Report Title: Rabbit Skin Irritation Patch Test

Test Type: Skin Irritation

Conducting Laboratory and Location: International Bio-Research Europe

Test Substance(s): #E2414.01 – 1% Octopirox in shampoo

Species: Rabbit

# of Animals: 3 animals per group

Test Conditions: Test material tested at 1 and 5% dilution. 0.4 ml of the substance applied to pad. Applied to intact and abraded skin. The site was graded at 24 and 72 hrs after application of patch.

Results: Primary Irritation Index at both 1 and 5 % dilution on both intact and abraded skin = 0. E2414.01 is considered to be non-irritating.

Study #: IBRE-1-3-599-84; IBRE-1-3-600-84
Report Date: 10/19/84

Accession #: 32038

BCH BTS : 930

BIOLOGICAL TEST FOR SAFETY : EUROPEAN OPERATIONS REQUEST DOCUMENT (EORD).

A

Originator	A. Cairns 1/5/84 (Name / Date)	Originator's SH	T.C. Bell 2/5/84 (Name / Date)	Originator's AD	R.E. Atkinson (Name / Date)
Toxicologist	D.J.G. Müller 9/5/84 (Name / Date)	P&RS SH	G. Calvin 7.5.84 (Name / Date)	P&RS Manager	T.M. McCarthy 28/8/84 (Name / Date)

Estimated Total Cost : £ 1400

Estimated Dates of : Availability of Analytical Data : _____

Receipt of Report : Summer 1984

Product Coordination Manager : J.B. Canden 29/8/84 (Name / Date)

B

Name of Test Substance : Head & Shoulder AR w/ 1% Octopirox

Identification Number E-2414.01

Substances required by (date) _____

Agreed by PDP _____

TSCH Completion Date _____

			Panel/Blind Test	Ship Test	Test Market	National
Type of Consumer Exposure(s) for Which Safety Clearance is Requested	No. of Subjects	:	200			
	Starting Date	:	Fall '84			
	Duration	:	6 weeks			
	Location	:	UK			

C

Safety Test Requirements (By P&RS)

Tests :

	Amount of Substance Needed	Cost
1. LD_{50} (rat), Up & Down method	200 g	£ 300
2. Eye Irritation (rabbit, low volume protocol)	20 g	£ 250
3. Skin Irritation (rabbit)	20 g	£ 100
4. Skin Sensitization (guinea Pig)	100 g	£ 750

D.J.G. Müller
Toxicologist

3-5-84
Date

/mp.w - 0229M

RESULTS AND CONCLUSIONS

1. Acute Oral Toxicity (rats) (HRC 85170D/P&G 1165/AC)

Test Material	Concentration	Dose	LD_{50}
E-2414.01 (R&S AR with 1% octopyrox)	undiluted	up & down	M 16.9 g/kg (13.0-22.1) F 10.7 g/kg (8.1-14.0)

At all doses (4.8 g/kg - 23.3 g/kg for the males; 4.8 g/kg - 13.8 g/kg for the females), animals showed pilo-erection, abnormal body carriage and increased salivation. Lethargy and diarrhoea were frequently observed. For the surviving animals, recovery was complete by day 8 and terminal autopsy did not reveal unusual findings apart from a subcutaneous abscess of a male rat dosed at 17.9 g/kg.

2. Eye Irritation (rabbit) (HRC 84981D/P&G 1164/SE)

Test Material	Treatment	MAS	Corneas Involved	Eyes Normal in Indicated Number of Days
E-2414.01	0.01 ml,NR	11	4/6	1 in 2, 1 in 3 3 in 7, 1 in 14
	0.01 ml,R	<1	0/3	2 in 1, 1 in 2

When no rinsing occurred, transient corneal opacities developed. Temporary iritis and conjunctivitis were observed. Considerable discharge was seen in one animal.

3. Skin Irritation (rabbit) (IBR 1-3-599-84 and 1-3-600-84)

Test Material	Concentration	Primary Irritation Index	Degree of Irritation
E-2414.01	5 % aq.	0	non irritating
	1 % aq.	0	non irritating

4. Skin Sensitization (guinea pig) (IBR 2-5-598-84)

Test Material	Concentration		Incidence of Sensitization
	Induction	Challenge	
E-2414.01	50 % aq.	50 % aq.	0/20

No signs of erythema or oedema were observed on the animal skin.

