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Dear Sir/Madam:

Elf Atochem North America, Inc. (Elf Atochem) has received the final report of a primary eye irritation study in rabbits and is submitting it to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e). This study provides information on phenyl acetic acid (CAS No. 103-82-2) and does not involve effects in humans. The title of the study is *Acute Eye Irritation in Rabbits*.

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

The results of this study showed the test material to be severely irritating to rabbit eyes. Results from the study report will be incorporated into the Elf Atochem material safety data sheet for this material.

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

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Best Regards,

Debra Randall

Debra Randall, DABT
Product Safety Manager

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SPONSOR

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

STUDY TITLE

ACUTE EYE IRRITATION
IN RABBITS

TEST SUBSTANCE

PHENYLACETIC ACID

STUDY DIRECTOR

Stéphane de Jouffrey

STUDY COMPLETION DATE

14 November 1997

PERFORMING LABORATORY

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

LABORATORY STUDY NUMBER

15417 TAL

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STATEMENT OF THE STUDY DIRECTOR

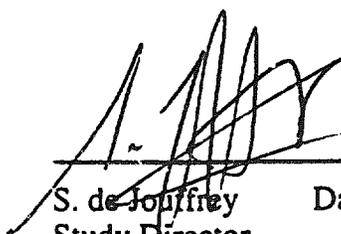
The study was performed in compliance with the principles of Good Laboratory Practice as described in:

- . 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.
- . Council Directive 87/18/E.E.C. of 18 December 1986 on the harmonization of laws, regulations or administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (O.J. n° L 15 of 17.1.87).
- . 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.

Toxicology



S. de Jouffrey Date: 14 November 1997
Study Director
Doctor of Veterinary Medicine
Head of Short-term and Environmental
Toxicology

OTHER SCIENTISTS INVOLVED IN THIS STUDY

For Pharmacy: P.O. Guillaumat
Doctor of Pharmacy

For Toxicology: C. Pelcot
Study Supervisor

STATEMENT OF QUALITY ASSURANCE UNIT

Type of inspection	Dates (day/month/year)		
	Inspection	Reported to Study Director (*)	Reported to Management (*)
Protocol	10 March 1997	26 March 1997	26 March 1997
Report	14 August 1997	19 September 1997	19 September 1997

At about the same time as this study, described in this report, "process-based" and routine facility inspections of critical procedures relevant to this study type were made by the Quality Assurance Unit.

The findings of these inspections were reported to the Study Director and to C.I.T. Management.

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

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



L. Valette-Talbi Date: 14 November 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 PHENYLACETIC ACID (batch No. S2969) 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., B₅, 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 the end of the study (day 22).

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: very slight to severe chemosis, very slight to moderate redness of the conjunctivae and clear or whitish purulent discharge were noted, from day 1 up to day 17 at the latest.

A slight iritis was observed in two animals on day 2; it persisted up to day 12 or 14. Reading was masked by corneal opacity in the remaining animal.

A moderate or severe corneal opacity was noted in all animals on day 1; a slight to severe corneal opacity persisted up to the end of the observation period (day 22) in two animals. The remaining animal was killed on day 7 for ethical reasons, because of the severity of ocular reactions.

A whitening of the conjunctivae was noted in all animals on day 1; it persisted up to day 17 at the latest. Neovascularisation was noted in two animals from day 5 up to day 14 or from day 7 up to the end of the observation period (day 22) and alopecia around the eye was recorded in one animal, from day 11 up to day 20.

Mean scores calculated for each animal over 24, 48 and 72 hours were 3.3, 3.0 and 3.0 for chemosis, 3.0, 2.7 and 3.0 for redness of the conjunctivae, 1.0 and 1.0 for iris lesions (not calculable in one animal) and 2.0, 4.0 and 2.3 for corneal opacity.

Conclusion

Under our experimental conditions and according to the classification criteria laid down in Directive 93/21/E.E.C. (27th April 1993) adapting to technical progress for the eighteenth time Council Directive 67/548/E.E.C., the test substance PHENYLACETIC ACID (batch No. S2969) is considered 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 PHENYLACETIC ACID (lot n° 2969) 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., B₅, 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 fin de l'étude (jour 22).

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 très léger à sévère, une rougeur de la conjonctive très légère à modérée et un larmoiement clair ou purulent sont notés, du jour 1 au jour 17 au plus tard.

