CENTRE DE RECHERCHES BIOLOGIQUES

Baugy, June 17, 1993

STUDY NO. 920083 E

[redacted]

PRIMARY CUTANEOUS IRRITATION

Sponsor :
ELF ATOCHEM SA
La Défense 10 Cedex 42
92091 PARIS LA DEFENSE
FRANCE

Company Sanitized. Does not contain TSCA CBI

CHEMIN DE MONTFAULT - 18800 BAUGY - TEL. (18) 48 26 18 26 - TÉLEX 782183 F - TÉLÉCOPIE (18) 48 26 11 87
SOCIÉTÉ A.R.L. - R.C.S. BOURGES B 775 124 452 - SIRET 775 124 452 00016 - A.P.E. 9311

TRIAL : Cutaneous primary irritation index.

COMPOUND : [redacted]

SPONSOR : ELF ATOCHEM SA.

SPONSOR CONTACT : Mr REGNIER

ADDRESS : La Défense 10 Cedex 42
92091 PARIS LA DEFENSE - FRANCE

SITE OF TRIAL : CENTRE DE RECHERCHES BIOLOGIQUES
Chemin de Montifault
18800 BAUGY - FRANCE

RESPONSIBLE STAFF FOR CERB :

Scientific and Technical Director :

S. RICHARD
Pharmacien
Docteur de 3ème Cycle
Maître en Pharmacologie

01:07:93
Date

Signature

Head of Toxicology Department :

C. AUDEVAL-GERARD
Docteur Vétérinaire
CES d'Ophtalmologie

30/06/93
Date

Signature

Study Director :

C. BESSON
DUT de Biologie Appliquée

30/06/93
Date

Signature

Quality Assurance :

C. VIGIER

28/06/93
Date

Signature

The present report is based upon the authentic experimental results obtained.

This report consists of 33 pages numbered from 1 to 33 including 5 appendices.

CONTENTS

I. SUMMARY

The aim of this study was objective determination in the Rabbit of the irritant properties and/or degree of corrosion induced by compound [redacted] following single cutaneous application.

0.5 ml of compound [redacted] were applied to the right flank of each of three rabbits. The left flank served as a control for the trial. A dressing held the compound in place for 4 hours on the flank of each animal.

Any possible lesions were evaluated approximately one hour after removal of the dressing, then 24 hours, 48 hours and 72 hours later.

Mean indices were calculated from results obtained from each rabbit at times 24 hours, 48 hours and 72 hours.

Cumulative means of mean indices were :

. Erythema : 0.

. Edema : 0.

Mean indices per rabbit, for the three times together were :

. Erythema : 0 in all animals.

. Edema : 0 in all animals.

In conclusion, compound [redacted] was found to be <u>non-irritant</u> for the skin of the Rabbit.

II. EXPERIMENTAL PROTOCOL ADOPTED

II.1 INTRODUCTION

The protocol used for study of cutaneous primary irritation, complied with requirements of OECD Guideline No. 404 (May 12, 1981) and EEC Directives (67/548, 79/831, 83/467, 84/449) and enabled full evaluation of the reversible or irreversible nature of the effects seen.

II.2 AIM

The aim of the study was objective determination in the Rabbit of the irritant properties and/or degree of corrosion caused by compound [redacted] following its single cutaneous application.

II.3 METHOD

Dermal irritation and/or corrosion following cutaneous application of compound [redacted] to the back of the Rabbit were evaluated by grading of the cutaneous irritation reactions seen, using a predetermined score system.
This method is not applicable to substances with a pH below 2 or above 11.5, with a predictable cutaneous corrosive action.

The protocol n° 92.04.10.02 signed by the responsible of the sponsor and by the experimenters may be found in appendix 1.

A pre-study was carried out using one rabbit.
Results showed no irritation, the study was continued in two other rabbits.

This study took place in accordance with rules of Good Laboratory Practices as published by :

- **The French Ministry of Social Affairs and National Solidarity :**
  State Secretariat Responsible for Health
  Instructions concerning Good Laboratory Practices (GLP) in the field of experimental toxicology.
  Instruction of May 31, 1983, Official Text No. 1065 ; Reference SN-S83/25.

