

Elf Atochem

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October 6, 1997

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Document Control Office (7407)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M St., S.W.
Washington, D.C. 20460

Subject: TSCA FYI Coordinator



FYI-97-001307

Dear Sir/Madam:

Elf Atochem North America, Inc. (Elf Atochem) is submitting the enclosed final report from an eye irritation study in rabbits to the Environmental Protection Agency (EPA) on a "For Your Information (FYI)" basis. This study does not involve effects in humans. The title of the study is *Acute Eye Irritation in Rabbits*.

This study recently came into our possession via our parent company in France and provides information on 10-undecynoic acid (CAS Number 2777-65-3). Elf Atochem does not currently manufacture, import or market 10-undecynoic acid.

Nothing in this letter or the enclosed study report is considered confidential business information of Elf Atochem.

The results of the study showed the test material to be corrosive to rabbit eyes.

Further questions regarding this submission may be directed to me at (215) 419-5890.

Sincerely,

Debra Randall
Debra Randall, D.A.B.T.
Product Safety Manager



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SPONSOR

Elf Atochem S.A.
Cours Michelet
La Défense 10
92091 Paris-la-Défense CEDEX
France

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STUDY TITLE

ACUTE EYE IRRITATION
IN RABBITS

TEST SUBSTANCE

10-UNDECYNOIC ACID

STUDY DIRECTOR

Stéphane de Jouffrey

STUDY COMPLETION DATE

7 April 1997

PERFORMING LABORATORY

Centre International de Toxicologie (C.I.T.)
Miseray - 27005 Evreux - France

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LABORATORY STUDY NUMBER

15021 TAL

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STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with the following Principles of Good Laboratory Practice Regulations:

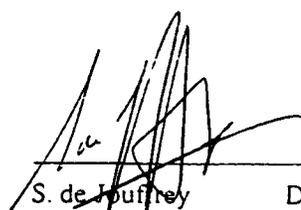
- . O.E.C.D. Principles of Good Laboratory Practice, Decision Concerning Mutual Acceptance of Data in the Assessment of Chemicals, C(81)30(final) Annex 2. May 12, 1981.
- . Décret N° 90-206 du 7 mars 1990 concernant les Bonnes Pratiques de Laboratoire (Journal Officiel du 9 mars 1990), Ministère de l'Industrie et de l'Aménagement du Territoire.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

This study was performed at the Centre International de Toxicologie (C.I.T.), Miserey, 27005 Evreux, France.

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Toxicology



S. de Jouffrey Date: 7 April 1997
Study Director
Doctor of Veterinary Medicine
Head of Short-term and Environmental
Toxicology

OTHER SCIENTISTS INVOLVED IN THIS STUDY

For Pharmacy: J. Richard
Doctor of Pharmacy

For Toxicology: C. Pelcot
Study Supervisor

STATEMENT OF QUALITY ASSURANCE UNIT

1. Specific study inspections

Type of inspections	Dates		
	Inspections	Report to Study Director (*)	Report to Management (*)
Protocol	22 November 1996	25 November 1996	25 November 1996
Report	19 March 1997	20 March 1997	20 March 1997

2. Routine inspections performed on other studies of the same type according to a frequency defined in Q.A.U. procedures

Inspected phase	Dates		
	Inspections	Report to Study Director (*)	Report to Management (*)
Treatment/test substance	2 October 1996	2 October 1996	2 October 1996
Preparation/test substance	15 October 1996	15 October 1996	15 October 1996

The inspections were performed in compliance with C.I.T. Quality Assurance Unit procedures and the Good Laboratory Practice Regulations.

(*) The dates mentioned correspond to the dates of signature of audit reports by Study Director and Management.

b 

L. Valette-Talbi Date: 7 April 1997
 Doctor of Biochemistry
 Head of Quality Assurance Unit
 and Scientific Archives

SUMMARY

At the request of Elf Atochem S.A., Paris-la-Défense, France, the potential of the test substance 10-UNDECYNOIC ACID (batch No. 1/BD4523) to induce ocular irritation was evaluated in rabbits according to O.E.C.D. (No. 405, 24th February 1987) and E.C. (92/69/E.E.C., B₃, 31st July 1992) guidelines. The study was conducted in compliance with the Principles of Good Laboratory Practice Regulations.

