BASF MAR 1 7 1995
Abteilung Toxikologie
Department of Toxicology
D-67056 Ludwigs-
hafen, FRG

cp; 0107

AMENDMENT No. 1

to the Report:

Penetration of **Uvinul T 150** (5 % in a Sunscreen Formulation) through Human Epidermis in vitro.

Project No.: 62V0398/943005

This amendment contains 3 pages

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Report, p. 17

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Based on the findings of this study it can be calculated that approx. 0.1 % (= approx. **0.72** µg/cm²) of the applied Uvinul T 150 in the high dose level and approx. 1.5 % (= approx. **0.84** µg/cm²) of the low dose has penetrated the epidermis 24 hours after applicaton.

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C. Pölloth March 17 1995
Study Director: Dr.med. C. Pölloth

BASF
Abteilung Toxikologie
Department of Toxicology

STATEMENT

of the Quality Assurance Unit

Number of test substance:	94/398
Name of test substance:	Uvinul T 150 / 5% Sunscreen Formulation
Title:	Report: Penetration of **Uvinul T 150** (5 % in a Sunscreen Formulation) through Human Epidermis in vitro.

The Quality Assurance Unit audited the amendment dated March 17, 1995 to the report of Feb 27, 1995.

Date of audit: March 17, 1995

Ludwigshafen, March 17, 1995

Dr. med. Dr. rer. nat. R. Rossbacher
(Quality Assurance Unit)

Report, p.3

The result of the reanalysis of the test substance is now available and the report is amended as follows (amended parts in bold print):

3.1. TEST SUBSTANCE

Stability at room temperature: **the stability of the test substance over the study period was proven by reanalysis**

C. Pölloth, May 03, 1995
Study Director: Dr.med. C. Pölloth

BASF
Abteilung Toxikologie
Department of Toxicology
D-67056 Ludwigshafen, FRG

MAR 17 1995

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Date of audit: May 03, 1995

Ludwigshafen, May 03, 1995 .....J. Hajok.....
J. Hajok
(Quality Assurance Unit)

MAY 0 4 1995

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Abteilung Toxikologie
Department of Toxicology
D-67056 Ludwigs-
hafen, FRG

cp; 0118

AMENDMENT No. 2

to the Report:

Penetration of **Uvinul T 150** (5 % in a Sunscreen Formulation) through Human Epidermis in vitro.

Project No.: 62V0398/943005

This amendment contains 3 pages

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Abteilung Toxikologie
Department of Toxicology
D-67056 Ludwigs-
hafen, FRG

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Ludwigshafen, May 03, 1995 .....J. Hajok.....
J. Hajok
(Quality Assurance Unit)

AMENDMENT N

to the Report

Penetration of **Uvinul T 150** (5 % in
through Human Epidermis

Project No.: 62V0398

This amendment contains 3 pages

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C. Pölloth March 17 1995
Study Director: Dr.med. C. Pölloth

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Study Director: Dr.med. C. Pölloth

BASF
Abteilung Toxikologie
Department of Toxicology

67056 Ludwigs-
hafen, FRG

FEB 2 7 1995
cp0084

REPORT

Penetration of **Uvinul T 150** (5% in a Sunscreen Formulation)
through Human Epidermis in vitro

Substance No.:	94/398
Project No.:	62V0398/943005
Testing facility:	BASF Aktiengesellschaft Department of Toxicology, Z 470 67056 Ludwigshafen/Rhein, FRG

This report consists of 19 pages + appendix

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From the Department of Toxicology of BASF Aktiengesellschaft,
Ludwigshafen/Rhein, FRG

Head: Prof. Dr. med. Dr. rer. nat. H.-P. Gelbke

Study director/conduct of study: C. Pölloth, Feb. 23, 1995
Dr. med. C. Pölloth

Analytics: Gans, Feb. 24, 1995
Dr. rer. nat. G. Gans

Head of section: Feb. 24 1995
Dr. rer. nat. H.D. Hoffmann

GLP STATEMENT

Title: Report. Penetration of **Uvinul T 150** (5% in a Sunscreen Formulation) through Human Epidermis in vitro.

This study was conducted in accordance with the GLP-provisions of the "Chemikaliengesetz" (Chemicals Act; Bundesgesetzblatt 1990, Teil 1, 22.03.90; FR Germany) and with the "OECD Principles of Good Laboratory Practice" (Paris, 1981).

Feb. 24, 1995
.....
Head of section

C. Pollath, Feb. 23, 1995
.....
Study director

STATEMENT

OF THE QUALITY ASSURANCE UNIT

Number of test substance: 94/398

Name of test substance: Uvinul T 150 / 5% Sunscreen Formulation

Title: Report. Penetration of **Uvinul T 150** (5% in a Sunscreen Formulation) through Human Epidermis in vitro.

The Quality Assurance Unit inspected the study, audited the final report, and reported findings to the Study Director and to Management.

Phase of study/ inspection	Date of inspection	Report to Study Director and to Management
Protocol:	Nov. 21, 1994	Nov. 29, 1994
Conduct of study:	Nov. 29, 1994 Dec. 20, 1994	Nov. 29, 1994 Dec. 20, 1994
Audit of the report:	Feb. 23, 1995	Feb. 23, 1995

Remarks: Parts of the analytics were inspected independently by the Quality Assurance Unit of the analytical laboratory.

Ludwigshafen, February 27, 1995

Dr.rer.nat. H. Fleig
(Head of Quality Assurance Unit)

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1. SUMMARY

The potential for skin penetration of **Uvinul T 150**, applied in a sunscreen formulation (5 % w/w) was evaluated in vitro following a single application to human epidermis. A static skin penetration chamber design was used in this study.

Start of study:	November 28, 1994
End of study:	February 10, 1995
Skin samples:	Epidermal preparations of human skin
Dose levels:	a) 1 mg of the formulation / cm^2 (corresponding to approx. 0.05 mg Uvinul T 150 / cm^2) b) 10 mg of the formulation / cm^2 (corresponding to approx. 0.5 mg Uvinul T 150 / cm^2)
Sampling times:	0; 1; 2; 4; 8; 24; 48; 72 hours after application
Mean absorption rate:	- time interval 1-8 h: approx. 0.06 µg Uvinul T 150 / cm^2 h^{-1} (low and high dose) - time interval 8-72 h: approx. 0.01 µg Uvinul T 150 / cm^2 h^{-1} (low and high dose)
Maximum absorption rate:	approx. 0.35 µg Uvinul T 150 /cm^2 h^{-1} (low and high dose) obtained within 2 hours post application

Recovery of Uvinul T 150 in receptor fluid:

after 72 hours: (measured)	low dose:	approx. 2.5 % of the applied dose
	high dose:	approx. 0.2 % of the applied dose
after 24 hours: (calculated)	low dose:	approx. 1.3 % of the applied dose
	high dose:	approx. 0.1 % of the applied dose

Assessment: It is concluded that **Uvinul T 150** has the potential to penetrate human epidermis with the maximal absorption rate obtained within 2 hours post application. Thereafter the flux declines and reaches a steady-state at approx. 8 hours post application.

