file Copy

Shaughnessy No.: 105501

Date Out of EAB: FEB 11 1988

To: Robert Taylor
Product Manager #25
Registration Division (TS-767C)

From: Paul Mastradone, Acting Chief
Environmental Chemistry Review Section #1
Exposure Assessment Branch/HED (TS-769C)

Thru: Paul F. Schuda, Chief
Exposure Assessment Branch/HED (TS-769C)

Attached, please find the EAB review of:

Reg./File Number: 1471-101

Chemical Name: Tebuthiruon

Type Product: Herbicide

Product Name: SPIKE, GRASLAN

Company Name: ELANCO

Purpose: Review terrestrial field study protocol, data waiver request, and extension of time request

Date Received: _____

Action Code: 650

Date Completed: 02/05/88

EAB #(s): 80096

Monitoring Study Requested: _____

Total Reviewing Time: 1.0days

Monitoring Study Voluntarily: _____

Deferrals To:

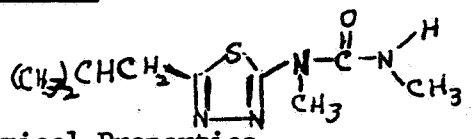
_____ Ecological Effects Branch

_____ Residue Chemistry Branch

_____ Toxicology Branch

I. CHEMICAL:

Shaughnessy No.: 105501
Year of Initial Registration: 1974
Common Name: Tebuthiuron
Chemical Name: N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N, N'-dimethylurea
Trade Name: SPIKE, Graslan
Type of Pesticide: Broad Spectrum Herbicide
Chemical Structure:



Physical/Chemical Properties:
Aqueous Solubility: 2.5 mg/ml (25°C)
Vapor Pressure: $2x10^{-6}$ mm Hg (25°C)
K_{ow} = 61 Log K = 1.79

II. TEST MATERIAL: N/A(protocol)

III. STUDY/ACTION TYPE: Review terrestrial field dissipation protocol, request for time extension, request for data waiver, request for change in field parameters

IV. STUDY IDENTIFICATION:

A. 3 Letters:
1. Letter from James D. Helmer (ELANCO) to Robert Taylor, dated 10/28/87
2. Letter from James D. Helmer (ELANCO) to Robert Taylor, dated 10/26/87
3. Letter from James D. Helmer (ELANCO) to Robert Taylor, dated 10/23/87

B. Terrestrial Field Dissipation Study Protocol

LX 199-03(Tebuthiuron) Field Dissipation--Terrestrial Protocol (FIFRA 164-1). October 23, 1987 (Draft). Prepared by Landis Associates, Inc., Valdosta, GA, for ELANCO Products Company, a division of Eli Lilly and Company.

V. REVIEWED BY:

Patricia Ott
Chemist
Section 1, FAB/HED

Signature: Pat Ott
Date: 2/5/88

VI. APPROVED BY:

Paul Mastradone
Acting Chief
Section 1, FAB/HED

Signature: Paul J. Mastradone
Date: FEB 11 1988

VII. CONCLUSIONS:

A. Environmental Fate Profile: See Pages 49-50 of the Tebuthiuron Registration Standard EAB Science Chapter, dated March 4, 1987.

B. Data Requirements:

Requirements That Have Been Satisfied: (page 47 of RS dated July 1987)
Hydrolysis

Requirements That Have Not Been Satisfied:

Photodegradation in Water	Leaching and Adsorption/Desortion
Photodegradation in Soil	Soil Dissipation
Aerobic Soil Metabolism	Aquatic Dissipation
Anaerobic Soil Metabolism	Irrigated Crop Stud
Aerobic Aquatic Soil Metabolism	Fish Bioaccumulation
Anaerobic Aquatic Soil Metabolism	*Monitoring Study: recommended by the Ground Water Team

Data Which Are Reserved: Long Term Soil Dissipation
Data Which Are Not Being Required At This Time: Reentry

C. Ground Water:
Tebuthiuron has the profile of a leacher (resistant to hydrolysis, photolysis, persistent in soil, leaches through soil). Its degradates also leach through soil.