CONCLUSIONS :

Head & Shoulders AR (TEA surfactant, Meridian perfume) with 1 % octopyrox is not acutely toxic. At the concentrations tested, this material is non irritating for the eye. Under the conditions of the treatment, E-2414.01 does not induce sensitization in guinea pigs.

V. Scaiteur P.H.S. Bay

Distribution :

Mr. A. Cairns
Mr. T.C. Bell
Mr. R.E. Atkinson
Mr. J. Crompton
Mr. R.A. Jamieson (+ reports)
Mr. J.E. Weaver
Mr. R.R. Balmbra
Mr. G.G. Clinckemaillie
Mr. W.P. Meier/G.J. Schmitt

5030K/VS/ab

TEST SUBSTANCE CHARACTERIZATION REPORT (TSCR)

A

Test Substance Identification Number E-2414.01

Biological Test for Safety Request Number ECM HTS 930

Originator: A. Cairns (Name) 16/8/94

B

Name of Product or Ingredient (or code designation) H&S AELCC (NORMAL/DRY)

Brand Notebook Ref. (including Production code if available) _____

Physical Form LOTION/SHAMPOO Colour GREEN/BLUE Density 1.034g/cc

Solubility SOLUBLE IN WATER pH (conc.) 4.6 (50% SOLN IN H_2O) Sample Expiration Date _____

Recommended Storage Conditions DO NOT FREEZE

Hazards (i.e. flammability, toxic gases) NONE

C

FORMULATED COMPOSITION

Component[a]	Nominal Level (%by Wt.)	Acceptable Range[b]	Stock Code No.	Supplier	Lot[b] Number
PROPYLENE GLYCOL	0.500		45661	DOW	)
KATHON CG (1)	0.033		45572	ROHM & HAAS	)
PRELL PASTE	55.560		64506	P&G UK	)
CITRIC ACID (2)	0.680		45076	PFISER	)
SODIUM CHLORIDE(2)	0.750		48070	BRITISH SALT	)
COCONUT AMIDE	3.000		64501	MANRO	)
EGDS	5.000		45470	EMERY INDUSTRIES	NK
OCTOPIROX	1.000			HOECHST AG	NK
COLOUR SOLUTION(2)	0.220		56516	KHONSTAMM	)
MERIDIAN PERFUME	0.600		55416	P&G (US)	)
WATER	TO 100 PTS		73819	P&G UK	)

(1) TOTAL KATHON CG IN FINISHED PRODUCT IS 5 PPM
(2) CAN BE VARIED TO MEET FINISHED PRODUCT LIMITS

(a) Ingredients will be listed by chemical name: non-chemical names such as Tergitol 15-3 or Yellow Dye D&C No. 10 may be acceptable but should be previewed with the responsible toxicologist. Chemical names which are inconveniently long may be abbreviated in table but should be listed in full in referenced footnotes. Non-definitive identifications (e.g. Arquad, BC-Base) are not acceptable).

(b) If information requested is not known then the symbol NK will be entered.

The above information provided by:

Process Development Person (PDP) A. CAIRNS (Name) (Signature) (Date) 16/8/94

Issue 2: 21.3

TSCR ANALYTICAL REQUEST FORM

D
Please carry out the following analyses according to your recorded procedures. This data is needed for non-clinical safety studies.

Signed [illegible] (Name) Date 7th December 1990

Agreed for Analytical Section _____ (Name) Date _____

Agreed for Human Safety _____ (Name) Date _____

Date Submitted / Re Submitted	Submitter Code	Component or Property	Measured Value	Analytical Notebook
7th Dec. 1990	27/93	% Octanoate	1.01	[illegible]
		Colour L	95.1	[illegible]
		a	-2.0	
		b	-14.9	
		% [illegible]	0.0	
		Cat SO_4	2.45	
		pH	4.31	
		Viscosity	1361	

Analytical Information verified by:

[illegible] (Name) (Signature) 7/12/90 (Date)

E
This test substance is suitable for non-clinical safety testing

Originator's SH: _____ (Name) (signature) _____ (Date)

Toxicologist: [illegible] (Name) (Signature) [illegible] (Date)

