

BACKGROUND: BASF corporation had submitted the six required tests in support of their product Dazomet and was reviewed as of October 3, 1976. The oral toxicity data was found to be acceptable, however the acute dermal and inhalation toxicity tests, the eye and dermal irritation and sensitization studies were found to be supplementary.

At the present time these studies are submitted for review: Acute Inhalation toxicity and eye and dermal irritation studies performed at the Toxicology Department of the BASF Aktiengesellschaft in West Germany.

RECOMMENDATION:

1. The inhalation study is core guideline data and is acceptable.
2. The eye irritation test is core minimum data but acceptable.

There must be indications that the eyes were examined during the 24 hours preceding the test. The absence or the presence of opacity must be confirmed by fluorescein dye, and conjunctival irritation must include discharge scores according to the guidelines.

3. Dermal irritation data is considered supplementary. According to the guidelines the test material, if solid, must be applied as is, but moistened by first weighing 0.5g and then moistening it with an appropriate amount of water which is generally indicated. An aqueous

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RECOMMENDATION: (cont)

suspension (50% w/w) does not fit this description.

The wappings must be semioclusive.

It is recommended that new data in dermal irritation be submitted that uses undiluted test material for the applications.

4. The applicant must still present acute Dermal Toxicity and sensitization data to complete the registration requirements.

The Review of the Label must be postponed until such time as the requested information is received and reviewed.

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The Animals were observed daily for 14 days - Body weights were taken at initiation and on days 7 and 14. Viability check was made daily. Necropsy was performed on all animals.

Results

Gravimetric Analysis	Group I	Group II	Group III
	4.05	5.73	6.21
	4.74	4.80	8.25
	3.09	4.85	8.91
	3.45	5.06	10.23
Mean	3.83 ± 0.72	5.11 ± 0.43	8.40 ± 1.68
Nominal Concentration	39.1	59.9	85.2
Particle Size			
5.5 μ m	14.6	26.4	19.6
2.2 μ m	38.1	37.0	32.5
1.2 μ m	10.8	9.6	11.4
< 1.2 μ m	11.2	—	5.3
M.M.A.D.	5.2 μ m	2.14 μ m	6.10 μ m
Geometric standard deviation	3.7	1.7	2.7

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The major signs of toxicity during exposure included diminished pain reflex after 1.5 hr in Group III and attempts to escape were noticed. Following the exposure tremulous gait, reddish nasal discharge, yellow smeared abdominal fur, red concentration of noses, piloerection, squatting posture, reddish urine, anemia in general and pinpoints observed are in group III. The reddish color of the nose and the blood in the reddish urine & anemia were confirmed by blood tests.

Although most of the symptoms subsided abnormalities such as blood in the urine, yellow smears on the fur, slightly dragging hindlimbs and piloerection persisted in group 3 animals. Weight gains were normal among the survivors.

The necropsy of the animals that succumbed to treatment in groups II & III showed general congestive hyperemia. At 3.4 mg/l one male showed minimal emphysema and 2 females intensified hyperemia.

No gross abnormalities were observed in the survivors.

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

Product Manager: (21) Reviewer: L. Markarian
 MRID No.: 415680-02 Report Date: 8/20/90
 Testing Laboratory: BASF Aktiengesellschaft Report No. 35-0389
 Author(s): Dr. J. Kieczka
 Species: Rabbit, Vienna white
 Sex: 2 ♂ 4 ♀ Weight: 2.82 - 2.94 kg
 Source: Gaukler, D-6050 Offenbach/Main FRG
 Dosage: 0.1 ml undiluted
 Test Material: Dozomet 85/312 technical active ingredient white powder
 Quality Assurance (40 CFR §160.12): included

Summary:

Tox. Category: IV Classification: core minimum

Procedure (Deviation From §81-4): 0.1 ml (pulverized powder 39 mg) of test material was instilled in the right conjunctival sac. No indication if the eyes were examined prior to test. Evaluations at 1, 24, 48 & 72 hrs after instillation. The presence or the absence of corneal lesions is not verified by fluorescein stain. No record of discharge at any interval

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	0/6	0/6	0/6	0/6				
Conjunctivae Redness	6/6	6/6	1/6	0/6				
Chemosis	4/6	0/6	0/6	0/6				
Discharge	-	-	-	-				
Pupil Contracted	5/6	0/6	0/6	0/6				

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Comments: The guidelines specify that the eyes must be examined within 24 hrs of the initiation of the test and the findings confirmed by the use of fluorescein dye. There is no indication that this was done, neither was the absence of any corneal lesion confirmed by fluorescein dye. No discharge evaluations were not made. Therefore the study is core minimum data.

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

Product Manager: (21) Reviewer: L. Markarian
 MRID No.: 416630-01 Report Date: 8/20/90
 Testing Laboratory: BASF Aktiengesellschaft Report No. 85/0389
 Author(s): Dr. H. Kieczka
 Species: Rabbit, white Vienna, Goukier: D-6050 Offenbach/Main Ger.
 Age: not specified
 Sex: 2 ♂ 4 ♀
 Weight: 2.82 - 3.14 Kg
 Dosage: 0.5 g of suspension 50% w/w
 Test Material: Dazomet (85/313) Technical active ingredient (98.2% pure)
 Quality Assurance (40 CFR §160.12): included

Summary:

The Primary Irritation Index = 0

Toxicity Category: _____

Classification: Supplementary

Procedure (Deviations From §81-5): The test material was applied to the skin by covering a 2.5 x 2.5 cm patch with 0.5 mm layer of the 50% w/w aqueous suspension and placing it on the skin. The diluent was distilled water. Exposure was for 4 hrs. The trunks of the rabbits were not wrapped in impervious material, but in porous bandage. Observations were at 4, 24, 48 & 72 hrs. Scoring was according to a scale similar to Draize

Results:

No irritation was recorded for any animal at any interval

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Special Comments:

Placement of 1mm of a suspension that weighed 0.5 gram on the patch and then applying this to the skin does not constitute a bona fide 0.5g application that has been moistened according to the guidelines. Therefore the test is classed as supplementary data.