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

JAN 13 2004

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OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Melvin M Graben
BASF Corporation
P.O. Box 13528
Research Triangle Park, NC 27709-3528

and

Susanne Lingard
BASF Canada Inc.
345 Carlingview Drive
Toronto, Ontario
M9W 6N9

Dear Mr. Graben and Ms. Lingard:

Subject: Review of BASF 670H Submission
BAS 670 H Technical
PMRA Sub. No. 2003-0839
EPA File Symbol 7969-ENU

The U. S. Environmental Protection Agency (EPA), is the lead agency for the joint review of BAS 670H data with the Pest Management Regulatory Agency (PMRA) of Canada. As part of the NAFTA Joint Review process described in the document entitled "Updated Procedures for Joint Review of Chemical Pesticides", after passing Step II (Receipt, screening, label review and reduced risk assessment) submissions undergo a Preliminary Review for Deficiencies.

This submission has been forwarded to the appropriate Evaluation Divisions for Deficiency Review. As a result of the Deficiency Review, it has been determined that this submission is incomplete. Outstanding data requirements resulting from the Deficiency Review are outlined in the attached *Deficiency Review Notes (D.R. Notes)* (Attachment 1). Additional deficiencies or data gaps may be identified during the full review process.

Both the Environmental Protection Agency (EPA) and PMRA will not consider a full data evaluation in the absence of a complete and reviewable submission. However, this submission will be retained by the Agencies for ninety (90) calendar days from the date of this letter in order for you to satisfactorily address the deficiencies outlined in this letter and attachment 1. If your written response is inadequate or is not received by both agencies within 90 days **(by April 12, 2004)** from the date of this letter, this submission will be returned to you at your expense.

(1)

If your submission is returned, it is suggested that the information contained in the *D.R. Notes* can be used in the preparation of future submissions.

Should you have any questions regarding the review of these submissions, please do not hesitate to contact Jim Stone of the EPA at (703) 305-7391 or Stone.James@epamail.epa.gov or Susan B. Wong of the PMRA at (613) 736-3671 or email Susan_B_Wong@hc-sc.gc.ca.

Sincerely,

/S/

Donald Stubbs, Chief
Herbicide Branch
Registration Division (7505C)

Enclosure: Attachment 1 Deficiency Review NOTES (BAS 670H Technical Herbicide)

cc: Lois Rossi, EPA
Anthony Gilbert, EPA
Joanne Miller, EPA
Mark Brohm, PMRA

Attachment 1:
Deficiency Review NOTES (PMRA Submission No. 2003-0839, EPA File Symbol 7969-ENU)

Please note that, in lieu of submitting the required data listed below, you may submit scientific rationales to waive the requirements. Upon receiving the rationales, the suitability of any waiver will be assessed during a full evaluation.

During the full evaluation, further clarification of minor information points may be required, but no additional data can be requested/accepted during full evaluation. Once all the review streams are complete and the results of one or more reviews indicate that further data are required, or if other issues are identified, you will be informed in a letter of evaluation deficiency.

PART 1 LABEL

DACO: 1.0
Title: Label

Deficiencies:

A BASF code " BAS 670 H" is used for the active ingredient instead of the common name.

The distinction between "BAS 670 H Acid" (which is M670H05) and the "BAS 670 336SC free acid" is unclear. According to the proposed label, 1 gallon of product contains 2.8 lbs of the free acid".

Required DATA:

An ISO common name should be used on the label once one is accepted.

Clarify the nature of "BAS 670 336C free acid"

NOTE: we are <u>not</u> requesting a revised label at this time. Please do <u>not</u> submit a revised label with your response.

PART 2 CHEMISTRY REQUIREMENTS FOR THE REGISTRATION OF A TECHNICAL GRADE OF ACTIVE INGREDIENT (TGAI) OR AN INTEGRATED SYSTEM PRODUCT

DACO: 2.2
Title: Manufacturer's Name and Office Address and Manufacturing Plant's Name and Address

Deficiencies:

The manufacturing plant location is listed as "BASF, Research Triangle Park, NC" under DACO 2.2 of the chemistry in the data

(3)

package and as "BASF, Germany" in box 6 of the Statement of Product Specification Form (SPSF).

Required Clarification: **The applicant is required to confirm the correct plant location where the TGAI is manufactured.**

DACO: 2.13.3
Title: Batch data

Deficiencies: The data submitted in support of the specifications of the TGAI, manufactured at the BASF Ludwigshafen, are based on five batches of the TGAI produced in pilot scale.

Required DATA: **Analytical data from five batches of the TGAI from full scale production are required when available, to support the specifications as per the requirements of DIR 98-04. In the interim, the applicant is required to provide the expected date of such data.**

DACO: 2.15
Title: Sample of Chemical Standard

Deficiencies: A 2.5 g analytical standard of the active ingredient was not submitted.