Un léger iritis est noté au jour 2 chez deux animaux : il persiste jusqu'au jour 12 ou 14. La lecture est masquée par une importante opacité cornéenne chez le dernier animal.

Une opacité cornéenne modérée ou sévère est observée chez tous les animaux au jour 1 : une opacité cornéenne légère à sévère persiste jusqu'à la fin de la période d'observation (jour 22) chez deux animaux. Le dernier animal est sacrifié au jour 7 pour des raisons éthiques, suite à la persistance de réactions oculaires sévères.

Un blanchiment de la conjonctive est noté chez tous les animaux au jour 1 : il persiste jusqu'au jour 17 au plus. Une néovascularisation de la cornée est observée chez deux animaux, du jour 5 au jour 14 ou du jour 7 jusqu'à la fin de la période d'observation (jour 22) et une alopecie sur le pourtour de l'oeil est notée chez un animal, du jour 11 au jour 20.

Les scores moyens calculés pour chaque animal après 24, 48 et 72 heures sont de 3,3 ; 3,0 et 3,0 pour le chémosis, de 3,0 ; 2,7 et 3,0 pour la rougeur de la conjonctive, de 1,0 et 1,0 pour les lésions de l'iris (non calculable chez un animal) et de 2,0 ; 4,0 et 2,3 pour l'opacité cornéenne.

Conclusion

Dans nos conditions expérimentales et d'après les critères de classification décrits dans la Directive 93/21/C.E.E. (27 avril 1993) portant dix-huitième adaptation au progrès technique de la Directive 67/548/C.E.E., le produit PHENYLACETIC ACID (lot n° 2969) est considéré irritant par voie oculaire chez le Lapin.

1. INTRODUCTION

The objective of this study was to evaluate the potential of the test substance PHENYLACETIC 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 PHENYLACETIC 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: PHENYLACETIC ACID
- . batch number:
 - protocol: S2969
 - labelling: none
- . Elf Atochem filing number: CAL 514/97
- . description: rough whitish crystalline flakes
- . container: one opaque plastic flask
- . date of receipt: 7 March 1997
- . storage conditions: at room temperature, protected from light and from humidity
- . purity: 99%
- . expiry date: February 1998.

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 batch number "S2969", which was absent from the label on the container was confirmed by the Study Monitor in a statement dated 8 April 1997.

The pH of the test substance at a concentration of 10% in purified water measured at C.I.T. was approximately 3.

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 Selle, 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 ± 0.2 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: 30 to 70%
- . light/dark cycle: 12 h/12 h
- . ventilation: approximately 12 cycles/hour of filtered, non-recycled air.

The temperature and relative humidity were recorded 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	15 April 1997	6 May 1997
02	18 April 1997	24 April 1997
03	18 April 1997	9 May 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 membranes)

. no swelling	0
. any swelling above normal (includes nictitating membranes)	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*
. nacrourous 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. Classification of the test substance is based on the criteria laid down in Council Directive 93/21/E.E.C. Commission Directive of 27th April 1993 adapting to technical progress for the eighteenth time Council Directive 67/548/E.E.C. on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances.

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. PROTOCOL ADHERENCE

The study was performed in accordance with the original protocol No. 15417 TAL and related amendments.

The minor fluctuations of relative humidity recorded outside of the target ranges specified in the protocol were not considered to have an impact on the validity or integrity of the study.

2.8. ARCHIVES

The study archives, 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 ten years after the end of the *in vivo* phase of the study. At the end of this period, the study archives will be returned to the Sponsor.

3. RESULTS (table 1)

Slight to severe conjunctival reactions were observed in all animals: very slight to severe chemosis (grades 1 to 4), very slight to moderate redness of the conjunctivae (grade 1 to 3) and clear or whitish purulent discharge were noted, from day 1 up to day 17 at the latest.

A slight iritis (grade 1) was observed in two animals on day 2; it persisted up to day 12 or 14. Reading was masked by corneal opacity in the remaining animal.

A moderate or severe corneal opacity (grade 3 or 4) was noted in all animals on day 1: a slight to severe corneal opacity (grades 2 to 4) persisted up to the end of the observation period (day 22) in two animals. The remaining animal was killed on day 7 for ethical reasons, because of the severity of ocular reactions.

