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| Document Title TOXICOLOGY STUDIES ON GLYCIDYL METHACRYLATE WITH ATTACHMENT AND COVER LETTER DATED 02/28/84 | | |
| Chemical Category GLYCIDOL & DERIVATIVES | | |

CAS # 100-91-2

40-8440 442

[21-0091]-92 VII-B

6(157)

Marubeni AMERICA CORPORATION

200 PARK AVENUE • NEW YORK, N. Y. 10166 • (212) 599-2222
3958

February 28, 1984

TSCA Public Information Office (TS-793)
Opts, Room E-108
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

1984 FEB 29 11 05 AM

To whom it may concern:

RE: ANPR-OPTS-42051

Enclosed please find copies of our manufacturer's comments in triplicate on ANPR-OPTS-42051 regarding our product Glycidyl Methacrylate (GMA).

Since these were sent from Japan by facsimile, you may have some difficulties in reading those. The original letters will be sent to you as soon as we receive from Japan.

Following are our sales records for our 28 customers in the U.S. and Mexico: (Unit: 1,000lbs)

| 1979 | 1980 | 1981 | 1982 | 1983 |
|------|------|------|------|------|
| 171 | 139 | 182 | 251 | 340 |

Our sales price has been in the range of US\$3.05 - 3.50 per lb. To our best knowledge, performance will be the key market factor because of high price of our product compared with other monomers.

We respectfully request that we be kept informed of the position regarding GMA relative to the other proposed glycidyl ester studies so that we may make the necessary scientific and business decisions concerning this product.

Sincerely yours,

H. Iwamoto
Vice President



NIPPON OIL & FATS CO., LTD.

(NIPPON YUSHI K. K.)

OIL & FAT PRODUCTS AND CHEMICALS DIV
EDIBLE OILS & FATS DIV.
PAINTS DIV.
CHEMICALS & EXPLOSIVES DIV
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OUR REF

YOUR REF

TSCA Public Information Office (TS-793)
Office of Pesticides and Toxic Substances
Environmental Protection Agency
Room E-108, 401 M St., SW.
Washington, D.C. 20460

Handwritten signature

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Reference : Document Control Number (OPTS-42051)

Gentlemen:

This notice is submitted in accordance with the EPA's "Toxic Substances; Glycidol and its Derivatives; Response to the Interagency Testing Committee, Advance Notice of Proposed Rulemaking" published on December 30, 1983, at FR/Vol. 48 No. 252.

The chemical substance in this subject is :

Glycidyl Methacrylate (GMA)

CAS Registry Nos.
106-91-2

This chemical substance is to be put into Subcategory VII.

It is manufactured by Nippon Oil & Fats Co., Ltd., Product and Chemicals Division which plant is located at Amagasaki city, Hyogo Prefecture, Japan and Marubeni America Corporation imports approximately 200,000 lbs. into the United States annually.

Toxicity tests were conducted in the period of Feb. 25 - Jul. 5, 1969 by "Kitazato University, Japan" by patch test, acute dermal toxicity and inhalation test. The following conclusion was reached:

"As long as the quantity of GMA is small, local and overall disorder so caused are mild."

Copies of test report by "Kitazato University" are enclosed herewith.

Nippon Oil & Fats has neither commissioned nor conducted any additional tests and has no other data which can disprove the result of Ames test on GMA whether it is mutagenic, carcinogenic and teratogenic.

However, it is understood that GMA does not give adverse health effects from chemical characteristic point of view as well as Nippon Oil & Fats's experience for 15 years production.

Vapour pressure at 50 c.degree is 2.5mmHg, while those of Butyl Glycidyl Ether and Allyl Glycidyl Ether are 9.2mmHg and 17.5mmHg respectively.

Accordingly the chances of inhalation and dermal contact of GMA can be relatively less.

Furthermore, GMA is used solely in formulation various plastics and resins, and is used at less than 10% of the formulation. In the reaction, GMA combines with the other polymeric moieties and no free monomer is expected to remain. Although these formulations include such consumer product as latex and acrylic paint, synthetic fiber and binders, the public is not exposed to GMA and we do not know of any complains.

