

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

JAN 13 2004

JAN 13 2004

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 336SC
PMRA Sub. No. 2003-0840
EPA File Symbol 7969-ENL

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 336 SC Herbicide)

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

5

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

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 not requesting a revised label at this time. Please do not submit a revised label with your response.

Required Clarifications: a) Under the section "Application Directions", the applicant is required to clearly state the maximum number of allowable applications of BAS 670 336 SC Herbicide per growing season.
b) Under the section "Spray Additives", the applicant must specify whether Assist is the required COC surfactant (i.e., "...addition of a COC surfactant (Assist) and ...").

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

**PART 3 CHEMISTRY REQUIREMENTS FOR THE REGISTRATION OF
MANUFACTURING CONCENTRATES AND END-USE PRODUCTS
FORMULATED FROM REGISTERED TECHNICAL GRADE OF
ACTIVE INGREDIENTS OR INTEGRATED SYSTEM PRODUCTS**

DACO: 3.1.2
Title: Formulating Plant's Name and Address

Deficiencies: The formulating plant location is listed as "BASF, Research Triangle Park, NC" under DACO 3.1.2 of the Chemistry data 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 EP is formulated.**

DACO: 3.5.10
Title: Storage stability data

Deficiencies: The product is stated to be stable for one year at ambient temperature without supporting data.

Required DATA: **The applicant is required to provide the results of one year storage stability study as per the requirements of DIR 98-03, if available. In the interim, the completion date of such study is required.**

PART 4 TOXICOLOGY

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

④

Attachment 1:

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

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.**

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

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.**

Attachment 1:

/ 5

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

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 5 EXPOSURE (OCCUPATIONAL AND/OR BYSTANDER)

DACO: 5.2
Title: Use Description/Scenario (Application and Postapplication)

Deficiencies: The applicant submitted a description of the use pattern to address this data requirement. Within this description, the applicant did not discuss a postapplication activity that occurs in seed corn, detasseling. In order to conduct the full evaluation, the applicant must clarify whether detasseling is expected to co-occur with application of BAS 670 336 SC Herbicide, and if not, the minimum number of days expected between application of BAS 670 336 SC Herbicide and detasseling in seed corn.

Required Clarification: Information describing whether the post-application activity, detasseling, is expected to co-occur with application of BAS 670 336 SC Herbicide in seed corn and if the two activities do not co-occur, the minimum number of days expected between application of BAS 670 336 SC Herbicide and detasseling in seed corn.

DACO: 5.6/5.7
Title: Postapplication

Deficiencies: The applicant proposes that postapplication exposure would be negligible and did not provide a quantitative estimate of postapplication exposure. Following application to sweet, seed or field corn, however, there is potential for postapplication exposure following scouting activities and an exposure estimate is required for scouters. In addition, depending on whether there is co-occurrence between application of BAS 670 336 SC Herbicide and detasseling in seed corn, there may be potential for postapplication

7

exposure following detasseling activities in seed corn and an exposure estimate would be required. If the applicant has exposure data to support a postapplication exposure assessment (e.g., dislodgeable foliar residue data) this should be submitted. In the absence of this information, a Tier 1 assessment using default inputs will be conducted during the full evaluation. Since the applicant is a member of the Agricultural Reentry Task Force (ARTF), transfer coefficients derived from ARTF studies may be used when appropriate.

Required Clarification: The applicant must clarify whether they have exposure data to support a postapplication exposure assessment (e.g., dislodgeable foliar residue data) for scouters (and potentially detassellers). In the absence of product specific data, a Tier 1 assessment using default inputs will be conducted during the full evaluation.

DACO:

5.8

Title:

In Vivo Dermal Absorption

Deficiencies:

The applicant submitted an *in vivo* dermal absorption study conducted with BAS 670 H in rats. A number of study limitations were noted in the preliminary review of the study. Specific study limitations include:

- Lack of details of the chemical composition of the formulation concentrate used in the study. The applicant should be advised that in order to determine the relevance of the test material to the proposed formulation, BAS 670 336 SC Herbicide, this information is required.
- Details on quantification and calculation of the actual dose administered to each animal (i.e., weight of pipette before and after dosing, sample calculations, etc.)
- Raw data. In order to verify the results which are presented as a percentage of the applied dose, raw data including dpm for each matrix and tissue weights should be submitted.

