UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

June 1, 2001

MEMORANDUM

Subject: D273135 – T535, EPA File Symbol 72992-U
D273364 – T427, EPA File Symbol 72992-G
D273124 – T344, EPA File Symbol 72992-E
D273148 – T426, EPA File Symbol 72992-O
D273347 – T345, EPA File Symbol 72992-L
D273350 – T428, EPA File Symbol 72992-T
D273360 – T333, EPA File Symbol 72992-I
D273362 – T430, EPA File Symbol 72992-A

From: Wallace Powell, Biologist
Product Science Branch
Antimicrobials Division (7510C)

06-01-01

Thru: Karen P. Hicks, Team Leader
Chemistry/Toxicology Team
Product Science Branch
Antimicrobials Division (7510C)

6/4/01

Michele E. Wingfield, Chief
Product Science Branch
Antimicrobials Division (7510C)

To: Adam Heyward, Product Manager, Team 34
Portia Jenkins, Team Reviewer, Team 34
Drusilla Copeland, Team Reviewer, Team 34
Regulatory Management Branch II
Antimicrobials Division (7510C)

BACKGROUND

The applicant, Pokon & Chrysal B.V. (as represented by an agent), has submitted papers in support of the acute toxicity data requirements (mammalian) for registration of the subject products: T535, T427, T344, T426, T345, T428, T333, and T430.

The submitted papers include the following study reports:

- For T535: acute oral toxicity (MRID 453257-03), acute dermal toxicity (MRID 453257-02), and skin sensitization (MRID 453257-04).
- For T427: eye irritation (MRID 453269-02), skin irritation (MRID 453269-03), and skin sensitization (MRID 453269-04).
- For T344: eye irritation (MRID 453255-02), skin irritation (MRID 453255-03), and skin sensitization (MRID 453255-04).

With the following exceptions, the above submitted studies were cited by the applicant to cover the remaining acute toxicity data requirements for the various products:

- For all the products, acute inhalation waivers were requested.
- For T535, eye irritation and skin irritation waivers were requested.

Each of the subject products is meant to provide conditioning for ornamental cut flowers by controlling microbial growth, activating water uptake, and preventing premature wilting. Each product contains the following active ingredients:

- 2-bromo-2-nitropropane-1,3-diol (i.e., Bronopol), EPA code 216400
- Poly(iminoimidocarbonyliminoimidocarbonyliminohexamethylene)hydrochloride (i.e., polymeric biguanide), EPA code 111801.

RECOMMENDATION

The submitted studies were initially reviewed for Product Science Branch (PSB) by Oak Ridge National Laboratory. The reviews are attached to this memorandum. Any PSB disagreement with the reviews appears below; the reviews themselves have not been edited by PSB.

A basic acceptability summary for the submitted studies is as follows:

- The test material identified in each study report appears to represent the product in support of which the study was submitted.
- Studies submitted for T535 (EPA File Symbol 72992-U):
  - MRID 453257-03 (acute oral toxicity): Acceptable
  - MRID 453257-02 (acute dermal toxicity): Acceptable
  - MRID 453257-04 (skin sensitization): Acceptable
- Studies submitted for T427 (EPA File Symbol 72992-G):
  - MRID 453269-02 (eye irritation): Unacceptable but potentially upgradable
  - MRID 453269-03 (skin irritation): Acceptable
  - MRID 453269-04 (skin sensitization): Acceptable
- Studies submitted for T344 (EPA File Symbol 72992-E):
  - MRID 453255-02 (eye irritation): Unacceptable but potentially upgradable
  - MRID 453255-03 (skin irritation): Acceptable
  - MRID 453255-04 (skin sensitization): Unacceptable but potentially upgradable

The acute toxicity regulatory status for the subject products is summarized in the table below. The table is followed by clarifying comments in the form of footnotes.

For each data requirement for each product, the table lists the means of support, followed by the study MRID if applicable, followed by the acute Toxicity Category indicated by the study results if applicable, followed by the acceptability rating for the data requirement. Footnote reference numbers are shown in square brackets.

2

As indicated in the table, there are three data requirements which remain outstanding for certain products. These are the acute inhalation toxicity, eye irritation, and skin sensitization data requirements. For each of these, the issues to be resolved and the information needed by PSB are identified in the table footnotes.

In regard to the submitted product labels, the first-aid statements and human-hazard precautionary statements will be reviewed after the outstanding data requirements have all been met. For the time being, note that the Signal Word for T535 (EPA File Symbol 72992-U) will have to be changed from CAUTION to DANGER because T535 is assigned to eye and skin irritation Category I.