2. INTRODUCTION

The purpose of this study was to determine the in vitro time course of the cutaneous penetration of **Uvinul T 150** when applied as a 5% sunscreen formulation in samples of human epidermis following a single application.

Dermal penetration may be assessed in vitro using various skin preparations, however, the use of epidermal membranes provides a representative barrier for substances such as the test substance **Uvinul T 150**. With respect to barrier functions there is no apparent difference between fresh or cadaver skin, if the latter is stored for not longer than 48 hours before use in the experiments [5].
The use of in vitro methods as a screening procedure for skin penetration potential has been validated in many studies [1-5].

3. MATERIAL AND METHODS

3.1. TEST SUBSTANCE

Name of test substance:	Uvinul T 150 / 5% Sunscreen Formulation
Chemical name:	2,4,6-Trianilino-p-(carbo-2-ethylhexyl-1-oxi)-1,3,5-triazin in a sunscreen formulation
Test substance no:	94/398
Number of batch:	Rezeptur 53/013 N vom 16.9.94
Batch No. of Uvinul T 150 used in the formulation:	37-0032 (Manufacturing Date: June 15, 1994)
Characterization:	Rezeptur 53/013 (see appendix) with 5.6 g Uvinul T 150 / 100 g (see analytical certificate ZAX/OO, 94LOO618 of Oct. 4, 1994)
Appearance:	white creamy paste
Homogeneity:	homogenous by visual inspection
Stability at room temperature:	is checked by re-analysis. Result not yet available. An instability is not to be expected.
Storage:	ambient temperature, in the dark
Preparation of the test substance:	the test substance formulation ("Uvinul T 150 / 5 % Sunscreen Formulation") is applied tel quel
Dose levels tested:	a) 1 mg of the formulation / cm^2 (corresponding to approx. 0.05 mg Uvinul T 150 / cm^2) b) 10 mg of the formulation / cm^2 (corresponding to approx. 0.5 mg Uvinul T 150 / cm^2)
Application Frequency:	Single application

3.2. HUMAN SKIN

Human skin specimens with no signs of skin disease were obtained from a local clinic. Data on the origin of the skin samples are given in Table 1. Further information pertaining to the source of the tissue, its condition and durage of storage is kept at the Department of Toxicology of BASF.

Table 1: Origin of Skin

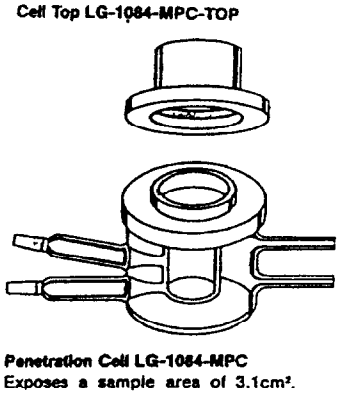
Donor		Skin from	Used for Epidermal Preparations No.
Sex	Age		
female	53	arm	6A
male	52	abdomen	7C
female	73	breast	8A, 8B
male	70	abdomen	9A, 9C, 9D, 9E
female	74	abdomen	11E, 11F

3.3. PENETRATION CHAMBER

The following modified Franz-System was used to mount the epidermal preparations (Laboratory Glass Apparatus Inc., Berkeley, USA)

Donor Chamber

Receptor Chamber



Exposed skin area:	3.14 cm^2
Receptor Chamber Volume:	7.0 ml
Receptor medium:	50 % aqueous ethanol (1:1, v/v) reason for selection: 50% aqueous ethanol has appropriate solvent properties and has been shown to predict the in vivo percutaneous absorption of a number of lipophilic penetrants [6]
Occlusion:	Parafilm^R

3.4. EXPERIMENTAL PROCEDURE

The potential of **Uvinul T 150** in a sunscreen formulation (5 %, w/w) to penetrate human epidermis was assessed in vitro. 3 independent experiments were carried out, each with 1-7 skin samples, using identical procedures.
In the following the main steps of the experimental procedure are described. Experimental details are kept in the raw data.

3.4.1. Preparation of the Epidermal Membranes

Epidermal membranes were prepared according to the method described in the laboratory's SOP on the day of the receipt of the skin. In brief, any subcutaneous tissue was trimmed off the skin. Then the skin was immersed in water of approx. 60 °C for 1-2 minutes. The epidermis was then gently peeled off and spreaded by immersion in water. If not used at once, the membranes were sealed in aluminium foil and stored at -20°C until use.

3.4.2. Assembly of the Penetration Chamber

a) Membrane Integrity Check
The receptor chamber (see 3.3.), containing a magnetic stirrer bar (of a volume of approx. 0.4 ml) was filled with physiological saline (0.9 % sodium chloride in aqua dest.) and maintained at 32-35 °C by circulating temperature-controlled water through the outer jacket.
The epidermis was mounted, strateum corneum side up, on the filled receptor cell, then covered with the donor chamber and the whole fixed with clamps.
After application of physiological saline to the epidermal surface the donor chamber was occluded with a layer of Parafilm^{R}.
The receptor phase was stirred at ca. 500 rpm using the Teflon coated bar and a motor placed beneath the chambers.

b) Main Experiments
For the main experiments the penetration chambers were assembled as given for the membrane integrity check experiments (see above) with the exception that 50 % aqueous ethanol (1:1, v/v) was used as receptor fluid instead of physiological saline.
After mounting the epidermis the appropriate amount of the formulation was applied to the epidermal surface (see 3.4.4.) and the donor chamber occluded as described above.