IBR
Forschungs GmbH
Südkampen Nr. 31
3030 Walsrode 1

Telefon: (05186) 1366
Telex: 924342 ibr d
Vormals in Hannover
Krumme Straße 7

October 1984 / ot

Project-No.: 1-3-599-84

RECEIVED : 19-10-1984	
CHECKED BY:	22.10.84
	22-10-84

Test article "E-2414.01"

(BCM BTS 930)

1 % in Aqua dest

Primary Skin Irritation in Rabbits

(Closed Patch Test)

Head & shoulders AR w/Cat pirex

Sponsor:
Procter & Gamble
European Technical Center
Temselaan 100
B - 1820 Grimbergen (Strombeek-Bever)

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I. INTRODUCTION

The objective of this study was to assess the relative level of primary skin irritation of the compound "E-2414.01 (SCM BTS 930) 1 % in Aqua dest" under occluded conditions in rabbits.

II. SUMMARY

The relative level of primary skin irritation of the test article "E-2414.01 (BCM BTS 930) 1 % in Aqua dest" was investigated in one group of three rabbits.

All signs of erythema, eschar and edema formation were recorded during the two day observation period.

The test compound induced during the entire observation period no skin alterations..

The Primary Irritation Index is 0,0.

The substance "E-2414.01 (BCM BTS 930) 1 % in Aqua dest" is considered to be non-irritating.

We, the undersigned, hereby declare that the work was performed under our supervision and according to the procedure herein described. The described symptoms, findings and data correspond to the results obtained in this test.

Dr. Dr. W. Sterner .....

Fachtierarzt für
Pharmakologie u. Toxikologie

Expert agrée
pharmacologue, toxicologue

Fachtierarzt für
klin. Laboratoriumsdiagnostik

Fachtierarzt für
Versuchstierkunde

Dr. G. Chibanguza .....

Fachtierarzt für
Pharmakologie u. Toxikologie

Sülkampen, Oktober 17, 1984

III. MATERIAL AND METHOD

1. Animals

1.1	Species:	Rabbit
1.2	Strain:	White New Zealanders
1.3	Source:	Harald Schriever, Kaninchenfarm, D - 2740 Bremervörde, Neuendamm 88
1.4	Colour:	white
1.5	Background of the strain:	1965 imported from the USA. Breeding by brother/sister mating. 1971 cross-breeding with bucks of danish breed Hawit-Land (WNZ with long ears). Continued breeding by brother/sister mating, supplied periodically with heterogeneous blood from selected prize winning bucks. Selections are conducted according to criterias of the Rabbit Breeding Association for White New Zealanders. The breeding is constantly under veterinary supervision and free of epidemics since commencement. At the age of 4 weeks the animals are treated once against coccidia with "Sulkanin" mixed into the drinking water.
1.6	Date of receipt:	02.10.84
1.7	Acclimatization time:	7 days at least
1.8	Randomisation:	by the way of lottery drawing
1.9	Animal identification:	cage card with the following information: dosage, earmark, sex, day of the beginning of the study.
1.10	Weight range at the beginning of the study:	ø 2,4 kg

2. Husbandry

2.1	Caging:	single caging in battery of cages
2.2	Cagetyp:	lattice plate boxes with fencel bassin underneath.
	Size:	35 cm high, 35 cm wide, 50 cm long
2.3	Lighting:	fluorescent light, 4000° K, 120 Lux
2.4	Lighting periods:	12 hours daily, from 7.00 a.m. to 7.00 p.m.
2.5	Temperature:	18° C ± 2° C
2.6	Relative humidity:	50 - 85 %
2.7	Registration:	by thermohygrometer

3. **Food and Feeding**

3.1 Producer: Pfeiff Spezialfutter GmbH
4750 Soest/Westfalen

3.2 Name: Mühmel Z Kaninchenzuchtkorn
(Alleinfutter für Zuchtkaninchen)

3.3 Type: Pellets, 1,0 - 1,5 cm large, 0,5 cm diameter

3.4 Composition:

Wheat red dogs	31,50 %
Oats	10,00 %
Soya meal	10,00 %
Dried sugar beet pulp	13,00 %
Lucerne meal	28,00 %
Molasses	4,00 %
Blend of vitamins	0,40 %
Blend of minerals	2,56 %
Calcium carbonate ($CaCO_3$)	0,50 %
Choline chloride	0,04 %