Table: Acute Toxicity Regulatory Profile for the Proposed Registrations

(Footnotes appear in square brackets [ ])

Product and Data Package	Means of Support, MRID, Acute Tox Category, Acceptability					
	Acute Oral Toxicity	Acute Dermal Tox.	Acute Inhalation Tox.	Eye Irritation	Skin Irritation	Skin Sensitization
T535 72992-U D273135	**Submitted** study MRID 453257-03 Category III Acceptable[1]	**Submitted** study MRID 453257-02 Category III[2] Acceptable	Waiver request (Cat. III requested) Category III[3] Waiver Acceptable	Waiver request (Cat. I requested) Category I[4] Waiver Acceptable	Waiver request (Cat. I requested) Category I[4] Waiver Acceptable	**Submitted** study MRID 453257-04 Sensitizer Acceptable
T427 72992-G D273364	Cited T535 study MRID 453257-03 Category III Citation Acceptable[5]	Cited T535 study MRID 453257-02 Category III Citation Acceptable[5]	Waiver request (Cat. III requested) Category III[3] Waiver Acceptable	**Submitted** study MRID 453269-02 Category unknown Unacceptable[6]	**Submitted** study MRID 453269-03 Category IV Acceptable	**Submitted** study MRID 453269-04 Sensitizer Acceptable
T344 72992-E D273124	Cited T535 study MRID 453257-03 Category III Citation Acceptable[5]	Cited T535 study MRID 453257-02 Category III Citation Acceptable[5]	Waiver request (Cat. III requested) Waiver Unacceptable[3]	**Submitted** study MRID 453255-02 Category unknown Unacceptable[6]	**Submitted** study MRID 453255-03 Category IV Acceptable	**Submitted** study MRID 453255-04 Non-sensitizer Unacceptable[7]
T426 72992-O D273148	Cited T535 study MRID 453257-03 Category III Citation Acceptable[5]	Cited T535 study MRID 453257-02 Category III Citation Acceptable[5]	Waiver request (Cat. III requested) Category III[3] Waiver Acceptable	Cited T427 study MRID 453269-02 Category unknown Citation Unacceptable[6]	Cited T427 study MRID 453269-03 Category IV Citation Acceptable[8]	Cited T427 study MRID 453269-04 Sensitizer Citation Acceptable
T345 72992-L D273347	Cited T535 study MRID 453257-03 Category III Citation Acceptable[5]	Cited T535 study MRID 453257-02 Category III Citation Acceptable[5]	Waiver request (Cat. III requested) Waiver Unacceptable[3]	Cited T344 study MRID 453255-02 Category unknown Citation Unacceptable[6]	Cited T344 study MRID 453255-03 (Study: Category IV) Cat. III assigned[9] Citation Acceptable	Cited T344 study MRID 453255-04 Non-sensitizer Citation Unacceptable[7]
T428 72992-T D273350	Cited T535 study MRID 453257-03 Category III Citation Acceptable[5]	Cited T535 study MRID 453257-02 Category III Citation Acceptable[5]	Waiver request (Cat. III requested) Category III[3] Waiver Acceptable	Cited T427 study MRID 453269-02 Category unknown Citation Unacceptable[6]	Cited T427 study MRID 453269-03 Category IV Citation Acceptable	Cited T427 study MRID 453269-04 Sensitizer Citation Acceptable
T333 72992-I D273360	Cited T535 study MRID 453257-03 Category III Citation Acceptable[5]	Cited T535 study MRID 453257-02 Category III Citation Acceptable[5]	Waiver request (Cat. III requested) Waiver Unacceptable[3]	Cited T344 study MRID 453255-02 Category unknown Citation Unacceptable[6]	Cited T344 study MRID 453255-03 Category IV Citation Acceptable	Cited T344 study MRID 453255-04 Non-sensitizer Citation Unacceptable[7]
T430 72992-A D273362	Cited T535 study MRID 453257-03 Category III Citation Acceptable[5]	Cited T535 study MRID 453257-02 Category III Citation Acceptable[5]	Waiver request (Cat. III requested) Category III[3] Waiver Acceptable	Cited T427 study MRID 453269-02 Category unknown Citation Unacceptable[6]	Cited T427 study MRID 453269-03 Category IV Citation Acceptable	Cited T427 study MRID 453269-04 Sensitizer Citation Acceptable

Table Footnotes:

[1] Although only 3 rats per sex were used, the acute oral toxicity study is being accepted because the clearly innocuous results – together with the use of a 2 g/kg limit dose which is well above the Category III limit – make the prospect of a more severe Toxicity Category than Category III to be highly unlikely. (Note: according to the 870.1100 Guidelines, the use of fewer animals than 5 per sex, or than 5 of the more sensitive sex, may be justified in individual circumstances.)

[2] Acute dermal toxicity study: Category III based on the limit test.

[3] Acute inhalation toxicity data is waived for T535, T427, T426, T428, and T430, based on lack of significant concern regarding product components at the concentrations present, when used for the proposed product use pattern. Category III is assigned in order to indicate the possibility of a mild or moderate hazard.

For the products which are in powder form – T344 (EPA File Symbol 72992-E), T345 (72992-L), and T333 (72992-I) – the acute inhalation waiver request is Unacceptable but potentially upgradable. The applicant reports that the particle size range for T344 is 200 to 800 microns. The applicant should submit the data that led to this conclusion. If an attrition resistance test was used, the test report should be submitted. (Such a test consists of an agitation to exaggerate conditions of shipping and handling, followed by a sieving with preferably a 106 micron filter.) Such data should also be submitted for T345 and T333.

[4] T535: Eye irritation Category I based on pH<2, as per 40 CFR 158.340(a)(2).