It has been found in shallow ground water in Texas. The GW Team recommended (Catherine Eiden's memo dated October 1987) the registrant do a small-scale retrospective ground water monitoring study.

It will be monitored in the National Pesticides in Ground Water Monitoring Survey.

VIII. RECOMMENDATIONS:

A. Change in Protocol, As Outlined in the RS (Letter from James D. Helmer (ELANCO) to Robert Taylor dated 10/28/87)

1. Using Field Studies to Satisfy Both RCB and EAB Data Requirements
The registrant can opt to do this; however, EAB will evaluate field studies according to the Subpart N Data Requirement Guidelines.

2. Geographic Sites (paragraph 2, page 1)
Geographic sites should be chosen that are both representative of usage and reflect a "worst case" scenario, with regard to ground water leaching potential. After the geographic sites are chosen by the registrant, but before the study begins, meteorological and site data should be sent to EPA. This should include: yearly rainfall data (by month), depth to water table, soil characteristics, yearly soil and air temperature data (by month), slope of land, specific geographic location.

3. Changing Application Rate from 6 lb/A to 4 lb/A (paragraph 3, page 1)
For the terrestrial field dissipation study, the maximum recommended rate on the label, for that use pattern, must be used. This is particularly important with

Tebuthiuron, since it has been found in ground water; all study parameters must be chosen to create a "worst case" scenario.

3. Ground Application Versus Aerial (paragraph 4, page 1)
Ground application is acceptable, if representative of the actual use pattern chosen for the study.

B. Request for Time Extensions (letter from James Helmer (ELANCO) to Robert Taylor dated October 26, 1987).

1. 6 Months' Extension for the Photodegradation in Water and Photodegradation in Soil Studies
Reason: Contract Laboratory scheduling
Response: EAB concurs with this request.

2. 3 Months' Extension for Soil Dissipation Study
Study is supposed to begin in the spring of 1988 and the registrant needs a short extension of time to complete the study.
Response: EAB concurs with this request.

C. Data Waivers (letter from James Helmer (ELANCO) to Robert Taylor dated 10/23/87)

1. 164-2, Aquatic Field Study

EAB does not concur because the studies cited were runoff studies conducted for rangeland application and this requirement is an aquatic dissipation study for the aquatic noncrop (ditchbank) use. Data are required.

2. Irrigated Crop Study
This data requirement is triggered by the aquatic noncrop use (ditchbank). The registrant has a label statement which says (for the ditchbank use): "Do not apply on ditches used to transport irrigation or potable water."
RD has a policy that, if there is a label statement, then the registrant does not have to do an irrigated crop study; therefore, EAB concurs with this waiver request.

D. Terrestrial Field Dissipation Protocol

1. The submitted protocol is written in too general a mannner; more detail and specificity must be added. For example, the registrant should state specifically which formulation will be used, which application equipment will be used, where exactly the study site is, etc. However, the sampling protocol presents a detailed discussion.
2. Because the agency has a concern about tebuthiuron's ability to leach to ground water, the protocol should reflect parameters which will give a "worst case" scenario, with respect to this concern.
3. One of the objectives of the field dissipation study is to monitor the formation and decline of degradates. EAB notes that no acceptable soil metabolism data are available for tebuthiuron. EAB suggests that acceptable aerobic and anaerobic metabolism data, accurately describing the degradates of tebuthiuron, be developed prior to or concurrent with submission of field dissipation data.
4. The protocol should give detailed geographic site information, meteorology data, depth to water table, slope of land, soil characteristics. Sites chosen

should reflect both the use pattern of interest and a "worst case" scenario with regard to ground water leaching. This information and a revised protocol, which addresses the points listed, should be submitted to EPA for approval.