Ingredients: (Charge control by "Weander Feed stuff analysis", EC - Tolerances of Jan.1980)

Crude protein	14,40 - 17,60 %
Methionin	0,20 - 0,26 %
(Methionin + Cystin)	0,38 - 0,58 %
Lysin	0,68 - 0,92 %
Crude fat	1,90 - 3,50 %
Crude fibre	11,20 - 14,80 %
Ash	8,40 - 10,20 %
Calcium	1,27 - 1,73 %
Phosphorus	0,45 - 0,75 %
Sodium	0,20 - 0,30 %
H_2O	11,00 - 13,00 %
N-free extract	difference on 100 %

Feed additives / kg feed

15.000 I.U. Vitamin A
1.875 I.U. Vitamin D_3
15 mg Vitamin E
Butylhydroxytoluol (Antioxidant)

4. **Bedding**

4.1	Producer:	Sniff Spezialfutter GmbH 4770 Soest/Westfalen
4.2	Name:	Sniff - Bedding
4.3	Production:	from pure spruce-, fir- and pine-wood, dried and disdusted.
4.4	Sterilisation:	180° C
4.5	Water binding capacity (% of bedding used):	276,5

5. **Water**

5.1	Administration:	ad libitum
5.2	System:	drinking nipples
5.3	Quality:	aqua fontana as for human consumption
5.4	Quality control:	Regular analysis by an official laboratory for water analysis.

6. Test material

The test compound "E-2414.0" was supplied by Procter & Gamble, European Technical Center, Grimbergen (Strombeek-Bever), Belgium.

6.1 DRD-number: EGM STS 930

6.2 General characteristics: The sample is a blue, turbid, strong viscous liquid.

6.3 Storage: ambient temperature

7. Experimental Design

7.1 Preparation of the animals

Following an acclimatisation period of 7 days at least to accustom the rabbits to the environmental conditions existing in the animal room, the test was initiated.
Prior to treatment the back of each animal was clipped with a small animal clipper. Two test sites of each animal were left intact and two test sites were abraded with a clean clipper blade, so as to penetrate the horny layer of the epidermis, but without causing bleeding.

7.2 Preparation of the test material

The sample "E-2414.01" was applied as a 1 % dilution in Aqua dest (v/v).

7.3 Procedure

0.4 ml of the substance to be tested was applied under a 2.5 x 2.5 cm gauze pad.
The test liquid was applied to both intact and abraded skin sites on the left half of the dorsal area.
The patches were secured with adhesive tapes by placing them around the border of the patches. The animals were immobilized in restrainers for 24 hours to prevent them from removing the patches.
After that time, the test sites were uncovered and the test substance was removed with wet disposable gauze.

7.4 Observations

Thirty minutes after the patches had been removed, the test sites were evaluated and this evaluation was reported as the 24-hour post-treatment evaluation.
Again an evaluation of the reactions was taken 48 hours after the removal of the patches and this was reported as 72-hour post-treatment evaluation.

The scores of the test substance on both intact and abraded skin sites of all animals for erythema and eschar formation (12 scores), and separately for edema formation (12 scores) were averaged. The sum of these two averages was the Primary Irritation Index of the corresponding test compound.

7.5 Classification of the Primary Irritation Index

See Appendix 1.

IV. RESULTS

Under the described conditions the following was recorded:

The sample "E-2414.01 (ECM BTS 930) 1 % in Aqua dest" induced during the entire observation period no skin alterations.

The Primary Irritation Index is 0,0.

The test compound "E-2414.01" is considered to be non-irritating.

V. GENERAL INFORMATION

Sponsor:	Procter & Gamble European Technical Center Temselaan 100 B - 1820 Grimbergen (Strombeek-Bever)
Study performed by:	IBR Forschungs GmbH Südkampen Nr. 31 3030 Walsrode 2
Study director:	Dr. Dr. W. Starner Fachtierarzt für Pharmakologie u. Toxikologie Expert agrée pharmacologue, toxicologue Fachtierarzt für klin. Laboratoriumsdiagnostik Fachtierarzt für Versuchstierkunde
Project leader:	Dr. med. vet. G. Chibanguza Fachtierarzt für Pharmakologie u. Toxikologie
Assistants:	M. Fürst, H. Händschke, H. Quaren
Quality assurance:	P. Volkmann
Time of study:	10.10. - 13.10.84
Archives and documents:	All raw data and a copy of the final report will be stored in the archives of IBR. The test substance will be returned to the sponsor.