Methods

The study design was established according to available information on the test substance and the above guidelines.

As possible irritant effects were anticipated, a first assay was conducted in one male New Zealand White rabbit.

Since the test substance did not show severe irritant properties in the first assay, it was evaluated in two other male New Zealand White rabbits in a second assay.

A single dose of 100 mg of the test substance was introduced into the left conjunctival sac. The right eye served as control.

The test substance was used in its original form.

The eyes were not rinsed after administration of the test substance.

Ocular reactions were observed approximately one hour, 24, 48 and 72 hours after the administration and then daily until reversibility of the ocular reactions.

The mean values of the scores recorded for each animal after 24, 48 and 72 hours were calculated.

Results

Slight to severe conjunctival reactions were observed in all animals: slight to severe chemosis, slight or marked conjunctival redness and clear to whitish purulent discharge were noted, from day 1 up to day 8, 14 or 15.

A slight iritis was noted in all animals on day 2; it persisted up to day 7 or 8, and was masked by corneal opacity in one animal between days 3 and 5.

A marked corneal opacity was observed in all animals on day 2. A slight to severe corneal opacity persisted up to day 8 in two animals, and up to the end of the observation period (day 22) in the remaining animal.

Neovascularisation was observed in all animals, from day 6 up to day 8, 13 or 21, and a myosis was recorded in two animals, between days 3 and 7 or between days 5 and 6.

The mean scores calculated for each animal over 24, 48 and 72 hours were 3.3, 3.3 and 2.3 for chemosis, 2.7, 3.0 and 2.7 for redness of the conjunctiva, 1.0 and 1.0 for iris lesions (not calculable for one animal) and 2.7, 2.3 and 3.7 for corneal opacity.

Conclusion

Under our experimental conditions, the test substance 10-UNDECYNOIC ACID (batch No. 1/BD4523) was considered severely irritant when administered by ocular route in rabbits.

RESUME

A la demande de Elf Atochem S.A., Paris-la-Défense, France, l'irritation oculaire pouvant être induite par le produit 10-UNDECYNOIC ACID (lot n° 1/BD4523) a été évaluée chez le Lapin conformément aux lignes directrices de l'O.C.D.E. (No. 405, 24th February 1987) et de la C.E.E. (92/69/E.E.C., B, 31st July 1992). L'étude a été réalisée conformément aux règles de Bonnes Pratiques de Laboratoire.

Méthodes

L'étude a été réalisée selon les informations disponibles sur le produit et les lignes directrices mentionnées ci-dessus.

Des effets irritants étant supposés, un premier essai a été effectué sur 1 lapin mâle New Zealand White.

Le produit n'ayant pas montré de propriétés irritantes graves lors de ce premier essai, il a été testé sur 2 autres lapins mâles New Zealand White lors d'un second essai.

Une dose unique de 100 mg de produit a été introduite dans le cul de sac conjonctival de l'oeil gauche. L'oeil droit a servi de témoin.

Le produit a été utilisé tel quel.

Aucun rinçage des yeux n'a été réalisé après l'administration du produit.

Les réactions oculaires ont été observées environ 1 heure, 24, 48 et 72 heures après l'administration puis quotidiennement jusqu'à la réversibilité des réactions oculaires.

La moyenne des scores enregistrés après 24, 48 et 72 heures a été calculée pour chaque animal.

Résultats

Des réactions conjonctivales légères à sévères sont observées chez tous les animaux : un chémosis léger à sévère, une rougeur de la conjonctive légère à marquée et un larmolement clair à purulent blanchâtre sont notés, du jour 1 aux jours 8, 14 ou 15.

Un léger iritis est noté chez tous les animaux au jour 2 ; il persiste jusqu'aux jours 7 ou 8, en étant masqué par l'opacité cornéenne chez un animal entre les jours 3 et 5.