4. Since tebuthiuron is persistent in soil, the study must continue for as long as is necessary to show decline of parent and formation and decline of degradates, which may mean several years of sampling.

5. Soil sampling strategy for both the site qualification and field application sampling must address soil heterogeneity. For example, one sample for site qualitifcation is unacceptable.

6. Soil samples must be taken 2 feet below the lowest detectable residues.

7. The exact analytical method to be used for soil analyses must be submitted, along with recovery data for parent and degradates, the limit of detection of the method for each compound, and extraction efficiency data for each type of soil.

8. Storage stability of the samples should be verified.

IX. Background:

A. Introduction

Tebuthiuron was initially registered in 1974. A Registration Standard for tebuthiuron was completed in July 1987. It was on the GWDCI list and has been found in shallow ground water in Texas. The data submitted under the GWDCI was found not to meet guidelines in the RS. The RS stated (page 18) that the agency was not requiring ground water advisory label statements.

It is on the priority #1 list of analytes to be monitored for the National Pesticides in Ground Water Survey.

In October 1987, Catherine Eiden (GW Team) recommended the registrant do a small scale retrospective ground water monitoring study.

This submission is in response to the RS and includes: request for time extensions, request for data waivers, a terrestrial field dissipation study protocol, and a request to change certain field study parameters.

Tebuthiuron

Page_____ is not included in this copy.

Pages 6 through 16 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.

____ The document is a duplicate of page(s) _____.

____ The document is not responsive to the request.

✓ Draft protocol

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.

Plant Science Projects Development and Registration Division
Lilly Research Laboratories
Elanco Products Company
Divisions of Eli Lilly and Company

P.O. Box 708
Greenfield, Indiana 46140
Telephone (317) 467-4000

ELANCO

Carthy

October 23, 1987

Mr. Robert J. Taylor
Product Manager (25)
Registration Division
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Taylor:

RE: TEBUTHIURON REGISTRATION STANDARD
REQUEST THAT CERTAIN REQUIREMENTS BE WAIVED

Elanco Products Company has reviewed the Tebuthiuron Registration Standard that was issued by the Agency on July 24, 1987. There are several requirements for studies within Parts 158.125, 158.130, 158.135, 158.145, and 158.150 which should be eliminated from the Standard and are as follows:

I. Part 158.125 RESIDUE CHEMISTRY

1. 171-4 - Nature of the Residue (Plants)
2. 171-4 - Nature of the Residue (Livestock)

II. Part 158.130 ENVIRONMENTAL FATE

Dissipation Studies - Field

1. 164-2 - Aquatic (Sediment)

Accumulation Studies

1. 165-3 - Irrigated Crops

III. Part 158.135 TOXICOLOGY

1. 83-1: Chronic Toxicity - Rodent
2. 83-2: Oncogenicity - Rat
3. 83-3: Teratogenicity - Rabbit
4. 84-2: Chromosomal Aberration
5. 84-2: Other Mechanisms of Mutagenicity
6. 85-1: General Metabolism

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animal had been preconditioned with unlabeled tebuthiuron, given a single dose of ^{14}C tebuthiuron, and sacrificed 24 hours later.

The nature of the residue study which was reviewed for the Registration Standard also contained data on the rate and route of excretion which showed that a single oral dose was rapidly excreted primarily in the urine. In addition, the report also included blood level data which showed that the peak blood level occurred 12 hours after a single dose which indicates that the compound is rapidly absorbed. Finally, data were presented on the characterization of urinary metabolites. This data showed that EL-103 was readily metabolized to a number of products. Only about 5% of the urinary radioactivity was found to be unmetabolized EL-103.

The fact that the residues characterized in tissues are essentially identical to those present in urine collected for five days after a single oral dose, indicates that the metabolite profile present in tissues 24 hours after a single oral dose contains the entire spectrum of metabolic products of EL-103 which are formed by the ruminant.

Elanco maintains that the data already submitted are scientifically valid and fulfill the requirement for nature of the residue in meat even though the study was conducted differently than required by current guidelines.