3.4.3. Assessment of Membrane Integrity

Following an equilibration period of approx. 15 minutes, the integrity of each epidermal preparation was tested by measuring its permeability to tritiated water. ^3H_2O (ca. 2 kBq; Amersham-Buchler) was applied to the epidermal surface, allowed to remain for 20 minutes, and then removed by blotting with a cotton-tipped applicator. Physiological saline was added to cover the epidermis and 60 minutes later the receptor solution was removed and a 1-ml aliquot assayed for radioactive content. Any residual tritiated water and receptor fluid were rinsed out of the donor and receptor chambers of the cells. The cells were then refilled with receptor fluid and left overnight while the samples were analysed by scintillation counting.
Skin preparations were regarded as being undamaged if not more than 2 % of the applied radioactivity was recovered from the receptor fluid.
Additionally, the membrane integrity was assessed after the end of the main experiments as described above.

3.4.4. Administration of Test Substance

The test substance was applied with a cotton-tip applicator to the epidermal surface according to the following dose scheme:

Table 2: Dose Scheme

Epidermal Preparation	Nominal Dose Level [mg Formulation / cm²]	Applied Dose / Chamber [mg Formulation]
6A	1	3.3
7C	1	3.3
8B	1	3.1
9D	1	3.0
11F	1	3.3
8A	10	30.0
9A	10	30.8
9C	10	30.7
9E	10	31.6
11E	10	30.0

3.4.5. Sampling

The rate and extent of **Uvinul T 150** absorption were determined by removing 1.5 ml of the receptor fluid at 0, 1, 2, 4, 8, 24, 48 and 72 hrs. The first 0.5 ml of each sample were discarded and the remaining 1.0 ml kept for analysis. The volume of fluid in the receptor chamber was maintained by the replacement of a volume of fresh receptor fluid equal to the sample volume after each sample has been taken.

At the end of each experiment **Uvinul T 150 / 5% Sunscreen Formulation** remaining on the surface of the skin was collected by gently blotting the surface with a cotton wool swab and then washing the surface twice with aqueous ethanol. Residual **Uvinul T 150** adhering to the receptor wall was removed by rinsing the chamber twice with aqueous ethanol.

Subsequent to the surface wash and after the terminal membrane integrity check (see 3.4.3), the epidermis was removed from the chamber and kept for analysis.

3.4.6. Sample Analysis

All samples were stored at -20° C until analysis.

The concentration of **Uvinul T 150** was determined in the receptor fluids, in the epidermis, in donor and receptor chamber washings and in Parafilm[R].

Liquid samples were analysed for **Uvinul T 150** content by measuring the extinction at 309 nm (E_{309}) in a Perkin-Elmer photometer. If necessary, the samples were diluted with dioxan or a dioxan:ethanol:water mixture before analysis. The concentration of **Uvinul T 150** in a sample was calculated according:

$$C = \frac{E_{309} \times D}{\varepsilon}$$

(C = concentration of Uvinul T 150 [µg/ml]; D = dilution factor, $\varepsilon = 0.130842$)

Parafilm[R] and epidermal membranes were extracted with dioxan or a dioxan:ethanol:water mixture and measured photometrically as described above

Radioactivity was determined by liquid scintillation counting in a Pharmacia counter (type Wallace 1409).

3.5. DATA ANALYSIS

The following parameters were analyzed for epidermal preparations with intact barrier function:

- concentration of **Uvinul T 150** in the receptor phase at different sampling times
- the cumulated amount of **Uvinul T 150** in all receptor samples (cumulative total absorption)
- concentration of **Uvinul T 150** in donor and surface washings, epidermis, receptor washings and Parafilm^R (mass balance).

Amounts are expressed either as the percentage of the applied dose of **Uvinul T 150** or in µg of **Uvinul T 150**.

The mean and standard deviations or range was calculated of all acceptable epidermal preparations (n=5 for each dose level) for all absorption and mass balance data.

The absorption rate was determined by regression analysis from the slope of the mean cumulated amount of the test substance divided by the skin area. Mean absorption rates for two time intervals (0-8 hrs and 8-72 hrs) were calculated.

The tables and figures of this report are computer generated with data rounded appropriately for inclusion in this report. Calculation of mean data from individual data presented in the report will therefore in some instances yield a minor variation in the value.

3.6. RETENTION OF RECORDS

The raw data, the protocol and the original of this report will be stored at BASF Aktiengesellschaft at least for the period of time specified in the GLP regulations.
Details concerning responsibilities or locations of archiving can be seen from the respective SOP's and from the raw data.

4. RESULTS AND DISCUSSION

The rate of **Uvinul T 150** penetration through isolated human epidermal preparations was investigated in vitro after a single application of a sunscreen formulation at nominal dose levels of 1 and 10 mg formulation / cm² (corresponding to approx. 0.05 and 0.5 mg **Uvinul T 150** / cm²)

4.1. Membrane Integrity Check

The results of the membrane integrity check are given in Table 3. Epidermal preparations were considered intact if less than 2 % of the applied radioactivity was recovered from the receptor fluid.

Additional integrity checks were performed immediately after the last sampling at 72 h to determine if the membrane was damaged during the experiment. No serious damage was apparent (Table 3).

4.2. Absorption Profile and Penetration Rate

The absorption profile of **Uvinul T 150** over 72 hours is given in Fig. 1 for the mean of all samples (n = 5 for each dose level; for values of the single membrane preparations see Appendix). Cumulative absorption at 72 hours after application of the test substance ranged from 0.4 µg/cm² to 2.1 µg/cm² (= 0.7 to 3.6 % of the applied dose) and averages 1.4 µg/cm² (= 2.5 % of the applied dose) in the low dose. For the high dose level the cumulative absorption ranged from 0.18 µg/cm² to 1.49 µg/cm² (= 0.03 to 0.28 % of the applied dose) and averages 1.09 µg/cm² (= 0.2 % of the applied dose).

The penetration rate (= permeation rate, flux; amount of **Uvinul T 150** in µg penetrating a square centimeter per hour) is presented in Figure 2. The data represent average values of all acceptable skin preparations (n = 5 for each dose level). For both dose levels the maximum penetration rate was achieved within 2 hours post-application and averages approx. 0.35 $\mu g/cm^2\ h^{-1}$ with large variations between individual samples (range: 0.1 - 0.55 $\mu g/cm^2\ h^{-1}$ at 1 h post-application and 0 - 0.17 $\mu g/cm^2\ h^{-1}$ or 0 - 0.53 $\mu g/cm^2\ h^{-1}$ for low and high doses respectively at 2 hours post-application). Thereafter the rate of penetration declines with time and reaches a steady-state after approx. 8 hours

For both dose levels the average absorption rate was determined by regression analysis from the slope of the respective absorption curves (Fig. 1; see Appendix for details). For the first 8 hours after application the average absorption rate in both dose levels amounted to appr. 0.06 $\mu g/cm^2\ h^{-1}$, thereafter it averaged to approx. 0.01 $\mu g/cm^2\ h^{-1}$ (time interval: 8-72 h, both dose levels).