Appendix 1

Primary Irritation Scoring

(a) 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
Highest possible erythema score	4

(b) Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure	4
Highest possible edema score	4

Classification of the Primary Irritation Index

0	=	Non-irritating
0,1 - 2	=	Mildly irritating
2 - 5	=	Moderately irritating
5 - 6	=	Moderately to severely irritating
6 - 8	=	Severely irritating

Appendix 2

Individual values

Animal 1

		Hours 24	Hours 72 (48)
intact	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0
abraded	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0

Animal 2

		Hours 24	Hours 72 (48)
intact	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0
abraded	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0

Animal 3

		Hours 24	Hours 72 (48)
intact	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0
abraded	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0

Primary Irritation Indices

	erythema					edema			
	intact		abraded			intact		abraded	
Animal-No.	24 h	72 h	24 h	72 h	Animal-No.	24 h	72 h	24 h	72 h
1	0	0	0	0	1	0	0	0	0
2	0	0	0	0	2	0	0	0	0
3	0	0	0	0	3	0	0	0	0
	= 0,0					= 0,0			
$\bar{x}$ 1	= 0,0				$\bar{x}$ 2	= 0,0			

$\bar{x}$ 1 + $\bar{x}$ 2 = 0,0

DECLARATION

The conditions for the performance of all studies, e.g. animal care, rooms, technical equipment and personnel are regularly controlled by the Quality Assurance Unit.

This report provides a correct and faithful record of the results obtained.

P. Volkmann .....

QAU

Südkempen, ..15.10.84.....

IBR
Forschungs GmbH
Südkampen Nr. 31
3030 Walsrode 1

Telefon: (05186) 1366
Telex: 924342 ibr d
Vormals in Hannover
Krumme Straße 7

October 1984 / ot

Project-No.: 1-3-500-84

RECEIVED : 19-10-1984	
CHECKED BY:	22.10.84
	23-10-84

Test article "E-2414.01"

(BCM BTS 930)

5 % in Aqua dest

Primary Skin Irritation in Rabbits

(Closed Patch Test)

Head & Shoulders AR w/ Colgate

Sponsor:
Procter & Gamble
European Technical Center
Temselaan 100
B - 1820 Strombeek-Bever (Strombeek-Bever)

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I. INTRODUCTION

The objective of this study was to assess the relative level of primary skin irritation of the compound "E-2414.01 (HOM 873 930) 5 % in aqua dest" under occluded conditions in rabbits.

II. SUMMARY

The relative level of primary skin irritation of the test article "E-2414.01 (ECM BTS 930) 5 % in Aqua dest" was investigated in one group of three rabbits.

All signs of erythema, eschar and edema formation were recorded during the two day observation period.

The test compound induced during the entire observation period no skin alterations.

The Primary Irritation Index is 0,0.

The substance "E-2414.01 (ECM BTS 930) 5 % in Aqua dest" is considered to be non-irritating.

II. SUMMARY

The relative level of primary skin irritation of the test article "E-2414.01 (ECM BTS 930) 5 % in Aqua dest" was investigated in one group of three rabbits.

All signs of erythema, escher and edema formation were recorded during the two day observation period.

The test compound induced during the entire observation period no skin alterations.

The Primary Irritation Index is 0,0.

The substance "E-2414.01 (ECM BTS 930) 5 % in Aqua dest" is considered to be non-irritating.

We, the undersigned, hereby declare that the work was performed under our supervision and according to the procedure herein described. The described symptoms, findings and data correspond to the results obtained in this test.

Dr. Dr. W. Sterner .....

Fachtierarzt für
Pharmakologie u. Toxikologie

Expert agréé
pharmacologue, toxicologue

Fachtierarzt für
klin. Laboratoriumsdiagnostik

Fachtierarzt für
Versuchstierkunde

Dr. G. Chibanguza .....

Fachtierarzt für
Pharmakologie u. Toxikologie

Stuttgart, October 17, 1984.

