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

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC SUBSTANCES

07/JULY/2003

MEMORANDUM

Subject: EPA Reg. No: 7969-ENL BAS 670 336SC Herbicide
DP Barcode: D290071
Decision No: 211978
PC Code: 123009

From: Masih Hashim, Toxicologist
Technical Review Branch
Registration Division (7505C)

To: James Stone, PM Team 23
Herbicide Branch
Registration Division (7505C)

Applicant: BASF Corporation (Agricultural Products)
26 Davis Drive
Research Triangle Park, NC 27709-3528

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
[3-(4,5-Dihydro-isoxazol)-4-methansulfonyl-2-methyl-phenyl]-(5-hydroxy-1-1methyl-1H-pyrazol-4-yl) methanone	29.7
Inert ingredients	70.3
Total:	100.0

(1)

ACTION REQUIRED: PM requests a review of the acute toxicity data for the File Symbol 7969-ENL, BAS 670 00 H, a herbicide.

BACKGROUND: BASF Corporation has submitted a set of (6) acute toxicity studies for registration of BAS 670 00 H. These studies were conducted in BASF Laboratories in Germany.

RECOMMENDATIONS: Each of the following studies (MRID 45901807 thru 45901812) is in compliance with the Sub Division F guidelines.

The toxicology profile for the File Symbol 7969-ENL is as follows:

acute oral toxicity	III	acceptable	MRID 45901807
acute dermal toxicity	III	acceptable	MRID 45901808
acute inhalation	IV	acceptable	MRID 45901809
primary eye irritation	III	acceptable	MRID 45901810
primary dermal irritation	IV	acceptable	MRID 45901811
dermal sensitization	neg.	acceptable	MRID 45901812

Labeling:

PRODUCT ID #: 007969-00205

PRODUCT NAME: BAS 670 336SC Herbicide

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals:

Harmful if absorbed through skin. Harmful if swallowed. Causes moderate eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Wear long-sleeved shirt and long pants, socks, shoes, and gloves. 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.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.

-Do not give anything by mouth to an unconscious person.

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If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-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.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE ORAL STUDY- RAT [OPPTS 870.1100]

PRODUCT MANAGER: 23 **REVIEWER:** M. HASHIM

TEST MATERIAL: Bas 670 336SC Herbicide, BAS 670 00 H (33.6%), Batch No. 2000-2 Liquid/ pink-turbid

CITATION: Garner, A., and Hofiman, H. (2002). BAS 670 H- Acute Oral Toxicity Study in Wistar Rats. Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany, Study No. 10A0440/001076 dated 5-30-2001. MRID No. 45901807 (Unpublished).

SPONSOR: BASF Corporation (Agricultural Products), Research Triangle Park, NC 27709-3528.

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 45901807), young adult (SPF) Wistar rats 3 m / f (Strain: Crl:WI [GLX/BRL/HAN]IGS BR, weight males 216-232 g, females 197-211 g, Source Charles River. Deutschland, Sandhofer Weg 7. Sulzfeld) were given a single oral dose of BAS 670 00 H (purity 33.6%- Batch No. 2000-2) in double distilled water at a dose of 2000 mg/kg for males and 4000 mg/kg for females. Animals were observed for clinical signs, mortality and body weight changes for 14 days.
(Note: A dose of 4000 mg/kg was given in error to female animals)

There were no deaths on the study. All animals gained weight during the study. No lesions were noted from any animal during necropsy.

Oral LD_{50} Males >2000 mg/kg bw
Females >4000 mg/kg bw
Combined >3000 mg/kg bw

BASF 670 00 H is Tox Category III.

This acute oral toxicity study is classified as Acceptable. This study satisfies the guideline requirement for (OPPTS 870.1100; OECD 401) in the rat.

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

RESULTS:

TABLE 1. Doses, mortality/animals treated		
Dose (mg/kg bw)	**Males**	**Females**
2000	0/3	-
4000	-	0/3

NECROPSY FINDINGS: Unremarkable.

(4)

DATA EVALUATION RECORD

STUDY TYPE: ACUTE DERMAL TOXICITY STUDY - RAT [OPPTS 870.1200]

PRODUCT MANAGER: 23 **REVIEWER:** M. HASHIM

TEST MATERIAL: Bas 670 336SC Herbicide, BAS 670 00 H, Batch No. 2000-2, purity 33.6%, Liquid, pink turbid

CITATION: Gamer, A., and Hoffman, H (2001). BAS 670 00 H- Acute Dermal Toxicity Study in Rats. Department of Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein. Germany, Study No. 11A0440/001077 dated 5-30-01. MRID No. 45901808 (Unpublished).

SPONSOR: BASF Corporation (Agricultural Products), Research Triangle Park, NC 27709-3528.

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 45901808), 5 male and 5 female young adult (SPF) Wistar rats (Strain: Crl:WI [GLX/BRL/HAN]IGS BR, weight males 227-236 g, females 216-228 g, Source Charles River, Deutschland, Sandhofer Weg 7, Sulzfeld) were given a single topical dose of BAS 670 00 H (Batch No. 2000-2, purity 33.6%) at 4000 mg/kg body weight. The test substance was applied on a clipped skin (dorsum) of the animal covered by a semi occlusive dressing for 24 hours. Animals were observed for clinical signs, mortality, and weekly body weights were taken. Necropsy findings were recorded.