The observed profile could be due to a rapid diffusion through the epidermal preparation during the early part of the absorption. Later on, as the epidermal capacity for the uptake of **Uvinul T 150** is saturated, a steady-state of **Uvinul T 150** uptake in and release from the epidermis becomes the predominant contribution to the overall absorption process. From the comparison of the two dose levels it can be concluded that maximum absorption is obtained already at the low dose level and that absorption is saturated at the high dose level.

4.3. Recovery of Uvinul T 150 at 72 hr (Mass Balance)

Data showing the recovery of **Uvinul T 150** at the end of the 72 h test period are presented in Table 4. Total recovery in all cases was found to be greater than 83 % of the applied dose and averaged 125 % for the low dose and 102 % for the high dose (see Appendix for single data).

Most part of the applied dose is found remaining on the epidermal surface in both dose levels.
The percentage found in the epidermis was higher for the low dose with large variation between the samples (mean: 48 % of the applied dose, range: 18-100 %).

The quantity found in the receptor chamber after 72 hours amounted to approx. 2.5 % of the applied dose in the low dose level and to approx. 0.2 % of the applied dose in the high dose level.

Table 3: Membrane Integrity Check - Results

Membr. No.	% of applied radioactivity before	after 72 hr	Comment
6A	0.93	0.49	only 0.2 kBq used for the assessment after 72 h
7C	0.72	0.82	
8A	0.50	1.27	
8B	1.21	2.76	considered as not seriously damaged although value > 2 % after 72 h
9A	0.04	1.16	
9C	0.29	1.42	
9D	0.38	2.01	
9E	1,97	0.77	
11E	0.59	0.91	
11F	1.42	0.61	

note: same numbers before the letter specify samples from the same donor (cf Table 1)

Fig. 1:

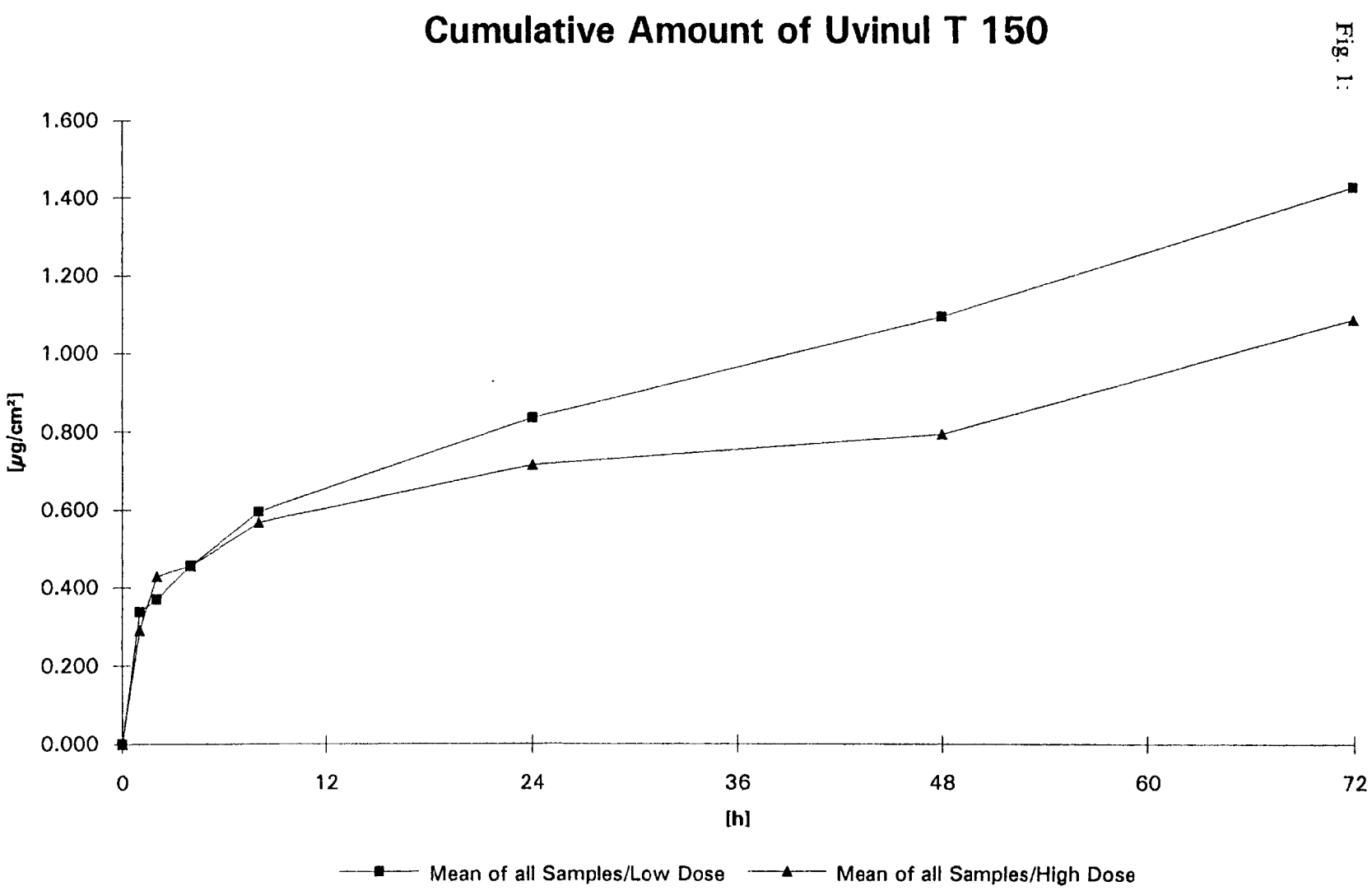

Cumulative Amount of Uvinul T 150
1.600
1.400
1.200
1.000
0.800
0.600
0.400
0.200
0.000
[µg/cm²]
0
12
24
36
48
60
72
[h]
Mean of all Samples/Low Dose
Mean of all Samples/High Dose

Fig. 2:

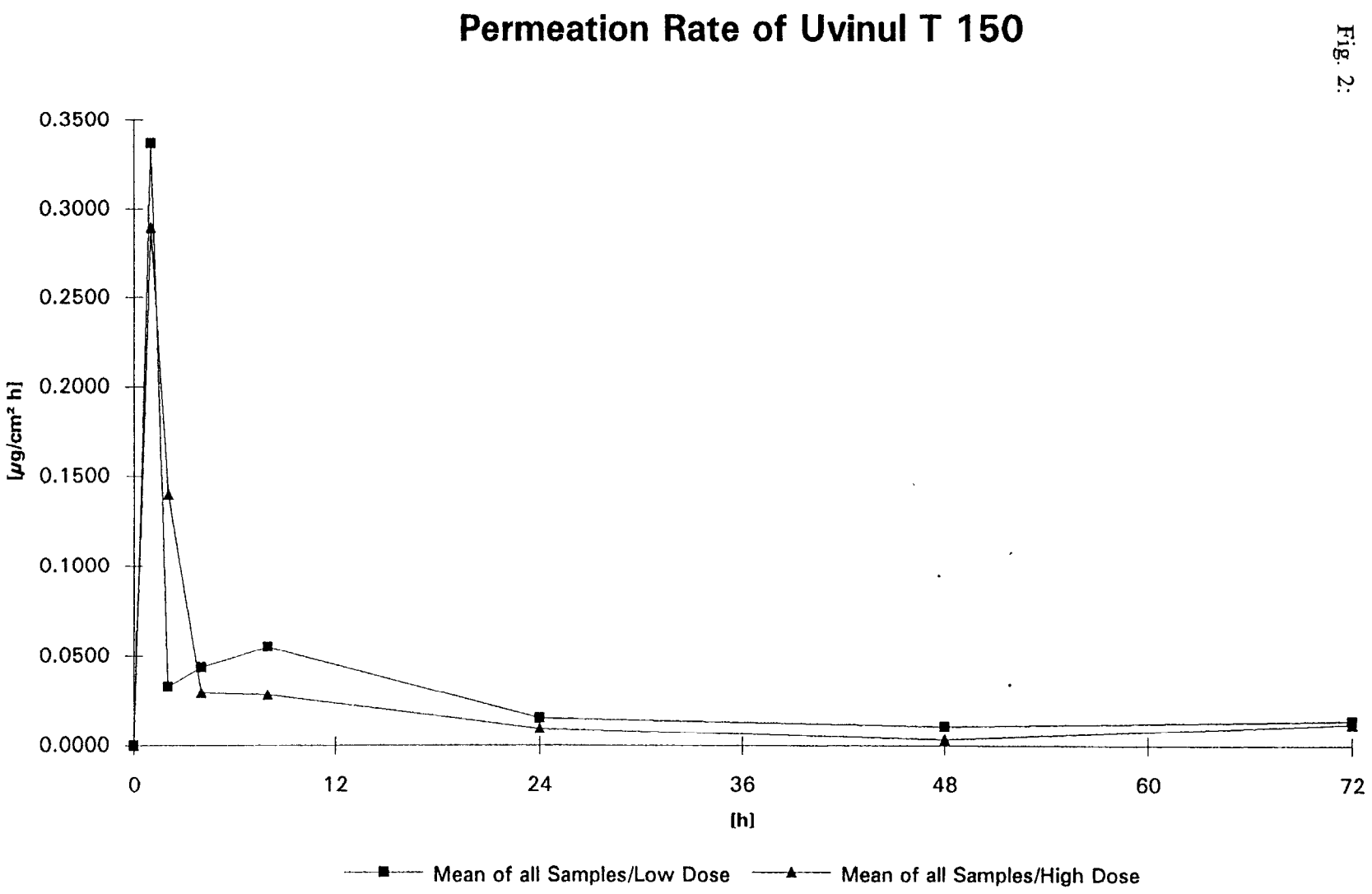

Permeation Rate of Uvinul T 150
0.3500
0.3000
0.2500
0.2000
0.1500
0.1000
0.0500
0.0000
[µg/cm² h]
0
12
24
36
48
60
72
[h]
Mean of all Samples/Low Dose
Mean of all Samples/High Dose

Table 4: Recovery of **Uvinul T 150** in different compartments at 72 hours after application

Compartment	Mean (Range) [% of applied dose]	
	Low dose	High dose
Swab + Donor Chamber Wash	73.9 (17.8 - 94.9)	92.8 (59.6-118.1)
Receptor	2.50 (0.71 - 3.60)	0.20 (0.03-0.28)
Epidermis	48.4 (17.7 - 99.5)	9.0 (2.1 - 25.2)
Total Recovery	124.9 (109.6 - 141.6)	102.0 (82.7-122.2)

Compartments with recoveries of less than 0.1 % of the applied dose:
Parafilm, Receptor Chamber Wash

5. CONCLUSION

Based on the findings of this study, it is concluded that under the chosen experimental conditions **Uvinul T 150** applied in a sunscreen formulation (5 % w/w) did penetrate human epidermis with the maximum penetration rate obtained within 2 hours post application. Thereafter the flux declines and reaches a steady-state at approx. 8 hours.
After 72 hours approx. 2.5 % (low dose = 1 mg formulation / cm^2) and approx. 0.2 % (high dose = 10 mg formulation / cm^2) of the applied **Uvinul T 150** were recovered in the receptor fluid. Based on the findings of this study it can be calculated that approx. 0.1 % (= approx. 0.05 $\mu g/cm^2$) of the applied **Uvinul T 150** in the high dose level and approx. 1.3 % (= approx. 0.065 $\mu g/cm^2$) of the low dose has penetrated the epidermis 24 hours after application.