A whitening of the conjunctivae was noted in all animals on day 1; it persisted up to day 17 at the latest. Neovascularisation was noted in two animals from day 5 up to day 14 or from day 7 up to the end of the observation period (day 22) and alopecia around the eye was recorded in one animal, from day 11 up to day 20.

Mean scores calculated for each animal over 24, 48 and 72 hours were 3.3, 3.0 and 3.0 for chemosis, 3.0, 2.7 and 3.0 for redness of the conjunctivae, 1.0 and 1.0 for iris lesions (not calculable in one animal) and 2.0, 4.0 and 2.3 for corneal opacity.

4. CONCLUSION

Under our experimental conditions and according to the classification criteria laid down in Directive 93/21/E.E.C. (27th April 1993) adapting to technical progress for the eighteenth time Council Directive 67/548/E.E.C., the test substance PHENYLACETIC ACID (batch No. S2969) is considered 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	2	3	3	3	3,0	(+)
		Discharge	2	S	S	S	(2)	
	Iris		0	1	1	1	1,0	(+)
	Corneal opacity	Intensity	3	2	2	2	2,0	(+)
		Area	2	4	4	3	3,7	
	Other		B	B	B	B		
	Fluorescein		/	U	U	U		
02	Conjunctivae	Chemosis	3	3	3	3	3,0	(+)
		Redness	1	2	3	3	2,7	(+)
		Discharge	0	S	S	S	(2)	
	Iris		OP	OP	OP	OP	(2)	(2)
	Corneal opacity	Intensity	4	4	4	4	4,0	(+)
		Area	1	2	2	3	2,3	
	Other		B	B	B	B		
	Fluorescein		/	U	U	U		
03	Conjunctivae	Chemosis	2	3	3	3	3,0	(+)
		Redness	2	3	3	3	3,0	(+)
		Discharge	0	S	S	S	(2)	
	Iris		0	1	1	1	1,0	(+)
	Corneal opacity	Intensity	4	3	2	2	2,3	(+)
		Area	2	2	2	2	2,0	
	Other		B	B	B	B		
	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

(2) = not calculated

U = Fluorescein batches Nos. 5691 and 7239

/ = Fluorescein not used

S = Whitish purulent discharge

OP = Scoring masked by marked corneal opacity

B = Whitening of conjunctivae

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	3	2	2	2	2	2	2	2	2	2
		Redness	3	3	3	3	2	2	2	2	2	2	1
		Discharge	S	S	0	0	0	0	0	0	0	0	0
	Iris		1	1	1	1	1	1	1	1	1	0	0
	Corneal opacity	Intensity	2	2	2	2	2	2	2	2	2	2	2
		Area	3	3	3	3	3	3	3	3	2	2	2
	Other Fluorescein		B	B	B/N	B/N	B/N	B/N	B/N/A	B/N/A	B/N/A	N/A	
			U	U	U	U	U	U	U	/	/	U	
02	Conjunctivae	Chemosis	3	3	3	M	M	M	M	M	M	M	
		Redness	3	3	3	M	M	M	M	M	M	M	
		Discharge	S	S	S	M	M	M	M	M	M	M	
	Iris		OP	OP	OP	M	M	M	M	M	M	M	
	Corneal opacity	Intensity	4	4	4	M	M	M	M	M	M	M	
		Area	3	4	4	M	M	M	M	M	M	M	
	Other Fluorescein		B	B	B	M	M	M	M	M	M		
			U	/	/	M	M	M	M	M	M		
03	Conjunctivae	Chemosis	3	3	3	3	2	2	1	1	1	1	
		Redness	3	3	3	3	3	3	2	2	2	2	
		Discharge	S	S	S	S	S	S	0	0	0	0	
	Iris		1	1	1	1	1	1	1	1	1	1	
	Corneal opacity	Intensity	2	2	2	2	2	2	2	2	2	2	
		Area	2	2	2	2	2	2	2	2	3	3	
	Other Fluorescein		B/N	B/N	B/N	B/N	B/N	B/N	B/N	B/N	B/N		
			U	U	U	U	U	U	U	/	/		

D = day

U = Fluorescein batches Nos. 5691 and 7239

/ = Fluorescein not used

S = Whitish purulent discharge

OP = Scoring masked by marked corneal opacity

B = Whitening of conjunctivae

N = Neovascularisation

A = Alopecia around the eye

M = Animal killed for humane reasons

Table 1 (continued)

