PC Code: 128008
EPA FILE SYMBOL: 7969-198

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

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

July 12, 2004

MEMORANDUM

Subject:	Name of Pesticide Product:	Boscalid Technical	
	EPA Reg. No.:	7969-198	
	DP Barcode:	D303310	
	Decision No.:	338664	
	PC Code:	128008	3-Pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)-

From: Breann Hanson, Toxicologist BH
Technical Review Branch
Registration Division (7505C) JCK

To: Robert Westin
Fungicide Branch, RM 22
Registration Division (7505C)

Applicant: BASF Corporation
Agricultural Products
26 Davis Drive, P.O. Box 13528
Research Triangle Park, NC 27709-3528

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt.
128008	3-Pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)- CAS No. 188425-85-6	99.00%
Inert Ingredient(s):		1.0%
	Total:	100.00%

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ACTION REQUESTED:

The Product Manager requests:

> "The attached studies were submitted in response to the requirements specified when this product was registered. Are these studies acceptable"

BACKGROUND: BASF Corporation has submitted a new dermal sensitization (MRID 462701-02) study in support of registration for Boscalid Technical, EPA Reg No. 7969-198. The study was conducted at Experimental Toxicology and Ecology Toxicology of BASF Aktiengesellschaft, Ludwigshafen, Germany. The acute oral toxicity, acute dermal toxicity, acute inhalation toxicity, primary eye irritation and primary dermal irritation (MRID 454048-14 through -18) were classified as acceptable in the review for the original submission of Boscalid Technical, EPA Reg No. 7969-198. (McAndrew; D278286; EPA File Symbol 7969-ROI; 31/JAN/2002). The dermal sensitization study was resubmitted due to it's unacceptability in the previous submission.

RECOMMENDATIONS: The dermal sensitization study has been reviewed and is classified as acceptable. The acute oral toxicity, acute dermal toxicity, acute inhalation toxicity, primary eye irritation and primary dermal irritation studies referenced above may be bridged to this product. The acute toxicity profile for Boscalid Technical, EPA Reg No. 7969-198 is:

Acute oral toxicity	IV	Acceptable	MRID 45404814
Acute dermal toxicity	III	Acceptable	MRID 45404815
Acute inhalation toxicity	IV	Acceptable	MRID 45404816
Primary eye irritation	IV	Acceptable	MRID 45404817
Primary skin irritation	IV	Acceptable	MRID 45404818
Dermal sensitization	Negative	Acceptable	MRID 46270102

LABELING: Based on the toxicity profile above, the following are the precautionary and first aid statements for this product as obtained from the Label Review System:

PRODUCT ID #: **007969-00198**

PRODUCT NAME: BOSCALID TECHNICAL

PRECAUTIONARY STATEMENTS

Hazards to Humans and Domestic Animals:

SIGNAL WORD: CAUTION

Harmful if absorbed through skin. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse.

First Aid:

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Breann Hanson **Date:** July 12, 2004
Risk Manager (EPA): Robert Westin, RM 22

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406

TEST MATERIAL: BAS 510 F (3-Pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)-: 94.3%; Batch #: N46; solid/white)

CITATION: Gamer, A.O.. (2003) BAS 510 F -Maximization Test in Guinea Pigs. Laboratory Project Identification: 30H0179/972226. Unpublished study prepared by Experimental Toxicology and Ecology Toxicology of BASF Aktiengesellschaft. December 22, 2003 MRID 46270102.

SPONSOR: BASF Corporation, Agricultural Products, 26 Davis Drive, P.O. Box 13528, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 46270102) with BAS 510 F (3-Pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)-: 94.3%; Batch #: N46; solid/white), 30 DH (SPF) female guinea pigs (Weight: 324-387 g females Source: Harlan Winkelmann GmbH, Borchen, FRG) were tested using the Magnusson-Kligman Design method.

During the preliminary testing phase, appropriate concentrations of the test substance to be used were determined for the intradermal induction (test substance 5% in 1% CMC-solution in distilled water), topical induction (test substance 25% in 1% CMC-solution in distilled water), and topical challenge (test substance 5% in 1% CMC-solution in distilled water).

The first induction phase involved 3, 0.1 mL intradermal paired injections into 20 guinea pigs of the test substance (test substance 5% in 1% CMC-solution in distilled water), test substance and Freund's Adjuvant (5% test substance in Freund's Adjuvant), and Adjuvant alone (Adjuvant/0.9% NaCl solution). Paired injections were also administered to 10 naive control guinea pigs of CMC-solution, CMC-solution in distilled water with Freund's Adjuvant, and Adjuvant alone. Immediately after patch removal the animals were scored for erythema.

One week later, a second induction phase was conducted consisting of a 0.5 mL topical application of the test substance 25% in 1% CMC-solution in distilled water applied directly to the dose site of the test animals, which was then covered with a gauze patch for 48 hours. Immediately after patch removal the animals were scored for erythema. The control group was not treated .