3. Part 158.130 ENVIRONMENTAL FATE
164-2 - Aquatic (Sediment)

Agency Position: The Registration Standard for tebuthiuron indicates this study is required for an "aquatic, nonfood use pattern".

Elanco Response: The description of this study in the Pesticide Assessment Guidelines indicates that it is required for "...aquatic food crop uses, for aquatic noncrop uses (which include antifouling paints and other outdoor protective uses where the pesticide-containing surface is in contact with water, and also pesticide application to ditchbanks and shorelines), and for any aquatic impact uses involving direct discharge of treated water into outdoor aquatic sites." This study is apparently only required when a pesticide is applied directly to water or when it is applied to an area that will come in contact with surface water. All labels for SPIKE

products containing tebuthiuron have the following precaution: "Ditchbank Usage - Do not apply SPIKE to any portion of the ditchbank that will come into direct contact with water as movement of SPIKE in this water to nontarget plant species may result in the injury or death of those plants. Do not apply on ditches used to transport irrigation or potable water." Since tebuthiuron is not applied directly to water or to an area that will come in contact with surface water, the requirement for a field dissipation study on aquatic sediment should be waived.

In addition, studies already submitted and not reviewed for this requirement provide sufficient information to indicate that any tebuthiuron that reaches the aquatic environment through runoff does dissipate and would not accumulate. In studies of two catchment ponds in watersheds treated with tebuthiuron (MRID 00090107 and 00090109), tebuthiuron dissipated from the ~~ponds over three~~ to five months. At most, a total of 4.53% of the tebuthiuron applied in one watershed could be accounted for in a pond which received runoff from a 7.1 inch rainfall event. The total amount of tebuthiuron accounted for in this pond declined in four months to 0.8% of that applied to the watershed. Only up to 0.08% of the tebuthiuron applied to the second watershed could be accounted for in another pond, and this level declined to 0.01% in about two months. Tebuthiuron is degraded by photolysis (half-life in laboratory study about two weeks). The highest concentration of tebuthiuron in the surface two inches of sediment from either pond calculated from a measured value was 0.42 ppm. The K_{ads} values for sediments from these two sites were estimated to be 2.7 and 3.9. Chemical characteristics of tebuthiuron, such as its solubility in water (2.3 g/L), its low n-octanol/water partition coefficient (log k_{ow} 1.79), and its low soil adsorption coefficients (K_{ads} of 0.2 in sand, 0.2 in sandy loam, 1.3 in clay and 10.0 in peat) also indicate that tebuthiuron would not accumulate in the aquatic environment. As concentrations of tebuthiuron decline in water due to photolysis, tebuthiuron concentrations in sediment would decrease due to desorption. Finally, tebuthiuron is not repeatedly applied to the same site within a year, so the amount of any tebuthiuron in runoff will generally become lower over time.

Aquatic animals will not be affected by exposure to even the highest concentration of tebuthiuron that might occur in surface water due to runoff. Elanco Products Company has proposed to reduce the highest application rate of tebuthiuron to 6 lb/A. A review article by Wauchope (J. Env. Qual., 1978, Vol. 7, pp 459-472) indicates that up to 5% of a water-soluble

agricultural chemical applied to a moderate slope (10-15%) could be lost in runoff. Even if it were possible for tebuthiuron to be added directly to six inches of water, the highest tebuthiuron concentration would be 4.4 ppm. This concentration is lower than all of the no-observed effect concentrations from chronic toxicity studies with rainbow trout, fathead minnows, and Daphnia magna.

Based on the label precaution against applying tebuthiuron to any part of a ditchbank that could come in contact with surface water, the environmental fate studies already submitted for tebuthiuron, the chemical characteristics of the compound, and the lower maximum application rate of tebuthiuron that has been proposed, Elanco Products Company believes there is sufficient information to conclude that tebuthiuron does not accumulate in the aquatic environment and is safe to aquatic animals. Elanco requests, therefore, that the requirement for an aquatic field dissipation study be waived.