One animal died on the study (accidental), there were no apparent signs or pathology from this animal. Mean body weight of the male animals had no adverse effects, while the female weight gains were affected by the treatment. No gross lesions were noted from any animal during necropsy.

Dermal LD_{50} Males >4000 mg/kg bw
Females >4000 mg/kg bw
Combined >4000 mg/kg bw

BASF 670 00 H is Tox Category III.

This acute dermal toxicity study is classified as Acceptable. This study satisfies the guideline requirement for (OPPTS 870.1200) in the rat.

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

RESULTS:

TABLE 1. Doses, mortality/animals treated		
Dose (mg/kg bw)	**Males**	**Females**
4000	0/5	0/5

NECROPSY: Not significant

(5)

DATA EVALUATION RECORD

STUDY TYPE: ACUTE INHALATION STUDY- Rat [OPPTS 870.1300]

PRODUCT MANAGER: 23 **REVIEWER:** M. HASHIM

TEST MATERIAL: Bas 670 336SC Herbicide, BAS 670 00 H, Batch No. 2000-2, Purity 33.6%, Solid yellow brown

CITATION: Gamer, A., Leibold, E, and Hoffmann, H. (2001). BAS 670 00 H- Acute Inhalation Toxicity Study in Wistar Rats, 4-hour exposure. Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany, Study No. 1310440/007016 dated 10-23-01. MRID No. 45901809 (Unpublished).

SPONSOR: BASF Corporation (Agricultural Products), Research Triangle Park, NC 27709-3528.

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 45901809), young adult Wistar rats, 5/sex (Strain: CrlGlxBrlHan:WI. Males: 8-12 wks, weight 233-244 g; females: 14-18 wks, wt. 218-228 g, Source: Charles River Deutschland, Sandhofer Weg 7, 97633 Sulzfeld) were exposed to BASF 670 00 H (33.6%, Batch No. 2000-2) as liquid aerosol at the analytical concentration of 5.8 mg/L for 4 hours. The MMAD was 5.4-5.9 µm. The animals were observed for 14 days for clinical signs and mortality. Weekly body weights were taken. Necropsy findings were recorded.

Inhalation LC_{50} Males >5.8 mg/L
Females > 5.8 mg/L
Combined> 5.8 mg/L

LC_{50} for BASF 670 00 H is 5.8 mg/L. and is considered as Toxicity Category IV.

Signs of toxicity included rapid respiration, squatting posture and smeared fur from one hour to two days, after which animals appeared normal. Body weights were not affected.

This acute inhalation study is classified Acceptable. This study satisfies the guideline requirement for (OPPTS 870.1300; OECD 403) in the rat.

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

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RESULTS:

Analytical Conc. (mg/L) LC_{50}	MMAD µm	GSD	Mortality (# dead/total)		
			Males	Females	Combined
5.8	5.4-5.7	2.0-2.2	0/5	0/5	0/10

Environment/Exposure

Conc./LC50	Inhalation system	Air Flow/supply	Exposure Temp.	R. humidity %
5.8 mg/L	55 L	1.5 m^3/h	22.5^0 C	54.5

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY EYE IRRITATION - Rabbit [OPPTS 870.2400]

PRODUCT MANAGER: 23 **REVIEWER**: M. HASHIM

TEST MATERIAL: Bas 670 336SC Herbicide, BAS 670 00 H, Batch No. 2000-2, purity 33.6%, Liquid, pink cloudy

CITATION: Wiemann, C. and Hellwig, J. (2001). BAS 670 00 H- Acute Eye Irritation Study in Rabbits. Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany, Study No. 11A0440/002140 dated 6-11-01. MRID No. 45901810 (Unpublished).

SPONSOR: BASF Corporation (Agricultural Products), Research Triangle Park, NC 27709-3528.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 45901810), 0.1 ml of BAS 00 H (Batch No. 2000-2, 33.6%) was instilled into the conjunctival sac of the right eyelid of 3 young adult NZW rabbits (Source: Harlan Winklemann GmbH, Borchen, FRG). The left eye served as a control. The eyes of these rabbits were washed 24 hours after the treatment. The animals were observed for ocular irritation for 72 hours

There was conjunctivitis but no corneal opacity or iritis in any of the animals. Rabbits showed an av. score of 0.4 for conjunctival redness, which subsided within 48 hours. The product is a moderate irritant.

BAS 00 H meets criteria of EPA Toxicity Category III.