6. REFERENCES

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7. LIST of ABBREVIATIONS

appl.	=	applied
approx.	=	approximately
C	=	concentration
cm^2	=	square centimeter (cm x cm)
D	=	dilution factor
E309, E_{309}	=	Extinction at 309 nm
ε	=	extinction factor
f	=	female
g/l	=	gram / liter
h, hrs	=	hour, hours
KBq	=	Kilobequerel
m	=	male
M	=	mean
mg	=	milligrams
Min, min	=	minimum
Max, max	=	maximum
ml	=	milliliter
µg	=	microgram
µl	=	microliter
N,n	=	number of values
NaCl	=	sodium chloride
n.d.	=	not determined
nm	=	nanometer
no., No.	=	number
ppm	=	parts per million
rpm	=	rounds per minute
SDEV	=	standard deviation
t	=	time
(t)	=	designates the sampling at the time point "t"
(t-1)	=	designates the sampling at the antecedent time point
(t=0)	=	designates the sampling before application of the test substance
≤	=	less than or equal
≥	=	greater than or equal
%	=	per cent
°C	=	Celsius

APPENDIX

EQUATIONS

Receptor Volume	=	7.0 ml minus volume of the stirring bar
	=	7.0 ml - 0.4 ml = 6.6 ml
Amount before Sampling $_{(t)}$	=	Amount in Receptor Chamber $_{(t-1)}$ - Amount Removed by Sampling $_{(t-1)}$
Amount in Receptor Chamber $_{(t)}$	=	Concentration $_{(t)}$ x 6.6
Amount Removed by Samplin $_{(t)}$	=	1.5 x concentration $_{(t)}$
Amount in Delta Time $_{(t)}$	=	Amount in Receptor Chamber $_{(t)}$ + Amount Removed by Sampling $_{(t-1)}$ - Amount in Receptor Chamber $_{(t-1)}$
Cumulated Amount $_{(t)}$	=	Cumulated Amount $_{(t-1)}$ + Amount in Delta Time $_{(t)}$
Cumulated Amount without Background $_{(t)}$	=	Cumulated Amount $_{(t)}$ - Cumulated Amount $_{(t=0)}$

Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 6A

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.059 mg Uvinul T 150/cm²
Applied Dose: 0.185 mg/Chamber
Date of Application: 29.11.1994

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	33	0.000	0.017	2	0.260	1.716	0.390	1.716	1.716	0.93	0.000	0.00
1	34	1.326	0.026	2	0.397	2.620	0.596	1.294	3.010	1.63	1.294	0.70
2	35	2.024	0.012	2	0.183	1.208	0.275	-0.816	2.194	1.19	0.478	0.26
4	36	0.933	0.018	2	0.275	1.815	0.413	0.882	3.076	1.66	1.360	0.74
8	37	1.402	0.022	2	0.336	2.218	0.504	0.816	3.892	2.11	2.176	1.18
24	38	1.714	0.029	2	0.443	2.924	0.665	1.210	5.102	2.76	3.386	1.83
48	39	2.259	0.032	2	0.489	3.227	0.734	0.968	6.070	3.28	4.354	2.36
72	40	2.493	0.038	2	0.581	3.835	0.872	1.342	7.412	4.01	5.696	3.08

Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 7C

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.059 mg Uvinul T 150/cm²
Applied Dose: 0.185 mg/Chamber
Date of Application: 17.01.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	41	0.000	0.000	2	0.000	0.000	0.000	0.000	0.000	0.00	0.000	0.00
1	42	0.000	0.010	2	0.153	1.010	0.230	1.010	1.010	0.55	1.010	0.55
2	43	0.780	0.013	2	0.199	1.313	0.299	0.533	1.543	0.83	1.543	0.83
4	44	1.014	0.009	2	0.138	0.911	0.207	-0.103	1.440	0.78	1.440	0.78
8	45	0.704	0.014	2	0.214	1.412	0.321	0.708	2.148	1.16	2.148	1.16
24	46	1.091	0.020	2	0.306	2.020	0.459	0.929	3.077	1.67	3.077	1.67
48	47	1.561	0.030	2	0.459	3.029	0.689	1.468	4.545	2.46	4.545	2.46
72	48	2.340	0.044	2	0.673	4.442	1.010	2.102	6.647	3.60	6.647	3.60

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Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 8B

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0 130842

Concentration: 0.055 mg Uvinul T 150/cm²
Applied Dose: 0.174 mg/Chamber
Date of Application: 17.01.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	57	0.000	0.001	2	0.015	0.099	0.023	0.099	0.099	0.06	0.000	0.00
1	58	0.076	0.017	2	0.260	1.716	0.390	1.640	1.739	1.00	1.640	0.94
2	59	1.326	0.017	2	0.260	1.716	0.390	0.390	2.129	1.23	2.030	1.17
4	60	1.326	0.009	2	0.138	0.911	0.207	-0.415	1.714	0.99	1.615	0.93
8	61	0.704	0.027	2	0.413	2.726	0.620	2 022	3.736	2.15	3.637	2.10
24	62	2.106	0.021	2	0.321	2.119	0.482	0.013	3.749	2.16	3.650	2.10
48	63	1.637	0.034	2	0.520	3.432	0.780	1.795	5.544	3.19	5.445	3.14
72	64	2.652	0.030	2	0.459	3.029	0.689	0.377	5.921	3.41	5.822	3.35

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Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 9D

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.054 mg Uvinul T 150/cm²
Applied Dose: 0.168 mg/Chamber
Date of Application: 17.01.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	89	0.000	0.008	2	0.122	0.805	0.183	0.805	0.805	0.48	0.000	0.00
1	90	0.622	0.009	2	0.138	0.911	0.207	0.289	1.094	0.65	0.289	0.17
2	91	0.704	0.010	2	0.153	1.010	0.230	0.306	1.400	0.83	0.595	0.35
4	92	0.780	0.015	2	0.229	1.511	0.344	0.731	2.131	1.27	1.326	0.79
8	93	1.167	0.009	2	0.138	0.911	0.207	-0.256	1.875	1.12	1.070	0.64
24	94	0.704	0.023	2	0.352	2.323	0.528	1.619	3.494	2.08	2.689	1.60
48	95	1.795	0.011	2	0.168	1.109	0.252	-0.686	2.808	1.67	2.003	1.19
72	96	0.857	0.018	2	0.275	1.815	0.413	0.958	3.766	2.24	2.961	1.76

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Uvinul T 150 / 5% Sunscreen Formulation

Date: 16.02.95

Project No.: 62V0398/943005

Skin 11F

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.059 mg Uvinul T 150/cm²
Applied Dose: 0.185 mg/Chamber
Date of Application: 07.02.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	113	0.000	0.004	2	0.061	0.403	0.092	0.403	0.403	0.22	0.000	0.00
1	114	0.311	0.002	2	0.031	0.205	0.047	-0.106	0.297	0.16	-0.106	-0.06
2	115	0.158	0.001	2	0.015	0.099	0.023	-0.059	0.238	0.13	-0.165	-0.09
4	116	0.076	0.002	2	0.031	0.205	0.047	0.129	0.367	0.20	-0.036	-0.02
8	117	0.158	0.005	2	0.076	0.502	0.114	0.344	0.711	0.38	0.308	0.17
24	118	0.388	0.004	2	0.061	0.403	0.092	0.015	0.726	0.39	0.323	0.17
48	119	0.311	0.008	2	0.122	0.805	0.183	0.494	1.220	0.66	0.817	0.44
72	120	0.622	0.011	2	0.168	1.109	0.252	0.487	1.707	0.92	1.304	0.71

Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 8A

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.535 mg Uvinul T 150/cm²
Applied Dose: 1.680 mg/Chamber
Date of Application: 17.01.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	49	0.000	0.000	2	0.000	0.000	0.000	0.000	0.000	0.00	0.000	0.00
1	50	0.000	0.010	2	0.153	1.010	0.230	1.010	1.010	0.06	1.010	0.06
2	51	0.780	0.005	2	0.076	0.502	0.114	-0.278	0.732	0.04	0.732	0.04
4	52	0.388	0.007	2	0.107	0.706	0.161	0.318	1.050	0.06	1.050	0.06
8	53	0.545	0.009	2	0.138	0.911	0.207	0.366	1.416	0.08	1.416	0.08
24	54	0.704	0.020	2	0.306	2.020	0.459	1.316	2.732	0.16	2.732	0.16
48	55	1.561	0.026	2	0.397	2.620	0.596	1.059	3.791	0.23	3.791	0.23
72	56	2.024	0.029	2	0.443	2.924	0.665	0.900	4.691	0.28	4.691	0.28

Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 9A

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.549 mg Uvinul T 150/cm²
Applied Dose: 1.725 mg/Chamber
Date of Application: 17.01.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	65	0.000	0.014	2	0.214	1.412	0.321	1.412	1.412	0.08	0.000	0.00
1	66	1.091	0.007	2	0.107	0.706	0.161	-0.385	1.027	0.06	-0.385	-0.02
2	67	0.545	0.008	2	0.122	0.805	0.183	0.260	1.287	0.07	-0.125	-0.01
4	68	0.622	0.024	2	0.367	2.422	0.551	1.800	3.087	0.18	1.675	0.10
8	69	1.871	0.021	2	0.321	2.119	0.482	0.248	3.335	0.19	1.923	0.11
24	70	1.637	0.010	2	0.153	1.010	0.230	-0.627	2.708	0.16	1.296	0.08
48	71	0.780	0.014	2	0.214	1.412	0.321	0.632	3.340	0.19	1.928	0.11
72	72	1.091	0.026	2	0.397	2.620	0.596	1.529	4.869	0.28	3.457	0.20

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Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 9C

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.548 mg Uvinul T 150/cm²
Applied Dose: 1.719 mg/Chamber
Date of Application: 17.01.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	81	0.000	0.010	2	0.153	1.010	0.230	1.010	1.010	0.06	0.000	0.00
1	82	0.780	0.011	2	0.168	1.109	0.252	0.329	1.339	0.08	0.329	0.02
2	83	0.857	0.025	2	0.382	2.521	0.573	1.664	3.003	0.17	1.993	0.12
4	84	1.948	0.013	2	0.199	1.313	0.299	-0.635	2.368	0.14	1.358	0.08
8	85	1.014	0.020	2	0.306	2.020	0.459	1.006	3.374	0.20	2.364	0.14
24	86	1.561	0.016	2	0.245	1.617	0.368	0.056	3.430	0.20	2.420	0.14
48	87	1.249	0.014	2	0.214	1.412	0.321	0.163	3.593	0.21	2.583	0.15
72	88	1.091	0.023	2	0.352	2.323	0.528	1.232	4.825	0.28	3.815	0.22

Uvinul T 150 / 5% Sunscreen Formulation

Date: 14.02.95

Project No.: 62V0398/943005

Skin 9E

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.564 mg Uvinul T 150/cm²
Applied Dose: 1.770 mg/Chamber
Date of Application: 17.01.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	97	0.000	0.008	2	0.122	0.805	0.183	0.805	0.805	0.05	0.000	0.00
1	98	0.622	0.012	2	0.183	1.208	0.275	0.586	1.391	0.08	0.586	0.03
2	99	0.933	0.023	2	0.352	2.323	0.528	1.390	2.781	0.16	1.976	0.11
4	100	1.795	0.021	2	0.321	2.119	0.482	0.324	3.105	0.18	2.300	0.13
8	101	1.637	0.019	2	0.290	1.914	0.435	0.277	3.382	0.19	2.577	0.15
24	102	1.479	0.031	2	0.474	3.128	0.711	1.649	5.031	0.28	4.226	0.24
48	103	2.417	0.018	2	0.275	1.815	0.413	-0.602	4.429	0.25	3.624	0.20
72	104	1.402	0.023	2	0.352	2.323	0.528	0.921	5.350	0.30	4.545	0.26

Uvinul T 150 / 5% Sunscreen Formulation

Date: 16.02.95

Project No.: 62V0398/943005

Skin 11E

Receptor Volume: 6.6 ml
Sample Volume: 1.5 ml
Extinction Factor: 0.130842

Concentration: 0.535 mg Uvinul T 150/cm²
Applied Dose: 1.680 mg/Chamber
Date of Application: 07.02.1995

Hours	Sample No.	Amount before Sampling [µg]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/ml]	Amount in Receptor Chamber [µg]	Amount Removed by Sampling [µg]	Amount in Delta Time [µg]	Cumulated Amount Uvinul T 150 [µg]	[%dose]	Cumulated Amount without Background Uvinul T 150 [µg]	[%dose]
0	105	0.000	0.000	2	0.000	0.000	0.000	0.000	0.000	0.00	0.000	0.00
1	106	0.000	0.017	2	0.260	1.716	0.390	1.716	1.716	0.10	1.716	0.10
2	107	1.326	0.003	2	0.046	0.304	0.069	-1.022	0.694	0.04	0.694	0.04
4	108	0.235	0.003	2	0.046	0.304	0.069	0.069	0.763	0.05	0.763	0.05
8	109	0.235	0.001	2	0.015	0.099	0.023	-0.136	0.627	0.04	0.627	0.04
24	110	0.076	0.000	2	0.000	0.000	0.000	-0.076	0.551	0.03	0.551	0.03
48	111	0.000	0.000	2	0.000	0.000	0.000	0.000	0.551	0.03	0.551	0.03
72	112	0.000	0.000	2	0.000	0.000	0.000	0.000	0.551	0.03	0.551	0.03