Une opacité cornéenne marquée est notée chez tous les animaux au jour 2 : une opacité cornéenne légère à sévère persiste jusqu'au jour 8 chez deux animaux, et jusqu'à la fin de la période d'observation (jour 22) chez le dernier animal.

Une néovascularisation est notée chez tous les animaux, du jour 6 jusqu'au jour 8, 13 ou 21, et un myosis est observé chez deux animaux, entre les jours 3 et 7 ou entre les jours 5 et 6.

Les scores moyens individuels calculés après 24, 48 et 72 heures sont de 3,3 ; 3,3 et 2,3 pour le chémosis, 2,7, 3,0 et 2,7 pour la rougeur de la conjonctive, 1,0 et 1,0 pour l'iritis (non calculable chez un animal), et 2,7 ; 2,3 et 3,7 pour l'opacité cornéenne.

Conclusion

Dans nos conditions expérimentales, le produit 10-UNDECYNOIC ACID (lot n° 1/BD4523) est considéré sévèrement irritant par voie oculaire chez le Lapin.

1. INTRODUCTION

The objective of this study was to evaluate the potential of the test substance 10-UNDECYNOIC ACID to induce ocular irritation following a single administration in rabbits.

In the assessment of the toxic characteristics of a test substance, determination of the irritant effects on the eyes of mammals is an important initial step.

Information derived from this test serves to indicate the possible existence of hazards to Man likely to arise from exposure of the eyes, and associated mucous membranes, to the test substance.

This study was conducted in compliance with:
. O.E.C.D. guideline No. 405, 24th February 1987.
. E.C. Directive No. 92/69/E.E.C., B₅, 31st July 1992.

2. MATERIALS AND METHODS

2.1. TEST SUBSTANCE

2.1.1 Identification

The test substance 10-UNDECYNOIC ACID used in the study was supplied by Elf Atochem S.A.

Documentation supplied by the Sponsor identified the test substance as follows:

- . name:
 - protocol and labelling: 10-UNDECYNOIC ACID
- . batch number:
 - protocol and labelling: 1/BD4523
- . Elf Atochem filing number: CAL 7693/96
- . description: whitish solid
- . container: one smoked glass flask
- . date of receipt: 22 November 1996
- . storage conditions: at room temperature and protected from light
- . purity: 97.65%.

Data relating to the characterization of the test substance are documented in a test article description and an analytical certificate (presented in appendix 1) provided by the Sponsor.

The pH of the test substance at a concentration of 10% in purified water measured at C.I.T. was 4.1.

2.1.2 Preparation

The test substance was used in its original form.

2.2. TEST SYSTEM

2.2.1 Animals

Sex, species, strain: male New Zealand White rabbits.

Reason for this choice: species commonly requested by the international regulations for this type of study.

Breeder: Elevage Cunicole de Val de Scelle, 80160 Prouzel, France.

Number of animals and identification: three animals were used, as recommended by the international regulations and taking into account that a good correlation of results can be obtained with either three or six animals (1). The animals were identified individually with a metal tag in the ear.

Weight: on the day of treatment, the animals had a mean body weight \pm standard deviation of 2.7 ± 0.3 kg.

Acclimatization: at least five days before the beginning of the study.

2.2.2 Environmental conditions

During the acclimatization period and during the main test, the environmental conditions in the animal room were set as follows:

. temperature: $18 \pm 3^\circ\text{C}$

. relative humidity: 50 to 70%

. light/dark cycle: 12 h/12 h

. ventilation: approximately 12 cycles/hour of filtered and cooled air

The temperature and relative humidity were measured continuously and records retained.

The housing conditions (temperature, relative humidity and ventilation) were checked monthly.

The animals were housed individually in polystyrene cages (35 cm x 55 cm x 32 cm or 48.2 cm x 58 cm x 36.5 cm). Each cage was equipped with a food container and a water bottle.