Although Nippon Oil & Fats's data provided herewith would appear poor to disprove the carcinogenicity and others, the experience for 15 years without adverse health effect could reasonably prove that overall disorders are mild.

Finally Nippon Oil & Fats company's point of view, the sales amount does not justify to share the test cost with respect to carcinogenicity, mutagenicity, teratogenicity, epidemiology and other chronic effects which is estimated a few million dollar at maximum level.

Meanwhile, although Nippon Oil & Fats believe the data of acute testing, enclosed herewith, on GMA is enough, Nippon Oil & Fats will consider to commission or conduct again acute toxicity test with respect to oral LD50, dermal LD50, primary eye irritation, primary dermal irritation and dermal sensitization, if it is required.

Should you have any questions concerning this notice, please feel free to contact to :

Mr. T. Banno
Marketing Manager of Chemical Dept.
Marubeni America Corporation
42nd Floor Pan American Bldg.
200 Park Ave. New York, N.Y.10166
Telephone : 599-3956

Vety truly yours,


Y. WADA, Manager
Overseas Trade Section
Nippon Oil & Fats Co., Ltd.
Product and Chemicals Div.



NIPPON OIL & FATS CO., LTD.

(NIPPON YUSHI K. K.)

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OUR REF

YOUR REF

TOXICOLOGY STUDIES

ON GLYCIDYL METHACRYLATE

Description: This is a summary of single exposure studies on animals. The data indicate the relative degree of hazard in handling the product. Increasing degrees of hazard are expressed by these terms: slight, moderate, definite, serious. It must be remembered that results of experiments on animals cannot be numerically translated to probable human response.

Result: Single Oral Dose To Rats: Definite Hazard.
LD₅₀ - 0.77 ml per kilogram body weight.
For comparison, ethyl acrylate has an LD₅₀
1.02 gm per kilogram which is in the general class of but less toxic than aniline.

Single Skin Penetration In Rabbits: Definite Hazard.
LD₅₀ - 0.45 milliliters per kilogram body weight.
This result suggests that skin penetration in harmful amounts may occur after moderate contact in terms of skin area involved and duration of contact. Skin contact is to be avoided.

Single Inhalation By Rats: Moderate Hazard.
A 4 hour exposure to concentrated vapors formed at room temperature killed 4 of 6 rats. A 4 hour exposure to a known concentration of 600 ppm did not kill any of 6 rats.

Skin Irritation: Definite Hazard.
The undiluted chemical caused redness and swelling comparable to a mild first-degree burn on the tender skin of the rabbit belly.

Eye Injury: Moderate Hazard.
This chemical produces injury no more severe than that seen with liquid hand soaps. In case of eye contact, the eye should be given a 15 minute emergency wash.

SPECIAL INSTRUCTIONS

BLEMNER-G HANDLING DATA

If you handle Blemmer-G, please notice the following:

"BLEMNER-G HAS MEMBRANE IRRITATION PROPERTY AND WHEN IT CONTACTS THE SKIN, INFLAMMATION OCCURS, SO SPECIAL CARE MUST BE TAKEN WHEN HANDLING."

1. Special care for the leakage of GMA production line.
"PLEASE AVOID ANY KIND OF GMA LEAKAGE."
2. Because of the vapors of GMA, it is necessary to have adequate ventilation.
3. All operators should wear rubber gloves, safety glasses, safety shoes and rubber aprons.
4. Before operation, each operator should use protective cream which is sold for epoxy resin from CIBA-GEIGY.
5. After each operation, each operator should wash his hands and face with soap.

When it contacts the skin, it must be washed away immediately with a large quantity of water or soapy water for ten minutes. Even though pain or itching is not felt after the skin has contact with GMA, burning symptoms may occur. So it is very important to wash the skin thoroughly with water. When vapors of GMA fill the room, and pain is felt, immediately the operator should leave the room and wash eyes with sufficient water.