The utility of the data in the occupational exposure and risk assessment will be determined during the full evaluation.

8

Required Clarification: In order to assess the utility of the submission the following clarifications are requested:

- the chemical composition of the formulation concentrate
- details on quantification and calculation of the actual dose
- raw data (dpm per matrix/sample, tissue weights, etc.)

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 7 FOOD, FEED AND TOBACCO RESIDUE STUDIES

DACO: 7.2.1
Title: Residue Analytical Method - PLANT MATRICES

Deficiencies:

1. The 10X LOQ chromatograms (0.1 and 0.5 ppm) do not reflect a 10-fold increase compared to the 1X LOQ chromatograms (0.01 and 0.05 ppm).
2. Linearity has been demonstrated for 0.1-10 pg/ μ L (ppb). However, the reported limits of quantitation are 10 ppb (K+CWHR, grain) and 50 ppb (forage, stover).

Required DATA:

1. Resubmit chromatograms (Study Number 56542; Pages 41, 42, 53 and 54; Figures 9, 10, 21 and 22), and provide an explanation for the discrepancy.
2. Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in plant matrices.

9

Attachment 1:

/ 8

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

DACO: 7.2.1

Title: Residue Analytical Method - ANIMAL MATRICES

- Deficiencies:**
1. Radiovalidation data for animal matrices was not provided to demonstrate extraction efficiency.
 2. The axes for the standard curves (Figures 12 and 13) are illegible. Also, detector response linearity cannot be accurately established as no r value was included for either standard curve.

- Required DATA:**
1. **Radiovalidation data for animal matrices.**
 2. **Please send revised BAS 670 H and M670H02 standard curves (Study Number 55913; Pages 33 and 34; Figures 12 and 13), including proper axes and correlation (r) values.**

DACO: 7.2.3

Title: Inter-Laboratory Analytical Method Validation - PLANT MATRICES

- Deficiencies:**
1. Linearity has been demonstrated for 2-20 pg/ μ L (ppb). However, the reported limits of quantitation are 10 ppb (maize seed) and 50 ppb (lettuce, oilseed rape seed and apple).
 2. Recoveries of BAS 670 H and M670H05 at 10-fold the LOQ (0.1 mg/kg for maize seed; 0.5 mg/kg for lettuce, oilseed rape seed and apple) were listed in the report. However, no chromatograms of matrices spiked at 10X LOQ were provided.
 3. Chromatograms of samples spiked at one-fold the LOQ are hard to read, making it impossible to determine if there are interferences in the area of analytical interest.

- Required DATA:**
1. **Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in plant matrices.**

10

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

2. Please submit chromatograms of samples spiked at 10X LOQ for all matrices (0.1 mg/kg for maize seed; 0.5 mg/kg for lettuce, oilseed rape seed and apple).
3. Please resubmit chromatograms of samples spiked at 1X LOQ (Study Number 135238; Pages 25-27, 30-31; Figures 7, 9, 11, 17 and 19).

DACO: 7.2.3

Title: Inter-Laboratory Analytical Method Validation - ANIMAL MATRICES

- Deficiencies:
1. The r values for the standard curves of both BAS 670 H and M670H02 are illegible.
 2. The 10X LOQ chromatograms (0.1 and 0.5 ppm) do not reflect a 10-fold increase compared to the 1X LOQ chromatograms (0.01 and 0.05 ppm) (Figures 15-18, 21-24).
 3. Linearity has been demonstrated for 0.1-10 pg/ μ L (ppb). However, the reported limits of quantitation are 10 ppb (whole milk) and 50 ppb (liver).

- Required DATA:
1. Please provide r values for standard curves (Study Number 56757; Pages 29-30; Figures 9-10).
 2. Resubmit chromatograms (Study Number 56757; Pages 33-34, 36-37; Figures 15-18, 21-24), and provide an explanation for the discrepancy.
 3. Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in animal matrices.

DACO: 7.2.5

Title: Determination of Stability in Various Solvents

- Deficiencies:
1. Storage intervals of stock analytes do not appear to be submitted for the following studies: plant and animal metabolism, plant and animal analytical methodology; supervised residue crop field trials.

