



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

AUG 26 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Subject: Azadirachtin Biochemical Pesticide. Product
Chemistry Data. EPA Reg. No. 62552-3. MRID No.
420865-01 to -11. DP Barcode D173864. CBRS Nos.
9959, 9960.

From: Michael S. Metzger, Chemist *Michael S. Metzger*
Chemistry Branch II - Reregistration Support
Health Effects Division (H7509C)

Thru: Edward Zager, Chief *EZager*
Chemistry Branch II - Reregistration Support
Health Effects Division (H7509C)

To: Phillip Hutton, Pm 18
Registration Division (H7505C)

Attached is the review of product chemistry data submitted in support of the registration of the biochemical pesticide azadirachtin (EPA Reg. No. 62552-3). This information was reviewed by Acurex Environmental Corporation under the supervision of CBRS, HED, and has been revised to reflect Agency policy.

Attachment 1: Azadirachtin (Chemical Code 121701) (CBRS Nos. 9959 and 9960; DP Barcode D173864). Task 4: Product Chemistry Data in Support of Registration.

cc (with attachment): M. Metzger (CBRS), SF, Acurex
cc (without attachment): RF, circu

AZADIRACTIN
(Chemical Code 121701)
(CBRS Nos. 9959 and 9960; DP Barcode D173864)

TASK 4

**Product Chemistry Data
in Support of Registration**

August 12, 1992

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

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Eastern Region Operations
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AZADIRACHTIN

(Chemical Code 121701)

(CBRS Nos. 9959 and 9960; DP Barcode D173864)

PRODUCT CHEMISTRY DATA IN SUPPORT OF REGISTRATION

Task 4

BACKGROUND

Azadirachtin is a biochemical pesticide manufactured by AgriDyne Technologies, Inc. (formerly Native Plants, Inc., or NPI). A REFS printout dated 7/92 lists the "technical" material as a 10% formulation intermediate (FI) (EPA Reg. No. 62552-3). NPI submitted product chemistry data to fulfill the data requirements of Subdivision M for biochemical pesticides which were reviewed by the Agency (M. Metzger, CB Nos. 7326, 7752, and 7753, 4/25/91). Data were still required for Guideline Reference Nos. 151-10 through -13, 151-15, 151-16, and several physical and chemical properties of 151-17. In response, AgriDyne submitted additional product chemistry data which were reviewed by the Agency (M. Metzger, CB Nos. 8236, 8237, 8238, and 8728, 11/12/91). The data were found acceptable for Guideline Reference No. 151-12 and several characteristics of 151-17, but additional data was required for the remainder of the 151 series topics. Consequently, AgriDyne submitted additional data (1991; MRIDs 420865-01 through -11), which are reviewed here for adequacy in fulfilling Subdivision M product chemistry requirements.

CONCLUSIONS/RECOMMENDATIONS

Residue data from this product are not required because the product contains a biochemical applied at ≤ 20 g ai/A. If the registrant proposes to increase the application rate in the future, residue data may be required.

The review of the current submitted data (1991; MRID 42086511) finds the flammability - flashpoint data (151-17) acceptable for the purpose of registration.

As concluded in the 11/91 review, adequate data were previously submitted to fulfill the requirements for the following sections of subdivision M of the Pesticide Assessment Guidelines for the azadirachtin technical:

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151-12

151-17 Melting point, pH, vapor pressure, and photostability only.

As described in detail in the 11/91 review, additional data are required for the following Subdivision M requirements:

151-10, 151-11, 151-13, 151-15, 151-16

151-17 Color, physical state, odor, density, oxidizing or reducing potential, storage stability, viscosity, corrosion characteristics, octanol/water partition coefficient, stability, and solubility.

Toxicological considerations permitting, CBRS has stated no objections to a 1-year conditional registration of this product provided a revised CSF is submitted for the end use product. However, CBRS recommends against extension of this conditional registration or full registration of this product until the remaining data deficiencies for product chemistry are resolved.

DETAILED CONSIDERATIONS

Introduction

AgriDyne responded to product chemistry data deficiencies for the azadirachtin technical (EPA Reg No. 62552-3) cited in the CBRS review of 11/12/91 (M. Metzger). The registrant provided 11 volumes of data (1991; MRIDs 420865-01 through -11). With the exception of flammability-flashpoint data contained in MRID 42086511, the remaining MRIDs are duplicates of the data reviewed by M. Metzger in the 4/91 and 11/91 reviews. The only additions to the MRIDs appear to be cover sheets with new MRID numbers and registrant GLP statements. Therefore, the conclusions reached by CBRS remain in effect for 151 series data requirements.

AgriDyne must clarify the issue of whether or not they will be producing azadirachtin by a new manufacturing process which does not isolate the technical, but rather uses an integrated system to create an end use product. As described in detail in the 9/91 review, the use of a continuous manufacturing process would require new studies to fulfill the requirements of Subdivision M product chemistry.

AgriDyne must submit a revised CSF for the end use product, and for the purposes of conditional registration, the revised CSF must establish certified limits for impurities (present at > 1% in any batch) at values which are 30% of the values found on the CSF for the technical material (the end use product is 3% a.i. and the technical is 10% ai). If aflatoxins

have been shown to be present in any batch of the technical material, an upper certified limit (included on the CSF) will be required for these impurities, regardless of concentration.