[5] With the possible exception of T345, the products would not be expected to be more hazardous by acute dermal toxicity than would the cited test material (T535). If there are any components of a product that are not present in the cited test material, they are not of significant concern with respect to acute dermal toxicity.

As for T345 (EPA File Symbol 72992-L), concentrations of most components are moderately higher than they are in the cited test material. However, the T345 components are not of significant concern in and of themselves at the concentrations present, and the pH of T345 suggests that corrosiveness would not be a factor. Moreover, the quantitative and qualitative data in the acute dermal toxicity study on the T535 test material (to which T345 is being compared) all suggest that that test material is probably nearly harmless by dermal absorption.

[6] PSB overrules the acceptability finding in the two attached eye irritation study reviews (MRID's 453269-02 and 453255-02): PSB finds the studies Unacceptable but potentially upgradable. The applicant should submit a description of the grading system for severity of chemosis and redness in individual animals. (This will help in interpreting Table 1 in both study reports).

PSB assumes that, upon test-article application, treated eyes were held shut for approximately 1 second and were not rinsed for 24 hours. If this is not the case, the applicant should let us know and explain the procedure used.

[7] PSB overrules the acceptability finding in the attached review of MRID 453255-04 (conducted on T344): PSB finds the study Unacceptable but potentially upgradable. For each animal in the Test Group (as distinct from the control groups), reactions to intradermal and topical inductions should be submitted. (This is to confirm that induction in these animals was adequate.) In addition, the treatment volumes, and a description of the grading system for severity of erythema and oedema, should be submitted.

T344, T345, and T333 will be classified as Non-sensitizers if MRID 453255-04 is upgraded to Acceptable. If it is not upgraded, then PSB will assign these products the Sensitizer classification based on their similarity to T535 and T427, products which tested positive for sensitization (MRID's 453257-04 and 453269-04, respectively).

[8] The skin irritation data citation is acceptable for T426 based on its comparability to two supported products: T427 (on which MRID 453269-03 was conducted) and T344 (on which MRID 453255-03 was conducted). Comparing T426 to the one product results in a concern regarding a pH difference; comparing T426 to the other product results in a concern regarding concentration differences. However, comparing T426 to both products together helps to allay these concerns (since the problems of the one comparison are different than those of the other).

[9] T345 is generally more concentrated than T344, on which the cited skin irritation study (MRID 453255-03) was conducted. Based on the non-irritating result of the cited study, however, the T345 skin irritation hazard is not expected to be much worse than that of T344. T344 is in skin irritation Category IV. It is suitable, then to assign Category III to T345. Product label statements consistent with skin irritation Category III will caution the user as to the possibility of a mild or moderate hazard.

DATA EVALUATION RECORD

POLY(IMINOIMIDOCARBONYLIMINOIMIDOCARBONYL-IMINOHEXAMETHYLENE) HYDROCHLORIDE (T344)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT [870.2400 (§81-4)]
MRID 45325502

Prepared for
Antimicrobial Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K274

Primary Reviewer:
Gary A. Sega, Ph.D. Signature: Gary Sega
Date: MAY 14 2001

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.),Ph.D., D.A.B.T. Signature: H T Borges
Date: MAY 14 2001

Robert H. Ross, M.S., Group Leader Signature: Robert H. Ross
Date: MAY 14 2001

Quality Assurance:
Lee Ann Wilson, M.A. Signature: L. A. Wilson
Date: MAY 14 2001

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC, for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Reviewer: Wallace Powell, Ph.D. _____ Date: _____

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D._____ Date: _____
Antimicrobial Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit [OPPTS 870.2400 (§81-4)]

DP BARCODE: D273124 SUBMISSION CODE: S593295
P.C. CODE: 111801 CASE NO.: 070079

TEST MATERIAL: T344

SYNONYMS: Chrysal Clear Professional 2 Powder (P 1162)

CITATION: Richeux, Francois, Study Director (1999) Assessment of acute irritant/corrosive effects of T344 on the eyes. Phycher Bio Developpement, 18, chemin de Lou Tribail, Z1 de Toctoucau, Cestas, France 33610. Laboratory report identification IO-OCDE-PH-99/299, August 16, 1999. MRID 45325502. Unpublished.

SPONSOR: Pokon & Chrysal B.V., Gooimeer 7, 1411 DD NAARDEN, The Netherlands

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 45325502) 0.1 g of T344 (Batch P1162) was instilled into one eye of each of three male New Zealand White rabbits. The contralateral eye of each rabbit served as control. The eyes of all rabbits were scored for ocular irritation 1, 24, 48, and 72 hours after instillation. Examinations were extended up to 6 days in animals still showing signs. No corneal opacity or iritis were found on any rabbit but the test material did induce slight to moderate conjunctival irritation. The maximum mean ocular irritation score was 11.3 at 1 hour after instillation.

T344 produced conjunctival irritation that lasted up to 5 days. It is in TOXICITY CATEGORY IV for acute eye irritation.