Rabbit number	Region of eye	Description of ocular reactions	Scores							
			D15	D16	D17	D18	D19	D20	D21	D22
01	Conjunctivae	Chemosis	1	1	1	0	0	0	0	0
		Redness	1	1	1	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	3	3	3	2	2	2	2	2
		Area	2	2	2	2	2	2	2	2
	Other	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N	N
	Fluorescein	U	/	/	U	/	/	/	/	/
02	Conjunctivae	Chemosis	M	M	M	M	M	M	M	M
		Redness	M	M	M	M	M	M	M	M
		Discharge	M	M	M	M	M	M	M	M
	Iris		M	M	M	M	M	M	M	M
	Corneal opacity	Intensity	M	M	M	M	M	M	M	M
		Area	M	M	M	M	M	M	M	M
	Other	M	M	M	M	M	M	M	M	
	Fluorescein	M	M	M	M	M	M	M	M	
03	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	2	2	2	2	2	2	2	2
		Area	2	2	2	2	2	2	2	2
	Other	B	B	B	*	*	*	*	*	
	Fluorescein	U	/	/	/	/	/	/	/	

D = day

U = Fluorescein batches Nos. 5691 and 7239

/ = Fluorescein not used

* = None

B = Whitening of conjunctivae

N = Neovascularisation

A = Alopecia around the eye

M = Animal killed for humane reasons

APPENDICES

1. Test article description and analytical certificate

TOXICOLOGY DEPARTMENT
CONFIDENTIAL
27 February 1997

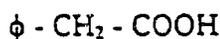
elf atochem s.a.

La défense 10
92091 Paris-la-Défense, France

TEST ARTICLE DESCRIPTION

PHENYL ACETIC ACID

STRUCTURAL FORMULA



IDENTITY

Test article name : PHENYLACETIC ACID
Chemical name : id
CAS number : 103-82-2
EINECS number : 203-148-6
Molecular formula : $C_8H_8O_2$
Molecular weight : 136.1
Purity : 99%
Origin : Elf Atochem UK, Widnes
Batch : S2969
Elf Atochem filing number : CAL 514/97

PHYSICAL AND CHEMICAL PROPERTIES

Appearance : Large cream flakes
Odour : Persistent, unpleasant
Specific gravity : 1.1
Melting point : 76.5°C
Boiling point : 265°C at 1013 mbar
Vapor pressure : 1.3 hPa at 97°C
Flash point : 132°C
Solubility : water: 1.66g/100 ml at 20°C (increasing temperature is likely to increase solubility)
: ethylic alcohol
: DMSO: unknown

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

see test substance data sheet

STORAGE AND DISPOSAL

Storage : in dark and at room temperature
Expiry date : February 1998
Disposal : incineration

elf atochem**ATO**

Elf Atochem UK Ltd
 Chlorotoluene Derivatives Division
 West Bank Dock Estate, Wigan, Cheshire WA3 6NY
 Tel: 0151 424 4281 Sales: Fax: 0151 423 2314
 Works: Fax: 0151 423 5757
 Engineering: Fax: 0151 423 5450

514/57

W/QC/011A

CERTIFICATE OF ANALYSIS

Customer CENTRE D'APPLICATION DE LEVALLOIS
 Quantity 250g SAMPLE Date 03 - 02 - 97
 Product PHENYL ACETIC ACID
 Customers Order No Order No. S 2969

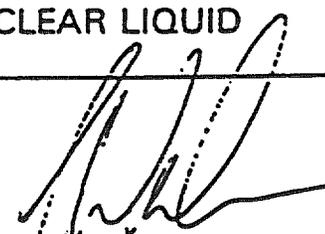
The product supplied against the above order has been tested and found to comply with the requirements of

Batch Numbers etc.

Analysis Results

BULK

8343	DESCRIPTION	:	LARGE CREAM FLAKES
	ASSAY	:	99.0%
	MELTING POINT	:	76.5° C
	MOISTURE	:	0.15%
	20% SOLUTION IN 10% NaOH	:	PALE YELLOW CLEAR LIQUID


 Quality Control Manager
 (I. WALKER)

2. Diet formula

Ref: 112

**COMPLETE DIET
RABBIT MAINTENANCE DIET**Appearance: 4.5 mm diameter granules
Conditioning: bags of 25 kgsDaily 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

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

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

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)

Best Available Copy

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