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Chemical Category	DEQUEST 2060S		

8(e)

CAP

(COMPLIANCE AUDIT PROGRAM)

9746

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NOTE: Peter provides data entry in CBITS for the 8(e) CAP Documents.

8EHQ-0892-9746

"Contains NO CBI",

Monsanto

92 AUG 28 PM 2:57

ENVIRONMENT, SAFETY & HEALTH

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

August 13, 1992



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Environmental Protection Agency
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88920008048

Attention: Section 8(e) Coordinator (CAP Agreement)

This submission is pursuant to the TSCA Section 8(e) Compliance Audit Program and CAP Agreement #8ECAP-0036.

The information included herein is characterized as follows:

Chemical Identity - DEQUEST 2060S; STABILIZED SOLUTION OF DIETHYLENE
TRIAMINE PENTA(METHYLENE PHOSPHONIC ACID)

Chemical CAS No. - 015827608

Information/Study Type - II,B,2,b/Acute Toxicity/Irritation Study

Information/Study Identification - Irritant Effects on Rabbit Skin of DEQUEST 2060S
HU-82-227

Identification of Reportable Endpoint: SEVERELY IRRITATING TO SKIN IN A PRIMARY
IRRITATION STUDY

Previous TSCA 8(e) or PMN submissions, if any, for the reference chemical can be found in
Appendix A.

It should be noted that this summary is not all inclusive. Therefore, it may not highlight all
adverse effects that EPA may judge to meet TSCA 8(e) reportability. This submission/report does
not contain confidential business information.

Sincerely,

J. R. Condray
Director, Regulatory Management
(314) 694-8883

MASTER FILE

PROJECT NO. HU-82-227

CONFIDENTIAL

CAS NO. 015827608

8337D/MTO 13/SE

IRRITANT EFFECTS ON RABBIT SKIN
OF DEQUEST 2060S
(Study reference HU-82-227)

Addressee:

Mr. N. G. H. Thomas,
Monsanto Europe S.A.,
Avenue de Tervuren 270-272,
Letter Box No. 1,
B-1150 Brussels,
BELGIUM.

1 February 1983.

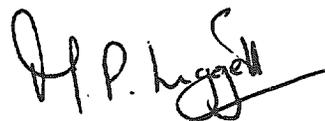
Author:

Michael P. Liggett.

Huntingdon Research Centre,
Huntingdon,
Cambridgeshire,
ENGLAND.

8337D/MOT'13/SE

I the undersigned, hereby declare that the work was performed under my supervision according to the procedures herein described, and that this report provides a correct and faithful record of the results obtained.

A handwritten signature in black ink, appearing to read "M. P. Liggett", with a stylized flourish at the end.

Michael P. Liggett,
Head of Unit - Acute Studies
Department of Industrial Toxicology

QUALITY ASSURANCE AUDIT STATEMENT

HRC REPORT NO. 8337D/MTO 13/SE

This report has been audited by HRC Quality Assurance Unit and is considered to be an accurate presentation of the data produced during the course of the study.

Kenneth W.G. Shillam

1.2.83

**Kenneth W.G. Shillam, B.Sc., Ph.D., F.I. Biol.,
Director, Quality Assurance**

Audit notes

An audit by the QAU consists of (a) a comparison of the reported findings with the raw data as recorded in notebooks and worksheets, and (b) a comparison of derived data and statements of fact with the reported raw data. Any computerized presentations which are the outcome of verified entry direct from the raw data and which are secure against manual alteration are not normally audited.

Short reports and some parts of longer reports are audited completely. Reports containing large amounts of data are divided into sections liable to have similar error rates and each is subjected to a sampling procedure according to the methods described in British Standards Institution, BS 6000, 6001 (1972) and US Military Standard 105D (1963). The Acceptable Quality Level (the maximum percentage errors considered satisfactory as a process average) is 0.4. Reports with any section not meeting the acceptance criteria are revised by the Study Director and this is followed by QAU re-audit.

The results of any investigations made by the sponsor and which are included in HRC reports are audited using the sponsor's report to HRC.



QAU STUDY INSPECTIONS

HRC Report No. 8337D/MTO 13/SE

Acute studies are conducted at HRC in a setting which involves frequent repetition of similar or identical procedures. At or about the time of this study, 'process-based' inspections were made by the QAU of the critical procedures relevant to this study type. For the inspection of each procedure, at least one study was selected at random.

The findings of these inspections were reported promptly to the Study Director and to HRC Management.

A handwritten signature in black ink, appearing to read 'K. W. G. Shillam', is positioned above the printed name.