This study is classified as Acceptable. It satisfies the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

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

OBSERVATIONS:

Table 1. Total Lesions/ Total No. of Animals

Lesion	**1 hr**	**24 hrs**	**48 hrs.**	**72 hrs.**
Conjunctivitis	1/3	1/3	0/3	0/3
Corneal opacity	0/3	0/3	0/3	0/3
Iritis	0/3	0/3	0/3	0/3

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY DERMAL IRRITATION - Rabbit [OPPTS 870.2500]

PRODUCT MANAGER: 23 **REVIEWER:** M. HASHIM

TEST MATERIAL: Bas 670 336SC Herbicide, BAS 670 00 H, Batch No. 2000-2, Purity 33.6%, Liquid / pink-cloudy

CITATION: Wiemann, C. and Hellwig, J. (2001). BAS 670 00 H- Acute Dermal Irritation/ Corrosion in Rabbits. Department of Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany, Project No. 18H0440/002141 dated 6-11-2001. MRID No. 45901811 (Unpublished).

SPONSOR: BASF Corporation (Agricultural Products), Research Triangle Park, NC 27709-3528.

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 45901811), 0.5 g of BAS 670 00 H, Batch No. 2000-4 Purity33.6%) was topically applied to 3 NZW (young adult) rabbits (SPF bred, Source: Boehringer Ingelheim Pharma KG) on a 2.5 cm^2 area of the dorsal skin. The test site was covered by a patch and a semi occlusive dressing for 4 hours. The animals were then observed for 72 hours.

All rabbits had mild degree of erythema. This was reversible within 48 hours. There was no edema. The mean irritation score based on 24-72 hour reading was 0.2.

The compound (BAS 670 00 H) is a mild irritant, and is classified as Toxicity Category IV.

This study is classified as Acceptable. This study satisfies the guideline requirement for a primary dermal irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

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

OBSERVATIONS: Three rabbits had erythema. The mean irritation score (erythema+edema) based on 24-72 hour reading was 0.2.

DATA EVALUATION RECORD

STUDY TYPE: DERMAL SENSITIZATION-Guinea pig [OPPTS 870.2600]

PRODUCT MANAGER: 23 **REVIEWER**: M. HASHIM

TEST MATERIAL : BAS 670 00 H. Batch No. 2000-2, Purity 33.6%. Liquid / pink cloudy

CITATION: Wiemann, C, and Hellwig, J. (2001). BAS 670 00 H- Modified Buehler Test (9 inductions) in Guinea Pigs. Experimental Toxicology and Ecology, BASF Aktiengesellschaft, 67056 Ludwigshafen/Rhein, Germany, Study No. 11A0440/002139 dated 6-11-01. MRID No. 45901812 (Unpublished).

SPONSOR: BASF Corporation (Agricultural Products), Research Triangle Park, NC 27709-3528.

EXECUTIVE SUMMARY: A Buehler test (MRID 45901812) was performed to assess the sensitization potential of BAS 670 00H (33.6 % a.i Lot No. 2000-2) in young adult Hartley guinea pigs (Source: Harlan Winklemann GmbH, Borchen, FRG). Based on the screening tests, the test substance was used as 100% for induction and 25% for the challenge. One test and two control groups (10 animals for each control and 20 for test group) were used. There were 9 inductions (3/week). Thirteen days after the last induction, a challenge was performed at 25% of the test substance.

After three 3 weeks of inductions, dermal irritation was observed in a few animals during (2nd-9th induction). There was discrete or patchy to moderate and confluent erythema and swelling on the test animals at 24 and 48 hours. However, after a challenge dose, there was no skin reaction in the control or test animals (24 or 48 hours evaluation). A historical control was used.

In this study, BAS 670 00 H was not a dermal sensitizer.

This study is classified as Acceptable. This study satisfies the requirement for a 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.

PROCEDURE :A Buehler test was performed to assess the sensitization potential of BAS 670 00H in young adult Hartley guinea pigs. Based on the screening tests, the test substance was used as 100% for induction and 25% for the challenge. One test and two control groups (10 animals for each control and 20 for test group) were used. There were 9 inductions (3/week). Thirteen days after the last induction, a challenge was performed at 25% of the test substance.

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ACUTE TOX ONE-LINERS

1. DP BARCODE: D290071
2. PC CODE: 123009
3. CURRENT DATE: 7-7-03
4. TEST MATERIAL: BAS 670 336SC Herbicide

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/ rat/ BASF-Department of Toxicology - BASF, Germany/ 10A0440/001076 / 5-30-01	45901807	Oral LD_{50}> 3000 mg/kg	III	A
Acute dermal toxicity / rat/ Department of Toxicology - BASF, Germany/ 11a0440-001077/ 5-30-01	45901808	Dermal LD_{50} > 4000 mg/kg	III	A
Acute Inhalation study/rat/ BASF-Toxicology Lab, Germany/ 13I10440/007016 / 10-23-01	45901809	LC_{50} >5.8 mg/L	IV	A
Eye irritation study / rabbit/ BASF Tox and Ecology Lab, Germany/ 11H0440/002140/ 6-11-01	45901810	moderate irritant	III	A
Skin irritation/ rabbit/ BASF Tox and Ecology Lab-Germany/ 18H0440/002141/ 6-11-01	45901811	mild irritant	IV	A
Dermal sensitization/ guinea pig/ BASF-Toxicology and Ecology- Germany/ 33H0440/002139 / 6-11-01	45901812	not a sensitizer	-	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated

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