This study is classified as **Acceptable/Guideline** and satisfies the guideline requirements for an primary eye irritation study [870.2400 (§81-4)] in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: T344

Description: white powder
Batch #: P1162
Composition: active ingredients; Bronopol [2-bromo-2-nitropropane-1,3-diol] (0.263%) and poly(iminoimidocarbonyl-iminoimidocarbonyliminohexamethylene) hydrochloride (1.250%). Other ingredients: [redacted]
CAS Nos.: not reported for active ingredients

2. Vehicle: None

3. Test animals

Species: rabbit
Strain: New Zealand White
Age and weight at dosing: age not stated; males: 2.02-2.43 kg
Source: Elevage Feuilletas (Campet Lamolere 40000 Mont de Marsan - France)
Acclimation period: 6 days
Diet: not reported
Water: not reported
Housing: kept in individual boxes
Environmental conditions:
Temperature: 19 - 23 °C
Relative Humidity: 54 - 74%
Air changes: not reported
Photoperiod: not reported

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 19, 1999; end: July 25, 1999

2. Animal assignment and treatment:

The test material (0.1 g) was instilled into one eye of each male rabbit. The contralateral eye was left untreated and served as control. Ocular examinations were performed on both eyes of each rabbit at 1, 24, 48, and 72 hours after instillation. When signs persisted, examination times were extended up to 6 days.

II. RESULTS AND DISCUSSION

A. Conjunctival irritation was noted on all 3 rabbits at 1 hour after instillation with a gradual reduction in irritation thereafter. Irritation on all animals cleared between day 3 and day 6. Chemosis was noted on the conjunctiva of all treated eyes with clearing by day 4. The average ocular irritation index was determined at each time point using the classification established in the Journal Officiel de la Republique Francaise dated July 10th, 1992. The average index values were 11.3, 6.7, 4.0, 2.0, 1.0, 2.0 and 0 for 1 hour, 1, 2, 3, 4, 5 and 6 days, respectively. No effect on the cornea or iris was noted on any animal.

The test material induced slight to moderate conjunctival irritation that lasted up to 5 days. T344 is in TOXICITY CATEGORY IV.

B. DEFICIENCIES

The age of the animals, diet, air changes and photoperiod were not reported, but it is unlikely that these parameters would have affected the study results.

DATA EVALUATION RECORD

POLY(IMINOIMIDOCARBONYLIMINOIMIDOCARBONYL-IMINOHEXAMETHYLENE) HYDROCHLORIDE (T344)

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT [870.2500 (§81-5)] MRID 45325503

Prepared for
Antimicrobial Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K274

Primary Reviewer: Gary A. Sega, Ph.D.	Signature: Date:	Gary Sega MAY 14 2001
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.),Ph.D., D.A.B.T.	Signature: Date:	H.T Borges MAY 14 2001
Robert H. Ross, M.S., Group Leader	Signature: Date:	Robert H. Ross MAY 14 2001
Quality Assurance: Lee Ann Wilson, M.A.	Signature: Date:	L. A. Wilson MAY 14 2001

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC, for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

11

EPA Reviewer: Wallace Powell, Ph.D. _____ Date: _____

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D._____ Date: _____
Antimicrobial Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit [OPPTS 870.2500 (§81-5)]

DP BARCODE: D273124
P.C. CODE: 111801

SUBMISSION CODE: S593295
CASE NO.: 070079

TEST MATERIAL: T344

SYNONYMS: Chrysal Clear Professional 2 Powder (P 1162)

CITATION: Richeux, Francois, Study Director (1999) Assessment of acute irritant/corrosive effect of T344 on the skin. Phycher Bio Developpement, 18, chemin de Lou Tribail, Z1 de Toctoucau, Cestas, France 33610. Laboratory report identification IC-OCDE-PH-99/299, August 16, 1999. MRID 45325503. Unpublished.

SPONSOR: Pokon & Chrysal B.V., Gooimeer 7, 1411 DD NAARDEN, The Netherlands

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 45325503) three male New Zealand albino rabbits were dermally exposed on the right flank to 0.5 g T344 (Batch #: P1162) for 4 hours. The animals were observed for 72 hours. No animal showed erythema, eschar or edema formation at any time during the study.

T344 did not cause any dermal reaction up to 72 hours post-treatment and is placed in Toxicity Category IV.

This study is classified as **Acceptable/Guideline** and satisfies the guideline requirements for a primary dermal irritation study [870.2500 (§81-5)] in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: T344

Description: white powder
Batch #: P1162
Composition: active ingredients; Bronopol [2-bromo-2-nitropropane-1,3-diol] (0.263%) and poly(iminoimidocarbonyl-

12

iminoimidocarbonyliminohexamethylene) hydrochloride (1.250%). Other ingredients: [redacted]

CAS Nos.: not reported for active ingredients

2. Vehicle: None

3. Test animals

Species: rabbit
Strain: New Zealand albino
Age and weight at dosing: age not stated; males: 2.10 - 2.36 kg
Source: Elevage Feuilletas (Campet Lamolere F- 40000 Mont de Marsan - France)
Acclimation period: 7 days
Diet: not reported
Water: not reported
Housing: kept in individual boxes
Environmental conditions:
Temperature: 19-23 °C
Relative Humidity: 58 - 74%
Air changes: not reported
Photoperiod: not reported

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 20, 1999; end: July 23, 1999

2. Animal assignment and treatment:

The neat test material (0.5 g) was applied as a patch during a 4-hour period on the undamaged skin on the right flank of three male rabbits. The left flank of each animal was treated with 0.5 mL of distilled water and served as a control. Skin reactions were noted 1, 24, 48 and 72 hours after removal of the patch.