III. MATERIAL AND METHOD

1. Animals

1.1	Species:	Rabbit
1.2	Strain:	White New Zealanders
1.3	Source:	Harald Schriever, Kaninchenfarm, D - 2740 Bremervörde, Neuendamm 88
1.4	Colour:	white
1.5	Background of the strain:	1965 imported from the USA. Breeding by brother/sister mating. 1971 cross-breeding with bucks of danish breed Hawit-Land (WHZ with long ears). Continued breeding by brother/sister mating, supplied periodically with heterogeneous blood from selected prize winning bucks. Selections are conducted according to criterias of the Rabbit Breeding Association for White New Zealanders. The breeding is constantly under veterinary supervision and free of epidemics since commencement. At the age of 4 weeks the animals are treated once against coccidia with "Sulkanin" mixed into the drinking water.
1.6	Date of receipt:	02.10.84
1.7	Acclimatization time:	7 days at least
1.8	Randomization:	by the way of lottery drawing
1.9	Animal identification:	cage card with the following information: dosage, earmark, sex, day of the beginning of the study.
1.10	Weight range at the beginning of the study:	ø 2,4 kg

2. **Husbandry**

2.1	Caging:	single caging in battery of cages
2.2	Cagetyp:	lattice plate boxes with faecal bassin underneath.
	Size:	45 cm high, 35 cm wide, 50 cm long
2.3	Lighting:	fluorescent light, 4000° K, 120 Lux
2.4	Lighting periods:	12 hours daily, from 7.00 a.m. to 7.00 p.m.
2.5	Temperature:	18° C ± 2° C
2.6	Relative humidity:	50 - 55 %
2.7	Registration:	by thermohygrometer

3. Food and Feeding

3.1 Producer: Semiff Spezialfutter GmbH
4770 Soest/Westfalen

3.2 Name: Mümmel Z Kaninchenzuchtkorn
(Alleinfutter für Zuchtkaninchen)

3.3 Type: Pellets, 1,0 - 1,5 cm large, 0,5 cm diameter

3.4 Composition:

Wheat red dogs	31,50 %
Oats	10,00 %
Soya meal	10,00 %
Dried sugar beet pulp	13,00 %
Lucerne meal	26,00 %
Molasses	4,00 %
Blend of vitamins	0,40 %
Blend of minerals	2,56 %
Calcium carbonate ($CaCO_3$)	0,50 %
Choline chloride	0,04 %

Ingredients: (Charge control by "Weender Feed stuff analysis", EC - Tolerances of Jan.1980)

Crude protein	14,40 - 17,60 %
Methionin	0,20 - 0,26 %
(Methionin + Cystin)	0,38 - 0,50 %
Lysin	0,68 - 0,92 %
Crude fat	1,90 - 3,50 %
Crude fibre	11,20 - 14,80 %
Ash	8,40 - 10,20 %
Calcium	1,27 - 1,73 %
Phosphorus	0,45 - 0,75 %
Sodium	0,20 - 0,30 %
H_2O	11,00 - 13,00 %
N-free extract	difference on 100 %

Feed additives / kg food

15.000 I.U. Vitamin A
1.875 I.U. Vitamin D_3
15 mg Vitamin E
Butylhydroxytoluol (Antioxidant)

4. **Bedding**

4.1	Producer:	Seniff Spezialfutter GmbH 4770 Soest/Westfalen
4.2	Name:	Seniff - Bedding
4.3	Production:	from pure spruce-, fir- and pine-wood, dried and disdusted.
4.4	Sterilisation:	180° C
4.5	Water binding capacity (% of bedding used):	276,5

5. **Water**

5.1	Administration:	ad libitum
5.2	System:	drinking nipples
5.3	Quality:	aqua fontana as for human consumption
5.4	Quality control:	Regular analysis by an official laboratory for water analysis.

6. Test material

The test compound "E-2414.01" was supplied by Procter & Gamble, European Technical Center, Grimbergen (Strombeek-Bever), Belgium.

6.1 DRD-number: ECM BTS 930

6.2 General characteristics: The sample is a blue, turbid, strong viscous liquid.

6.3 Storage: ambient temperature

7. Experimental Design

7.1 Preparation of the animals

Following an acclimatization period of 7 days at least to accustom the rabbits to the environmental conditions existing in the animal room, the test was initiated.
Prior to treatment the back of each animal was clipped with a small animal clipper. Two test sites of each animal were left intact and two test sites were abraded with a clean clipper blade, so as to penetrate the horny layer of the epidermis, but without causing bleeding.

