#9E5052
Metconazole (P.C. Code 125619)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC SUBSTANCES

28/DEC/2004

MEMORANDUM

Subject: EPA File Symbol: 9E5052 Metconazole
DP Barcode: D308761
Decision No: 302638
PC Code: 125619

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

To: Lana Coppolino, RM 21
Fungicide Branch
Registration Division

Applicant: BASF Corporation
P. O. Box 13528
Research Triangle Park, NC 27709-3528

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Metconazole	95.2
Inert ingredients/ Impurities	49.8
Total:	100.00

#9E5052
Metconazole (P.C. Code 125619)

ACTION REQUIRED: PM requests a review of the acute toxicity data for the File Symbol #9E5052, Metconazole Fungicide (5-[(4-chlorophenyl methyl]-2,2-dimethyl-1-(1H-1, 2, 4-triazol-1-ylmethyl) cyclopentanol submitted by BASF Corporation, originally by Kureha Chemical Industry.

BACKGROUND: Acute toxicity studies for Metconazole were conducted in UK and USA during 1990 to 1994. Oral study has several replicates. The test substance has three lot numbers. All studies are reported under three MRID numbers (44721512, 44721513 and 44721514).

RECOMMENDATIONS: Each of the submitted studies is in compliance with the Sub-Division F guidelines.

There were several replicates of the oral tox study with differences in the outcome for LD_{50}. For safety concern, we will select the lowest value from such studies.

In the future the Registrant has to submit OECD 425 (Up and Down Method) for acute oral study. OECD 401 may not accepted.

Acute inhalation study is not submitted in the package This forms a data gap for registration.

The toxicology profile for the File Symbol #9E5052 is as follows:

acute oral toxicity -mouse	III	acceptable	MRID 44721512
acute oral toxicity-rat	III	acceptable	MRID 44721512
acute oral toxicity-rat	III	acceptable	MRID 44721513
acute oral toxicity-rat	IV	acceptable	MRID 44721514
acute dermal toxicity-rat	III	acceptable	MRID 44721512
acute dermal toxicity-rat	III	acceptable	MRID 44721513
acute dermal toxicity-rabbit	III	acceptable	MRID 44721512
acute inhalation study	-	data gap	
primary eye irritation	III	acceptable	MRID 44721513
primary dermal irritation	IV	acceptable	MRID 44721513
dermal sensitization	neg..	acceptable	MRID 44721513

Labeling: Labeling will be provided after receiving the inhalation study.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 12-23-04

Risk Manager (EPA): 21

STUDY TYPE: Acute Oral Toxicity- OPPTS 870-1100; OECD 401

TEST MATERIAL: Metconazole (95%), WL148271

CITATION: Gardner, J. R. (1990). 148271: Acute Oral and Dermal Toxicity. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR 89.214 study date 4-4-90 MRID 44721512.

SPONSOR: BASF Corporation BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: Mouse- (MRID 44721512): LD_{50} of Metconazole (95%) was determined in (5 male and 5 female) CD-1 (ICR) BR strain mice (Wt. 18-26 g, fe 16-21 g, Source: Charles River-UK) dosed at 391, 625, 1000, 1600 mg/kg b.w. The test material was administered in corn oil. Evaluation parameters included signs of gross toxicity and mortality for a subsequent period of 14 days. Initial and weekly body weights and necropsy findings were recorded on all animals.

Oral LD_{50} for male mice was 718 and for females 410, combined 566 mg/kg bw.

Several animals died on the study (Table 1). Main clinical signs developed within 5 hours of dosing. The signs were (in general) abasia/ataxia, abnormal posture, pallor of skin and eyes and stereotype behaviour. Before death animals showed prostration, coma, hypothermia or cyanosis in all doses. Isolated signs were piloerection, lethargy, tremor and convulsion. Tissue alterations at necropsy showed exaggerated lobular pattern of the liver, distension of cecum and congestion or hyperaemia of urinary bladder. All these signs were seen in a single or few animals.