II. RESULTS AND DISCUSSION

A. No animal showed erythema, eschar or edema formation at any time during the study.

Since the test material did not induce any dermal reaction up to 72 hours post-treatment, T344 is considered a non-irritant to skin and is placed in Toxicity Category IV.

B. DEFICIENCIES

The exact method of application of the test material was not stated. The age of the animals, diet, air changes and photoperiod were not reported. It is unlikely that these parameters would have affected the study results.

DATA EVALUATION RECORD

POLY(IMINOIMIDOCARBONYLIMINOIMIDOCARBONYL-IMINOHEXAMETHYLENE) HYDROCHLORIDE (T344)

STUDY TYPE: DERMAL SENSITIZATION - GUINEA PIG [870.2600 (§81-6)]
MRID 45325504

Prepared for
Antimicrobial Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K274

Primary Reviewer:
Gary A. Sega, Ph.D.

Signature: Gary Sega
Date: MAY 14 2001

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.),Ph.D., D.A.B.T.

Signature: H.T Borges
Date: MAY 14 2001

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: MAY 14 2001

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: MAY 14 2001

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC, for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Reviewer: Wallace Powell, Ph.D. _____ Date: _____

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D._____ Date: _____
Antimicrobial Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Skin Sensitization - Guinea Pig [OPPTS 870.2600 (§81-6)]

DP BARCODE: D273124
P.C. CODE: 111801

SUBMISSION CODE: S593295
CASE NO.: 070079

TEST MATERIAL: T344

SYNONYMS: Chrysal Clear Professional 2 Powder (P 1162)

CITATION: Richeux, Francois, Study Director (1999) Assessment of sensitizing properties of T344 on albino guinea pig. Phycher Bio Developpement, 18, chemin de Lou Tribail, Z1 de Toctoucau, Cestas, France 33610. Laboratory report identification SMK-PH-99/299, September 29, 1999. MRID 45325504. Unpublished.

SPONSOR: Pokon & Chrysal B.V., Gooimeer 7, 1411 DD NAARDEN, The Netherlands

EXECUTIVE SUMMARY: In a skin sensitization study (MRID 45325504) 12 Dunkin-Hartley albino guinea pigs were induced with T344 (Batch #: P1162) according to the method of Magnusson and Kligman. After a rest period of 18 days the animals were subjected to a Challenge Phase, involving dermal exposure to the test material followed by 2 days of observation. No erythema or edema were noted on the skin of treated animals compared to controls during this time. The report also included a neomycin sulfate positive control study which was carried out within six months of the current study. The results were appropriate.

In this study, T344 was not a dermal sensitizer .

This study is classified as **Acceptable/Guideline** and satisfies the guideline requirements for a skin sensitization study [870.2600 (§81-6)] in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

16

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: T344

Description: white powder
Batch No.: P1162
Composition: active ingredients; Bronopol [2-bromo-2-nitropropane-1,3-diol] (0.263%) and poly(iminoimidocarbonyl-iminoimidocarbonyliminohexamethylene) hydrochloride (1.250%). Other ingredients: [redacted]
CAS Nos.: not reported for active ingredients

2. Vehicle: None or distilled water

3. Test animals

Species: guinea pig
Strain: Dunkin-Hartley albino
Age and weight at dosing: age not stated; females: 298-332 g
Source: Elevage St. Antoine (F-22740 Pleudaniel)
Acclimation period: 5 days
Diet: guinea pig breeding diet, certified 114
Water: not reported
Housing: not reported
Environmental conditions:
Temperature: 19-26 °C
Relative Humidity: 44-77%
Air changes: not reported
Photoperiod: not reported

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 21, 1999; end: August 19, 1999

2. Animal assignment and treatment

The animals were induced and challenged according to the scheme shown in Table 1.

TABLE 1 Scheme for induction and challenge with test material
***Induction Phase**
1st induction: intradermal injection into scapular region of a 1.56% concentration of the test material**
2nd induction: 1 week after 1st induction; topical application of undiluted test material*** on the same zone, 24 hours after brushing with 0.5 mL of a 10% sodium lauryl sulfate solution
Rest Phase (18 days)
***Challenge Phase**
Topical application under occlusive dressing of a 25 and 12.5% concentration of the test material****
24 hour reading
48 hour reading

From p. 8, MRID 45325504
*No treatment volumes were given.
**Preliminary studies showed that the highest intradermal dose causing no necrosis was a 1.56% solution of the test material in saline.
***Preliminary studies showed that the pre-maximum, non-irritant concentration of the test material causing no erythema when applied topically was pure (100%) test material.
****Preliminary studies showed that the maximum concentration of the test material causing no erythema when applied topically was a 25 % solution in distilled water.