K. W. G. Shillam
Director, Quality Assurance

Sample designation: Dequest 2060S (SPE 8207).

Examination for: Irritant effects on rabbit skin.

1. INTRODUCTION

1.1. This study was designed to assess skin irritation potential.

The test substance may come into contact with the skin during handling or use.

1.2. The albino rabbit was chosen as it has been shown to be a suitable model for skin irritation studies and is the animal recommended in the test protocol.

1.3. The study plan was agreed by the Study Director on 6 January 1983 and the study was undertaken between 12 January and 14 January 1983.

2. TEST SUBSTANCE

2.1. Dequest 2060S, a clear brown liquid, was received on 20 December 1982 and was stored at ambient temperature.

2.2. The stability and absorption of the test substance were not determined.

2.3. The test substance was administered as supplied by the Sponsor.

3. EXPERIMENTAL PROCEDURE

3.1. Protocol

The experimental procedure used was based on that prescribed by the Consumer Product Safety Commission of the U.S.A. in The Code of Federal Regulations, Title 16, Section 1500.41.

3.2. Animal management

3.2.1. Two New Zealand White strain rabbits weighting 2.3 and 2.5 kg and approximately 11 weeks of age were obtained from Buxted Rabbits, Buxted, Sussex, England. The rabbits selected for the study were suitably acclimatised to the laboratory environment.

- 3.2.2. Both animals were identified by a numbered aluminium tag placed through the edge of one ear. This number was unique within the HRC Industrial Toxicology Department throughout the duration of the study.
- 3.2.3. The rabbits were individually housed in metal cages with perforated floors in Building R 14 Room 1. They had free access to tap water and laboratory animal diet Grain Harvester 474 Special Rabbit Pellets.
- 3.2.4. Animal room temperature was maintained at approximately 19°C and relative humidity at 30-70%.

Air exchange was maintained at approximately 19 air changes per hour and lighting was controlled by means of a time switch to give 12 hours of artificial light per day.
- 3.2.5. Both animals were observed daily for signs of ill health or toxicosis.

3.3. Treatment procedure

- 3.3.1. Approximately 24 hours prior to application of Dequest 2060S, hair was removed with electric clippers from the dorso-lumbar region of each rabbit exposing an area of skin approximately 10 cm square.
- 3.3.2. Immediately prior to application of the test substance, an area of skin approximately 2.5 cm square on the right side of the spine was abraded using the tip of a scalpel blade to make minor incisions through the stratum corneum. These were not deep enough to disturb the dermis or cause bleeding. A similar site on the left side remained intact.
- 3.3.3. A 0.5 ml aliquot of Dequest 2060S was applied under a 2.5 cm square gauze pad to one intact and one abraded skin site on each animal.
- 3.3.4. The treatment sites were occluded with "Elastoplast" elastic adhesive dressing backed with "Sleek" plaster for approximately 24 hours. The animals were not restrained during the exposure period and were returned to their cages.

At the end of the exposure period the occlusive dressing and gauze pads were removed and the treatment sites wiped to remove any residual test substance.

3.4. Observations and scoring

- 3.4.1. Examination of the treated skin sites was made approximately 24 and 72 hours after application of the test substance.

3.4.2. The dermal reactions were assessed using the following numerical scoring system:

Erythema and eschar formation:

No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Oedema formation:

No oedema	0
Very slight oedema (barely perceptible)	1
Slight oedema (edges of area well-defined by definite raising)	2
Moderate oedema (raised approximately 1 millimeter)	3
Severe oedema (raised more than 1 millimeter and extending beyond the area of exposure)	4

A note was also made of any lesion not covered by this scoring system.

3.4.3. The numerical scores for erythema and oedema at both the 24 and 72 hours readings for both intact and abraded skin sites were added together and divided by 8 to give an estimated Primary Irritation Index.

4. EVALUATION*

The Primary Irritation Index was used to classify the test substance as follows:

<u>Primary Irritation Index</u>	<u>Classification</u>
0	non-irritant
>0 - 2	mildly irritating
>2 - 5	moderate irritant
>5 - 6	moderate to severe irritant
>6	severe irritant

5. ARCHIVES

All specimens, raw data and other documents generated at HRC during the course of this study, together with a copy of this Final Report, have been lodged in the Huntingdon Research Centre Archives, Huntingdon, England.

* Based on "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics", published by the Association of Food and Drug Officials of the United States, 1959, p.46.

6. RESULTS

The numerical scores awarded to the dermal reactions elicited by Dequest 2060S are given in Table 1.