Required DATA: **As per Dir98-04, a 2.5 g analytical standard of the active ingredient is required. It should be sent directly to:**

Laboratory Services
Pest Management Regulatory Agency
Health Canada
Laboratory Services Building, No. 22
Central Experimental Farm
Ottawa, Ontario
K1A 0C6
Attn: Mary O'Neil

PART 4 TOXICOLOGY

Study Title: Developmental neurotoxicity study in Wistar rats (MRID 45902304), (Report

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number 67R0124/98140)

Notes: No positive control data was submitted.

Required Data: Positive control data from the laboratory performing the test that demonstrate the sensitivity of the procedures being used. These data do not need to be from studies using prenatal exposures. However, the laboratory must demonstrate competence in evaluation of effects in neonatal animals perinatally exposed to chemicals and establish test norms for the appropriate age group.

DACO: 4.0
Title: Toxicology

Notes: Studies were submitted without Certificates of Analysis for the test article.

Required Clarification: **Please provide Certificates of Analysis for batches N3, N14, N33, 30786/22, 01311-230, 01586-177, and WH 20089. (Several Reports).**

DACO: 4.3.1
Title: Short-term oral, 90-day rodent

Notes: A study (Report Number 50S0124/98062) is mentioned as being in progress in Report Number 50S0124/98142.

Required Clarification: **Please provide this study (Report Number 50S0124/98062).**

DACO: 4.3.3
Title: Short-term oral, 21-day to 30-day

Notes: A range-finding study (Report Number 50S0124/98062) is mentioned as being the basis for dose selection in Report Number 50S0124/98142.

Required Clarification: **Please provide this range-finding study (Report Number 50S0124/98062).**

DACO: 4.5.2-1 (Report Number 30R0124/98120)
Title: Teratogenicity, rodent

Notes: The batch used for stability analysis does not match batch used in the study.

Required Clarification: **Please explain the use of batch N14 for the stability analysis when batch N26 was the one used in the study.**

DACO: 4.5.3-1 (Report Number 40R0124/989167)
Title: Teratogenicity, non-rodent

Notes: Some tables on pages 288-291 have darkened table headers which are not legible.
Acclimation period and rationale for dose selection were not found.

Required Clarification: **Please provide clear copies of these pages.**
Please provide acclimation period and rationale for dose selection.

DACO: 4.5.3-2 (Report Number 40R0124/98170)
Title: Teratogenicity, non-rodent

Notes: Study states that fetal skeletal observations 'were abandoned'.

Required Clarification: **Please explain the lack of fetal skeletal observations.**

DACO: 4.5.3-4 (Report Number 40R0124/98150)
Title: Teratogenicity, non-rodent

Notes: The chromatographic fractions of batch N17 were not adequately described.

Required Clarification: **Please provide details of the components and purity for the chromatographic fractions of batch N17.**

DACO: 4.5.9 (Report Numbers 02B0022/996002 & 55908)
Title: Metabolism/Toxicokinetics in mammals

Notes: Acclimation period and the method of sacrifice were not found.

Required Clarification: **Please provide the acclimation period and the method of sacrifice.**

(6)

DACO: 4.5.12 (Report Number 67R0124/98140)
Title: Developmental Neurotoxicity

Notes: Positive control data that demonstrate the sensitivity of the procedures used in the study were not submitted.

Required Clarification: **Please submit positive control data. These data do not need to be from studies using prenatal exposures. However, the laboratory must demonstrate competence in evaluation of effects in neonatal animals perinatally exposed to chemicals and establish test norms for the appropriate age group.**

DACO: 4.8-7, 4.8-8 (Report Numbers 99S0124/98164, 99S0124/98165)
Title: Other studies

Notes: Concentration analysis of the test substance in the feed was not performed.

Required Clarification: **Please provide a rationale for this omission.**

PART 6 METABOLISM/TOXICOKINETICS STUDIES

DACO: 6.2
Title: Nature of the residue in Livestock - HEN

Deficiencies: Residues are identified by only 1 analytical technique (HPLC) with no confirmatory data using a spectroscopic method (Residue Chemistry Guidelines Dir98-02, Section 2 and OPPTS 860.1300).

Required DATA: **Data that confirms residue identity by a spectroscopic method.**

PART 8 ENVIRONMENTAL CHEMISTRY AND FATE

General: The screening of the environmental fate package has identified several issues that we believe should be clarified and/or corrected by the applicant prior to the full review of the studies by the contractor. One major issue is the lack of information on the fate and transport of degradates containing only the pyrazole ring. Formation of the major degradate "M670H05"(which does not have the pyrazole ring) implies formation of pyrazole ring products. From the data presented in the

studies, it is unclear which pyrazole-ring products form, how persistent they are, and how strongly they bind to soils..

The screening of the environmental fate suggests that a same degradate may have been identified by multiple company codes. This unnecessarily complicates the interpretation of results. To address this concern, the applicant should provide the following information for each degradate:

1. All of the company codes assigned to each degradate.
2. Common name, if any.
3. Chemical name (CAS and IUPAC).
4. Chemical Abstract Registry Number (if assigned).
5. Chemical structure.

Beyond the deficiencies or issues identified in the screening of the studies, it is important to note that there may be other issues with the data that will not surface until each study is reviewed in depth.