7.2 Preparation of the test material

The sample "E-2414.01 (BCM BTS 930)" was applied as a 5 % dilution in Aqua dest (v/v).

7.3 Procedure

0.4 ml of the substance to be tested was applied under a 2.5 x 2.5 cm gauze pad.

The test liquid was applied to both intact and abraded skin sites on the left half of the dorsal area.
The patches were secured with adhesive tapes by placing them around the border of the patches. The animals were immobilized in restrainers for 24 hours to prevent them from removing the patches.
After that time, the test sites were uncovered and the test substance was removed with wet disposable gauze.

7.4 Observations

Thirty minutes after the patches had been removed, the test sites were evaluated and this evaluation was reported as the 24-hour post-treatment evaluation.
Again an evaluation of the reactions was taken 48 hours after the removal of the patches and this was reported as 72-hour post-treatment evaluation.

The scores of the test substance on both intact and abraded skin sites of all animals for erythema and eschar formation (12 scores), and separately for edema formation (12 scores) were averaged. The sum of these two averages was the Primary Irritation Index of the corresponding test compound.

7.5 Classification of the Primary Irritation Index

See Appendix 1.

IV. RESULTS

Under the described conditions the following was recorded:

The sample "E-2414.01 (ECM BTS 930) 5 % in Aqua dest" induced during the entire observation period no skin alterations.

The Primary Irritation Index is 0,0.

The test compound "E-2414.01 (ECM BTS 930) 5 % in Aqua dest" is considered to be non-irritating.

V. GENERAL INFORMATION

Sponsor:	Procter & Gamble European Technical Center Temselaan 100 B - 1820 Grimbergen (Strombeek-Bever)
Study performed by:	IBR Forschungs GmbH Südkampen Nr. 31 3030 Walsrode 2
Study director:	Dr. Dr. W. Sterner Fachtierarzt für Pharmakologie u. Toxikologie Expert agrée pharmacologue, toxicologue Fachtierarzt für klin. Laboratoriumsdiagnostik Fachtierarzt für Versuchstierkunde
Project leader:	Dr. med. vet. G. Chibanguza Fachtierarzt für Pharmakologie u. Toxikologie
Assistants:	H. Fürst, H. Hädschke, W. Queren
Quality assurance:	P. Volkmann
Time of study:	10.10. - 13.10.84
Archives and documents:	All raw data and a copy of the final report will be stored in the archives of IBR. The test substance will be returned to the sponsor.

Appendix 1

Primary Irritation Scoring

(a) 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
Highest possible erythema score	4

(b) Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure	4
Highest possible edema score	4

Classification of the Primary Irritation Index

0	=	Non-irritating
0,1 - 2	=	Mildly irritating
2 - 5	=	Moderately irritating
5 - 6	=	Moderately to severely irritating
6 - 8	=	Severely irritating

Appendix 2

Individual values

Animal 1

		Hours 24	Hours 72 (48)
intact	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0
abraded	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0

Animal 2

		Hours 24	Hours 72 (48)
intact	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0
abraded	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0

Animal 3

		Hours 24	Hours 72 (48)
intact	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0
abraded	1. Erythema, eschar formation	0	0
	2. Edema formation	0	0

Primary Irritation Indices

	erythema					edema			
	intact		abraded			intact		abraded	
Animal-No.	24 h	72 h	24 h	72 h	Animal-No.	24 h	72 h	24 h	72 h
6	0	0	0	0	6	0	0	0	0
7	0	0	0	0	7	0	0	0	0
8	0	0	0	0	8	0	0	0	0

$= 0,0$ $\qquad$ $= 0,0$

$\bar{x}\ 1 = 0,0$ $\qquad$ $\bar{x}\ 2 = 0,0$

$\bar{x}\ 1 + \bar{x}\ 2 = 0,0$

DECLARATION

The conditions for the performance of all studies, e.g. animal care, rooms, technical equipment and personnel are regularly controlled by the Quality Assurance Unit.

This report provides a correct and faithful record of the results obtained.

F. Volkmann .....
QAU

Stöckumpen, 14.10.84