The test substance is of **moderate toxicity** based on the LD_{50} in mice, EPA Toxicity Category III.

This acute oral study is classified as Acceptable. This study does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100) in the mice.

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

statements were provided.

RESULTS and DISCUSSION:

391	0 / 5	1 / 5
625	2 / 5	5 / 5
1000	4 / 5	5 / 5
1600	5 / 5	5 / 5

A. **Mortality** - Table 1. There were several death on the study.

B. **Clinical observations** - Main clinical signs developed within 5 hours of dosing. The signs (in general)were abasia/ataxia, abnormal posture, pallor of skin and eyes, and stereotype behaviour. Before death animals showed prostration, coma, hypothermia or cyanosis in all doses. Isolated signs were piloerection, lethargy, tremor and convulsion.

C. **Gross Necropsy** Tissue alterations at necropsy were exaggerated lobular pattern of the liver, distension of cecum and congestion or hyperaemia of urinary bladder. All these lesions were seen in a single or a few animals.

D. **Reviewer's Conclusions**: TRB accepts the study author's conclusion.

E. **Deficiencies** - none.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 12-23- 04

Risk Manager (EPA): 21

STUDY TYPE: Acute Oral Toxicity- OPPTS 870-1100; OECD 401

TEST MATERIAL: Metconazole (95%), WL148271

CITATION: Gardner, J. R. (1990). 148271: Acute Oral and Dermal Toxicity. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR.89.214 study date 4-4-90 MRID 44721512.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: Rats oral (MRID 44721512): An acute oral toxicity study was conducted to determine the LD_{50} of WL148271 (Metconazole 95%) in Fischer 344 rats (Wt. 186-218 g, fe 126-147, Source: Charles River-UK). The doses selected were 255, 357, 500, 700 and 980 mg/kg b.w. The test material was administered in corn oil. Evaluation parameters included signs of gross toxicity and mortality for a subsequent period of 14 days. Initial and weekly body weights and necropsy findings were recorded on all animals.

Oral LD_{50} for male rats was 727 and for females 595, combined 660 mg/kg bw.

Several animals died on the study (Table 1). Main clinical signs were diarrhea noted primarily at 255, 500, 700 and 980 mg/kg dose. Abasia or ataxia was seen on doses at 357 and 500 mg/kg and in all higher doses. Chromodacryorrhea and salivation were seen at 357 mg/kg and higher dose levels. In addition lachrymation prostration, hypothermia was preclude to death. Piloerection, lethargy, pallor of the skin and eyes were also noted. Most signs appeared from 4 hours to day 4-11. Most surviving rats lost weight in the first week of the test, then gained back slowly. Necropsy lesions of the decedents showed liver, stomach, intestine and kidney alterations. Terminal animals showed discoloration of liver and lymph nodes, and distention of large intestine; cecum and colon.

The test substance is of **moderate toxicity** based on the LD_{50} in male and female rats, classified as EPA Toxicity Category III.

This acute oral study is classified as Acceptable. This study does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100) in the rat.

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

RESULTS and DISCUSSION:

255	0 / 5	0 / 5
357	0 / 5	0 / 5
500	1 / 5	3 / 5
700	1 / 5	2 / 5
980	5 / 5	5 / 5

A. Mortality - There were several death on the study (Table 1).

B. Clinical observations - Main clinical signs were diarrhea was noted at 255, 500, 700 and 980 mg/kg. Abasia or ataxia was seen on doses 357 and 500 mg/kg and in all higher doses. Chromodacryorrhea and salivation at 357 mg/kg and higher dose levels. In addition lachrymation prostration, hypothermia was a preclude to death. Piloerection, lethargy, pallor of the skin and eyes was also noted. Most signs appeared from 4 hours to day 4-11. Most surviving rats lost weight in the first week of the test, then gained back slowly.

C. Gross Necropsy Necropsy lesions of decedents showed liver, stomach, intestine and kidney alterations. Terminal animals showed discoloration of liver and lymph nodes and distention of large intestine; cecum and colon.