Well-defined to severe reactions, accompanied by necrotic lesions, were observed in both animals.

Due to the severity of the reactions only two animals were exposed to Dequest 2060S.

The Primary Irritation Index was estimated to be: 6.3.

7. CONCLUSION

Based on the limited data generated in this study Dequest 2060S is considered to be a severe irritant producing corrosive reactions on rabbit skin.

TABLE 1

Dermal reactions elicited by Dequest 2060S

Rabbit Number and Sex	E = Erythema O = Oedema	24 Hours		72 Hours	
		Intact	Abraded	Intact	Abraded
925c	E	2	2	4A	4A
	O	3	3	3	3
926f	E	4A	4A	4A	4A
	O	3	3	2	2

Estimated Primary Irritation Index = 6.3
 A necrotic lesions



OUTLINE PROTOCOL

*Spoke Elliot 11/10
Amend quotes
see below x*

ASSESSMENT OF EYE IRRITATION

INTRODUCTION

This protocol outlines a study designed to comply with the code of Federal Regulations (CFR) of the U.S.A., Title 16, Section 1500.42 as published by the Consumer Product Safety Commission in the Federal Register Vol. 38, No. 187, September 27 1973.

OBJECTIVE

To determine the degree of ocular irritation produced by a substance that is introduced into the rabbit eye.

EXPERIMENTAL DESIGN

Duration

Three day observation period following dose administration with provision for additional observation to a maximum of 21 days.

Animals

Six rabbits of the New Zealand White strain, approximately 2.5 - 3.5 kg and 4 - 6 months old.

Husbandry

Animals are caged individually in metal cages with wire mesh floors, and have free access to tap water and a standard laboratory animal diet. The animal room temperature is maintained at approximately 20°C, and although humidity is not controlled it is recorded daily. Air exchange is maintained at at least 12 changes per hour, and lighting controlled on a 12 hour light/dark cycle.

Pre-dose examination

Before testing, both eyes of each animal are examined and any animals with eye defects are rejected.

Dose administration

A single dose is applied to one eye of each animal. The dose is determined by the nature of the test substance, as follows:

- liquid: 0.1 ml per animal
- solid or paste: 100 mg per animal
- flake or granule (of low bulk-density): that weight (not to exceed 100 mg) which when compacted but uncrushed occupies a volume of 0.1 ml.

x Start with Laminals.



The lower lid is gently pulled away from the eyeball to form a cup into which the test substance is placed. The eyelids are gently held together for one second and then released. The other eye, remaining untreated, serves as a control.

The animals are restrained during, and for one hour after, instillation of the test substance. Except as noted below, the eyes are not washed following instillation.

OBSERVATIONS (Note 1)

The eyes are examined, and the grade of ocular reaction recorded at 1, 2, 3, 4, 7, 14 and 21 days after instillation, unless the eye is normal at 7 or 14 days. The additional observations in excess of the CFR requirements (i.e. day 4 onwards) will determine whether the reactions are of a transient or persistent nature. For examination at, or subsequent to, Day 1, the eyes may be washed with sodium chloride injection BP, 0.9% w/v or distilled water. Any or all eyes may be further examined at, or subsequent to, Day 1 by application of fluorescein stain. One drop of fluorescein sodium B.P., 2% w/v, is dropped directly onto the cornea, and excess reagent removed by flushing with sodium chloride solution or distilled water.

The following subjective numerical scoring system is used to grade the ocular lesion:

Cornea

No ulceration or opacity	0
Scattered or diffuse areas of opacity (other than slight dulling of normal lustre), details of iris clearly visible	(1)
Easily discernible translucent areas, details of iris slightly obscured	2
Nacreous areas, no details of iris visible size of pupil barely discernible	3
Complete corneal opacity, iris not discernible	4

Iris

Normal	0
Markedly deepened folds, congestion, swelling, moderate circumcorneal injection (any of these or combination or any thereof), iris still reacting to light, (sluggish reaction is positive)	(1)
No reaction to light, haemorrhage, gross destruction (any or all of these)	2

Conjunctivae

<u>Redness</u> (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	
Vessels normal	0
Some vessels definitely injected	1
Diffuse, crimson red, individual vessels not easily discernible	(2)
Diffuse, beefy red	3

Chemosis

No swelling	0
Any swelling above normal (including nictating membrane)	1
Obvious swelling with partial eversion of lids	(2)
Swelling with lids about half closed	3
Swelling with lids more than half closed	4



RESULTS

An animal shall be considered as exhibiting a positive reaction if the test substance produces at any of the readings ulceration of the cornea (other than a fine stippling), or opacity of the cornea (other than a slight dulling of the normal lustre), or inflammation of the iris (other than a slight deepening of the folds (or rugae) or a slight circumcorneal injection of the blood vessels), or if such substance produces in the conjunctivae (excluding the cornea and iris) an obvious swelling with partial eversion of the lids or a diffuse crimson red with individual vessels not easily discernible.