TEST RESULTS

Material tested : Blemmer G
Kind of tests : Toxicity tests
Requested by : Nippon Oil & Fats Co., L.T.D.
1-5, Yuraku-cho, Chiyoda-ku, Tokyo, Japan

The results of our tests on the above material which was submitted to our Department on February 5, 1969 are given in the attached papers.

August 13, 1969

Sadakichi Fukuzumi Professor,
Section of Drug Investigation,
Department of Pharmacy,
Kitasato University

Toxicity Tests on Blenmer G

Material tested: Blenmer G (Lot No. 81102, PH 5.0)

Experimental animals: Male albino rabbits

Test period: Feb. 25 - Jul. 5, 1969

Animal feeding conditions:

Housed in constant - temperature constant-humidity feeding chambers
($20^{\circ} \pm 2^{\circ}$, 50 - 60%)

Diet : Rabbit-use pellets made by Oriental
(RC-5)

Water given : Tap water

Feeding chambers: Individual-use rabbit feeding chambers
made by Tokiwa

The rabbits were fed under the above-mentioned conditions for about a week after being purchased (from Itsukida Shoten in Tokyo), and were then subjected to the Tests.

Testing Method

1. Patch Test

After 12 rabbits were fed for a week; they were divided into 2 groups (6 each), one of which then had their back skin abraded, the other left with theirs intact.

Intact skin : It was obtained by shearing back hairs with electric clippers.

Abraded skin : It was obtained by shearing back hairs with electric clippers and then abrading scarf skin with the aid of BaS hydrophilic ointment.

2 days later, 6 round pieces of lint of a 15mm diameter impregnated with different solutions were attached on the abraded or intact back skin of each rabbit. The pieces of lint (patch test-use adhesive plaster by Torii, Yakuhin K.K.) were beforehand impregnated respectively with 0.25ml and 0.13ml of Blemmer G and, as control, 0.25ml each of dilute hydrochloric acids of PHs 5.0 and 4.4. 24 hours after the attachment, the patches were removed and observations were made to assess the degrees of skin irritation 24 hours and 72 hours after the start of the patch application.

In addition, the rabbits were also observed for their symptoms, body weights and daily average feed consumptions.

2. Acute Dermal Toxicity

6 rabbits were divided into 2 groups and had their backs pretreated in the same manner as in the Patch Test. Then, the following quantities of Blemmer G were each applied on the portion of the back of each rabbit which was equivalent to about 10% of his total body surface area. 1 ml/kg of body weight, 2 ml/kg and 3 ml/kg were applied respectively on 3 rabbits of each group for observation of time required for death, symptoms, body weight change and feed consumption. Immediately after death, autopsy and then histopathological observations were made.

3. Inhalation Test

3 rabbits were fixed in an exposure chamber. 1.5 ml/kg of Blemmer G was sprayed over them with a sprayer for 5 seconds and they were kept in the foggy environment for 15 minutes. This procedure was repeated 20 times successively (total quantity: 30 ml/kg).

Each rabbit was examined before and 72 hours after start of the inhalation for urine (urine proteins, urine sugars, urine PH), liver and renal functions (S-GPT, urea nitrogen) and blood. Upon completion of the above examinations, dissection was made for histopathological examination on various organs.

For the histopathological examination, tissues after autopsy were treated by 10% formalin fixation and paraffin embedding to obtain sample sections, which then undertook microscopic observations upon having hematoxylin and eosin stains and as necessary, lipophilic stain.

Patch Test

Patch Test

Symptoms

No particular symptoms were found.

Body weight

No significant changes were found in body weights, except slight decrease tendency for 2 cases of the intact skin group (No. 3 and No. 4) and 1 case of the abraded skin group (No. 10).

Average feed consumption

The above-mentioned rabbits with slight weight decrease also showed decrease in feed ingestion. However no remarkable change was found on other rabbits.

Assessment of patch test results

Application of 0.25 ml of Blenner G gave marks of 5.2, meaning "Medium" irritation. The cases with 0.13 ml showed marks of 3.6, also meaning "medium" irritation.

The rabbits with abraded skin showed medium erythema mostly with crust formation. 3 cases (Nos. 7, 9 and 12) showed pyogenesis. The crusts did not disappear even 3 weeks later. The intact skin group showed no crust formation and their erythema disappeared before more than a week elapsed after removing patches.

