

US EPA ARCHIVE DOCUMENT

6-5-90

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215B

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 50534-115 Tuffcide 404
50534-9 Daconil 2787
50534-8 Bravo 500
50534-188 Bravo 720

FROM: William S. Woodrow WSW 5-24-90
Precautionary Review Section E 6/5/90
Registration Support Branch
Registration Division (H7505C)

TO: Lewis/Stone (PM 21)
Fungicide - Herbicide Branch
Registration Division (H7505C)

APPLICANT: Fermenta ASC Corporation
5466 Heisley Road
P.O. Box 8000
Mentor, Ohio 44061-8000

FORMULATION FROM LABEL:

Active Ingredient(s):		-115
<u>Chlorothalonil (tetrachloroisophthalonitrile)</u>		-9
		-8
		-188
		% by wt.
		40.4
		54.0
Inert Ingredient(s):		
		59.6
		45.0
Total		100.0%

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BACKGROUND

The Fermenta A.S.C. Corp. requested precautionary labeling changes and/or the addition of label use claims for the following chlorothalonil products; whose Confidential Statements of formula are similar enough to utilize a single set of supporting acute toxicity data:

EPA 50534-115 Tuffcide 404

chlorothalonil	40.4%
Inerts	59.6%

50534-9 Daconil 2787

chlorothalonil	40.4%
Inerts	59.6%

50534-8 Bravo 500

chlorothalonil	40.4%
Inerts	59.6%

50534-188 Bravo 720

chlorothalonil	54.0%
	46.0%

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RECOMMENDATIONS

1) Precautionary labeling change requests:
a. Request to delete "May be a potential skin sensitizer", under Precautionary Statements for:

50534-115 Tuttleide 404;

50534-9 Daconil 2787;

50534-8 Bravo 500, and;

50534-188 Bravo 720

RSB/PRS recommendation: This request is not justified. The only dermal sensitization study representing the above four products (conducted using Bravo 720; MRID #405460-02), showed that Bravo 720 was a weak contact sensitizer.

b. Fermenta Corp. is justified in removing all statements from the following labels referring to "chlorothalonil... or this product may produce temporary allergic side effects...", or "Note to physicians: Persons having an allergic reaction respond to treatment with

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antihistamines"

50534-115 Tuffade 404

50534-9 Daconil 2787

50534-8 Bravo 500

50534-188 Bravo 720

c. Fermenta Corp. requests adding the following
to the 50534-115; labels:
50534-9;
50534-8, and;
50534-188

"Note to Physician: Persons having
temporary irritation symptoms may respond
to treatment with antihistamines or steroid
creams and/or systemic steroids" is
acceptable to RSB/PRS. Note to PRS:
The Fermenta Note To Physician is
acceptable provided "may" is inserted
into the phraseology suggested by
Fermenta.

The "Note to User: This product may
produce mild bronchial irritation and
temporary irritation of the skin
characterized by redness or rash on
exposed skin areas. Affected persons

should call a physician", proposed by Fermenta is also acceptable to RSB/PTS, for the following product labels:

50534-115 ;

50534-9 ;

50534-8, and ;

50534-188

2) The Fermenta Corp. requests permission to add "prevents fungal growth on caulks, non-food grade sealants and adhesives", to the 50534-115 Tuffcide 404 product label.

The Fermenta Corp. request to add caulks, non-food grade sealants and adhesives to the 50534-115 Tuffcide 404 label is not acceptable to RSB/PTS ^{UNTIL DATA BASE IS COMPLETE} 9 current acute toxicity profile for 50534-115, as well as for the products listed below follows:

50534-115 ;

50534-9 ;

50534-8, and ;

50534-188

A current acute toxicity profile for the products listed above consists of:

Acute oral study (Bravo 500; 50534-8,
40.4 % A.I.)

87306, 10-19-77

Tox. Category III

Core Guidelines

Acute dermal study (Bravo 500; 50534-8,
40.4 % A.I.)

87307, 10-24-77

Tox. Category IV

Core Guidelines

Acute dermal study (Bravo-720; 50534-188,
54.07 % A.I.)

158494, 2-7-86

Tox. Category III

Core Guidelines

Acute inhalation study (Bravo-500; 50534-8,
40.4 % A.I.)