Fourteen days after the topical application of the induction phase the challenge phase was conducted by applying 0.5 mL of a topical application of the test substance 5% in 1% CMC-solution in distilled water to a naive site on both the test and control guinea pigs, which was then covered with a gauze patch for 24 hours. 24 and 48 hours after patch removal the animals were

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scored for erythema.

Due to inconclusive results after the challenge phase a re-challenge was conducted 7 days after the previous challenge dose. The procedure was repeated as stated above using the same 10 test naive control guinea pigs from the previous challenge.

The procedures were validated using alpha-Hexylcinnamaldehyde (HCA) as the positive control substance.

Based on this study, BAS 510 F is not a dermal sensitizer.

During the induction phase, observations at all dose sites for test animals treated with the test substance during both the injection and topical application phases ranged from moderate to intense erythema (score 2-3) with swelling and/or incrustation (score E-K). At challenge positive (grade 1) irritation was noted for 3/20 test animals at 24 hours. This irritation did not persist to 48 hours. No positive response was noted in the control animals. Since a sensitization response of only 20% was noted in the test animals, with no irritation persisting at 48 hours, these results were deemed inconclusive and a re-challenge was conducted.

During the re-challenge phase, 2/20 test animals exhibited positive (grade 1) irritation at 24 hours with this irritation persisting to 48 hours in one animal. None of the control animals exhibited a positive response at 24 or 48 hours.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal sensitization study (OPPTS 870.2600; OECD 406) in the Guinea pig .

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

I. PROCEDURE

A. Preliminary Testing - During the preliminary testing phase, appropriate concentrations of the test substance to be used were determined for the intradermal induction (test substance 5% in 1% CMC-solution in distilled water), topical induction (test substance 25% in 1% CMC-solution in distilled water), and topical challenge (test substance 5% in 1% CMC-solution in distilled water).

B. Induction - The first induction phase involved 3, 0.1 mL intradermal paired injections into 20 guinea pigs of the test substance (test substance 5% in 1% CMC-solution in distilled water), test substance and Freund's Adjuvant (5% test substance in Freund's Adjuvant), and Adjuvant alone (Adjuvant/0.9% NaCl solution). Paired injections were also administered to 10 naive control guinea pigs of CMC-solution, CMC-solution in distilled water with Freund's Adjuvant, and Adjuvant alone. Immediately after patch removal the animals were scored for erythema.

One week later, a second induction phase was conducted consisting of a 0.5 mL topical application of the test substance 25% in 1% CMC-solution in distilled water applied directly to the dose site of the test animals, which was then covered with a gauze patch for 48 hours. Immediately after patch removal the animals were scored for erythema. The control group was not treated .

C. Challenge - Fourteen days after the topical application of the induction phase the challenge phase was conducted by applying 0.5 mL of a topical application of the test substance 5% in 1% CMC-solution in distilled water to a naive site on both the test and control guinea pigs, which was then covered with a gauze patch for 24 hours. 24 and 48 hours after patch removal the animals were scored for erythema.

Due to inconclusive results after the challenge phase a re-challenge was conducted 7 days after the previous challenge dose. The procedure was repeated as stated above using the same 10 test naive control guinea pigs from the previous challenge.

D. Naive Controls - During the first induction phase, paired injections were administered to 10 naive control guinea pigs of CMC-solution, CMC-solution in distilled water with Freund's Adjuvant, and Adjuvant alone.

At the second induction phase, the control group was not treated.

At challenge, the naive controls received 0.5 mL of a topical application of the test substance 5% in 1% CMC-solution in distilled water to a naive site. 24 and 48 hours after patch removal the animals were scored for erythema.

II. RESULTS and DISCUSSION:

A. Reactions and duration - During the induction phase, observations at all dose sites for test animals treated with the test substance during both the injection and topical application phases ranged from moderate to intense erythema (score 2-3) with swelling and/or incrustation (score E-K). At challenge positive (grade 1) irritation was noted for 3/20 test animals at 24 hours. This irritation did not persist to 48 hours. No positive response was noted in the control animals. Since a sensitization response of only 20% was noted in the test animals, with no irritation persisting at 48 hours, these results were deemed inconclusive and a re-challenge was conducted.

During the re-challenge phase, 2/20 test animals exhibited positive (grade 1) irritation at 24 hours with this irritation persisting to 48 hours in one animal. None of the control animals exhibited a positive response at 24 or 48 hours.

B. Positive control - Results were appropriate with HCA study to validate test procedures. The most recent validation of this procedure was performed Oct.2 - Nov. 28, 2003. The test dates for the study on BAS 510 F were Sep. 23 - Oct. 24, 2003.

C. Reviewer's Conclusions: Agree with study author.

1. **DP BARCODE:** D303310
2. **PC CODE:** 128008
3. **CURRENT DATE:** JUL/12/2004
4. **TEST SUBSTANCE:** BAS 510 F (3-Pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)-: 94.3%; Batch #: N46; solid/white)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Dermal sensitization/guinea pig Experimental Toxicology and Ecology Toxicology of BSF Aktiengesellschaft 30H0179/972226 12-22-2003	46270102	is not a sensitizer	–	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived**