4-23-93

MEMORANDUM:

Subject: EPA File Symbol/EPA Reg. No.:63836-R

From: Lucy D. Markarian, Biologist 4 3/9/93
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

To: Cynthia Giles-Parker, PM 22
Fungicide-Herbicide Branch
Registration Division (H7505C)

Thru: Thomas C. Ellwanger, Section Head E 4/23/93
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

Applicant: Foster Products Corporation
3200 Labore Road
Vadnais Heights, MN 55110

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Barium Metaborate	9.00 %
3-Iodo-2-propynyl Butyl Carbamate	0.16 %
Inert Ingredient(s):	
.....	90.84 %
Total:	100%

94

BACKGROUND

Foster products has submitted six tests to support the registration of Foster 40-20 Fungicidal Protective Coating under EPA symbol 63836-R

RECOMMENDATION

With the exception of the inhalation data the submitted tests are accepted as support for the registration of Foster 40-20 FB-71. A new inhalation test is recommended that is conducted as suggested below. The rationale for the evaluation of the test is as follows:

Oral toxicity- Core minimum

Whenever there is mortality at the limit test, the guidelines recommend that an LD_{50} study must be conducted. The test used only two levels to estimate the LD_{50} of the product. There was 1/10 death at the second and lower level also. There should have been another level to comply with the guidelines.

Inhalation Toxicity - Supplementary

It is not certain what the concentration of the diluted test material was after the lumps were removed from the diluted material. The sample was not analyzed. The concentration in the chamber was extrapolated on the belief that there was a real 50 % w/w dilution. By the removal of the clumps of material by sieving it is not known if the concentration remained the same or was in effect more dilute.

The MMAD of 6.6 um is too large to be respirable by the test model. Even when it is claimed that 22 % were 3.3 um or under. According to the presented results from the particle size analyses, only 10 to 12 % were under 2.9 um. This is not acceptable even with more relaxed requirements for particle mass.

During the trial efforts particle size should also have been considered. There is no record of this. Particle size is just as important as the concentration. Regardless of concentration the test material has to be respirable if the test is to be considered valid.

It is recommended that a new inhalation test be submitted. One that determines the particle size prior to exposure during trials and uses a known concentration of the test material that is determined prior to exposure if any clumps are to be removed from the solution.

Dermal sensitization- Core minimum

The results of the challenge were not as clear cut as desirable. A rechallenge at a slightly lower concentration would have been more decisive. Persistence of ± reaction in 8/10 animals suggests the possibility of sensitization. This was twice the number that showed irritation in the control group. The test is accepted ,because ± effects are not considered positive.
PRS would like to see the results of the most recent control test rather than the summarized results of what the laboratory considers positive results, to reach independent conclusions. The submission of these results is recommended for future submissions.

LABELING

At the present time the signal word is CAUTION as it appears on the presented label.

The precautionary statement needs to be revised to read:

Harmful if swallowed or absorbed through skin. Causes moderate eye irritation. Avoid contact with skin or eyes or clothing. Wash thoroughly with soap and water after handling.

The statement of practical treatment should read:

If swallowed	Call physician or poison control center. Drink one or two glasses of water and induce vomiting by placing finger at the back of throat. 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 eyes with plenty of water. Get medical attention if irritation persists.

The precautionary labell[ing] may have to be revised if the requested data necessitates it.

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

Product Manager:22 **Reviewer:** L. Markarian
MRID No.: 424948-01 **Report Date:**9/2/92
Testing Facility: Springborn Laboratories **Report No.**3285.1
Author(s): Rusty E. Rush
Species: Rat, Sprague Dawley
Age: Young adult
Weight:M 217-258 g, F 212-239 g
Source: Charles River Laboratories, Portage, Michigan
Test Material: Foster 40-20 FB-71
Quality Assurance (40 CFR §160.12): Included

Conclusion:

1. **The estimated LD_{50} is** > 4000 mg/kg
2. **Tox. Category:**III **Classification:**core minimum

Procedure (Deviations from §81-1):

Fasted animals were intubated with the test material at two levels. Observations were frequent on the day of intubation and daily thereafter. Body weights were recorded at initiation and on days 7 and 14. Necropsy was performed on all animals.

Results:

Dosage mg/kg	(Number Killed/Number Tested)		
	Males	Females	Combined
5000	2/5	3/5	5/10
4000	0/5	1/5	1/10

Symptoms & Gross Necropsy Findings:

Among the animals that died included decreased activity, shallow or labored respiration, rales, soft stools or diarrhea, salivation, prostration and staining of the face, urine and fecal stains. The survivors at 5000 mg/kg showed few feces/soft stools, decreased activity and salivation. At 4000 mg/kg the survivors were generally asymptomatic.
Among the decedents necropsy revealed signs of gastrointestinal distress and congested meningeal vessels of the brain, and mottled lungs.

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

Product Manager:22 **Reviewer:** L. Markarian
MRID No.: 424948-02 **Report Date:**9/2/92
Testing Laboratory: Springborn Laboratories **Report No.:**3285.2
Author(s): Rusty E. Rush
Species: Rabbit, New Zealand White
Weight:2050 to 2934 g
Source: Mohican valley Rabbitry, Loudunville, Ohio
Test Material: Foster 40-20 FB-71
Quality Assurance (40 CFR §160.12): Included

Summary:

1. **The estimated LD_{50} is** > 2000 mg/kg

2. **Tox. Category:**III **Classification:**Guideline

Procedure (Deviation From §81-2):

Undiluted test material was applied to the clipped skin of the animals. Effort was made to spread the test material on an area covering 10 % of the body surface. However an area of 4 X 8 inches could be covered. The site was covered with 8 ply gauze and plastic wrap secured with tape. At 24 hrs the wrappings were removed and the site wiped with gauze moistened with distilled water. It was not possible to remove all the test material. Elizabethan collars were placed around the necks to avoid ingestion.
Observations were frequent on the day of application and daily thereafter. There were twice daily mortality checks. Body weights were recorded at initiation a nd on days 8 and 15. Necropsy was performed on all animals.

Results:

Reported Mortality

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

Symptoms & Gross Necropsy Findings:

Symptoms of toxicity included fecal or urine stains, soft stools, dark exudate around the nose and dermal irritation. The females showed weight loss on day 8,however, showed gains at termination. Dermal irritation was manifested as mild to moderate erythema and edema, desquamation and thickening of skin.
Necropsy revealed no product related abnormalities. The periovarian cysts in the females are considered normally occurring by the laboratory.

98

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

Product Manager:22 **Reviewer:** L. Markarian
MRID No.: 424948-03 **Report Date:**9/3/92
Testing Laboratory: Springborn Laboratories **Report No.:**3285.3
Author(s): Rusty E. Rush
Species: Rat, Sprgue Dawley
Weight: M 233-250 g, F 230-246 g
Source: Charles River Laboratories, Portage, Michigan
Test Material: Foster 40-20 FB-71
Quality Assurance (40 CFR §160.12): Included

Summary:

1. **The estimated LC_{50} is**

2. **Mean Concentration:**

3. **Tox. Category:** **Classification:**Supplementary

Procedure (Deviation From §81-3):

Several generation systems were tested prior to the study to achieve the highest possible concentration in the exposure chamber. None of the trials, however makes any reference to measuring the particle size distribution at any of these generation systems.

Exposure was in a RHS-100L whole body inhalation chamber for four hours. There was a 3 minute equilibration period. This and another 3 minutes for deequilibration was added to the exposure time.

The test atmosphere was generated using two spraying systems 1650/73160 SS atomizers in conjunction with initially with one (first 33 minutes), and then with two RH-1 nebulizers. Dried filtered and pressurized air was used in the generation. The chamber was maintained at a slightly negative pressure during exposure.

Prior to aerosolization the test material was diluted to 50 % with distilled water and passed through a 60 mesh sieve, because it was too viscous and had clumps of material that would clog the atomizer. The laboratory states that the sponsor was responsible for any necessary evaluations related to the composition, purity strength, and stability of the product. The diluted product was not analyzed after the clumps were removed.

Chamber air flow, temperature and humidity were monitored continuously and recorded at 30 minute intervals.

Chamber concentrations were determined at 30 minute intervals starting at 3 minutes (equilibration time) by sampling from the breathing zone with a glass fiber filters. The determined weights were multiplied by 0.5 to account for the 50 % dilution of the test material.

99

Particle size determination was made twice during the exposure using an ITP 7 L/minute cascade impactor.

Upon removal from the exposure chamber the animals were washed with lukewarm water and dried to remove residue from the fur of the animals and avoid ingestion.
Observations were made twice on the day of exposure, and daily thereafter. There were twice a day mortality checks.

Body weights were recorded at initiation and on days 8 and 15. Necropsy was performed on all animals.

Results:

Chamber Concentration	5.15 mg/L
Range	4.38 - 6.06
MMAD Average	6.6 um
% under 2.9 um	10 - 12
Temperature ^{o}**F**	72.3 - 74.8
Humidity %	89.2 - 98.9
Air flow Time weighted mean	263 lpm
Mortality	
Males	0/5
Females	0/5

Clinical signs	Test material matted on coat
	Rough coat
	Decreased activity
	Swollen eye lids
	Dark material around nose/eyes/ mouth
	Urine stains
	Few Feces
	Hair Loss
Necropsy Findings	9/10 no gross pathology
	1/10 dark red foci on both lobes of thymus

8

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

Product Manager:22
MRID No.: 424948-04
Testing Laboratory: Springborn Laboratories
Author(s): Rusty E.Rush
Species: Rabbit, New Zealand White
Sex: 3 M and 3 F
Weight:2.2 - 2.4
Source: Mohican Valley Rabbitry, Loudonville, Ohio
Dosage:0.1 ml
Test Material: Foster 40-20 FB-71 opaque white liquid
Quality Assurance (40 CFR §160.12):

Reviewer: L. Markarian
Report Date:9/2/92
Report No.:3285.4

Summary:

1. **Toxicity Category:**III

2. **Classification:** Guideline

Procedure (Deviations From §81-4):
Undiluted test material was instilled in the conjunctival sacs of six pre examined eyes. Observations were at 1, 24, 48, and 72 hrs. Fluorescein was used to confirm corneal findings. Draize scoring system was used.