- **Directive 87/18/EEC, this directive referring to Recommendation CC81/30 Appendix 2 of the OECD.**

- **The Food and Drug Administration : GLP 21 CFR Part 58 of December 22, 1978 and amendments of April 11, 1980 and September 4, 1987.**

II.4 COMPOUND

The technical data and the analytical certificate concerning the compound are attached to the study report in Appendix 2.

- Name : [redacted]
- Origin and batch number : [redacted]
- Record number (CAL) : [redacted]
- Origin : ELF ATOCHEM SA
- Date received : Saturday April 18 1992
- Amount : 1 bottle of approximately 107 g
- Appearance : [redacted]
- pH : [redacted]

II.5 ANIMALS

- SPECIES : New Zealand Albino Rabbit.
- ORIGIN : CEGAV specialized breeding establishment (Les Hautes Noës, Saint Mars d'Egrenne, 61350 PASSAIS LA CONCEPTION, FRANCE).
- WEIGHT : Between 1.5 kg and 2.5 kg at the start of the trial.
- SEX : female.
- NUMBER : 3.
- DATE OF DELIVERY : On 01.04.1992.
- ACCLIMATIZATION : For at least 5 days before the trial, in the zone where the experiment was to take place. Animals were selected on the basis of their general condition.
- IDENTIFICATION : Animals were identified individually by ear clipping.
- HOUSING : Animals were kept in cages of standard size. Excreta were eliminated by unrolling plastified brown paper which was placed under the cages.
  These cages were kept in an air-conditioned (17°C-21°C) animal house, kept at relative humidity between 45 per 100 and 65 per 100, apart from during cleaning, in which non-recycled filtered air was changed approximately ten times per hour. The artificial daylight cycle was 12 hours light and 12 hours darkness.

- FOOD : UAR 112.
  An analytical certificate concerning this foodstuff is provided with the study report in Appendix 3.

- DRINKING WATER : Tap water distributed ad libitum in polycarbonate feeder bottles with a stainless steel teat. A water sample was obtained every three months and sent to the Direction des Services Vétérinaires, 216 Rue Louis Mallet, 18014 BOURGES Cedex, FRANCE for analysis.The water analytical certificate in Appendix 4 corresponds to the sample obtained on the date closest of the start of the study.

II.6 APPLICATION OF COMPOUND

Compound [redacted] was applied to the dorsal cutaneous region. For this purpose, on the day prior to application, the dorsal region of each rabbit was carefully shaved over two symmetrical zones, measuring at least 14 cm x 5 cm, in relation to the vertebral axis. An AESCULAP FAVORITA II GT 104 electric trimmer was used, avoiding any damage to the skin. Any animal with damaged skin was eliminated from the study at the time of application.

The left flank of each of the animals was left intact.

A dose of 0.5 ml of compound [redacted] was applied to the right flank of each of the animals. The non-treated flank of each animal served as a control for the trial.

Compound [redacted] was deposited on a gauze square of approximately 6 cm^2. The side of the gauze in contact with the compound was applied to the skin.

This gauze square was protected by a swab held in place with a URGOPORE® microporous and non-allergic non-occlusive dressing, and the whole being held in place by COHEVET coalescent elastic and cohesive hypoallergenic tape. Dressings were held in place for 4 hours after application.

The day of application was taken as D1 of the study.

II.7 CLINICAL MONITORING OF ANIMALS

Approximately one hour after removal of the dressing and of compound [redacted] then 24 hours, 48 hours and 72 hours later, possible cutaneous lesions which may have appeared on the right flank of each of the animals were evaluated using the following score system.

ERYTHEMA AND ESCHARS FORMATION

No erythema	0
Slight erythema (scarcely visible)	1
Clearly visible erythema	2
Moderate to marked erythema	3
Severe erythema (reddish purple) with formation of slight eschars (deep lesions)	4

FORMATION OF EDEMA

No edema	0
Very slight edema (scarcely visible)	1
Slight edema (contours well defined, visible swelling)	2
Moderate edema (thickness approximately 1 mm)	3
Severe edema (thickness more than 1 mm and area greater than that of application)	4

II.8 CALCULATION OF CUTANEOUS IRRITATION INDEX

Mean indices are calculated from results obtained for each rabbit at times 24 hours, 48 hours and 72 hours.