There were 12 treated animals and 7 negative controls. The controls were treated similarly to the test animals with the exception that, in the Induction Phase, the test material was omitted from the intradermal injection and topical application. Erythema and edema were scored at each reading and the percentage of animals showing a positive response reported.

II. RESULTS AND DISCUSSION

A. INDUCTION REACTIONS AND DURATION

No dermal irritation was noted on any test or control animals during the Induction Phase.

B. CHALLENGE REACTIONS AND DURATION

No macroscopic cutaneous reaction was seen at 24 or 48 hours post-challenge on any control or treated animal receiving a 25 or 12.5% concentration of the test material in the Challenge Phase.

C. POSITIVE CONTROL

The report included a neomycin sulfate positive control study (archived data) that was carried out within six months of the current study. The results were appropriate.

D. ADDITIONAL TESTING

It is the reviewer's opinion that the study was conducted in a manner suitable to detect the sensitization potential of the test material. No additional testing is needed.

E. DEFICIENCIES

The treatment volumes were not given. There was no description given of the grading system. The age of the animals, housing, amount of drinking water, air changes and photoperiod were not reported. It is unlikely that these parameters would have affected the study results.

DATA EVALUATION RECORD

POLY(IMINOIMIDOCARBONYLIMINOIMIDOCARBONYL-IMINOHEXAMETHYLENE) HYDROCHLORIDE (T344)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT [870.2400 (§81-4)] MRID 45325502

Prepared for
Antimicrobial Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K274

Primary Reviewer: Gary A. Sega, Ph.D.	Signature: Date:	Gary Sega MAY 14 2001
Secondary Reviewers: H. Tim Borges, M.T.(A.S.C.P.),Ph.D., D.A.B.T.	Signature: Date:	HT Borges MAY 14 2001
Robert H. Ross, M.S., Group Leader	Signature: Date:	Robert H. Ross MAY 14 2001
Quality Assurance: Lee Ann Wilson, M.A.	Signature: Date:	L. A. Wilson MAY 14 2001

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC, for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

20

EPA Reviewer: Wallace Powell, Ph.D. _____ Date: _____

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D._____ Date: _____
Antimicrobial Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit [OPPTS 870.2400 (§81-4)]

DP BARCODE: D273124
P.C. CODE: 111801

SUBMISSION CODE: S593295
CASE NO.: 070079

TEST MATERIAL: T344

SYNONYMS: Chrysal Clear Professional 2 Powder (P 1162)

CITATION: Richeux, Francois, Study Director (1999) Assessment of acute irritant/corrosive effects of T344 on the eyes. Phycher Bio Developpement, 18, chemin de Lou Tribail, Z1 de Toctoucau, Cestas, France 33610. Laboratory report identification IO-OCDE-PH-99/299, August 16, 1999. MRID 45325502. Unpublished.

SPONSOR: Pokon & Chrysal B.V., Gooimeer 7, 1411 DD NAARDEN, The Netherlands

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 45325502) 0.1 g of T344 (Batch P1162) was instilled into one eye of each of three male New Zealand White rabbits. The contralateral eye of each rabbit served as control. The eyes of all rabbits were scored for ocular irritation 1, 24, 48, and 72 hours after instillation. Examinations were extended up to 6 days in animals still showing signs. No corneal opacity or iritis were found on any rabbit but the test material did induce slight to moderate conjunctival irritation. The maximum mean ocular irritation score was 11.3 at 1 hour after instillation.

T344 produced conjunctival irritation that lasted up to 5 days. It is in TOXICITY CATEGORY IV for acute eye irritation.

This study is classified as **Acceptable/Guideline** and satisfies the guideline requirements for an primary eye irritation study [870.2400 (§81-4)] in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

21

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: T344

Description: white powder
Batch #: P1162
Composition: active ingredients; Bronopol [2-bromo-2-nitropropane-1,3-diol] (0.263%) and poly(iminoimidocarbonyl-iminoimidocarbonyliminohexamethylene) hydrochloride (1.250%). Other ingredients: [redacted]
CAS Nos.: not reported for active ingredients

2. Vehicle: None

3. Test animals

Species: rabbit
Strain: New Zealand White
Age and weight at dosing: age not stated; males: 2.02-2.43 kg
Source: Elevage Feuilletas (Campet Lamolere 40000 Mont de Marsan - France)
Acclimation period: 6 days
Diet: not reported
Water: not reported
Housing: kept in individual boxes
Environmental conditions:
Temperature: 19 - 23 °C
Relative Humidity: 54 - 74%
Air changes: not reported
Photoperiod: not reported

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 19, 1999; end: July 25, 1999

2. Animal assignment and treatment:

The test material (0.1 g) was instilled into one eye of each male rabbit. The contralateral eye was left untreated and served as control. Ocular examinations were performed on both eyes of each rabbit at 1, 24, 48, and 72 hours after instillation. When signs persisted, examination times were extended up to 6 days.

II. RESULTS AND DISCUSSION

A. Conjunctival irritation was noted on all 3 rabbits at 1 hour after instillation with a gradual reduction in irritation thereafter. Irritation on all animals cleared between day 3 and day 6. Chemosis was noted on the conjunctiva of all treated eyes with clearing by day 4. The average ocular irritation index was determined at each time point using the classification established in the Journal Officiel de la Republique Francaise dated July 10th, 1992. The average index values were 11.3, 6.7, 4.0, 2.0, 1.0, 2.0 and 0 for 1 hour, 1, 2, 3, 4, 5 and 6 days, respectively. No effect on the cornea or iris was noted on any animal.