Table 1

Patch Test in Rabbits by Blemmer G

24 hours

| | | Intact Skin | | | | | | Abraded Skin | | | | | |
|--------------------------|------------|-------------|---|---|---|---|---|--------------|---|---|----|----|----|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| Blemmer G Stock soln. | 0.25 ml | 3 | 1 | 3 | 2 | 1 | 1 | 4 | 3 | 4 | 2 | 1 | 4 |
| | 0.13 ml | 2 | 1 | 2 | 0 | 0 | 1 | 4 | 3 | 4 | 2 | 4 | 4 |
| Control | PH 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | PH 4.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |

72 hours

| | | Intact Skin | | | | | | Abraded Skin | | | | | |
|--------------------------|------------|-------------|---|---|---|---|---|--------------|---|---|----|----|----|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| Blemmer G Stock soln. | 0.25 ml | 2 | 1 | 2 | 2 | 0 | 1 | 4 | 3 | 4 | 2 | 1 | 2 |
| | 0.13 ml | 2 | 1 | 2 | 0 | 0 | 0 | 4 | 3 | 4 | 2 | 0 | 2 |
| Control | PH 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | PH 4.4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Rating Criteria and Calculating Method for Skin-Irritative Reaction
in Patch Test, as well as Assessment of Rating Results

Rating Criteria

| Erythema and Crust Formation | | Edema Formation | |
|--------------------------------------|--------|-------------------------------|--------|
| None | 0 mark | None | 0 mark |
| Very slight erythema | 1 | Very slight edema | 1 |
| Remarkable erythema | 2 | Slight edema | 2 |
| Medium erythema | 3 | Medium edema | 3 |
| Severe erythema with a few crusts | 4 | Severe edema (1mm or more) | 4 |

Calculating Method

For each of the abraded and the intact skin groups, all marks for erythema and edema 24 hours and 72 hours after start of the patch application are summed up and the sum is divided by the number of animals to obtain the mean value. Assessment is made on the sum of the mean values for both groups.

Assessment of Rating Results

| <u>Rating results</u> | <u>Assessment</u> |
|-----------------------|------------------------|
| 0 - 2 | Mild skin irritation |
| 2 - 5 | Medium skin irritation |
| 6 or more | Severe skin irritation |

Table 2

Body Weight Changes of Rabbits in Patch Test

(Kg)

| Days after purchase | Intact Skin | | | | | | Abraded Skin | | | | | |
|---------------------|--------------|------|------|------|------|------|--------------|------|------|------|------|------|
| | Rabbit No. 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| 1 day | 1.84 | 2.26 | 1.60 | 1.52 | 1.78 | 1.51 | 1.62 | 2.12 | 1.54 | 1.89 | 1.89 | 1.96 |
| 3 | 1.90 | 2.30 | 1.75 | 1.90 | 1.71 | 1.85 | 1.45 | 2.15 | 1.75 | 1.98 | 2.07 | 2.04 |
| 5 | 1.81 | 2.32 | 1.69 | 1.80 | 1.96 | 1.95 | 1.58 | 2.22 | 1.94 | 1.90 | 2.13 | 2.18 |
| depilation 7 | 1.84 | 2.40 | 1.92 | 2.06 | 1.98 | 2.0 | 1.70 | 2.20 | 1.73 | 2.04 | 2.26 | 2.0 |
| applying 8 | 1.77 | 2.32 | 1.77 | 1.83 | 2.03 | 3.05 | 1.63 | 2.14 | 1.83 | 1.97 | 2.18 | 2.10 |
| 9 | 1.74 | 2.05 | 1.65 | 1.72 | 2.10 | 2.07 | 1.65 | 2.17 | 1.80 | 1.84 | 2.10 | 2.12 |
| 10 | 1.75 | 2.08 | 1.55 | 1.90 | 2.05 | 2.12 | 1.67 | 2.12 | 1.90 | 1.70 | 2.03 | 2.08 |
| 11 | 1.75 | 2.03 | 1.45 | 1.85 | 2.14 | 2.05 | 1.70 | 2.15 | 2.07 | 1.78 | 2.0 | 2.08 |
| 12 | 1.78 | 2.05 | 1.36 | 1.70 | 2.15 | 2.02 | 1.80 | 2.06 | 2.08 | 1.70 | 2.0 | 2.13 |

Table 3

Average Feed Consumptions of Rabbits in Patch Test

(g)

| Days incl. and after date of purchase | Intact Skin. | | | | | | Abraded Skin. | | | | | |
|---------------------------------------|--------------|-----|-----|-----|-----|-----|---------------|-----|-----|-----|-----|-----|
| | Rabbit No. 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| 2 days | 100 | 150 | 100 | 150 | 180 | 200 | 60 | 210 | 60 | 210 | 190 | 150 |
| 4 | 60 | 160 | 180 | 115 | 20 | 220 | 40 | 200 | 235 | 155 | 230 | 230 |
| 6 | 80 | 140 | 40 | 40 | 120 | 180 | 50 | 160 | 30 | 20 | 180 | 120 |
| 8 | 20 | 115 | 70 | 50 | 200 | 200 | 150 | 40 | 180 | 135 | 120 | 120 |
| 9 | 10 | 80 | 20 | 140 | 210 | 200 | 80 | 0 | 150 | 40 | 100 | 170 |
| 10 | 20 | 80 | 20 | 100 | 220 | 170 | 120 | 0 | 150 | 0 | 100 | 160 |
| 11 | 40 | 60 | 0 | 30 | 160 | 100 | 160 | 0 | 160 | 50 | 120 | 160 |
| 12 | 60 | 80 | 0 | 20 | 180 | 120 | 170 | 0 | 30 | 40 | 160 | 170 |
| 13 | 100 | 80 | 0 | 0 | 120 | 180 | 180 | 0 | 60 | 40 | 120 | 150 |

Acute Dermal Toxicity

Results

| | Rabbit No. | Doses | Results |
|--------------|------------|---------|---------------------------|
| Intact skin | 1 | 1 ml/kg | Died after 4 applications |
| | 2 | 2 ml/kg | " 1 application |
| | 3 | 3 ml/kg | " 1 application |
| Abraded skin | 4 | 1 ml/kg | Died after 4 applications |
| | 5 | 2 ml/kg | " 2 " |
| | 6 | 3 ml/kg | " 1 application |

Symptoms

When 1 ml/kg of Blemmer G was applied per dose, both the abraded and the intact skin groups died after 4 repetitions of application (totaling to 4 ml/kg). When 2 ml/kg or 3 ml/kg was applied per dose, both groups died with 1 - 2 doses each. No remarkable symptoms were found.

Body weight and feed consumption

On the rabbits which eventually died, no remarkable changes in body weight were found after applying 1 - 2 doses of Blemmer G. Those rabbits which undertook application of a small quantity (1 ml/kg) also did not show significant change in body weight, but showed gradual decrease in feed ingestion after application.

Histopathological examination

1) Skin

o Intact skin group

Abscesses were formed in scarf skin and further extended up to the top part of corium. They slightly infiltrated into sweat glands and hair roots, and their infiltration also appeared in a few spots on the skin side of dermal muscles in some areas.

o Abraded skin group

Lots of fibrin formed edemata in the upper and lower soft tissues centering around dermal muscles, and moderate amounts of neutrophils and macromonocytes appeared among those edemata. Muscle fiber showed remarkable degeneration and gave heavy bleeding. The fiber formed masses or disintegrated. Moderate penetration of leukocytes was found among fibers. Blood vessels were expanded by leukocytes which filled them fully. There was appearance of leukocytes and macromonocytes in the top layer of corium. However no remarkable changes were found in adnexa.

2) Liver

One case each of both groups showed remarkable congestion in bile ducts and appearance of cells inside Glisson capsules. No other remarkable changes were found. No other tracts and organs than mentioned above showed any noticeable aspects.

Table 4

Body Weight Changes of Rabbits in Acute Dermal Toxicity Test
(kg)

* parenthesized numbers: average (daily) feed ingestion (g)

| Days after Rabbits purchase | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|-----------------------------|------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Intact Skin | 2.35 | 2.30 (210) | 2.49 (210) | 2.58 (190) | 2.62 (200) | 2.68 (130) | 2.60 (180) | 2.65 (140) | 2.69 (30) | 2.65 (25) | 2.55 (25) | 2.55 (0) |
| | 2.45 | 2.45 (220) | 2.61 (210) | 2.70 (210) | 2.76 (240) | 2.80 (250) | 2.70 (120) | 2.81 (120) | 2.80 (40) | | | |
| | 3.15 | 3.16 (240) | 3.18 (240) | 3.20 (230) | 3.25 (240) | 3.30 (280) | 3.30 (200) | 3.32 (200) | 3.23 (30) | | | |
| Abraded Skin | 2.24 | 2.21 (90) | 2.30 (200) | 2.45 (210) | 2.53 (220) | 2.58 (160) | 2.47 (160) | 2.60 (200) | 2.65 (190) | 2.67 (130) | 2.76 (110) | 2.43 (20) |
| | 2.10 | 2.14 (210) | 2.18 (210) | 2.19 (180) | 2.24 (220) | 2.24 (190) | 2.17 (290) | 2.37 (200) | 2.34 (50) | 2.16 (10) | | |
| | 2.35 | 2.42 (210) | 2.48 (210) | 2.52 (210) | 2.62 (180) | 2.71 (180) | 2.68 (160) | 2.70 (240) | 2.62 (80) | | | |
| Non-treated | 2.60 | 2.64 (120) | 2.78 (210) | 2.82 (190) | 2.85 (210) | 2.88 (200) | 2.98 (180) | 3.0 (200) | 3.15 (230) | 3.10 (210) | 3.10 (240) | 3.15 (180) |
| | 2.72 | 2.76 (220) | 2.85 (180) | 2.86 (210) | 2.88 (190) | 2.91 (140) | 2.91 (210) | 3.05 (220) | 3.11 (260) | 3.18 (210) | 3.11 (200) | 3.10 (210) |

Table 5

Organ Weights of Rabbits in Acute Dermal Toxicity Test by Blemmer G

(g)

| Rabbits | Body weight (kg) | Liver | Kidneys left right | Spleen | Lungs | Heart | Adrenal glands left right | Brain | Testicles | Stomach |
|---------|------------------|-------|--------------------|--------|-------|-------|---------------------------|-------|-----------|---------|
| 1 | 2.55 | 100 | 9.9 9.9 | 1.8 | 12.0 | 8.0 | 0.2 0.2 | 8.9 | 5.6 5.8 | 31 |
| 2 | 2.80 | 114 | 9.2 9.1 | 1.2 | 19.1 | 9.9 | 0.2 0.2 | 9.8 | 3.0 3.0 | 34 |
| 3 | 2.16 | 130 | 12.0 14.0 | 2.6 | 21.0 | 26.5 | 0.3 0.4 | 10.2 | 3.5 3.5 | 33.5 |
| 4 | 2.43 | 106 | 11.0 11.7 | 1.5 | 32.0 | 20.0 | 1.5 1.5 | 10.0 | 4.2 4.0 | 30 |
| 5 | 2.16 | 95 | 9.4 9.1 | 1.6 | 11.0 | 8.1 | 0.3 0.3 | 9.5 | 2.2 2.2 | 33 |
| 6 | 2.62 | 116 | 11.6 10.7 | 5.5 | 14.2 | 13.5 | 0.3 0.4 | 8.7 | 3.0 2.9 | 40.2 |

Inhalation Test

Inhalation Test

Changes in body weight and feed consumption

All rabbits showed decrease both in body weight and feed ingestion 24 hours after spraying (See Table 6).

Symptoms

After spraying Blemmer G, every rabbit was found shedding tears, showing a symptom of conjunctivitis, which however disappeared 72 hours later. No other remarkable changes were noticed.