The following are noted :

- for each parameter, mean of indices for each rabbit for the three times (= mean index per parameter, per animal for the three times = Mi)
  The maximal theorical score is 4 (erythema/edema).

- for each parameter, the cumulative mean (= sum of mean indices for the three animals / 3 = sum of Mi/3).
  The maximal theorical score is 4 (erythema/edema).

II.9 STEPS OF THE STUDY :

A pre-study was carried out using one rabbit.
Results showed no irritation, therefore the study was continued in two other rabbits.

II.10 CLASSIFICATION

The compound [redacted] was classified irritant or non irritant on the basis of irritation indices obtained in accordance with the Directive 83/467/EEC proposed by the Official Gazette of the European Community.

Compound is found to be irritant if :

- cumulative mean (Cm = sum of Mi/3) is higher or equal to the values indicated in table I for at least one parameter.
- or if, for at least one parameter, mean indices (Mi) are higher or equal to the values indicated in the table I in at least 2 animals.

TABLE I

PARAMETER	THRESHOLD IRRITATION VALUE
Erythema	2
Edema	2

II.11 DATA ENTRY OF RESULTS

All data were recorded as and when obtained using files classified by the study number.

II.12 REPORT

The report of experiment included all findings noted during the course of the study, and in particular :

- cutaneous reaction observed,
- cutaneous irritation indices,
- classification of the compound [redacted]

II.13 QUALITY ASSURANCE

The Quality Assurance Unit ensured that working procedures relating to this type of study were strictly adhered to, by periodic inspections of random, over the course of the year.

Data included in the report of the experiment were audited by the Quality Assurance Unit, in accordance with standard procedures at the Centre.

II.14 RECORDS

The protocol, raw data, the correspondance, the report and a sample of the compound have been stored for five years at CERB, 18800 BAUGY, FRANCE, starting from the date of the final report.

At the end of this period, CERB will contact the sponsor in order to jointly determine to either :

- continue the records,
- return the data to the sponsor,
- destroy the data.

III. RESULTS

III.1 DEVIATION FROM PROTOCOL N° 92.04.10.02 :

No deviation from the protocol was recorded during the study.

The study was performed according to protocol n° 92.04.10.02.

III.2 DATES OF TRIAL

- Date of start of the pré-study : 23.04.1992.
- Date of end of the pre-study : 26.04.1992.

- Date of start of the main study : 28.04.1992.
- Date of end of the main study : 01.05.1992.

III.3 CUTANEOUS TOLERANCE

The results of findings are shown in Tables II (irritation indices at 24 hours, 48 hours and 72 hours and mean indices per parameter) and III (cumulative means for the three animals) as well as in the results sheet included in Appendix 5.

Cutaneous application of compound [redacted] caused no irritation reaction.

TABLE II

[redacted]

Irritation indices
(24h - 48h - 72h evaluations)
and mean indices per parameter

Rabbit No	EVALUATION TIME			MEAN INDEX (Mi)
	24 H	48 H	72 H	
920457	ER = 0 ED = 0	ER = 0 ED = 0	ER = 0 ED = 0	ER = 0 ED = 0
920458	ER = 0 ED = 0	ER = 0 ED = 0	ER = 0 ED = 0	ER = 0 ED = 0
920459	ER = 0 ED = 0	ER = 0 ED = 0	ER = 0 ED = 0	ER = 0 ED = 0

ER = erythema
ED = edema

TABLE III

[redacted]

Cumulative means for the three animals

	Sum of mean indices of three animals	Cumulative mean (sum/3) = CM
ERYTHEMA	0	0
EDEMA	0	0

- Cumulative means (Cm) of mean indices were :

. Erythema : 0.

. Edema : 0.

- Mean indices per rabbit (Mi), for the three times together were :

. Erythema : 0 in all animals.

. Edema : 0 in all animals.

Classification of the compound is : non-irritant compound for the skin of the Rabbit.

IV. CONCLUSION

Cutaneous primary irritation following application of compound [redacted] was evaluated in the Rabbit.

Under the experimental conditions adopted, the classification of compound [redacted] is : non-irritant compound for the skin of the Rabbit.

APPENDIX 1

Protocol n° 92.04.10.02

CERB - PROTOCOL N° 92.04.10.02

TRIAL : [redacted]
Cutaneous primary irritation index.