The test material induced slight to moderate conjunctival irritation that lasted up to 5 days. T344 is in TOXICITY CATEGORY IV.

B. DEFICIENCIES

The age of the animals, diet, air changes and photoperiod were not reported, but it is unlikely that these parameters would have affected the study results.

DATA EVALUATION RECORD

POLY(IMINOIMIDOCARBONYLIMINOIMIDOCARBONYL-IMINOHEXAMETHYLENE) HYDROCHLORIDE (T344)

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT [870.2500 (§81-5)]
MRID 45325503

Prepared for
Antimicrobial Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K274

Primary Reviewer:
Gary A. Sega, Ph.D.

Signature: Gary Sega
Date: MAY 14 2001

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.),Ph.D., D.A.B.T.

Signature: H.T Borges
Date: MAY 14 2001

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: MAY 14 2001

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L. A. Wilson
Date: MAY 14 2001

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC, for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Reviewer: Wallace Powell, Ph.D. _____ Date: _____

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D._____ Date: _____
Antimicrobial Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit [OPPTS 870.2500 (§81-5)]

DP BARCODE: D273124
P.C. CODE: 111801

SUBMISSION CODE: S593295
CASE NO.: 070079

TEST MATERIAL: T344

SYNONYMS: Chrysal Clear Professional 2 Powder (P 1162)

CITATION: Richeux, Francois, Study Director (1999) Assessment of acute irritant/corrosive effect of T344 on the skin. Phycher Bio Developpement, 18, chemin de Lou Tribail, Z1 de Toctoucau, Cestas, France 33610. Laboratory report identification IC-OCDE-PH-99/299, August 16, 1999. MRID 45325503. Unpublished.

SPONSOR: Pokon & Chrysal B.V., Gooimeer 7, 1411 DD NAARDEN, The Netherlands

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 45325503) three male New Zealand albino rabbits were dermally exposed on the right flank to 0.5 g T344 (Batch #: P1162) for 4 hours. The animals were observed for 72 hours. No animal showed erythema, eschar or edema formation at any time during the study.

T344 did not cause any dermal reaction up to 72 hours post-treatment and is placed in Toxicity Category IV.

This study is classified as **Acceptable/Guideline** and satisfies the guideline requirements for a primary dermal irritation study [870.2500 (§81-5)] in the rabbit.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: T344

   Description: white powder
   Batch #: P1162
   Composition: active ingredients; Bronopol [2-bromo-2-nitropropane-1,3-diol] (0.263%) and poly(iminoimidocarbonyl-

iminoimidocarbonyliminohexamethylene) hydrochloride (1.250%). Other ingredients: [redacted]

CAS Nos.: not reported for active ingredients

2. Vehicle: None

3. Test animals

Species: rabbit
Strain: New Zealand albino
Age and weight at dosing: age not stated; males: 2.10 - 2.36 kg
Source: Elevage Feuilletas (Campet Lamolere F- 40000 Mont de Marsan - France)
Acclimation period: 7 days
Diet: not reported
Water: not reported
Housing: kept in individual boxes
Environmental conditions:
Temperature: 19-23 °C
Relative Humidity: 58 - 74%
Air changes: not reported
Photoperiod: not reported

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 20, 1999; end: July 23, 1999

2. Animal assignment and treatment:

The neat test material (0.5 g) was applied as a patch during a 4-hour period on the undamaged skin on the right flank of three male rabbits. The left flank of each animal was treated with 0.5 mL of distilled water and served as a control. Skin reactions were noted 1, 24, 48 and 72 hours after removal of the patch.

II. RESULTS AND DISCUSSION

A. No animal showed erythema, eschar or edema formation at any time during the study.

Since the test material did not induce any dermal reaction up to 72 hours post-treatment, T344 is considered a non-irritant to skin and is placed in Toxicity Category IV.

B. DEFICIENCIES

The exact method of application of the test material was not stated. The age of the animals, diet, air changes and photoperiod were not reported. It is unlikely that these parameters would have affected the study results.

DATA EVALUATION RECORD

POLY(IMINOIMIDOCARBONYLIMINOIMIDOCARBONYL-IMINOHEXAMETHYLENE) HYDROCHLORIDE (T344)

STUDY TYPE: DERMAL SENSITIZATION - GUINEA PIG [870.2600 (§81-6)] MRID 45325504

Prepared for
Antimicrobial Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by
Chemical Hazard Evaluation Group
Toxicology and Risk Analysis Section
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Action No. K274

Primary Reviewer:
Gary A. Sega, Ph.D. Signature: Gary Sega
Date: MAY 14 2001

Secondary Reviewers:
H. Tim Borges, M.T.(A.S.C.P.),Ph.D., D.A.B.T. Signature: H.T Borges
Date: MAY 14 2001

