB has been requested by the Data Call-In (DCI) staff to review and develop an appropriate response to the September 25, 1987 letter from Roger A. Novak, Maneb Task Force (MTF) to Doug McKinney, SRB/RD, and to comment on a new storage stability study protocol for mane b and ethylene-thiourea (ETU) residues in/on animal products.

Protocol Deficiency Remaining to be Resolved (as delineated in RCB's July 31, 1987 memorandum - RCB No. 2535).

With respect to the animal products protocol, no deficiency remains.

Conclusions With Respect to the New Animal Products Protocol

All outstanding deficiencies originally cited in RCB's May 28, 1987 memorandum re: draft protocols for animal commodity storage stability studies have now been resolved. Therefore, the currently submitted new protocol "Determination of The Stability of Maneb and Ethylenethiourea Residues In/On Animal Products" (MTF Protocol 87-1500) is in compliance with EPA's 3(c)(2)(B) Storage Stability/Residue Data DCI Notice for Maneb dated March 31, 1987 and thus acceptable to RCB.

Background

MTF has now submitted the above new animal commodity storage stability study protocol for both mane and ETU in response to RCB's M.F. Kovacs, Jr., May 28, 1987 memorandum re: "Evaluation of Frozen Storage Stability Study Protocols for Maneb and ETU on RACs, Processed Commodities, and Animal Products" and to a subsequent meeting between RCB staff and representatives of the MTF on May 29, 1987 to discuss RCB's recommended revisions to the protocols evaluated in the aforementioned memorandum.

The following animal commodity protocols were originally submitted by MTF and evaluated by RCB in the May 28, 1987 memorandum:

1. Draft protocol "Pilot Study for the Determination of the Stability of Maneb and Ethylenethiourea Residues in Stored Frozen Samples of Milk, Eggs, Beef Tissues, and Poultry Tissues," prepared by Hazleton Laboratories America, Inc., Madison, Wisconsin 53704 dated, March 24, 1987.
2. Draft protocol "Determination of the Stability of Maneb Residues in Stored Frozen Samples of Milk, Eggs, Beef Tissues, and Poultry Tissues," prepared by Hazleton Laboratories America, Inc., Madison, Wisconsin 53704, dated March 24, 1987.

Present Considerations

Since the aforementioned draft protocols were not revised as separate items or resubmitted as such by the registrant in response to RCB's May 28, 1987 memorandum, they will not be discussed further in this review. The above draft protocols were integrated by the registrant into a new protocol, which is presently submitted as "Determination of the Stability of Maneb and Ethylenethiourea Residues In/On Animal Products"

(MTF Protocol 87-1500). This new protocol will be reviewed in its entirety in light of the deficiencies noted in both of the previously submitted draft protocols.

Determination of the Stability of Maneb and Ethylenethiourea Residues In/On Animal Products

A. Purpose of the Study

Registrant's Remarks

The purpose of this study is to generate storage stability data for laboratory fortified animal commodities to complement mane b and ethylenethiourea residue data on/in various animal commodities.

RCB's Comments: No objections.

B. Test Article(s)

Registrant's Remarks

Identification

Compound: Maneb

Common Name: Maneb

Trade Name: DITHANE

Chemical Name: Manganese ethylenebisdithio-
carbamate

Metabolite: Ethylenethiourea (2-imidazolidine-
thione)

Analytical Standards: Analytical reference standards of mane b and its degradate, ethylene-thiourea, will be supplied by the Sponsor.

Storage Conditions: Store frozen or refrigerated until use. Protect from light and heat.

Safety Precautions: Handle with care; observe proper precautions for handling pesticides.

Purity and Identity: Maneb and ethylenethiourea
purity and identity will
be provided by the Sponsor.

RCB's Comments: No objections.

C. Animal Commodity Matrices

Registrant's Comments

Animal Commodity Matrices. The following animal commodities will be utilized to generate storage stability data: whole eggs, poultry muscle, and milk, liver, kidney, and fat of cattle.

RCB's Comments: No objections.

D. Selection of Control Commodities

Registrant's Comments

Selection of Control Commodities. Control (untreated or store-bought) samples of each matrix will be analyzed prior to initiation of the study to assure they are not contaminated with either mane b or ethylenethiourea. Should residues be detected, screening of controls will continue until uncontaminated commodities are found. In the event that control tissues contain detectable levels of mane b or CS₂ "generators" screening shall continue to aid in selection of control tissues with the lowest possible levels of CS₂ "generators." The selected control commodities will be divided into nine subsamples. Solid tissue commodities (muscle, etc.) will be diced. Liquid commodities (eggs, milk) will be homogenized and aliquoted. Each individual subsample will be stored frozen. Eight subsamples, each containing at least 1/2 lb commodity, will be used for method controls and method spikes at the designated analysis intervals (with two serving as backups) and will remain stored frozen and until needed. The ninth subsample containing at least 4 lb commodity will be diced or aliquoted, where applicable, to allow for preparation of the stability spikes.

RCB's Comments

The registrant's preparation of control tissue samples prior to fortification (i.e., diced or cut-up) is consistent with RCB's earlier recommendations in the May 28, 1987 memorandum.