11

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

2. The standard curves for BAS 670 H and M670H05 are not visible.
3. The axes for all chromatograms (Figures 5-11) are not legible.

Required DATA:

1. **Provide storage intervals of stock analytes for the following studies: Corn metabolism (Study Number 98129), Goat metabolism (Study Number 55911), Hen metabolism (Study Number 55910), Plant analytical methodology (Study Number 56542), Animal analytical methodology (Study Number 55913), Supervised residue crop field trial (Study Number 63882).**
2. **Please resubmit standard curves for BAS 670 H and M670H05 (Study Number 56755; Pages 40-41; Figures 3-4).**
3. **Please resubmit chromatograms (Study Number 56755; Pages 42-48; Figures 5-11) with legible axes.**

DACO: 7.3

Title: Freezer Storage Stability

Deficiencies:

1. Linearity has been demonstrated for 0.1-10 pg/ μ L (ppb). However, the reported limits of quantitation are 10 ppb (corn grain), and 50 ppb (corn stover, corn forage and radish root).
2. The standard curves for BAS 670 H and M670H05 (Figure 15) are not visible.
3. Chromatograms of typical control corn forage (Figure 16), control radish root (Figure 19), control corn forage ((Figure 22) and control corn stover (Figure 25) are difficult to read.

Required DATA:

1. **Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in corn and radish matrices.**

12

2. Please resubmit standard curves for BAS 670 H and M670H05 (Study Number 56750; Page 55; Figure 15).
3. Please resubmit chromatograms of control matrix samples (Study Number 56750: Pages 56, 59, 62, 65; Figures 16, 19, 22, 25).

DACO: 7.4.1
Title: Supervised Residue Crop Field Trial

- Deficiencies:**
1. Linearity has been demonstrated for 0.2-10 pg/ μ L (ppb). However, the reported limits of quantitation are 10 ppb (fresh corn K+CWHR, corn grain), and 50 ppb (corn stover, corn forage).
 2. The r value for BAS 670 H 05 from the standard curve was reported as "1...".

- Required DATA:**
1. **Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in corn forage and stover.**
 2. **Please provide the actual r value (to at least 3 decimal places) for BAS 670 H 05 from the standard curve.**

DACO: 7.4.3
Title: Confined Rotational Crop Trial

- Deficiencies:**
1. Linearity has been demonstrated for 0.2-10 pg/ μ L (ppb). However, the reported limits of quantitation are 10 ppb (fresh corn K+CWHR, corn grain), and 50 ppb (corn stover, corn forage).
 2. The r value for BAS 670 H 05 from the standard curve was reported as "1...".

- Required DATA:**
1. **Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in corn forage and stover.**
 2. **Please provide the actual r value (to at least 3 decimal places) for BAS 670 H 05 from the standard curve.**

13

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

DACO: 7.4.4
Title: Field Accumulation in Rotational Crops

- Deficiencies:**
1. Data to demonstrate efficiency of the method for metabolite BAS 670 H 05 was not submitted.
 2. Chromatograms of samples spiked at 10X LOQ do not reflect a 10-fold response compared to chromatograms of samples spiked at LOQ.
 3. Linearity has been demonstrated for 0.2 to 10 pg/ μ L (ppb). However, the reported limit of quantitation for all rotational crop matrices is 0.05 ppm (50 ppb).

- Required DATA:**
1. **Data to determine efficiency of the method for metabolite BAS 670 H 05.**
 2. **Provide an explanation for the discrepancy in the chromatograms.**
 3. **Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in rotational crop matrices.**

DACO: 7.5
Title: Livestock Feeding Study - COW

- Deficiencies:**
1. Linearity has been demonstrated for 0.1 to 2.0 pg/ μ L (ppb). However, the reported limit of quantitation for liver, kidney and fat is 0.05 ppm (50 ppb) and 0.01 ppm (10 ppb) for muscle and milk.
 2. Chromatograms of milk and fat samples spiked at 10X (fat) or 50X (milk) LOQ do not reflect either a 10-fold or 50-fold response, compared to chromatograms of samples spiked at LOQ.