87310, 12-6-77

Tox. Category - not determined Supplementary

(no particle size/size distribution; No-
MMAD/GSD. Accuracy of cloud conc.
questionable, respirable particle fraction
was an inaccurate, crude estimation.

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Eye irritation study (Bravo-500; 50534-8,
40.47% A.I.)

87177 4-17-81

Tox. Category II Core Guidelines

Eye irritation study (Bravo-500; 50534-8,
40.47% A.I.)

87177 4-17-81

Tox. Category III Core Guidelines

Eye irritation study (Bravo-500; 50534-8,
40.47% A.I.) # 87178

Tox. Category III Core Guidelines

Eye irritation study (Bravo 720; 50534-188,
54% A.I.) # WIL-11006

Tox. Category II Core Guidelines

Skin irritation study (Bravo 500; 50534-8
40.47% A.I.) # 4503-77, 87308

Tox. Category IV Core Guidelines

Dermal sensitization study (Bravo 720; 50534-188
54.07% A.I.) # 405460-02

A weak contact sensitizer.

Core Guidelines

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LABELING : 50534-115, 50534-9, 50534-8,
50534-188.

- 1) The WARNING signal word is appropriate.
- 2) 50534-115 Tuffide 404

Precautionary Statements

- a. Do not remove the "May be a potential skin sensitizer" statement.

Under First Aid:

Add, "If Swallowed: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person."

- 3) 50534-9 Daconil 2787

Precautionary Statements

- a. Do not remove the "May be a potential skin sensitizer" statement.
- b. Add "Harmful if swallowed or absorbed through skin, and causes eye injury."

Under First Aid:

Add, "If Swallowed: Call a physician or

Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person.

If on skin: Wash with plenty of soap and water. Get medical attention.

If in eyes: Flush with plenty of water. Call a physician.

4) 50534-8 Bravo 500

Precautionary Statements

- a. Do not remove the "May be a potential skin sensitizer" statement.
- b. Add: "Harmful if swallowed, absorbed through skin, and causes eye injury".

Under First Aid:

Add: If swallowed: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce

vomiting or give anything by mouth to an unconscious person.

If on skin: Wash with plenty of soap and water. Get medical attention.

5) 50534-188 Bravo 720

Precautionary Statements

- a. Do not remove the "May be a potential skin sensitizer" statement.
- b. Add "Harmful if swallowed, absorbed through skin, and causes eye injury."

Under First Aid:

Add: "If Swallowed: Call a physician or Poison Control Center. Drink 1 or 2 glasses of water and induce vomiting by touching back of throat with finger. Do not induce vomiting or give anything by mouth to an unconscious person.

If on skin: Wash with plenty of soap and water. Get medical attention.

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6) Deletion of statements regarding temporary allergic side effects, and Note to Physician as indicated on sample labels provided by the registrant is acceptable to RSB/PPS. The deletion of "Note to User" under Directions for Use (50534-115, 50534-9) is acceptable.

7) The addition of a "Note to Physician", as indicated on sample labels, is acceptable provided the word "may" is inserted between the words "... symptom and respond - - - - -".

8) The addition of a "Note to User", as shown on the sample label is acceptable.

9) The label additions shown under 7) and 8) above concern products:

50534-115 ; Tuffcide 404

50534-9 ; Daconil 2787

50534-8, 9nd ; Bravo 500

50534-118 Bravo 720

ADDITIONAL RECOMMENDATION

3) The Registrant must submit an acceptable acute inhalation toxicity study, using one of the following Fermenta products: 50534-115 (Tuffcide 404), or 50534-9 (Daconil 2787), or 50534-8 (Bravo 500).

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1)

Product Manager: (21)
 MRID No.: 87306
 Testing Facility: Bio/Dynamics
 Author(s): W.E. Rinkelert
 Species: Rat, Wistar
 Age: not stated
 Weight: 210-257
 Source: Matland Farms, N.J.
 Test Material: compound 8641-125 (Bravo 500), liquid
 Quality Assurance (40 CFR §160.12):

Reviewer: M. Waller
 Report Date: 5-11-90
 Report No. 4501-77

Conclusion:

- LD₅₀ (mg/kg): Males = ; Females = ; Combined =
- The estimated LD₅₀ is 4.2 g/kg (2.9-6.1) g/kg 95% C.I.
- Tox. Category: III. Classification: guidelines

Procedure (Deviations from §81-1): 5mL 5F rats were dosed by oral intubation (5mL 5F/group), at 5 different dose levels - t.m.t. administered as 25% W/V solution in water. Animals dosed for mortality and toxic symptoms @ 0-2, 4-6 hrs post treatment, and at daily intervals to 14 days. Gross necropsies on all animals.