E. Storage Containers and Storage Conditions

Registrant's Comments

Storage containers will be screw-cap glass or polyethylene containers previously shown to be free of interferences. Freezer storage will be conducted at -20 ± 2 °C.

RCB's Comments: No objections.

F. Maneb Sample Amendment

Registrant's Comments

Maneb Stability in Fortified Animal Commodities. Animal commodities fortified with maneb only will be analyzed following various intervals of time for maneb and ethylenethiourea residues. To accomplish this, separate spiked samples of the various commodities will be fortified with maneb. At each time interval two samples will be analyzed for maneb and two for ethylenethiourea. Prior to fortification the representative matrices selected for analysis will be diced or aliquoted and immediately frozen. All fortifications will be with 2.0 ppm maneb.

Ten grams of frozen control commodity in a screw-cap bottle will be fortified with a small volume of a maneb suspension in water to achieve a final concentration of 2.0 ppm. The fortification solution will be dispersed over the frozen commodity and allowed to soak in. The bottle will then be sealed and immediately returned to the freezer. Prepare quadruplicate stability spikes for each time interval plus eight backup spikes for a total of 32 fortified samples per commodity.

RCB's Comments

No objection to fortification level. In addition fortification of diced or cut-up samples including specification of number of samples to be fortified per commodity is consistent with RCB's earlier recommendations (See May 28, 1987 memorandum).

G. ETU Sample Amendment

Registrant's Comments

Ethylenethiourea Stability in Fortified Animal Commodities. Ethylenethiourea will be analyzed at various intervals on animal commodities fortified with ethylenethiourea only. All fortifications will be done at 0.5 ppm.

Ten grams of frozen, chopped control commodity in a screw-cap bottle will be fortified with a small volume of an ethylenethiourea solution in water to achieve a concentration of 0.5 ppm. The fortification solution will be dispersed over the commodity and allowed to soak in. The jar will then be sealed and immediately returned to the freezer. Prepare duplicate stability spikes for each time interval plus four backup spikes for a total of 16 fortified samples per commodity.

RCB's Comments: See comments under Item F.

H. Analysis Scheme

Registrant's Comments

After the animal commodities are fortified, they will be analyzed at 0 day, and 1, 2, 4, 13, 26 week intervals. Fortified commodities for two additional intervals will also be prepared and stored to serve as backups. Two fortified commodities (stability spikes), one method control, and two method spikes (2.0 ppm for maneb and 0.5 ppm for ETU) will be analyzed for each compound for each storage interval for each matrix.

RCB's Comments

No objections to sampling intervals. The number and type of samples analyzed at each sampling interval is consistent with RCB's earlier recommendations (see May 28, 1987 memorandum).

I. Analytical Methods

Registrant's Comments

Maneb. Maneb residues will be measured according to the attached analytical method "Hazleton Laboratories America, Inc., A Gas-Chromatographic Method for Measurement of Dithane," dated August 14, 1986.

Ethylenethiourea (ETU). ETU residues will be measured according to the attached analytical method "Hazleton Laboratories America, Inc., An Analytical Method for Determining Ethylenethiourea in Chicken Tissues, Eggs, and Excreta."

RCB's Comments

No objections to the overall principle of both methods. However, these analytical procedures must be properly validated via recovery runs with each test substance at each sampling interval.

J. Study Reporting Requirements

Registrant's Remarks

Documentation. All pertinent chronological information shall be recorded in bound laboratory notebooks in indelible ink. These notebooks shall be exclusively dedicated to this study and become part of the raw data upon study termination. Data to be recorded shall include but not be limited to the actual time and date of sample receipt, sample processing including weights, and sample analysis and appropriate comments pertaining thereto; receipt and preparation of analytical standards; preparation of other solutions necessary for the analytical methods; and other information to fully document laboratory procedures, balance calibration, important events, etc.

Reports

A report will be issued by the testing facility detailing results of the storage stability studies and will contain:

1. A description of the methods and procedures used for the determination of maneb and ETU residues.
2. The results of samples analyzed, expressed in ppm and recovery where indicated, expressed in percent.
3. Recovery and control values for each analytical run.
4. A graphic display that shows results obtained versus time of storage for each matrix.

The final report will conform to EPA's PR Notice 86-5 and applicable Data Reporting Guidelines (proposed or final) available on the date of report issue and be suitable for direct submission to the Agency.

Good Laboratory Practices Statement

This study will be conducted in accordance with EPA Pesticide Program Good Laboratory Practice Standards (40 CFR Part 160). Amendments to this protocol must be signed by the sponsor and the study director and become a part of the protocol.

The Quality Assurance Unit of the testing facility will audit the study at frequent intervals and review the final report consistent with its internal SOPs.

Maintenance of Raw Data

Original data, or copies thereof, will be available at HLA to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data generated by HLA, as well as the final report, will be retained in the HLA archives for the period specified by the EPA Good Laboratory Practice Standards.

RCB's Comments

It appears that the registrant is making adequate provision for recordkeeping in conjunction with the proposed study.

cc: W. Boodee, E. Zager, Reviewer - M. Kovacs, S.F., R.F.,
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