SPONSOR :

ELF ATOCHEM
La Défense 10 - Cedex 42
92091 PARIS LA DEFENSE

SITE OF TRIAL : CENTRE DE RECHERCHES BIOLOGIQUES
Chemin de Montifault
18800 BAUGY, FRANCE

APPROBATION :

SPONSOR CONTACT :

Mr REGNIER

22/04//92 ---------- Date ---------- Signed

RESPONSIBLE STAFF FOR CERB :

Scientific and Technical Director :

S. RICHARD
Pharmacien, Docteur de 3ème Cycle
Maître en Pharmacologie

16/04/92 ---------- Date ---------- Signed

Head of Toxicology Department :

C. AUDEVAL-GERARD
Docteur Vétérinaire

16/04/92 ---------- Date ---------- Signed

Study Director :

C. BESSON

14/04/92 ---------- Date ---------- Signed

Quality Assurance :

C. VIGIER

16/04/92 ---------- Date ---------- Signed

[redacted]

CUTANEOUS PRIMARY IRRITATION INDEX

I AIM

The aim of the study is objective determination in the Rabbit of the irritant properties and/or degree of corrosion caused by compound [redacted] following its single cutaneous application.

II METHOD

Dermal irritation and/or corrosion following cutaneous application of compound [redacted] to the back of the Rabbit are evaluated by grading of the cutaneous irritation reactions seen, using a predetermined score system.

The protocol used for study of cutaneous primary irritation, complies with requirements of OECD Guideline No. 404 (May 12, 1981) and EEC Directives (67/548, 79/831, 83/467, 84/449) and enables full evaluation of the reversible or irreversible nature of the effects seen.

This method is not applicable to substances with a pH below 2 or above 11.5, with a predictable cutaneous corrosive action.

A pre-study is carried out using one rabbit.
If results shows no irritation or only slight irritation, the study is continued in two other rabbits.
If results reveals an irritant effect (grade ≥ 3 erythema and/or edema), the pre-study can be continued until D8 and D15 to indicate the possible reversibility of lesions, though the study is not repeated in two other rabbits.

This study took place in accordance with rules of Good Laboratory Practices as published by :

- **The French Ministry of Social Affairs and National Solidarity :**
  State Secretariat Responsible for Health
  Instructions concerning Good Laboratory Practices (GLP) in the field of experimental toxicology.
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- **Directive 87/18/EEC, this directive referring to Recommendation CC81/30 Appendix 2 of the OECD.**
- **The Food and Drug Administration : GLP 21 CFR Part 58 of December 22, 1978 and amendments of April 11, 1980 and September 4, 1987.**

III. COMPOUND FORAPERLE 321 :

DATA SUPLIED BY THE SPONSOR :
The substance information sheet and the analytical certificate were received on April 10,1992.

DATA TO BE SUPPLIED BY THE SPONSOR : please fill in the test substance information sheet.

AMOUNT OF COMPOUND TO BE SUPPLIED : 5 ml of compound [redacted] are required for the study.

IV - GENERAL CHARACTERISTICS OF STUDIES :

IV-1 ANIMALS

- SPECIES : New Zealand Albino Rabbit.
- ORIGIN : From CEGAV specialized breeding establishment (Les Hautes Noës, Saint Mars d'Egrenne, 61350 PASSAIS LA CONCEPTION, FRANCE).
- WEIGHT : Generally between 1.5 kg and 2.5 kg at the start of the trial.
- SEX : male or female.
- NUMBER : 3.
- ACCLIMATIZATION : For at least 5 days before the trial, in the zone where the experiment is to take place. Animals are selected on the basis of their general condition.
- IDENTIFICATION : Animals are identified individually by ear clipping.
- HOUSING : Animals are kept in cages of standard size. Excreta are eliminated by unrolling plastified brown paper which is placed under the cages.
  These cages are kept in an air-conditioned (17°C-21°C) animal house, kept at relative humidity between 45 per 100 and 65 per 100, apart from during cleaning, in which non-recycled filtered air is changed approximately ten times per hour. The artificial daylight cycle is 12 hours light and 12 hours darkness.
- FOOD : UAR 112 foodstuff.
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- DRINKING WATER : Tap water distributed ad libitum in polycarbonate feeder bottles with a stainless steel teat. A water sample is obtained every three months and sent to the Direction des Services Vétérinaires, 216 Rue Louis Mallet, 18014 BOURGES Cedex, FRANCE for analysis. A water analytical certificate is included in the study report.