Reported Mortality

DOSAGE (g /kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2.0 g / kg	3/5	0/5	3/10
2.8 g / kg	2/5	0/5	2/10
4.0 g / kg	5/5	2/5	7/10
5.6 g / kg	4/5	3/5	7/10
8.0 g / kg	5/5	5/5	10/10

Symptomology & Gross Necropsy Findings:

Clinical: Terminal body weights showed losses for all animals.
 Prominent in life: soft stool, piloerection, "sawtooth" appearance, fecal staining.
 Necropsy: Prominent: soft stool, nasal & oral discharge, red & yellow liquid, tan kidneys, mottled liver, mottled lungs, vesicular & focal staining of abdomen.

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: (21)

Reviewer: Ward
Report Date: 5-11-90
Report No. 4502-77

ARID No.: 81307
Testing Laboratory: Big Dynamics

Author(s): P.R. Neenchan

Species: Rabbit + NZ white

Sex: 3M & 3F Wt.: 2.3-2.7 kg

Test Material: Compound 8641-175 (Bravo 500)

Quality Assurance (40 CFR §160.12):

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Summary:

- LD50 (mg/kg): Males = _____; Females = _____; Combined = _____;
- The estimated LD50 is > 20.0 g/kg
- Tox. Category: IV. Classification: Guidelines

Procedure (Deviations From §81-2): Back of 3M & 3F rabbits clipped to
expose approx. 30% of surface (body). 1/2 of clipped skin abraded
longitudinally (each rabbit) 20.0 g/kg dose to each animal
(15.9 ml), based on 1.26 g/ml density. T.m.t. held in place by
plastic mass of infusious material. Animals observed for mortality
& toxic signs daily to 4 days. 2 hr exposure; observations for
Reported Mortality

DOSAGE (20/kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
<u>20 g/kg</u>	<u>0/3</u>	<u>0/3</u>	<u>0/6</u>

Symptomology & Gross Necropsy Findings:

edema/cystema & escher formation. Body wts. 0 to 4 days. All
animals subjected to gross necropsy.
Clinical: Moderate to severe erythema (all) slight edema in
5 animals @ 24 hrs. Soft stool in 4 animals through day 6.
Necropsy: Kidneys pale or tan; lungs mottled - 1 animal

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DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: (21)

RID No.: 158494

Testing Laboratory: WIL-11005/SPS Biotech

Author(s): N.H. Wilson

Species: Rabbit, NZ White (SMAS F)

Sex: Blind compound # T-194-1 Wt.: Not stated

Test Material: T-194-1 (Tech. chlorothalonil) Dose 720 is 54%

Quality Assurance (40 CFR §160.12): adequate A.I.

Reviewer: ~~W. H. H. H.~~

Report Date: 5-11-99 00895

Report No. SPS-2787

Summary:

1. LD50 (mg/kg): Males = ; Females = ; Combined =

2. The estimated LD50 is 2000 mg/kg

3. Tox. Category: III Classification: Slightly Toxic

Procedure (Deviations from §81-2): 2000 mg/kg applied 10% of surface

skin on clipped dorsal of SMAS Fitter; Maintained in contact for

24 hours. Animals were observed for toxic signs and/or

mortality frequently during day 1 post treatment, 2 rabbits to

4 dogs - Application sites healed for irritation on days 1, 3, 7,

10 & 14. Bolyto recorded days 0, 7, 7 & 14

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2000 mg/kg	0/5	0/5	0/10

Pathology & Gross Necropsy Findings:

Necropsies performed on all animals.

Clinical: Local dermal irritation only; low incidence of desquamation for most animals - All rabbits showed body wt. loss at some intervals during study.

Necropsy: Prominent gross findings included dark red of firm lungs (possibly pulmonary infection). No compound-related findings.