D. Reviewer's Conclusions: TRB accepts the study authors conclusion.

E. Deficiencies - None.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 12-23-2004

Risk Manager (EPA): 21

STUDY TYPE: Acute Oral Toxicity-Rat, OPPTS 870-1100; OECD 401

TEST MATERIAL: Metconazole (95%), WL136184 (KNF-S-474 cis isomer), Batch 12; F900250, White powder

CITATION: Gardner, J. R. (1991). Acute Oral and Dermal Toxicity in Rat, Skin and Eye irritancy in Rabbit and Skin Sensitization potential in Guinea Pig. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR.91.103 dated 10-11-91.MRID 44721513.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: (MRID 44721513) Rat- LD_{50} of WL136184 (Metconazole 95%) was determined in Fischer 344 rats (Wt. 189-229 g, fe 136-156 , Source: Source of Animals, Charles River-UK) dosed at 850, 1190, 1666 and 2332 mg/kg. The test material was administered in corn oil at a constant dose volume of 10.0 ml/kg. Evaluation parameters included signs of gross toxicity and mortality for a subsequent period of 14 days. Initial and weekly body weights, and terminal necropsy findings were recorded on all animals.

Oral LD_{50} for male rats was 1627 and for females 1312, combined 1459 mg/kg bw.

Nineteen animals died on the study (Table 1). Animals on all doses showed lethargy, salivation, lacrimation, periorbital encrustation and diarrhea.. Rats at dose 1190 mg/kg and above showed piloerection, ataxia or prostration. Tachypnea and coma were seen in animals that did not survive the test. There was partial recovery in most rats. There was body weight loss in animals surviving over 1190 mg/kg dose and above.

In decedents, gross necropsy lesions were mainly exaggerated hepatic pattern, areas of pallor or darkening of the liver, darkening of thymus, spleen and kidneys, abnormal fluid in the intestinal tract and inflamed stomach. Terminal animals showed white/yellow areas on the liver of a single male treated at the high dose level.

The test substance is of **moderate toxicity** based on the LD_{50} in female rats, EPA Toxicity Category III.

This acute oral study is classified as Acceptable. This study does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100) in the rat.

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

RESULTS and DISCUSSION:

850	0 /5	0 / 5
1190	1 / 5	3 / 5
1666	3 / 5	3 / 5
2332	4 /5	5 / 5

A. Mortality - Table 1. There were several death on the study.

B. Clinical observations - All doses shows lethargy, salivation, lacrimation, periorbital encrustation and diarrhea.. Rats at dose 1190 mg/kg and above showed piloerection, ataxia or prostration. Tachypnea and coma were seen in animals that did not survive the test. There was partial recovery in rats, however, it was incomplete. There was body weight loss recorded in animals surviving over 1190 mg/kg and above.

C. Gross Necropsy Gross necropsy lesions were mainly in decedents was exaggerated hepatic pattern, areas of pallor or darkening of the liver, darkening of thymus, spleen and kidneys, abnormal fluid in the intestinal tract and inflamed stomach. Terminal animals showed white/yellow areas on the liver of a single male treated at the high dose level.

D. Reviewer's Conclusions: TRB accepts the study authors conclusion.

E. Deficiencies - None.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 12-23-04

Risk Manager (EPA): 21

STUDY TYPE: Acute Oral Toxicity- Rat - OPPTS 870-1100; OECD 401

TEST MATERIAL: Metconazole 91.5%, AC 382390 Lot No. AC11021-26A, Cyclopentanol (91.5%), Powder

CITATION: Lowe, C., and Bradley, D. (1994). Oral LD_{50} in Albino Rats with AC 382390. Agricultural Products Research Division, Princeton, NJ. Study No. T-0959 dated 5-13-94. MRID 44721514.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: Rats (MRID 44721514): Acute oral toxicity (LD_{50}) of AC 382390 (Metconazole 91.5%) was determined in SD rats (Wt. 227-243g, fe 172-182 g, Source: Charles River< Raleigh, NC) at 5000 mg/kg body wt. The test material was administered in 0.5% carboxymethylcellulose. Evaluation parameters included signs of gross toxicity and mortality for a subsequent period of 14 days. Initial and weekly body weights and necropsy findings were recorded on all animals.