Results:

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

Comments:

9

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

Product Manager:22
MRID No.:424948-05
Testing Laboratory: Springborn Laboratories
Author(s): Rusty E. Rush
Species: Rabbit, New Zealand White
Age: Young adult
Sex: 3 M and 3 F
Weight:2.2 - 2.5 K
Dosage:0.5 ml
Test Material: Foster 40-20 FB-71
Quality Assurance (40 CFR §160.12): Included

Reviewer: L. Markarian
Report Date:9/2/92
Report No.:3285.5

Summary:

1. **The Primary Irritation Index** =0.83

2. **Toxicity Category:**IV

3. **Classification:** Guideline

Procedure (Deviations From §81-5):

Undiluted test material was applied to the clipped backs of six animals on 1 X 1 inch area, covered with gauze patch and the trunks of the animals wrapped in elastic semiocclusive bandage. At 4 hrs the wrappings were removed and the sites wiped with moistened gauze. The sites were evaluated at 1, 24, 48, and 72 hrs according to Draize.

Results:

At one hour all sites showed grade 1 or 2 erythema with 4/4 showing grade 1 edema and 1/6 grade 2 edema. At 24 hrs all sites showed grade 1 erythema with no edema. At 48 hrs all irritation had resolved.

Special Comments:

10

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

Product Manager:22
MRID No.: 424948-06
Testing Laboratory: Springborn Laboratories
Author(s): Rusty E. Rush
Species: Guinea Pig, Hartley
Weight:325 - 379
Source: Harlan Sprague Dawley, Inc.,Indianapolis Indiana
Test Material: Foster 40-20 FB-71
Positive Control Material:DNCB
Quality Assurance (40 CFR §160.12): Included

Reviewer: L. Markarian
Report Date:9/2/92
Report No.:3285.6

Method: Modified Buehler

Summary:

1. **This Product is not a dermal sensitizer.**

2. **Classification:**Core minimum

Procedure (Deviation From §81-6):

A pretest screening was made for the definition of the induction and elicitation concentrations. Four aqueous concentrations were applied to four guinea pigs for six hours in 0.4 ml aliquots on Webril patches. The trunks of the animals were wrapped in Expandovar stretchable bandage. the results were evaluated at 24 and 48 hrs. At 100 % there were 3/4 ± reactions and 1/4 0 reactions, At 50 % there were 4 ± reaction and 3/3 0 reactions. The induction and elicitation were conducted at 100 %.
All applications were made in the same manner as the preliminary screening. there were three inductions applied one week apart for three weeks. Challenge was two weeks after the last induction made at a naive site. A group of naive controls were also challenged. There were ten animals in each group. The skin was depilated prior to evaluation. The Buehler scoring system was used.

Reference is given to 21 control tests conducted between 9/90 and 3/92 using 0.5 % DNCB in acetone ethanol solvent for induction and 0.1 to 0.3 % of the same for challenge. Naive controls were used. The actual results of the tests are not given. The laboratory claims 99 % sensitization.

Results:
After the first induction 8/10 animals showed ± reactions at 24 hrs. After the two subsequent inductions 5/10 animals showed the same degree of slight irritation. At challenge all animals in both groups showed ± reactions at 24 hrs. This reaction persisted in 8/10 animals at 48 hrs in the test group, and 4/10 in the naive control group. The laboratory has concluded that the test material is not a sensitizer.

Tox Chem No: 011101 Barium Metaborate
107801 Iodo-2-Propynyl Butylcarbamate

Current date 3/9/93

Laboratory: Springborn Laboratories, Inc., Life Sciences Division
553 North Broadway, Spencerville, Ohio 45887

STUDY	MATERIAL	MRID NO	RESULTS	TOX CAT	CORE GRADE
Oral Toxicity Limit test 3285.1 9/2 /92	Foster 40-20 FB-71	424948-01	LD_{50} > 4000 mg/kg	III	Minimum
Dermal Toxicity Limit test 3285.2 9/2/93	" " " "	424948-02	LD_{50} >2000 mg/kg	III	Guideline
Acute Inhalation Limit test 3285.3 9/3/92	" " " "	424948-03		Supplementary	
Eye Irritation In rabbits 3285.4 9/2/92	" " " "	424948-04	Clear within 7 days	III	Guideline
Dermal irritation In rabbits 3285.5 9/2/92	" " " "	424948-05	PII 0.83	IV	Guideline
Dermal Sensitization	" " " "	424948-06	Not sensitizer	NA	Minimum

401