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: (21)
 MRID No.: 87310
 Testing Laboratory: Bio/Dynamics
 Author(s): W.E. Reinhardt
 Species: Rat, Sprague Dawley
 Sex: 5M & 5F
 Source: Charles River
 Test Material: Compound 8641-125 (Bravo 500), liquid
 Quality Assurance (40 CFR §160.12):
 Reviewer: W. Woodrow
 Report Date: 5-11-90
 Report No. 77-1946

Summary:

1. LC₅₀ (mg/kg): Males = _____; Females = _____; Combined = _____
2. The estimated LC₅₀ is 71.072 mg/L
3. Mean Concentration: _____
4. Tox. Category: ____ Classification: Supplementary (see 2nd page)

Procedure (~~Deviations From §81-2~~): Test mat. placed in 3-neck flask fitted with a "Luskia" aerosol generator. Dry air @ 9.0 L/min. passed through generator. Aerosol → 26.5 L flow effluent chamber - 4 hour exposure. Nominal concentration determined: wt. material expended ÷ L air thru chamber. Animals observed for

Results:

Reported Mortality

Exposure Concentration (mg/L)	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
1.072 mg/L	0/5	0/5	0/10

~~Symptomatology & Gross Necropsy Findings:~~

mortality and toxicity during exposure & daily to 14 days. Body weights recorded @ 0, 1, 2, 4, 7 & 14 days. Gross necropsies performed on all animals.

During exposure, chamber atmosphere sampled hourly by a GCA respirable dust monitor (Model RDM 201).

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equipped a cyclone precollector, which is "100%" efficient removing 10μ particles or $>$, $\pm$ "50%" efficient in removing 3.5μ particles, or $>$. Samples taken with and without precollector - to determine 10μ particles or $<$. (3.5 to 10μ).

Results Nominal Concentration of 7.16 mg/L .
Total mass concentration (mg/L) (without Cyclone Precollector) = 1.072 (av. of 4 measurements)

No animals died, all gained weight. No "definitive" toxic signs during study observation period. Necropsy findings suggested possibility of some pulmonary toxicity.

No particle size distribution studies; NO MMAD, GS Deviation.

Accuracy of total mass/mg cloud concentration needed mass verification.

Respirable particles (mg) was only rough estimation, with no verification of accuracy.

Supplementary Data: see above records.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (21)

Reviewer: Woodrow

ID No.: 87177

Report Date: 5-11-90

Testing Laboratory: Bio/Dynamics, Inc.

Report No. 64380-465000

Author(s): N. H. Wilson

Species: Monkeys & Rats, Cynomolgus

Sex: female

Weight:

Source: Primate Imports, Port. Wash., L.I., N.Y.

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Dose: 0.1ml

Test Material: T-111-3 (B-avo 500), liquid

Quality Assurance (40 CFR §160.12): adequate

Summary:

Tox. Category: II Classification: Guidelines

Procedure (~~Deviation From §81-4~~): 0.1ml test material instilled into
eye of each of 9 monkeys, to the conjunctival sac - 20 sec.
after treatment, eyes of 3 monkeys washed for 1 minute c
100 ml water - treated eyes examined and scored at 24, 48, 72
hours, and at 4, 7, 14 & 21 days for irritation.

Observations

	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Corneal opacity		6/9	6/9	6/9	4/9	2/9	2/9	0/9
Conjunctivae redness		0/9	0/9	0/9	0/9	0/9	0/9	0/9
Chemosis		0/9	0/9	0/9	0/9	0/9	0/9	0/9
Discharge		0/9	0/9	0/9	0/9	0/9	0/9	0/9

Comments: Corneal opacity through Day 14, absent by Day 21.
No iris involvement - Conjunctival irritation absent by
Day 14.

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DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (211)

ID No.: 87178

Testing Laboratory: Bio/Pharmaceutical, Inc.

Author(s): P.R. Neenehah

Species: Rabbit, M 2 white

Sex: 3M 3F

Weight:

Source: Maryland Breeding Farms - N.J.

Dose: 0.1ml

Test Material: Compound 8641-125 (Bkavo 500 - 40.4 to A.I.)

Quality Assurance (40 CFR §160.12): none

Summary:

Tox. Category: III Classification: Guidelines

Procedure (Deviation from §81-4): 0.1ml test material into one eye of each.
 (3M 3F subjects, Eyes unwashed. Eyes examined and scored for irritation on days 1, 2, 3 and 7, according to the Draize system.)