Oral LD_{50} for male/male rats was 5000 mg/kg bw.

There were no deaths on the study nor any clinical signs. Body weight gains were normal. Necropsy findings were unremarkable.

The test substance is of **low toxicity** based on the LD_{50} in female rats, EPA Toxicity Category IV.

This acute oral study is classified as Acceptable. This study does satisfy the guideline requirement for an acute oral study (OPPTS 870.1100) in the rat.

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

#9E5052
Metconazole (P.C. Code 125619)

RESULTS and DISCUSSION:

[redacted]		
5000	0 / 5	0 / 5

A. Mortality - Table 1. There were no deaths on the study.

B. Clinical observations -There were no clinical signs. Body weight gains were normal.

C. Gross Necropsy Necropsy findings were unremarkable.

D. Reviewer's Conclusions: TRB accepts the study authors conclusion.

E. Deficiencies - None.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 23/DEC/2004

Risk Manager (EPA): RM 21

STUDY TYPE: Acute Dermal Toxicity- SD Rat; OPPTS 870-1200; OECD 402.

TEST MATERIAL: Metconazole (95%), WL136184 (KNF-S-474 cis isomer), Batch 12; F900250, White powder

CITATION: Gardner, J. R. (1991). Acute Oral and Dermal Toxicity in Rat, Skin and Eye irritancy in Rabbit and Skin Sensitization potential in Guinea Pig. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR.91.103 dated 10-11-91.MRID 44721513.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: Dermal Toxicity- Rat (MRID 44721513). An acute dermal study was performed to determine the LD_{50} of Metconazole (95%) in Fischer 344 rats (Wt. males- 213-241 g, females 144-158 g, Source Ace Animals, Charles River-UK). The test substance was applied on the skin of rats as a single application (powder moistened in water) at 2000 mg/kg bw, and covered with a gauze and tape for 24 hours. Then the dressing was removed and the residual test substance was wiped/ cleaned. Animals were observed for 14 days. Terminal necropsy findings were recorded.

Dermal LD_{50} Males >2000 mg/kg bw
Females > 2000 mg/kg bw
Combined > 2000 mg/kg bw

There were no deaths on the study. There were no clinical signs. There was dermal irritation (erythema) in two animals that subsided by day 3.

The test substance is of **moderate toxicity** and is classified as EPA Toxicity Category III.

This acute dermal study is classified Acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402).

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

RESULTS and DISCUSSION:

[redacted]			
2000	0 / 5	0 / 5	0 / 10

A. Mortality - None.

B. Clinical observations - There were no toxic signs on the study. There was dermal irritation in two animals which subsided by day 3.

C. Gross Necropsy - Necropsy findings were unremarkable.

D. Reviewer's Conclusions: TRB agrees with the Study author's conclusion.

E. Deficiencies - None.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 23/DEC/2004

Risk Manager (EPA): RM 21

STUDY TYPE: Acute Dermal Toxicity- Rat; OPPTS 870-1200; OECD 402.

TEST MATERIAL: Cyclopentanol (95%), WL148271

CITATION: Gardner, J. R. (1990). Acute Oral and Dermal Toxicity. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR 89.214 dated 1-4-1990 MRID 44721512.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: (Dermal Toxicity)-Rat. An acute dermal toxicity study (MRID 44721512) was conducted to determine the LD_{50} of WL148271 (Metconazole 95%) in Fischer 344 rats (Wt. males- 215-250 g, females 130-151 g, Source Ace Animals, Charles River-UK). The test substance was applied on the skin of rats as a single application (powder moistened in water) at 2000 mg/kg bw and covered with a gauze and waterproof adhesive tape for 24 hours. Then the gauze pads and tapes were removed and the residual test substance was wiped/ cleaned. Animals were observed for 14 days. Terminal necropsy findings were recorded.