Examinations

(1) Blood examinations

As shown in Tables 7 and 8, no noticeable changes were found in either leukocytes or erythrocytes before and after spraying.

(2) Liver function examination

Compared with before spraying, S-CPT (Serum-Glutamic-Pyruvic Transaminase) activity increased for all the 3 cases (Table 7).

(3) Urine and renal function examinations

Except some protein found in Urine for 2 of the 3 cases, there were no noticeable changes in urine sugars, urine pH or serum urea nitrogen (Table 7).

(4) Histopathological examination

No particular differences were found in weights of various organs between the rabbits with inhalation and those without. Macroscopic observation on various organs detected no remarkable changes

either (Table 9).

Microscopic observations

- Trachea: All cases showed remarkable congestion under the mucous membrane of trachea and also slight appearance of erythrocytes and lymphocytes there.
- Lungs: There were no remarkable changes except that 1 case showed very porous air vesicles and hypertrophy in connective tissue cells of alveolar dissepiment, indicating local pneumonia.
- Liver: 1 case showed remarkable congestion but no cellular infiltration nor any noticeable changes in liver cells. In another case, remarkable congestion was found together with granulomas, which were composed mainly of lymphocytes and had giantocytes and parasitelike corpuscles at their center. Slight change was found in Glisson capsules. Feces-like albuminoid material was found inside ~~the~~^{the} ducts and it reduced stainability of the surrounding liver cells. However no changes were found in liver cells themselves.
- Kidneys: Though some local congestion was noticed, there were no remarkable changes in finer ureters, etc.

No other organs showed any particular changes.

Table 6. Inhalation Test

| | Blood Examination | | | | Liver Function | Renal Function Ex. | | | | |
|-----|--|-------------------------------|-----------------|--------------|----------------|--------------------|-----------------------|---------------|-------------|----------|
| | Erythrocytes (10 ⁴ /mm ³) | Leukocytes (mm ³) | Hb value (g/dl) | Ht value (%) | | S-GPT Karmar unit | Urea nitrogen (mg/dl) | Urine protein | Urine sugar | Urine PH |
| I-1 | Before inhalation | 561 | 9,700 | 12.2 | 40.6 | 29.0 | 27.5 | - | - | 7 |
| | 72 hours after inhal. | 579 | 7,200 | 11.8 | 40.0 | 51.0 | 28.5 | + | - | 8 |
| I-2 | Before inhal. | 645 | 10,400 | 15.0 | 46.9 | 32.6 | 27.5 | - | - | 8 |
| | 72 hours after inhal. | 320 | 14,600 | 8.7 | 31.2 | 89.0 | 32.0 | - | - | 8 |
| I-3 | Before inhal. | 568 | 6,500 | 13.2 | 43.0 | 25.8 | 30.0 | - | - | 8 |
| | 72 hours after inhal. | 566 | 6,400 | 13.6 | 42.2 | 47.5 | 31.5 | + | - | 8 |

Table 7. Hemogram in Inhalation Test

| | Baso | Eosino | Pseuds eosinophile (Neutrocytes) | | | | | Lympho | Mono | Others | | |
|-----|-----------------------|--------|----------------------------------|------|----|-----|----|--------|------|----------|---|---|
| | | | Met | Stab | II | III | IV | | | | V | |
| I-1 | Before inhalation | 0 | 0 | 0 | 11 | 24 | 17 | 3 | 0 | 45 | 0 | 0 |
| | 72 hours after inhal. | 0 | 1 | 0 | 3 | 8 | 14 | 3 | 0 | 69 69 | 1 | 1 |
| I-2 | Before inhal. | 0 | 1 | 0 | 15 | 18 | 2 | 3 | 0 | 41 | 2 | 0 |
| | 72 hours after inhal. | 0 | 0 | 0 | 6 | 19 | 13 | 2 | 0 | 52 | 7 | 1 |
| I-3 | Before inhal. | 0 | 3 | 0 | 2 | 10 | 16 | 3 | 1 | 64 | 0 | 1 |
| | 72 hours after inhal. | 0 | 1 | 0 | 3 | 3 | 2 | 0 | 0 | 85 | 6 | 0 |