Results:

	Observations (number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea		2/6	1/6	0/6		0/6		
Opacity		0/6	0/6	0/6		0/6		
Lids		5/6	5/6	2/6		0/6		
Conjunctivae		4/6	2/6	0/6		0/6		
Redness		4/6	3/6	0/6		0/6		
Chemosis		4/6	3/6	0/6		0/6		
Discharge								

Comments: No iris involvement, Corneal involvement absent by day 3. Conjunctival redness absent by day 7 (present through day 3)

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DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (211)

ID No.: 87177

Testing Laboratory: Bio/Dynamics

Author(s): N. H. Wilson

Species: Rabbit, N2 White

Sex: 9 M/F

Weight:

Source: Dutchland Lab. animals, Denver, PA.

Age: 0.1 ml

Test Material: T-111-3 (Bravo 500), liq

Quality Assurance (40 CFR §160.12): adequate

Reviewer: M. Waller

Report Date: 5-11-90

Report No. 6504-80

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Summary:

Tox. Category: III Classification: Guidelines

Procedure (Deviation from §81-4): 0.1 ml instilled into eye of each of 9 subjects. 20 sec. after application (to conjunctival sac), treated with 3 rabbits washed for 1 minute in 100 ml water. All treated eyes examined and scored for irritation @ 24, 48, 72 hours and at 4, 7, 14 days, and at 21 days.

	Observations (number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea		6/9	5/9	3/9	0/9	0/9	0/9	
Opacity		0/9	0/9	0/9	0/9	0/9	0/9	
Conjunctivae		9/9	9/9	5/9	3/9	0/9	0/9	
Redness		7/9	7/9	6/9	11/9	6/9	0/9	
Hemorrhage		8/9	6/9	3/9	0/9	0/9	0/9	
Discharge								

Comments: No iris involvement, Corneal involvement absent by day 4. Conjunctival irritation absent by day 7.

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DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: (21)

Reviewer: ~~W. Waller~~ Woodrow

MRID No.: 158493

Report Date: 5-10-90

Testing Laboratory: WIL Res. Labs., INC.

Report No. WIL-11006

Author(s): D. J. Nass

SDS-2787

Species: Rabbit, NZ White

Sex: 6M & 3F NZ+

Weight: _____

Source: Mexican Valley Rabbitry, O.

Dosage: 0.1ml

Test Material: Bevo 720 (54.0% A.I.), liquid

Quality Assurance (40 CFR §160.12): adequate

Summary:

Tox. Category: II

Classification: Guidelines

Procedure (Deviation From §81-4): 0.1ml undiluted test material

instilled into the conjunctival sac of 6 male & 3 female, 20-30
 seconds after treating eyes of 3 males, these eyes were
 flushed ~ 100ml tap water. Eyes examined and scored for
 irritation according to Draize @ 1, 2, 4, 48, 72 hours, and days 4, 7,
 10, 14, and 24 post dosing.

	Observations (number "positive"/number tested)								
	Hour	Days							
	1	1	2	3	4	7	14	21	
Cornea	0/6	2/6	3/6	1/6	0/6	0/6	0/6	0/6	
Opacity	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	
Iris	0/6	0/6	0/6	0/6	0/6	0/6	0/6	0/6	
Conjunctivae	6/6	6/6	6/6	6/6	6/6	3/6	0/6	0/6	
Redness	5/6	6/6	6/6	6/6	6/6	3/6	1/6	0/6	
Chemosis	3/6	3/6	4/6	3/6	1/6	1/6	1/6	0/6	
Discharge									

Comments: The scores for the 3 washed (treated) rabbit eyes were
 considerably lower than comparable scores for unwashed eyes;
 therefore washed scores were not utilized to derive Tox. Cat.

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Worleiw

Product Manager: (211)

Reviewer: M. Miller

MRID No.: 81308

Report Date: 5-10-90

Testing Laboratory: Bio/dynamics, Inc.

Report No.: 4503-77

Author(s): P.H. Heenchan

Species: Rabbit, N 2 white

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Age: not stated

Sex: 3M/3F

Weight: 2.15-2.45 kg.