4. Part 158.130 ENVIRONMENTAL FATE
165-3 - Irrigated Crops

Agency Position: The Registration Standard for tebuthiuron indicates this study is required because of ditchbank label usage.

Elanco Response: Adequate, restrictive labeling currently exists on all tebuthiuron end use products concerning ditchbank usages which should negate the need for accumulation studies in irrigated crops. Labels currently state "Do not apply to any portion of the ditchbank that will come into direct contact with water as movement in this water to non-target plant species may result in injury or death of those plants. Do not apply on ditches used to transport irrigation or potable water." Also, all labels prohibit the use of tebuthiuron on field crops.

In view of the above labeling, Elanco requests that the requirement for accumulation studies in irrigated crops for tebuthiuron be waived.

5. Part 158.135 TOXICOLOGY
83-1 - Chronic Toxicity - Rodent
83-2 - Oncogenicity - Rat

Agency Position: The Registration Standard for tebuthiuron indicates a combined chronic rodent and rat oncogenicity study is required.

In light of all of the above, Elanco requests a wavier from the necessity of any nontarget area phytotoxicity requirements in the re-registration process of tebuthiuron.

We appreciate your cooperation and consideration in these requests. If further clarification or discussion on any items in this correspondence is needed, please advise so a mutual meeting date can be arranged.

Sincerely,

ELANCO PRODUCTS COMPANY

James D. Helmer

James D. Helmer, Ph.D., Project Manager
Plant Science Projects Development
and Registration Division

JDH:cj

Attachment: Metabolism Of A New Herbicide, Tebuthiuron (1-[5-(1,1-Dimethylethyl)-1,3,4-Thiadiazol-2-yl]-1,3-Dimethylurea) In Mouse, Rat, Rabbit, Dog, Duck and Fish. Journal of Toxicology and Environmental Health 1:757-768, 1987.

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ELANCO

October 28, 1987

Mr. Robert J. Taylor
Product Manager (25)
Office of Pesticide Programs (TS-767-C)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Taylor:

RE: GUIDANCE FOR THE RE-REGISTRATION OF PESTICIDE PRODUCTS CONTAINING TEBUTHIURON AS THE ACTIVE INGREDIENT, DATED JULY 1987

We have reviewed the environmental chemistry and residue requirements as outlined in the subject document. Based upon our review, we believe that the questions regarding the environmental effects and residues of tebuthiuron resulting from application to rangeland and pastures can be more accurately defined by conducting the enclosed program.

We believe that submission of data from our proposed program will show that the residue patterns from Texas into California, and Oklahoma into Nebraska, are essentially similar and, therefore, do not warrant the more diverse but less intense program outlined in the subject Registration Standard. Furthermore, data from our proposed program will be obtained on both environmental and residue requirements from the same application locations and timings, and thus, will define more accurately the environmental and residue fate of tebuthiuron resulting from rangeland and pasture applications.

In this proposed program, we have identified the rate to be 4 lb/A active ingredient rather than 6 lb/A which is identified as the rate in the subject Re-registration Standard. Our basis for this is that the 6 lb/A rate is an atypical rate based upon the basal treatment for perennial shrubs and is, therefore, not used over a large unit area (i.e., in actual use, there may be 6 lb/A at the base of the shrub, but only 0.01 of the acre containing the shrub treated).

We also believe that these studies should not be conducted using aerial application. Because of the physical characteristics of the product (pellets) and the sampling methodology which has been

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developed for uptake and decline residue studies, it will be necessary to ground apply the pellets to a specific, confined area in order to obtain the maximum possible residue load. If the pellets are not applied uniformly, either the target crop will have lower than optimum residues or it will be killed by excess residues and unavailable for analysis.

If there are any questions following review by the Residue Chemistry Branch and Exposure Assessment Branch, we will request a meeting to discuss the program.