2.2.3 Food and water

All the animals had free access to 112 C pelleted diet (U.A.R., 91360 Villemoisson-sur-Orge, France). Each batch of food was analysed (composition and contaminants) by the supplier. The diet formula is presented in appendix 2.

Drinking water filtered by a F.G. Millipore membrane (0.22 micron) was provided *ad libitum*. Bacteriological and chemical analysis of the water and diet and detection of possible contaminants (pesticides, heavy metals and nitrosamines) are performed periodically. Results are archived at C.I.T.

It was verified that no contaminants in the diet or water at levels likely to influence the outcome of the study were present.

(1) Talsma, D.M.; Leach, C.L.; Hatoum, N.S.; Gibbons, R.D.; Roger, J.C.; Garvin, J.P.: Reducing the number of rabbits in the Draize eye irritancy test: A statistical analysis of 155 studies conducted over 6 years. *Fundamental and Applied Toxicology*. **10**: 1, 146-153 (1988).

2.3 TREATMENT

2.3.1 Selection of the animals

The day before treatment, the eyes of each animal were examined in order to use only animals without any signs of ocular irritation. Animals showing signs of ocular irritation, ocular defects or pre-existing corneal injury were not used.

2.3.2 Study design

The study design was established according to available information on the test substance and according to the O.E.C.D. and E.C. guidelines.

As possible irritant effects were anticipated, the test substance was evaluated in one animal (animal No. 01) in a first assay. Since the test substance did not show severe irritant properties in this first assay, it was evaluated in a second assay (animal Nos. 02 and 03).

2.3.3 Administration of the test substance

The test substance was used in its original form.

A single dose of 100 mg of the test substance was introduced into the conjunctival sac of the left eye after gently pulling the lower lid away from the eyeball.

The lower and upper eyelids were held together for about one second to avoid any loss of test substance. The right eye, which remained untreated, served as a control.

The eyes were not rinsed after administration of the test substance.

2.3.4 Date of treatment

Animal number	Date of treatment (day 1)	End of the observation period
01	7 January 1997	28 January 1997
02	14 January 1997	29 January 1997
03	14 January 1997	22 January 1997

2.4. OCULAR EXAMINATIONS

The eyes were examined approximately one hour, 24, 48 and 72 hours after administration of the test substance.

Following the O.E.C.D. and E.C. guidelines:

- when there is no evidence of irritation after 72 hours, the study is ended.
- when there is persistent ocular irritation after 72 hours, the observation period is extended to a maximum of 21 days (until day 22) in order to determine the progress of the lesions and their reversibility.
- when severe irritant effects are observed, the animals are killed on humane ground.

Any change in the animals' behaviour was noted.

2.5. DESCRIPTION AND EVALUATION OF OCULAR REACTIONS

Ocular reactions were evaluated for each animal according to the following numerical scale:

2.5.1 Conjunctival lesions and discharge

Chemosis (lids and/or nictitating membrane)

. no swelling	0
. any swelling above normal (includes nictitating 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*

Redness (refers to palpebral and bulbar conjunctivae, cornea and iris)

. blood vessels normal	0
. a number of blood vessels definitely hyperaemic (injected)	1
. diffuse, crimson colour, individual vessels not easily discernible	2*
. diffuse, beefy red	3*

Discharge

. absence of discharge	0
. slight discharge (does not include small amounts normally found in inner canthus)	1
. discharge with moistening of lids and hairs adjacent to lids	2
. discharge with moistening of lids and hairs on wide area around the eye	3

2.5.2 Iris lesions

. normal	0
. markedly deepened rugae, congestion, swelling, moderate circum-corneal hyperaemia, or injection, any of these or combination of 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*

2.5.3 Corneal lesions

Cornea (direct examination or, if necessary, with an Ultra-Violet lamp)

To determine the presence or absence of corneal opacification and to evaluate the affected area, one or two drops of 0.5% sodium fluorescein solution can be instilled into the eye (however, this must be performed before the 24-hour reading).