Dosage: 0.5ml undiluted

Test Material: Bravo 500 (compound 8641-125) - 40.4% Tech. Chlorothalonil

Quality Assurance (40 CFR §160.12): none

Summary:

The Primary Irritation Index = 1.3

Toxicity Category: IV

Classification: Guidelines

Procedure (Deviations From §81-5): 0.5ml undiluted test material applied to 1 intact and to 1 abraded test site of on clipped back of each of 6 rabbits under 1" sq. gauge. Dress secured with tape/cinnimils wrapped in plastic sheeting secured E. tape 24 hours contact. Animals observed and scored for Results: irritation at 24 and 72 hours post application.

(Erythema/edema/eschar)		mean scores
24hrs intact skin	Erythema	0.7
	Edema	0.5
Abraded skin	Erythema	0.8
	Edema	0.7
72hrs intact skin	Erythema	0.8
	Edema	0.3
abraded skin	Erythema	1.2
	Edema	0.2

Special Comments:

$5.2 = 1.3 = \text{P.I. Index}$

total 5.2

mild or slight irritation @ 72 hrs: Tox.

Category IV

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DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: (211) Reviewer: Woodrow
 MRID No.: 405460-02 Report Date: 5-8-90
 Testing Laboratory: WIL Ros. Lab., Inc. Report No. SDS/2787
 Author(s): S.K. Schultz, M.H. Wilson
 Species: Swine pigs
 Sex: 24M, 24F Weight: 300-450 g
 Source: Buckshire Corp.
 Test Material: Bravo 720 (Batch NO. J-194-1) 54.0% w.i.
 Positive Control Material: dinitrochlorobenzene (DNCB)
 Quality Assurance (40 CFR §160.12): Adequate
 Method: Modified Bruker closed patch - repeated irrit.

Summary:

1. This product ☒ is / is not a dermal sensitizer.
2. Classification: Guidelines

Procedure (Deviation From §81-6): Arrange finding study was conducted to determine the irritation potential of the test material (Bravo 720) & + control dinitrochlorobenzene (DNCB). Undiluted Bravo 720 & concentrations in 80% ethanol and acetone were used.
 Results: in the main study.

Procedure: quoted from the test's report:

Group	Test/Control Materials	Number of Animals	Concentration		
			Induction	Challenge	Rechallenge
I	Bravo® 720	12 (♂, ♀)	100%	100%	100%
II	DNCB (Positive Control)	12 (♂, ♀)	0.1%	0.05%	0.05%
III ^b	Bravo® 720 (Irritation Control-Challenge)	12 (♂, ♀)	--	100%	--
	DNCB (Irritation Control-Challenge)		--	0.05%	--
IV ^c	Bravo® 720 (Irritation Control-Rechallenge)	12 (♂, ♀)	--	--	100%
	DNCB (Irritation Control-Rechallenge)		--	--	0.05%

^aBravo® 720 was administered in undiluted form during the induction, challenge and rechallenge phases of the study. DNCB was administered in 80% ethanol for the induction phase and in acetone for the challenge and rechallenge phases of the study.

^bThis irritation control group was treated only at challenge. The same twelve animals served as irritation controls for the test and positive control materials.

Unquote.

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Induction: 3 applications per week, 9 total; to clipped backs of animals. Dose volume was 0.4 ml. Daxypatches, dental dam & tape secured patches. 6 hour exposures. Irritation scored for @ 24 & 48 hours after the initial application, and 24 hours after subsequent applications. (4 days after last induction application animals challenged at a previously unexposed (naive) site. Naive (control) animals challenged at separate sites with test and positive control materials - sites scored at 24 & 48 hours after application. Each animal in test and positive control groups re-challenged at naive sites. All animals spanned 2x daily for health.

Results:

- 1) Positive control: DNCB did irritate guinea pigs.
- 2) Bravo 720. In order to calculate numbers for each challenge & re-challenge individual results @ 24 hours, $\pm$ results were considered 0.5 :

Challenge	24 hrs	Irritation	24 hrs
Bravo 720 Mean =	<u>0.66</u>	control	<u>0.38</u>
Rechallenge Mean =	<u>0.54</u>	control	<u>0.17</u>
Bravo 720			

Conclusion:

Bravo 720 is a weak irritating agent.