①

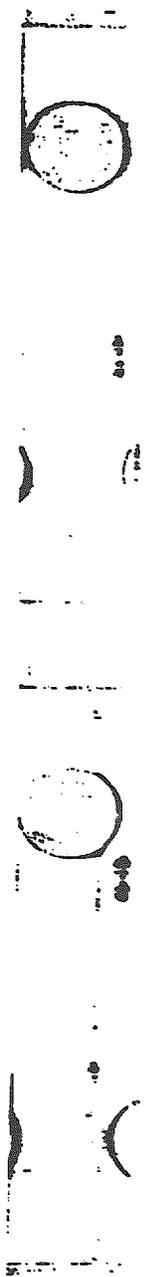


Table 8. Organ Weights of Rabbits in Inhalation Test

| | Body Weight (kg) | Liver | Kidneys left right | Spleen | Lungs | Heart | Adrenal glands left right | Brain | Stomach | Testicles left right | | | | |
|----------------------------|------------------|-------|--------------------|--------|-------|-------|---------------------------|-------|---------|----------------------|------|----|-----|-----|
| Rabbits with inhalation | I-1 | 3.33 | 120 | 15.5 | 14.8 | 3.4 | 31 | 4.6 | 0.3 | 0.3 | 10.2 | 34 | 5.4 | 4.4 |
| | I-2 | 3.06 | 140 | 11.0 | 12.0 | 1.9 | 26 | 10.1 | 0.5 | 0.4 | 9.3 | 29 | 5.2 | 4.8 |
| | I-3 | 2.95 | 98 | 14.0 | 13.0 | 1.9 | 19 | 8.0 | 0.4 | 0.4 | 10.6 | 35 | 5.2 | 5.0 |
| Rabbits without inhalation | C-1 | 2.76 | 106 | 15.0 | 15.0 | 2.0 | 31 | 8.0 | 0.6 | 0.6 | 9.0 | 32 | 4.5 | 5.0 |
| | C-2 | 2.70 | 124 | 13.0 | 12.5 | 2.3 | 29 | 9.0 | 0.4 | 0.4 | 10.0 | 26 | 4.5 | 4.5 |
| | C-3 | 3.02 | 163 | 13.0 | 13.0 | 7.0 | 28 | 12.0 | 0.4 | 0.4 | 11.0 | 46 | 4.0 | 4.0 |

Table 9. Body Weights and Feed Ingestions of Rabbits in Inhalation Test

| | days after purchase | 5 | 7 | spray | 8 | 9 | dissection | 10 |
|-----|---------------------|---------------|---------------|---------------|---------------|---------------|---------------|----|
| I-1 | 3.18 (180) | 3.26 (180) | 3.24 (200) | 3.28 (180) | 3.32 (210) | 3.10 (110) | 3.33 (180) | |
| I-2 | 2.80 (160) | 2.80 (210) | 2.88 (180) | 3.05 (200) | 3.05 (180) | 3.00 (120) | 3.06 (140) | |
| I-3 | 2.95 (210) | 3.18 (180) | 3.20 (180) | 3.28 (210) | 3.25 (140) | 3.15 (60) | 2.95 (80) | |

Conclusion

1. In patch test, the extent of skin irritation on rabbits by Blemmer G, according to "assessment of rating results", is "medium". However it gives high protein vagulation.
2. Applying 3 ml/kg of Blemmer G on the back of a rabbit causes his death within 24 hours.
3. Skin contact or inhalation of a large quantity of Blemmer G causes some physical disorders.
4. If the quantity of Blemmer G is small, local and overall disorders so caused are mild.

It is suggested that enough care should be taken in handling Blemmer G for its application.

CERTIFICATE OF AUTHENTICITY

THIS IS TO CERTIFY that the microimages appearing on this microfiche are accurate and complete reproductions of the records of U.S. Environmental Protection Agency documents as delivered in the regular course of business for microfilming.

Data produced 8 8 90 Marcia Rubolino
(Month) (Day) (Year) Camera Operator

Place Syracuse New York
(City) (State)