- Required DATA:**
1. **Data and sample calculations to demonstrate linearity in the range that encompasses the respective LOQs in livestock matrices.**

Deficiency Review NOTES (PMRA Submission No. 2003-0840, EPA File Symbol 7969-ENL)

2. Sample calculations, injection volume used and chromatograms (Study Number 56760; Pages 122-123, 140-141; Figures 16-19, 52-55) and provide an explanation for the discrepancy.

PART 10 VALUE

DACO: 10.2.3.3
Title: Efficacy: Small-Scale Trials

Deficiencies: The efficacy data provided indicates the application of BAS 670 336 SC Herbicide at the rate of 25 g ai/ha + Assist at 1.25 % v/v + UAN 28% at 1.25 % v/v is necessary to provide consistent control of the several of the requested weeds under various growing conditions. Therefore, the rate of BAS 670 336 SC Herbicide at 25 g ai/ha + Assist at 1.25 % v/v + UAN 28% at 1.25 % v/v is acceptable to appear on the BAS 670 336 SC Herbicide label.

Limited efficacy data provided also indicated the application of BAS 670 336 SC Herbicide at rates below 25 g ai/ha + Assist at 1.25 % v/v + UAN 28% may be effective in controlling common ragweed, green pigweed, eastern black night shade and wild mustard. However, there is insufficient data to establish the lowest effective rate for these weeds.

Required DATA: **Additional efficacy data may be required in order to establish that the lowest effective rate for BAS 670 336 SC Herbicide for control of common ragweed, green pigweed, eastern black nightshade and wild mustard. These trials should test the efficacy of 20, 15 and 12.5 g ai/ha in comparison with 25 g ai/ha on the subject weeds.**

DACO: 10.3.2
Title: Non-safety Adverse Effects

Deficiencies: 1. Seed Corn- Seed corn is proposed as a crop on the BAS 670 336 SC Herbicide label, however, no crop tolerance data was provided, and no rationale was given for the lack of data.

15

2. Sweet Corn- A limited number of trials over three years (seven dedicated weed-free trials, and four combined efficacy crop tolerance trials) showed inconsistencies between the crop tolerance and yield of sweet corn to BAS 670 336SC Herbicide alone. Only three trials in one year reported crop tolerance and yield of sweet corn to the two-way tank-mix of BAS 670 336 SC Herbicide + Atrazine 90WG.
3. Corn Heat Units- The proposed product label requests use in Eastern Canada, however, the range of crop heat units covered in the majority of the trials is approximately 2800-3400 CHU.

Required DATA:

1. **Ten dedicated weed-free crop tolerance trials per year over two years are required to determine the crop tolerance of seed corn to BAS 670 336 SC Herbicide alone and in tank-mix with Atrazine and Atrazine + Frontier. Trials should report crop injury three times (early, mid, and late-season) throughout the growing season, as well as measure crop yield. Trials should be conducted in areas representative of seed corn production in eastern Canada, and therefore cover a range of soil types, environments, and crop heat units.**
2. **Additional dedicated weed-free crop tolerance trials are required to show the crop tolerance of sweet corn to BAS 670 336 SC Herbicide alone and in tank-mix with Atrazine and Atrazine + Frontier. Trials should report crop injury three times (early, mid, and late-season) throughout the growing season, as well as measure crop yield as marketable yield. Trials should be conducted in areas representative of sweet corn production in eastern Canada, and therefore cover a range of soil types, environments, and crop heat units.**
3. **Additional trials are required to show the crop tolerance of field corn varieties that rate below 2700 CHU to BAS 670 336 SC Herbicide alone and in tank-mix with Atrazine and Atrazine + Frontier. Trials should report crop injury three times (early, mid, and**

late-season) throughout the growing season, as well as measure crop yield. Trials should be conducted in areas representative of field corn production in eastern Canada with crop heat units below 2700.

DACO: 10.3.3
Title: Damage to Rotational Crops

Deficiencies: A limited quantity of crop rotation data, 6 trials conducted in one year, was submitted in order to support the various recropping options as presented on the draft BAS 670 336 SC Herbicide label. These trials did not test the requested recropping interval for several of the crops i.e. requesting 9 month interval but the crops were planted 10 or 11 months after application. Based on the limited quantity of the data package and the fact the trials did not reflect the requested recropping interval, additional data must be provided to support the requested recropping options and the intervals.

Required DATA: Additional data must be provided in order to support the requested crops at the requested intervals.