Dermal LD_{50} Males >2000 mg/kg bw
Females > 2000 mg/kg bw
Combined > 2000 mg/kg bw

There were no deaths on the study. There was dermal irritation in 3 animals between Day 2-5. All animals gained weight during the study. Necropsy findings were unremarkable.

The test substance is of **moderate toxicity** and is classified as EPA Toxicity Category III.

This acute dermal study is Acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402).

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

RESULTS and DISCUSSION:

2000	0 / 5	0 / 5	0 / 10

A. **Mortality** - None.

B. **Clinical observations** - There were no deaths nor any toxic signs on the study. There was dermal irritation in 3 animals which subsided by day 5.

C. **Gross Necropsy** - Necropsy findings were unremarkable.

D. **Reviewer's Conclusions:** TRB agrees with the Study author's conclusion.

E. **Deficiencies** - None.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 12-23-04

Risk Manager (EPA): RM 21

STUDY TYPE: Acute Dermal Toxicity- OPPTS 870-1200; OECD 402.

TEST MATERIAL: Metconazole (95%), WL148271

CITATION: Gardner, J. R. (1990). Acute Oral and Dermal Toxicity. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR 89.214, 1-4-1990 dated 1-4-1990. MRID 44721512.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: (Dermal Toxicity-rabbit) (MRID 44721512)- An acute dermal toxicity study was performed to determine the LD_{50} of WL148271 (Metconazole 95%) in NZW rabbits (Wt.2.6-3.4 kg, Source: Foxfield Farms-UK). The test substance was applied on the skin of rabbits at a limit dose of 2000 mg/kg in a single application (powder moistened in water). This was covered with a gauze and waterproof adhesive tape for 24 hours. The dressing was removed and the residual test substance was wiped/ cleaned. Animals were observed for 14 days. Terminal necropsy findings were recorded.

Dermal LD_{50} Males rabbits >2000 mg/kg bw
Females > 2000 mg/kg bw
Combined > 2000 mg/kg bw

There were no deaths on the study. Desquamation of skin in two animals was seen during 8-14 days. There was congestion of lungs (4/10) animals, pale dark foci on lungs (2/10) and (3/10) animals with kidney lesions such as petechia, paleness and raised areas.

The test substance is of **moderate toxicity** and is classified as EPA Toxicity Category III.

This acute dermal study is classified Acceptable. It does satisfy the guideline requirement for an acute dermal study (OPPTS 870.1200; OECD 402).

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

RESULTS and DISCUSSION:

2000	0 / 5	0 / 5	0 / 10

A. Mortality - None.

B. Clinical observations - Desquamation of skin in two animals during 8-14 days.

C. Gross Necropsy - There was congestion of lungs (4/10), pale dark foci on lungs (2/10) and 3/10 with kidney lesions such as petechia, pale and raised areas.

D. Reviewer's Conclusions: TRB agrees with the Study author's conclusion.

E. Deficiencies - None.

#985052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 12-23-04

Risk Manager (EPA): 21

Type of Test: Primary Eye Irritation Study, OPPTS 870.2400; OECD 405

TEST MATERIAL: Metconazole (95%), WL136184 (KNF-S-474 cis isomer), Batch 12; F900250, White powder

CITATION: Gardner, J. R. (1991). Acute Oral and Dermal Toxicity in Rat, Skin and Eye irritancy in Rabbit and Skin Sensitization potential in Guinea Pig. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR.91.103 dated 10-11-91. MRID 44721513.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: (MRID 447121513) In a primary eye irritation study, six NZW rabbits (Source: Foxfield Farms, UK) were treated with Metconazole (95%). One eye of each rabbit was instilled (into the conjunctival sac) with 42 mg (0.1 mL) of the powdered test substance, the other eye served as the control. The eyes were not irrigated. Animals were then observed for 7 days. Ocular irritation was evaluated by Draize Method for seven days.