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Compound [redacted] is applied to the dorsal cutaneous region. For this purpose, on the day prior to application, the dorsal region of each rabbit is carefully shaved over two symmetrical zones, measuring at least 14 cm x 5 cm, in relation to the vertebral axis. An AESCULAP FAVORITA II GT 104 electric trimmer is used, avoiding any damage to the skin. Any animal with damaged skin is eliminated from the study at the time of application.

The left flank of each of the animals is left intact.

A dose of 0.5 g of compound [redacted] is applied to the right flank of each of the animals. The non-treated flank of each animal serves as a control for the trial.

The substance is deposited on a gauze square of approximately 6 cm^2. The side of the gauze in contact with the compound is applied to the skin.

This gauze square is protected by a swab held in place with a URGOPORE® microporous and non-allergic non-occlusive dressing, and the whole being held in place by COHEVET coalescent elastic and cohesive hypoallergenic tape. Dressings are held in place for 4 hours after application.

The day of application is taken as D1 of the study.

Steps of the study :

A pre-study is carried out using one rabbit.
If results shows no irritation or only slight irritation, the study can be continued in two other rabbits.

If results reveal an irritant effect (grade ≥ 3 erythema and/or edema), the pre-study can be continued until D8 and D15 to indicate the possible reversibility of lesions, though the study is not repeated in two other rabbits.

IV-3 CLINICAL MONITORING OF ANIMALS

Approximately one hour after removal of the dressing then 24 hours, 48 hours and 72 hours later, possible cutaneous lesions which may have appeared on the right flank of each of the animals are evaluated using the following score system. Observation can be continued until D8 and D15 if signs of irritation persist at 72 hours.

ERYTHEMA AND ESCHARS FORMATION

No erythema	0
Slight erythema (scarcely visible)	1
Clearly visible erythema	2
Moderate to marked erythema	3
Severe erythema (reddish purple) with formation of slight eschars (deep lesions)	4

FORMATION OF EDEMA

No edema	0
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Slight edema (contours well defined, visible swelling)	2
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The following are noted :

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  The maximal theorical score is 4 (erythema/edema).

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  The maximal theorical score is 4 (erythema/edema).

IV-5 CLASSIFICATION

The compound [redacted] is classified irritant or non irritant on the basis of irritation indices obtained in accordance with the Directive 83/467/EEC proposed by the Official Gazette of the European Community.

Compound is found to be irritant if :

- cumulative mean (Cm = sum of Mi/3) is higher or equal to the values indicated in table I for at least one parameter.

- or if, for at least one parameter, mean indices (Mi) are higher or equal to the values indicated in the table I in at least 2 animals.

PARAMETER	THRESHOLD IRRITATION VALUE
Erythema	2
Edema	2

V - RESULTS

All data are recorded as and when obtained using files classified by the study number.

VI - REPORT

The report of experiment includes all findings noted during the course of the study, and in particular :

- irritation reaction observed,
- cutaneous irritation indices,
- classification of the studied compound.

VII - QUALITY ASSURANCE

The Quality Assurance Unit ensures that working procedures relating to this type of study are strictly adhered to, by periodic inspections of random, over the course of the year.

Data included in the report of the experiment are audited by the Quality Assurance Unit, in accordance with standard procedures at the Centre.

VIII - RECORDS

The protocol, any possible amendments, raw data, the correspondance and the report, and a sample of the compound are stored for five years at CERB, 18800 BAUGY, FRANCE, starting from the date of the final report.

At the end of this period, CERB will contact the sponsor in order to jointly determine to either :

- continue the records,
- return the data to the sponsor,
- destroy the data.

IX - PLANIFICATION :

Date of start of study : Week of April 27, 1992.
Results by telex : at the end of the study.
Date of submission of the draft report : end of May 1992.
Date of submission of the English summary : at the final report submission.