If corneal opacification is difficult to determine, the eye can be examined under a U.V. lamp (a clear fluorescence is visible in the areas of opacification).

Opacity (degree of intensity: area most dense taken for reading)

. no ulceration or opacity	0
. scattered or diffuse areas of opacity (other than slight dulling or normal lustre), details of iris clearly visible	1*
. easily discernible translucent area, details of iris slightly obscured	2*
. macrous areas, no details of iris visible, size of pupil barely discernible	3*
. opaque cornea, iris not discernible through the opacity	4*

* indicates positive effect

Area of opacity

. one quarter (or less) but not zero	1
. greater than one quarter but less than a half	2
. greater than one half but less than three quarters	3
. greater than three quarters up to whole area	4

Any other lesions observed were noted.

2.6. INTERPRETATION OF RESULTS AND CLASSIFICATION OF SUBSTANCES

The results obtained were evaluated in conjunction with the nature and the reversibility of the scores observed, whilst taking into account all the reactions of the treated animals.

2.6.1 Interpretation of the results

Criteria for irritation

A substance or a preparation is considered irritant for the eyes if, when applied to the eye of the animal, significant severe ocular lesions are caused within 72 hours after exposure and which persist for 24 hours or more after treatment with the test substance.

All the scores at each reading time (24, 48 and 72 hours) and for an effect are used by calculating the respective mean values.

2.6.2 Classification of the test substances

- Xi symbol, indication of danger "irritant".

- phrases indicating the nature of special risks:

R 36: "Irritating to eyes"

Ocular lesions are significant if the mean score has any of the following values:

- . opacity of the cornea ≥ 2 , but < 3 ,
- . lesion of the iris ≥ 1 , but ≤ 1.5 ,
- . redness of the conjunctivae ≥ 2.5 ,
- . oedema of the conjunctivae (chemosis) ≥ 2 .

Or else, if the test is performed on three animals, if at least two of them show lesions equal to one of the following values:

- . opacity of the cornea ≥ 2 , but < 3 ,
- . lesion of the iris ≥ 1 , but ≤ 2 ,
- . redness of the conjunctivae ≥ 2.5 ,
- . oedema of the conjunctivae (chemosis) ≥ 2 .

R 41: "Risk of serious damage to eyes"

Ocular lesions are severe:

if the mean score has any of the following values:

- . opacity of the cornea ≥ 3 ,
- . lesion of the iris > 1.5 .

Or else, if the test is performed on three animals, if at least two of them show lesions equal to one of the following values:

- . opacity of the cornea ≥ 3 ,
- . lesion of the iris = 2.

Or if they persist at the end of the observation period.

If the test substance or preparation induces irreversible colouration of the eyes, the phrase R 41 should also be applied.

2.7. ARCHIVES

The study documentation and materials, namely:

- . protocol and possible amendments,
- . raw data,
- . correspondence,
- . final report and possible amendments,

are stored in the archives of C.I.T., Miserey, 27005 Evreux, France, for five years after the end of the *in vivo* phase of the study. At the end of this period, the study documentation will be returned to the Sponsor.

3. RESULTS (table 1)

Slight to severe conjunctival reactions were observed in all animals: slight to severe chemosis (grades 2 to 4), slight or marked conjunctival redness (grade 2 or 3) and clear to whitish purulent discharge were noted, from day 1 up to day 8, 14 or 15.

A slight iritis (grade 1) was noted in all animals on day 2; it persisted up to day 7 or 8, and was masked by corneal opacity in one animal between day 3 and day 5.

A marked corneal opacity (grade 3) was observed in all animals on day 2. A slight to severe corneal opacity (grades 2 to 4) persisted up to day 8 in two animals, and up to the end of the observation period (day 22) in the remaining animal.

Neovascularisation was observed in all animals, from day 6 up to day 8, 13 or 21, and a myosis was recorded in two animals, between day 3 and day 7, or between day 5 and day 6.