DACO: 8.2.3.5.6

Title: Anaerobic Aquatic Metabolism Study

Notes: On page 13, "M670H11 metabolite" is referred to as "structural isomer of BAS 670 H". Is the author referring to a "tautomer"? Also, the degradate M670H10 appears to partition predominantly to the sediment.

Required clarification: Clarify the nature of the "M670H11 metabolite". Submit information with supporting data on the adsorption/desorption of the degradate M670H10, such as batch-equilibrium studies.

DACO: 8.2.2
Title: Analytical Methodology (parent compound and transformation products)

Notes: 1. Apart from those shown below, the applicant has not specifically stated if there are any other major transformation products/metabolites expected in each environmental matrix.

In soil:	M670H05
In sediment	Not identified
In water	Not identified

In plant matrix:	M670H05
In animal matrix	M670H02

2. In the Animal Method (D0104), BASF Reg. Doc. # 2003/7004046, the metabolite of BAS 670H was referred to as (M670H02). The chemical structure and name of this metabolite were not provided.

Required Clarification:

1. **The applicant is requested to clarify if there are any other major transformation products/metabolites other than M670H05 in all matrices mentioned above, if there are a specific and validated method is required for their determination.**

   Please note that any transformation products / metabolites present at level greater than 10% of the initial concentration of the pesticide at any time during the study, as well as those products that have not attained 10% (e.g., 8 - 9%), but show a continuous increase in concentration up until the termination of the study is considered to be major. Also, transformation products / metabolites that are of toxicological concern (i.e., predicted or demonstrated toxicity) are considered to be major, even if their maximum concentrations are less than 10% of the initial parent concentration.

2. **The applicant is requested to provide the chemical structure and name for the metabolite (M670H02), if it is in fact another metabolite and not a typo.**

DACO: 8.2.2.2
Title: Sediment

Notes: An analytical method provided for the determination of soil samples was referenced for sediment samples. No rationale has been provided.

Required Clarification: **The applicant is requested to provide scientific rationale for extending the method which is used for soil samples to sediment samples. Please note that in order to do that, 2**

(9)

conditions must be met. They are:

1. **The extraction efficiency of the compounds in soil must be comparable to those in sediment.**

2. **No new major transformation products are present in sediment.**

PART 9 ENVIRONMENTAL TOXICOLOGY

General Clarification: A structural similarity between the BAS 670 H transformation product M670H05 has been identified, and isoxaflutole. A preliminary examination of fate data shows that M670H05 is a major transformation product in water/sediment systems (i.e., occurring at >10% total active radiation), and is moderately persistent to persistent (DT_{50} in water of 180 days). The applicant is asked to share any eco-toxicological information they may already have for this transformation product.

DACO: 9.5.3.1
Title: Fish, Early Life-Cycle Toxicity Test

Deficiencies: It is felt that the acceptability of this study has been compromised due to a number of factors: a) 14-d mean embryo survival in the viability control was marginal (83%), which may suggest difficulties in acclimatizing the off-site fertilized eggs, b) lime (calcium carbonate) precipitates were formed during the test necessitating a change in dilution water tanks, c) significant non-test material related mortalities occurred in nearly all treatments, coinciding with larvae accidentally leaving their hatching cups and coming in contact with carbonate deposits on the bottom of the container, d) sublethal effects, including reduced activity, apathy, and decreased respiration rate, were reported in several control fish.

Required DATA: **A new early life-cycle toxicity test with rainbow trout must be submitted. Survivorship in controls must be acceptable, and the test must be run without the**

presence of precipitates. For acceptable study guidelines refer to U.S. EPA 540/9-86-138, OPPTS 850.1400, and OECD No. 210.

DACO: 9.6.2.1
Title: Wild Birds - Acute Studies - Oral (LD50) Bobwhite Quail (Zok 2000).

Required Clarification: **The applicant is required to submit environmental data for the test chambers confirming that target temperature and humidity levels were achieved.**

DACO: 9.6.2.4/9.6.2.5
Title: Wild Birds - Acute Studies - Dietary (LC50): Bobwhite Quail (Zok 2001), and Mallard Duck (Zok 2000).

Required Clarification: **The applicant is required to submit a) environmental data for the test chambers confirming that target temperature and humidity levels were achieved, and b) the LOQ for analysis of BAS 670 H.**

DACO: 9.8.2
Title: Non-target Plants: Freshwater Algae - Study 01 (Kubitza 2001), and Study 02 (Kubitza 2001).

Required Clarification: **The applicant is required to provide a) temperature data to demonstrate that vessels were maintained within the specified range over the course of the test, and b) data verifying that initial cell densities were ~3.0 x 10^4 cells/mL.**

DACO: 9.8.3
Title: Non-target Plants: Marine Algae (Palmer et al., 2002).

Required Clarification: **The applicant is required to provide a) the non-linear regression equation (including r^2-value) used to derive the 96-h EC_{50}-value, and the associated 95% confidence intervals, and b) data verifying that refrigeration of the algal samples for up to 17 days was sufficient to inhibit cell growth during this period.**