Sincerely,

ELANCO PRODUCTS COMPANY

James D. Helmer

James D. Helmer, Ph.D., Project Manager
Plant Science Projects Development
and Registration Division

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ELANCO

October 26, 1987

Mr. Robert J. Taylor
Product Manager (25)
Office of Pesticide Programs (TS-767-C)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Taylor:

RE: TEBUTHIURON REGISTRATION STANDARD
REQUESTS FOR EXTENSIONS OF TIME

Elanco Products Company received the tebuthiuron Registration Standard on July 31, 1987. After reviewing the indicated generic data requirements, it is apparent that certain Agency submission deadlines can not be met. Thus, an outline of various requests for extensions of time follows:

I. RESIDUE CHEMISTRY

A. 171-4 - Nature of Residue (Plants)
[Nine (9) Months Extension of Time]

Reason: A waiver of this data requirement was requested to the Agency in a letter dated October 23, 1987. If the request is denied, then an extension of time is needed since grass growth is seasonal and the earliest study initiation date would be the spring of 1988.

B. 171-4 - Magnitude of the Residue (Storage Stability)
[Twenty-two (22) Months Extension of Time]

Reason: Trial initiation is planned for the spring of 1988 (when grass begins active growth after winter dormancy) in conjunction with the Magnitude of Residue in Grass and Hay. The Agency has requested that sampling be continued for a 24-month period of time after application. Thus, the Agency's time allotment of 15 months for this data requirement is impossible to meet and an extension of time is necessary.

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C. 171-4 - Magnitude of Residue (Grass and Hay)
[Nineteen (19) Months Extension of Time]

Reason: The justification for the request has been outlined in (B) above. Although the Agency's time allotment is 18 months for this data requirement, a 24-month sampling period again mandates an extension of time.

II. ENVIRONMENTAL FATE

A. 161-2 - Photodegradation in Water and
161-3 - Photodegradation in Soil
[Six (6) Months Extension of Time]

Reason: Both of these studies are to be conducted through a contract laboratory. The contract laboratory has indicated that the earliest possible start date is 01/88. Thus, an extension of time is required.

B. 161-1 - Soil Dissipation
[Three (3) Months Extension of Time]

Reason: Study initiation is scheduled for the spring of 1988. Based on the sampling time required for completion of this requirement, the Agency allotment of 27 months is insufficient and a short extension of time is needed.

III. TOXICOLOGY

A. 83-3 - Teratogenicity - Rabbit
[Six (6) Months Extension of Time]

Reason: A waiver of this data requirement was requested to the Agency in a letter dated October 23, 1987. If the request is denied, then an extension of time is needed since in order to do a pilot study first, the Agency allotment of 15 months is insufficient.

IV. PLANT PROTECTION

A. 121-1 - Seed Germination/Seedling Emergence and Vegetative Vigor
[Three (3) Months Extension of Time]

Reason: A waiver of this data requirement was requested to the Agency in a letter dated October 23, 1987. If this request is denied, then a short extension of time is being requested in order to adequately search the archives

for surrogate data and properly format as per PR Notice 86-5.

V. NONTARGET INSECT TESTING

A. 141-1 - Honey Bee Acute Contact Toxicity
[Six (6) Months Extension of Time]

Reasons: Since honey bees are only available on a seasonal basis for this kind of test, we will not be able to initiate the study until June 1988. Therefore, a six-month extension of time is requested.

Elanco Products Company is committed to diligently pursue fulfilling the necessary data requirements for re-registering tebuthiuron. The majority of the data requirements will be submitted within the Agency's time allotment; however, there are a few exceptions where reasonable time extensions are needed and trust the Agency is in agreement.

Thank you for your consideration in this matter. Please call if you have any questions.

Sincerely,

ELANCO PRODUCTS COMPANY

James D. Helmer

James D. Helmer, Ph.D., Project Manager
Plant Science Projects Development
and Registration Division

JDH:cj