The mean scores calculated for each animal over 24, 48 and 72 hours were 3.3, 3.3 and 2.3 for chemosis, 2.7, 3.0 and 2.7 for redness of the conjunctiva, 1.0 and 1.0 for iris lesions (not calculable for one animal) and 2.7, 2.3 and 3.7 for corneal opacity.

4. CONCLUSION

Under our experimental conditions, the test substance 10-UNDECYNOIC ACID (batch No. 1/BD4523) was considered severely irritant when administered by ocular route in rabbits.

Table 1: Individual ocular examinations and mean values of the scores recorded at each reading (24, 48 and 72 hours) for each animal

Rabbit number	Region of eye	Description of ocular reactions	Scores				Mean irritation score (1)	Interpretation (+) (-)
			1h D1	24h D2	48h D3	72h D4		
01	Conjunctivae	Chemosis	3	4	3	3	3,3	(+)
		Redness	0	2	3	3	2,7	(+)
		Discharge	2	S	S	2	(2)	
	Iris		0	1	OP	CP	(2)	(2)
	Corneal opacity	Intensity	0	2	3	3	2,7	(-)
		Area	0	3	4	4	3,7	
	Other		*	*	*	*		
Fluorescein		/	U	U	U			
02	Conjunctivae	Chemosis	3	4	3	3	3,3	(-)
		Redness	0	3	3	3	3,0	(-)
		Discharge	2	S	S	S	(2)	
	Iris		0	1	1	1	1,0	(+)
	Corneal opacity	Intensity	0	3	2	2	2,3	(-)
		Area	0	3	4	4	3,7	
	Other		*	*	*	*		
Fluorescein		/	U	U	U			
03	Conjunctivae	Chemosis	3	3	2	2	2,3	(+)
		Redness	0	2	3	3	2,7	(+)
		Discharge	2	S	1	1	(2)	
	Iris		0	1	1	1	1,0	(+)
	Corneal opacity	Intensity	0	3	4	4	3,7	(+)
		Area	0	3	2	2	2,5	
	Other		*	*	My	My		
Fluorescein		/	U	U	U			

(1) mean of scores on days 2, 3 and 4

h = hour

D = day

(+) = irritant according to E.E.C. criteria

(-) = non-irritant according to E.E.C. criteria

* = None

(2) = not calculated

U = Fluorescein batch No. 5691

/ = Fluorescein not used

S = Whitish purulent discharge

OP = Scoring obscured by marked corneal opacity

My = Myosis

Table 1 (continued)

Rabbit number	Region of eye	Description of ocular reactions	Scores										
			D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	
01	Conjunctivae	Chemosis	3	2	2	2	2	2	2	2	1	1	1
		Redness	3	3	3	2	2	2	2	2	1	1	1
		Discharge	2	1	1	0	0	0	0	0	0	0	0
	Iris		OP	1	1	1	0	0	0	0	0	0	
	Corneal opacity	Intensity	3	2	2	2	2	2	2	2	2	2	2
		Area	4	4	4	4	3	3	3	3	3	3	3
	Other:		*	N	N	N	N	N	N	N	N	N	
	Fluorescein		U	U	U	U	U	U	U	U	U	U	
02	Conjunctivae	Chemosis	2	2	2	1	1	1	1	1	1	1	1
		Redness	3	2	2	1	1	0	0	0	0	0	0
		Discharge	2	1	1	0	0	0	0	0	0	0	0
	Iris		1	1	1	0	0	0	0	0	0	0	
	Corneal opacity	Intensity	2	2	2	2	0	0	0	0	0	0	0
		Area	4	3	2	2	0	0	0	0	0	0	0
	Other		My	My/N	N	N	N	N	N	N	N	*	
	Fluorescein		U	U	U	U	U	/	/	/	/	/	
03	Conjunctivae	Chemosis	2	1	1	1	0	-	-	-	-	-	-
		Redness	2	2	2	1	0	-	-	-	-	-	-
		Discharge	0	0	0	0	0	-	-	-	-	-	-
	Iris		1	1	1	1	0	-	-	-	-	-	
	Corneal opacity	Intensity	3	2	2	2	0	-	-	-	-	-	-
		Area	4	2	2	2	0	-	-	-	-	-	-
	Other		My	My/N	My/N	N	*	-	-	-	-	-	
	Fluorescein		U	U	U	U	U	-	-	-	-	-	