Table 1. Inflamed conjunctiva was noted in the first hour of treatment in all animals. There was corneal opacity in one animal that subsided within 7 days.

The test substance is a **moderate irritant** to the rabbit eye. The test substance meets EPA Toxicity Category III.

This study is classified as Acceptable. It does satisfy 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.

RESULTS AND DISCUSSION:

Table 1. No of Animals affected. Total animals 6

lesion	One hr	24 hrs	48 hrs	72 hrs	day 7
corneal opacity	0 / 6	1/ 6	1 / 6	1 / 6	0 / 6
iritis	0 / 6	0 / 6	0 / 6	0 / 6	0 / 6
conjunctivitis	6 / 6	0 / 6	0 / 6	0 / 6	0 / 6

A. **Observations** - Table 1. Table 1. Ocular irritation subsided within 7 days.

B. **Reviewer's Conclusions:** The Reviewer agrees with the Study Author's conclusion.

C. **Deficiencies** : None.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 12-23-04

Risk Manager (EPA): 21

TYPE OF STUDY: Primary Skin Irritation Study in Rabbits- 870-2500, OECD 404.

TEST MATERIAL: Metconazole (95%), WL136184 (KNF-S-474 cis isomer), Batch 12; F900250, White powder

CITATION: Gardner, J. R. (1991). Acute Oral and Dermal Toxicity in Rat, Skin and Eye irritancy in Rabbit and Skin Sensitization potential in Guinea Pig. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR.91.103 dated 10-11-91.MRID 44721513.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: Dermal irritation-rabbit. In a primary dermal irritation study (MRID 44721513), 6 young adult NZW rabbits (Source: Foxfield Farm-UK) were topically treated with 0.5 g of Metconazole (95%). The test substance (in a powder form) was applied to the dorsal part of the body on a (6 cm ^{2}) lint patch moistened in dist. water. The test sites were covered with a gauze and a semi occlusive adhesive bandage for 4 hours. After the dressing was removed the test site was wiped/cleaned and scored by Draize Method for 72 hours.

Application of the test substance produced no irritation of the skin (edema or erythema), and is **not an irritant** to the rabbit skin. It meets EPA Tox Category IV.

This study is classified as Acceptable. It does satisfy 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.

RESULTS and DISCUSSION:

A. **Observations** - Application of the test substance produced no irritation of the skin (edema or erythema), and is not an irritant to the rabbit skin. It meets EPA Tox Category IV.

B. **Results** -The PDII was 0 (assumed).

C. **Reviewer's Conclusions:** The Reviewer is in agreement with the Study Author.

D. **Deficiencies** - None.

#9E5052
Metconazole (P.C. Code 125619)

Reviewer: M. Hashim **Date:** 23 Dec., 2004

STUDY TYPE: Dermal Sensitization - Guinea Pig; OPPTS 870.2600; OECD 406, 429

Risk Manager (EPA): 21

TEST MATERIAL: Metconazole (95%), WL136184 (KNF-S-474 cis isomer), Batch 12; F900250, White powder

CITATION: Gardner, J. R. (1991). Acute Oral and Dermal Toxicity in Rat, Skin and Eye irritancy in Rabbit and Skin Sensitization potential in Guinea Pig. Sittingbourne Research Centre, Sittingbourne, Kent ME9 8AG, England. Report No. SBGR.91.103 dated 10-11-91.MRID 44721513.

SPONSOR: BASF Corporation, Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: A Buehler study (MRID 44721513) was conducted to assess the sensitization potential of Metconazole (95%) in guinea pigs (Source: Harlan Porcellus, UK). A 0.45 mL of Metconazole (95%) was topically applied, once a week, for three consecutive weeks (using a 16 cm/x16 cm patch of the filter paper in dist. water) to 20 Hartley albino guinea pigs. Ten guinea pigs were used as the controls. (Topical induction and challenge made in 50% Vaseline). Test and control animals were challenged on day 28 by 0.15 mL of the test substance (as the highest non irritating concentration for this study). Animals were evaluated for dermal reaction at 24 and 48 hours after each exposure. Positive (historical) control was transcinnnamaldehyde and benzocaine.