The test shall be considered positive if four or more of the animals in the test group exhibit a positive reaction. If only one animal exhibits a positive reaction, the test shall be regarded as negative. If two or three animals exhibit a positive reaction, the test may be repeated using a different group of six animals (see Note 2). The second test shall be considered positive if three or more of the animals exhibit a positive reaction. If only one or two animals in the second test exhibit a positive reaction, the test shall be repeated with a different group of six animals. Should a third test be needed the substance shall be regarded as an irritant if any animal exhibits a positive response.

REPORT

Unless otherwise requested, 2 unbound copies of the report will be issued. The report will contain:

- a description of the experimental procedures used;
- a summary of all observations made;
- an evaluation of the test substance as a potential eye irritant.

NOTES

1. Figures in brackets indicate the lowest grades considered positive under Section 1500.42 of the Code of Federal Regulations.
2. A second test will not be undertaken routinely and is not included in the basic cost of the study.



ASSESSMENT OF PRIMARY SKIN IRRITATION

INTRODUCTION

This protocol outlines a study designed to comply with the Code of Federal Regulations of the USA, Title 16, Section 1500.41 as published by the Consumer Product Safety Commission in the Federal Register Vol. 38, No. 187, September 27, 1973.

OBJECTIVE

To evaluate local irritant effects to rabbit skin of the test substance following a single 24 hour occluded exposure.

EXPERIMENTAL DESIGN

Duration

Three day observation period following the 24-hour exposure period.

Animals

Six rabbits of the New Zealand White strain, approximately 2.5 – 3.5 kg and 4 – 6 months old.

Husbandry

All animals are caged individually in metal cages with wire mesh floors, and have free access to tap water and a standard laboratory animal diet. The animal room temperature is maintained at approximately 20°C, and although humidity is not controlled it is recorded daily. Air exchange is maintained at at least 12 changes per hour, and lighting controlled on a 12 hour light/dark cycle.

Skin preparation

Twenty-four hours before treatment the back and flanks of each rabbit are closely clipped with electric clippers, exposing an area of skin approximately 10 cm x 10 cm.

One area of skin on each rabbit 2.5 cm x 2.5 cm is abraded by making minor incisions through the stratum corneum, but not into the dermis or deep enough to cause bleeding.

Dose administration

Application is made to one intact and one abraded skin site on the clipped dorsum of each rabbit. The test material is applied under a patch of surgical gauze approximately 2.5 cm x 2.5 cm. For liquid substances or pastes 0.5 ml per site is used and for solids 0.5 g moistened with 0.5 ml distilled water. When the patches are in place the trunk of the animal is wrapped with an occlusive bandage of elastic adhesive dressing backed with a waterproof plaster.

The bandages and gauze patches remain in place for 24 hours. The animals are not restrained during this period.



OBSERVATIONS

The condition of each intact and abraded skin site is observed immediately, and at 72 hours, following removal of bandages and gauze patches. Skin reaction is subjectively assessed and recorded according to the following numerical system:

Observed reaction	Score
Erythema and eschar formation:	
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Oedema formation:	
No oedema	0
Very slight oedema (barely perceptible)	1
Slight oedema (edges of area well-defined by definite raising)	2
Moderate oedema (raised approximately 1 millimetre)	3
Severe oedema (raised more than 1 millimetre and extending beyond the area of exposure)	4

RESULTS

Calculation of Primary Irritation Index

The numerical scores for erythema and oedema in the intact and abraded skin sites for all six rabbits, and at both the 24 and 72 hour readings, are totalled. This sum is divided by 24 and the value obtained is termed the Primary Irritation Index.

Interpretation

The test substance is classified according to the following statement taken from page 46 of "Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics", Association of Food and Drug Officials of the United States, 1959:

"Compounds producing combined averages (primary irritation indices) of 2 or less are only mildly irritating; whereas those with indices from 2 to 5 are moderate irritants, and those with scores above 6 are considered severe irritants".

REPORT

Unless otherwise requested, 2 unbound copies of the report will be issued. The report will contain:

- a description of the experimental procedures used;
- a summary of all observations made;
- the calculated Primary Irritation Index and classification.

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.

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