D = day

U = Fluorescein batch No. 5691

/ = Fluorescein not used

* = None

OP = Scoring obscured by marked corneal opacity

N = Neovascularisation

My = Myosis

- = Ocular examination not performed

Table 1 (continued)

Rabbit number	Region of eye	Description of ocular reactions	Scores							
			D15	D16	D17	D18	D19	D20	D21	D22
01	Conjunctivae	Chemosis	0	0	0	0	0	0	0	0
		Redness	0	0	0	0	0	0	0	0
		Discharge	0	0	0	0	0	0	0	0
	Iris		0	0	0	0	0	0	0	0
	Corneal opacity	Intensity	1	1	1	1	1	1	1	1
		Area	2	1	1	1	1	1	1	1
Other Fluorescein		N	N	N	N	N	N	N	*	
		U	U	U	U	U	U	U	U	
02	Conjunctivae	Chemosis	1	0	-	-	-	-	-	-
		Redness	0	0	-	-	-	-	-	-
		Discharge	0	0	-	-	-	-	-	-
	Iris		0	0	-	-	-	-	-	-
	Corneal opacity	Intensity	0	0	-	-	-	-	-	-
		Area	0	0	-	-	-	-	-	-
Other Fluorescein		*	*	-	-	-	-	-	-	
		/	/	-	-	-	-	-	-	
03	Conjunctivae	Chemosis	-	-	-	-	-	-	-	-
		Redness	-	-	-	-	-	-	-	-
		Discharge	-	-	-	-	-	-	-	-
	Iris		-	-	-	-	-	-	-	-
	Corneal opacity	Intensity	-	-	-	-	-	-	-	-
		Area	-	-	-	-	-	-	-	-
Other Fluorescein		-	-	-	-	-	-	-	-	
		-	-	-	-	-	-	-	-	

D = day

U = Fluorescein batch No. 5691

/ = Fluorescein not used

* = None

N = Neovascularisation

- = Ocular examination not performed

APPENDICES

1. Test article description and analytical certificate

TOXICOLOGY DEPARTMENT
CONFIDENTIAL
13 November 1996

elf atochem s.a.
La défense 10, cedex 42
92091 Paris-la-Défense, France

TEST ARTICLE DESCRIPTION

10-UNDECYNOIC ACID

STRUCTURAL FORMULA



IDENTITY

Test article name	: 10-undecyric acid
CAS number	: 2777-65-3
EINECS number	: 220-471-8
Molecular formula	: $\text{C}_{11}\text{H}_{19}\text{O}_2$
Molecular weight	: 183
Purity	: 97.65
Origin	: Elf Atochem, CRRA
Batch	: I/B 04523
Elf Atochem filing number	: CAL 7693/96

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	: Solid
Specific gravity	: 0.906
Melting point	: 40-43°C
Solubility	: 227 mg/l in water soluble in ethylic alcohol, DMSO, corn oil

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

See « Fiche de données de sécurité »

STORAGE AND DISPOSAL

Storage	: in dark and at room temperature
Expiry date	: September 2006
Disposal	: incineration

elf atocem⁷³⁶

CENTRE DE RECHERCHE RHONE-ALPES

Pierre Bénite le : 01/10/96

BULLETIN D'ANALYSE

Référence AGILAN: 010999

Référence demandeur: 29798

Destinataires:

GILLET
CRRA CHIMIE ORGANIQUE
ELF ATOCHEM PIERRE-BENITE

Copies:

RMN

Votre demande : ACIDE 10-UNDECYNOIQUE PILOTE LOT 1/ BD4523

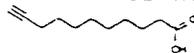
Du : 26/09/95

Séquentiel : 771903

Etude : 890619

Opérateur : L. Le Gleut

DETERMINATION DE PURETE



L'examen RMN H-1 permet d'identifier et de doser les espèces suivantes :