APPENDIX 2

Technical data and Analytical certificate
concerning compound

SERVICE DE TOXICOLOGIE
CONFIDENTIEL
Avril 1992

elf atochem sa
La Défense 10, cédex 42
92091 Paris-La Défense
France

FICHE D'INFORMATIONS

[redacted]

IDENTIFICATION

Nom commun : [redacted]
Nom chimique :

Origine; n° de lot :
N° d'archivage (CAL) :

PROPRIETES PHYSICO-CHIMIQUES

Apparence :
Viscosité :
Température ébullition :
pH :
Densité :
Point d'éclair :
Solubilité :

INFORMATIONS TOXICOLOGIQUES ET PRECAUTION D'EMPLOI

Aucune information disponible.

CONDITIONS DE CONSERVATION ET DE DESTRUCTION

Conservation	: A l'obscurité et à l'abri de la chaleur.
Stabilité	: Stable jusqu'en Avril 1993 dans ces conditions de stockage
Destruction	: Incinération.

elf atochem sa
4, cours Michelet, cedex 42
92091 Paris La Défense 10
France

ATO

BULLETIN D'ANALYSE

[redacted]

[redacted]

8 Avril 1992

Jean-François Régnier

Service de Toxicologie

APPENDIX 3

Analytical certificate concerning foodstuff

Réf. [redacted]

ALIMENT COMPLET

LAPINS - ENTRETIEN

Granulés : 4,5 mm

Ration journalière du Lapin : suivant la race, de 100 à 150 g — Eau à volonté.

FORMULE %

Céréales, sucre	42,8
Issues et légumineuses	49
Protéines végétales (tourteaux)	4,2
Composé minéral vitaminisé	4

ANALYSE MOYENNE %

Valeur calorifique (Cal/kg)	2.200
Eau	10
Protides	13
Lipides	2,7
Glucides (ENA)	49,3
Cellulose (Weende)	17
Minéraux	8

ACIDES AMINES
(calculés en mg/kg)

Arginine	6.800
Cystine	2.100
Lysine	4.600
Méthionine	1.600
Tryptophane	1.400
Glycine	5.200

MINERAUX
(calculés en mg/kg)

	App. Nat. (moy.)	App. par CM	TOTAUX
P	4.100	3.500	7.600
Ca	4.500	4.600	9.100
K	10.600	0	10.600
Na	1.150	1.950	3.100
Mg	2.100	130	2.230
Mn	40	40	80
Fe	160	140	300
Cu	12	15	27
Zn	30	45	75
Co	0,1	1,5	1,6
I	apporté sous forme assimilable par algues marines.		

VITAMINES
(calculées au kg)

	App. Nat. (moy.)	App. Synthét.	TOTAUX
Vitam. A	2.850 UI	6.500 UI	9.350 UI
- D 3	30 -	1.000 -	1.030 -
- B 1	4,30 -	0,00 mg	4,30 mg
- B 2	3,80 -	0,00 -	3,80 -
- B 3	16 -	0,00 -	16 -
- B 6	1 -	1 -	2 -
- E	16 -	10 -	26 -
- K 3	6 -	1 -	7 -
- PP	55 -	5 -	60 -
Choline	850 -	200 -	1.050 -

7, Rue Galliéni, 91 - VILLEMOISSON-SUR-ORGE • Tél. (1) 016-13-69 - (1) 016-21-37

APPENDIX 4

Analytical certificate concerning water

CONSEIL GÉNÉRAL DU Cher

LABORATOIRE DÉPARTEMENTAL VÉTÉRINAIRE

Agréé par le Ministère de la santé

RESULTAT D'ANALYSE D'EAU

N°d'Analyse: 920794 **N° d'Ordre:** 1236

***Type d'analyse:** C7B3

Prélèvement d'eau parvenu le: Lundi 11 Mai 1992

Effectué par: C.E.R.B. **Agent:**

Origine:

Lieu: ZONE PROTEGEE LAPIN COULOIR PROPRE

Commune: BAUGY

Physicochimie		Résultats	Normes*
Turbidité en U Jackson	:	0,3	< 2 U
Conductivité µS/cm		652	.....
PH	:	7,5	6,5-9
Oxydabilité KMnO4 mg/l	:	1	< 5
Dureté en °Français	:	37	.....
T.A.C en °Français	:	25	.....
Ammoniaque en mg/l	:	0	< 0,5
Nitrites en mg/l	:	0	< 0,1
Nitrates en mg/l	:	57	< 50
Sulfates en mg/l	:	65	< 250
Chlorures en mg/l	:	20	< 200
Fer en mg/l	:	0	< 0,2
Manganèse en mg/l	:		< 0,05
Fluor en mg/l	:		< 1,5
			.....
			< 5