A discussion of the information submitted for Subdivision M and a description of the data remaining outstanding is provided in the 11/91 Agency review and its corresponding Confidential Appendix.

151-17: Physical and Chemical Properties

Previous CBRS Response to 151-17

The 11/91 review stated that adequate data had been submitted for melting point, pH, vapor pressure, and photostability. Physical and chemical data requirements were found deficient for solubility and thermal stability. New data reflecting the use of the newest manufacturing process (to be clarified and described) are required for the remaining 151-17 characteristics.

AgriDyne's Response

AgriDyne submitted additional data (1991; MRIDs 420865-01 through -11) in response to the 11/91 review. The MRIDs are duplicates of the data reviewed by M. Metzger in the 4/91 and 11/91 reviews, with the exception of MRID 42086511 regarding flashpoint - flammability.

The flashpoint of the azadirachtin Azatin Technical® (NPI-720/11) was determined to be 126 °C using a tag closed cup procedure (ASTM Flash Point Method D56-82). These data fulfill the data requirement for the flash point - flammability determination of the azadirachtin Azatin Technical (EPA Reg. No. 62552-3).

CBRS Comments

The remainder of the 151-17 characteristics described and delineated in the 11/91 review are still outstanding for the azadirachtin technical. Additional data are required.

References:

Citations for the MRID documents referenced in this review are presented below. Submissions reviewed in this document are indicated by shaded print.

42086501 Ellenberger, S. (1991) Purification and Identification of Impurities Present in NPI-720 Technical Using HPLC, NMR and Mass Spectroscopy: Revised Final Report: (Supplement to MRIDs 41626401; 41626405; 41626406). Unpublished study prepared by Native Plants, Inc. 99 p.

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- 42086502 Ellenberger, S. (1990) Color Determination of NPI-720 and NPI-720F: Revised Final Report. (Supplement to MRIDs 41626309; 41626409; 41626910). Unpublished study prepared by Native Plants, Inc. 11 p.
- 42086503 Ellenberger, S. (1990) Determination of Physical State of NPI-720 and NPI-720F: Revised Final Report (Replaces MRIDs 41626310; 41626410; 41626911; 41774309). Unpublished study prepared by Native Plants, Inc. 5 p.
- 42086504 Ellenberger, S. (1990) Odor Determination of NPI-720 and NPI-720F: Revised Final Report: (Replaces MRIDs 41626311; 41626411; 41626912; 41774310). Unpublished study prepared by Native Plants, Inc. 4 p.
- 42086505 Ellenberger, S. (1990) Report for Melting Point Range Determination: Revised Final Report (Replaces MRIDs 41626312; 41626412; 41626919; 41774311). Unpublished study prepared by Brigham Young Univ. 9 p.
- 42086506 Ellenberger, S. (1990) Determination of Density of NPI-720 and NPI-720F: Revised Final Report (Replaces MRIDs 41626313; 41626413; 41626913; 41774312). Unpublished study prepared by Native Plants, Inc. 5 p.
- 42086507 Ellenberger, S. (1990) Determination of Density of NPI-270 and NPI-270F: Revised Final Report (Supplement to Original MRID 41626413 and to Revised Final MRID 42086506; Replaces MRID 41923208). Unpublished study prepared by Galbraith Labs, Inc. 5 p.
- 42086508 Ellenberger, S. (1990) Determination of Solubility of NPI-720: Revised Final Report (Replaces MRIDs 41626314; 41626414; 41626914; 41774313). Unpublished study prepared by Native Plants, Inc. 5 p.
- 42086509 Ellenberger, W. (1990) Determination of Solubility of NPI-720: Revised Final Report (Supplement to Original MRID 41626414 and Revised Final MRID 42086508; Replaces MRID 41923209). Unpublished study prepared by Univ. of Ariz., Coll. of Pharmacy. 10 p.
- 42086510 Ellenberger, S. (1990) Determination of pH of NPI-270 and NPI-270F: Revised Final Report (Replaces MRIDs 41626315; 41626415; 41626915; 41774314). Unpublished study prepared by Native Plants, Inc. 5 p.
- 42086511 Ellenberger, S. (1990) Flash Point Determination of NPI-270 and NPI-270F: Revised Final Report (Replaces MRID 41626318; 41626418; 41626918; 41774317). Unpublished study prepared by Native Plants, Inc. 5 p.

Agency Memoranda

CB Nos.: 7326, 7752, 7753
Subject: Azadirachtin Biochemical Pesticide. Product Chemistry Data in Support of Registration.
To: P. Hutton, W. Nelson
From: M. Metzger
Thru: F. Suhre
Dated: 4/25/91
MRID(s): 416264-01 through -18, 416269-01 through -19, and 416263-01 through -13.

CB Nos.: 8236, 8237, 8238, 8728
Subject: Azadirachtin Biochemical Pesticide. Response to Product Chemistry Data Deficiencies.
To: W. Nelson, T. McClintock
From: M. Metzger
Thru: W. Hazel
Dated: 11/12/91
MRID(s): 419232-00 through -14

CB Nos.: none
Subject: Registration of Azadirachtin Biochemical Pesticide. SACB Review of Supplemental Information for Product Chemistry Data and Toxicity Studies (HED Project Nos. 1-1717 and 1-2399; I.D. No. 000275-AO).
To: P. Hutton, W. Nelson
From: T. McClintock
Thru: R. Engler
Dated: 12/13/91
MRID(s): 419232-00 through -20

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