The test substance showed no positive response in any of the 20 guinea pigs.

Under the conditions of the study Metconazole is **not a sensitizer.**

COMPLIANCE: The test (870-2600) meets GLP requirements. It is Acceptable in accordance with the Sub Division F guide line.

This study is classified as Acceptable.. It does satisfy the guideline requirement for a sensitization study (OPPTS 870.2600; OECD 406, 429) in the Guinea pig .

I. PROCEDURE A Buehler study was conducted to assess the sensitization potential of Metconazole (95%) in guinea pigs. A 0.45 mL of Metconazole (95%) was topically applied, once a week, for three consecutive weeks (to a 16 cm/x16 cm patch of the filter paper in dist. water) to 20 Hartley albino guinea pigs. Ten guinea pigs were used as the controls. (Topical induction and challenge made in 50% Vaseline). Test and control animals were challenged on day 28 by 0.15 mL of the test substance (as the highest non irritating concentration for this study). Animals were evaluated for dermal reaction at 24 and 48 hours after each exposure. Positive (historical) control was transcinnnamaldehyde and benzocaine. .

A. **Induction** - 50% Vaseline + 0.45 ml test substance used

B. **Challenge** - 50% vaseline 0.15 ml test substance used.

C. **Naive Controls** - Challenged similarly as the test group.

RESULTS and DISCUSSION: The test showed 0/20 at 24 and 48 hours, respectively.

A. **Reactions and duration:** none

B. **Positive control** - Showed appropriate results.

C. **Reviewer's Conclusions:** The Reviewer agrees with study author.

D. **Deficiencies** - None.

#9E5052
Metconazole (P.C. Code 125619)

TOX ONE LINER:
Bar Code: 308761
#9E5052
TEST MATERIAL: Metconazole Fungicide 95%
Date: 12-28-04

Study/ Species/ #/ Lab/ date	MRID #	Results	Tox Cat.	Core grade
Acute oral toxicity study/ mouse/ Sittingbourne Res. Centre, Kent-UK/ 89.214/ 4-4-90	44721512	LD_{50} >566 m/f	III	A
Acute oral toxicity study/ rat/ Sittingbourne Res. Centre, Kent-UK/ 89.214/ 4-4-90	44721512	LD_{50} >566 m/f	III	A
Acute oral toxicity study/ rat/ Sittingbourne Res. Centre, Kent-UK/ 91.103/10-11-91	44721513	LD_{50} >1459 m/f	III	A
Acute oral toxicity study/ rat/ Ag Products Res Div - Princeton/ T-0959/ 5-13-94	44721514	LD_{50} >5000 m/f	IV	A
Acute dermal toxicity study/ rat/ Sittingbourne Res. Centre, Kent-UK/ 91.103/10-11-91	44721513	Dermal LD_{50} > 2000 m/f	III	A
Acute dermal toxicity study/ rat/ Sittingbourne Res. Centre, Kent-UK/SBGR 89.214/1-4-90	44721512	Dermal LD_{50} > 2000 m/f	III	A
Acute dermal toxicity study/ rabbit/ Sittingbourne Res. Centre, Kent-UK/ SBGR 89.214/1-4-90	44721512	Dermal LD_{50} > 2000 m/f	III	A
Eye irritation study/ rat/ Sittingbourne Res. Centre, Kent-UK/ 91.103/10-11-91	44721513	moderate irritant	III	A
Primary dermal irritation study/rabbit Sittingbourne Res. Centre, Kent-UK/ 91.103/10-11-91	44721513	mild irritant	IV	A
Sensitization study/ guinea pig Sittingbourne Res. Centre, Kent-UK/ 91.103/10-11-91	44721513	neg.	-	A