Bactériologie		Résultats	Normes*
Coliformes thermotolérants/100ml	:	0	0
Streptocoques fécaux/100ml	:	0	0
Coliformes/100ml	:	2	0-95%
Dénombrement des bactéries aérobies revivifiables à 37°C/ml	:	< 1	.....
" " à 22°C/ml	:	2	.....
Spores de bactéries anaérobies sulfito-réductrices/20ml	:	0	≤ 1
" " /100ml	:		0
Salmonelles	:		0
Staphylocoques pathogènes	:		0
			0

*:Selon decret N°89-3 et suivants.

Bourges,le: Lundi 18 Mai 1992

Adj. Dir. du Laboratoire — Erick PRENGERE

Le Directeur du Laboratoire — Jean Marie GUERAUD

Company Sanitized. Does not contain TSCA CBI

APPENDIX 5

Results data sheet

CERTIFIÉ CONFORME 2
A L'ORIGINAL

CERB

IRRITATION PRIMAIRE CUTANEE
PRODUIT CHIMIQUE

ETUDE N °: 920083E

PRODUIT : [redacted]

N° LOT : [redacted]

VOLUME ~~ou~~
~~MASSE~~ ADMINISTRÉE : 0,5ml

ESPECE : Lapin Néo - Zélandais

SEXE : ~~mâle~~ / femelle

DEBUT D'ETUDE : 23.04.92

FIN D'ETUDE : 26.04.92

HEURE DE DEBUT DE L'APPLICATION / PARAPHE : 10H45 / CS

HEURE DE DEBUT DU DEMAILLOTAGE / PARAPHE : 14H50 / CS

TEMPS LECTURE NUMERO LAPIN	24 H DATE : 24.04	48 H DATE : 25.04	72 H DATE : 26.04	TOTAL/INDICE /ANIMAL	INDICE MOYEN *
920457	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0
.....	E = O =	E = O =	E = O =	E = O =	E = O =
.....	E = O =	E = O =	E = O =	E = O =	E = O =
PARAPHE HEURE	16H20 / CS	14H / A	14H30 / A	CB	CB

OBSERVATIONS DIVERSES

T.LECTURE N°LAPIN	5 H 23.04.	J 8	J 15
920457	E = 0 O = 0	E = O =	E = O =
.....	E = O =	E = O =	E = O =
.....	E = O =	E = O =	E = O =
PARAPHE HEURE	16H00 / CB	/	/

CERB

CERTIFIÉ CONFORME A L'ORIGINAL

3

IRRITATION PRIMAIRE CUTANEE
PRODUIT CHIMIQUE

ETUDE N°: 920083E

PRODUIT : [redacted]

N° LOT : [redacted]

VOLUME ~~ou~~ MASSE ADMINISTREE : 0,5ml

ESPECE : Lapin Néo – Zélandais

SEXE : ~~mâle~~ / femelle

DEBUT D'ETUDE : 28.04.92

FIN D'ETUDE : 1.05.92

HEURE DE DEBUT DE L'APPLICATION / PARAPHE : 9H45 / CB

HEURE DE DEBUT DU DEMAILLOTAGE / PARAPHE : 13H50 / CB

TEMPS LECTURE / NUMERO LAPIN	24 H DATE : 29.04	48 H DATE : 30.04	72 H DATE : 1.05	TOTAL/INDICE /ANIMAL	INDICE MOYEN *
920458	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0
920459	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0	E = 0 O = 0
.....	E = O =	E = O =	E = O =	E = O =	E = O =
PARAPHE HEURE	16H30 / CS	16H25 / CS	12H00 / MJ	CB	CB

OBSERVATIONS DIVERSES

T.LECTURE N°LAPIN	5 H 28.04.92	J 8	J 15
920458	E = 0 O = 0	E = O =	E = O =
920459	E = 0 O = 0	E = O =	E = O =
.....	E = O =	E = O =	E = O =
PARAPHE HEURE	15H00 / CB	/	/