	% molaire relatif
Acide 10-undécynoïque	97,65
Acide 9-undécynoïque (*)	0,31
CHBr=CH-R	0,45
CH ₂ =CBr-R	0,05
CH ₂ =CH-R	0,32
R-CH=CH-R	0,16
Inconnu (□)	0,95
CH ₃ -O-CH ₂ -CH ₂ -O-C(=O)-R	0,09
Bu ₄ N ⁺	0,04

Le 2ème chiffre après la virgule n'est, bien sûr, qu'indicatif.

(*) Hypothèse bâtie sur la présence d'un triplet à 1,77 ppm.

(□) A votre demande nous n'avons pas poursuivi la tentative d'identification des signaux, liés, à 4,65 et 5,08 ppm. Cette identification nécessiterait probablement un enrichissement en vue d'un examen C-13 et éventuellement un couplage GC-MS.

Nous ne constatons pas d'excès des CH₂ 'non fonctionnels' par rapport aux CH₂ 'fonctionnels': la présence de polymères peut donc être rejetée.

Il reste de très faibles signaux difficilement exploitables.

Responsable d'analyse : BEATRICE ALLARD-BRETON

Visa :

2. Diet formula

0-0-2-5

Ref: 112
COMPLETE DIET
RABBIT MAINTENANCE DIET
 Appearance: 4.5 mm diameter granules
 Conditioning: bags of 25 kgs

Daily portion: in accordance with race and body weight, Rabbits 100-150 g, water *ad libitum*.

FORMULA %

Cereals	43.8
Grain biproducts and legumes	49
Vegetable proteins (soya bean meal, yeast)	4.2
Vitamin and mineral mixture ..	3

AVERAGE ANALYSIS %

Calorific value (KCal/kg).....	2200
Moisture	10
Proteins	13
Lipids	2.7
Carbohydrates (N.F.E.)	49.3
Fibre	17
Minerals (ash)	8

MINERALS (calculated in mg/kg)

	Nat. val.	CMV val.	Total
P	3500	3500	7000
Ca	4500	4500	9000
K	11600	0	11600
Na	400	1600	2000
Mg	2100	100	2200
Mn	40	40	80
Fe	160	140	300
Cu	12	15	27
Zn	30	45	75
Co	0.1	1.5	1.6
I	0	0	0
Cl	500	3000	3500

AMINO ACID VALUES
(calculated in mg/kg)

Arginine	6800
Cystine	2100
Lysine	4600
Methionine	1600
Tryptophan	1400
Glycine	5200

FATTY ACID VALUES
(calculated in mg/kg)

Palmitic acid.....	6400
Palmitoleic acid.....	0
Stearic acid.....	600
Oleic acid.....	6400
Linoleic acid.....	12100
Linolenic acid.....	2400

VITAMINS (calculated per kg)

	Nat. val.	CMV val.	Total
Vitamin A	2850 IU	6500 IU	9350 IU
Vitamin D3	30 IU	1000 IU	1030 IU
Vitamin B1	4.3 mg	0 mg	4.3 mg
Vitamin B2	3.8 mg	0 mg	3.8 mg
Vitamin B3	16 mg	0 mg	16 mg
Vitamin B6	1 mg	1 mg	2 mg
Vitamin B12	0 mg	0 mg	0 mg
Vitamin E	16 mg	10 mg	26 mg
Vitamin K3	6 mg	1 mg	7 mg
Vitamin PP	55 mg	5 mg	60 mg
Folic acid	0 mg	0 mg	0 mg
Biotin	0 mg	0 mg	0 mg
Choline	850 mg	200 mg	1050 mg
Meso-Inositol	0 mg	0 mg	0 mg

Available under quality "Control Ref.: 112 C"

U.A.R., 7 rue Galliéni, 91360 Villemoisson - Tel: 69.04.03.57 - Fax : 69.04.81.97
 (Ref. Doc. UAR: 1992)