Robert H. Ross, M.S., Group Leader Signature: Robert H Ross
Date: MAY 14 2001

Quality Assurance:
Lee Ann Wilson, M.A. Signature: L. A. Wilson
Date: MAY 14 2001

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC, for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Reviewer: Wallace Powell, Ph.D. _____ Date: _____

EPA Work Assignment Manager: Bonaventure Akinlosotu, Ph.D._____ Date: _____
Antimicrobial Division (9510C)

DATA EVALUATION RECORD

STUDY TYPE: Skin Sensitization - Guinea Pig [OPPTS 870.2600 (§81-6)]

DP BARCODE: D273124
P.C. CODE: 111801

SUBMISSION CODE: S593295
CASE NO.: 070079

TEST MATERIAL: T344

SYNONYMS: Chrysal Clear Professional 2 Powder (P 1162)

CITATION: Richeux, Francois, Study Director (1999) Assessment of sensitizing properties of T344 on albino guinea pig. Phycher Bio Developpement, 18, chemin de Lou Tribail, Z1 de Toctoucau, Cestas, France 33610. Laboratory report identification SMK-PH-99/299, September 29, 1999. MRID 45325504. Unpublished.

SPONSOR: Pokon & Chrysal B.V., Gooimeer 7, 1411 DD NAARDEN, The Netherlands

EXECUTIVE SUMMARY: In a skin sensitization study (MRID 45325504) 12 Dunkin-Hartley albino guinea pigs were induced with T344 (Batch #: P1162) according to the method of Magnusson and Kligman. After a rest period of 18 days the animals were subjected to a Challenge Phase, involving dermal exposure to the test material followed by 2 days of observation. No erythema or edema were noted on the skin of treated animals compared to controls during this time. The report also included a neomycin sulfate positive control study which was carried out within six months of the current study. The results were appropriate.

In this study, T344 was not a dermal sensitizer .

This study is classified as **Acceptable/Guideline** and satisfies the guideline requirements for a skin sensitization study [870.2600 (§81-6)] in the guinea pig.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: T344

Description: white powder
Batch No.: P1162
Composition: active ingredients; Bronopol [2-bromo-2-nitropropane-1,3-diol] (0.263%) and poly(iminoimidocarbonyl-iminoimidocarbonyliminohexamethylene) hydrochloride (1.250%). Other ingredients: [redacted]
CAS Nos.: not reported for active ingredients

2. Vehicle: None or distilled water

3. Test animals

Species: guinea pig
Strain: Dunkin-Hartley albino
Age and weight at dosing: age not stated; females: 298-332 g
Source: Elevage St. Antoine (F-22740 Pleudaniel)
Acclimation period: 5 days
Diet: guinea pig breeding diet, certified 114
Water: not reported
Housing: not reported
Environmental conditions:
Temperature: 19-26 °C
Relative Humidity: 44-77%
Air changes: not reported
Photoperiod: not reported

B. STUDY DESIGN AND METHODS

1. In life dates

Start: July 21, 1999; end: August 19, 1999

2. Animal assignment and treatment

The animals were induced and challenged according to the scheme shown in Table 1.

TABLE 1 Scheme for induction and challenge with test material
***Induction Phase**
1st induction: intradermal injection into scapular region of a 1.56% concentration of the test material**
2nd induction: 1 week after 1st induction; topical application of undiluted test material*** on the same zone, 24 hours after brushing with 0.5 mL of a 10% sodium lauryl sulfate solution
Rest Phase (18 days)
***Challenge Phase**
Topical application under occlusive dressing of a 25 and 12.5% concentration of the test material****
24 hour reading
48 hour reading

From p. 8, MRID 45325504.
*No treatment volumes were given.
**Preliminary studies showed that the highest intradermal dose causing no necrosis was a 1.56% solution of the test material in saline.
***Preliminary studies showed that the pre-maximum, non-irritant concentration of the test material causing no erythema when applied topically was pure (100%) test material.
****Preliminary studies showed that the maximum concentration of the test material causing no erythema when applied topically was a 25 % solution in distilled water.

There were 12 treated animals and 7 negative controls. The controls were treated similarly to the test animals with the exception that, in the Induction Phase, the test material was omitted from the intradermal injection and topical application. Erythema and edema were scored at each reading and the percentage of animals showing a positive response reported.

II. RESULTS AND DISCUSSION

A. INDUCTION REACTIONS AND DURATION

No dermal irritation was noted on any test or control animals during the Induction Phase.

B. CHALLENGE REACTIONS AND DURATION

No macroscopic cutaneous reaction was seen at 24 or 48 hours post-challenge on any control or treated animal receiving a 25 or 12.5% concentration of the test material in the Challenge Phase.

C. POSITIVE CONTROL

The report included a neomycin sulfate positive control study (archived data) that was carried out within six months of the current study. The results were appropriate.

D. ADDITIONAL TESTING

It is the reviewer's opinion that the study was conducted in a manner suitable to detect the sensitization potential of the test material. No additional testing is needed.

E. DEFICIENCIES

The treatment volumes were not given. There was no description given of the grading system. The age of the animals, housing, amount of drinking water, air changes and photoperiod were not reported. It is unlikely that these parameters would have affected the study results.