Summary Tables: Cumulative Amount

Low Dose

Time [h]	0	1	2	4	8	24	48	72
Skin Area	[µg/cm²]							
6A	0.000	0.412	0.152	0.433	0.693	1.078	1.387	1.814
7C	0.000	0.322	0.491	0.459	0.684	0.980	1.447	2.117
8B	0.000	0.522	0.646	0.514	1.158	1.162	1.734	1.854
9D	0.000	0.092	0.189	0.422	0.341	0.856	0.638	0.943
11F	0.000	*-0.034	*-0.053	*-0.011	0.098	0.103	0.260	0.415
Mean	0.000	0.337	0.370	0.457	0.595	0.836	1.093	1.429
Min	0.000	0.092	0.152	0.422	0.098	0.103	0.260	0.415
Max	0.000	0.522	0.646	0.514	1.158	1.162	1.734	2.117

High Dose

Time [h]	0	1	2	4	8	24	48	72
Skin Area	[µg/cm²]							
8A	0.000	0.322	0.233	0.334	0.451	0.870	1.207	1.494
9A	0.000	*-0.123	*-0.040	0.533	0.612	0.413	0.614	1.101
9C	0.000	0.105	0.635	0.432	0.753	0.771	0.823	1.215
9E	0.000	0.187	0.629	0.732	0.821	1.346	1.154	1.447
11E	0.000	0.546	0.221	0.243	0.200	0.175	0.175	0.175
Mean	0.000	0.290	0.430	0.455	0.567	0.715	0.795	1.087
Min	0.000	0.105	0.221	0.243	0.200	0.175	0.175	0.175
Max	0.000	0.546	0.635	0.732	0.821	1.346	1.207	1.494

* = not considered for calculations

Summary Tables: Flux

Low Dose

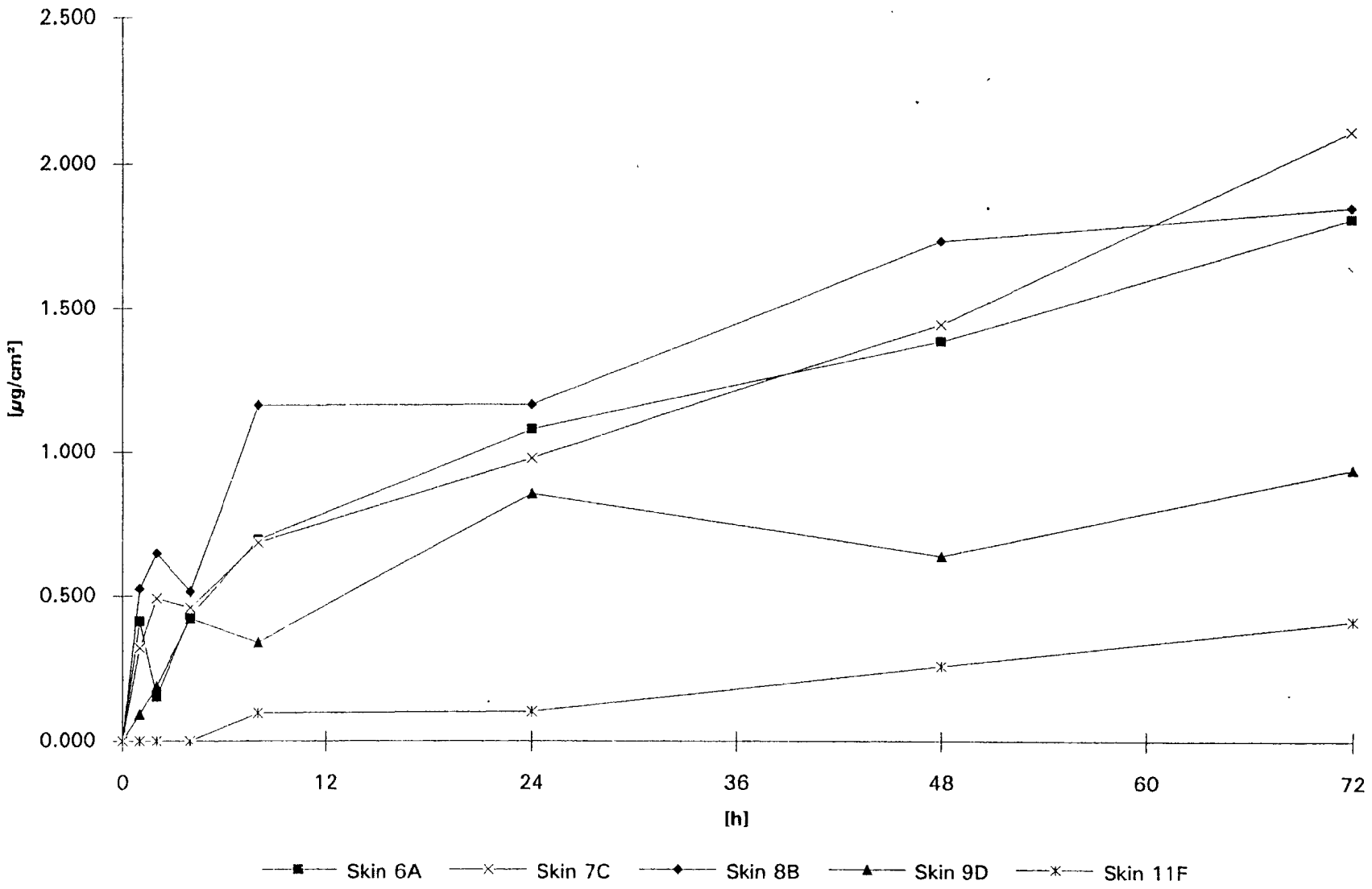
Time [h]	0	1	2	4	8	24	48	72
Skin Area	[µg/(cm² h)]							
6A	0.0000	0.4121	-0.2599	0.1404	0.0650	0.0241	0.0128	0.0178
7C	0.0000	0.3217	0.1697	-0.0164	0.0564	0.0185	0.0195	0.0279
8B	0.0000	0.5223	0.1242	-0.0661	0.1610	0.0003	0.0238	0.0050
9D	0.0000	0.0920	0.0975	0.1164	-0.0204	0.0322	-0.0091	0.0127
11F	0.0000	*-	*-	*-	0.0123	0.0003	0.0066	0.0065
Mean	0.0000	0.3370	0.0329	0.0436	0.0548	0.0151	0.0107	0.0140
Min	0.0000	0.0920	-0.2599	-0.0661	-0.0204	0.0003	-0.0091	0.0050
Max	0.0000	0.5223	0.1697	0.1404	0.1610	0.0322	0.0238	0.0279

High Dose

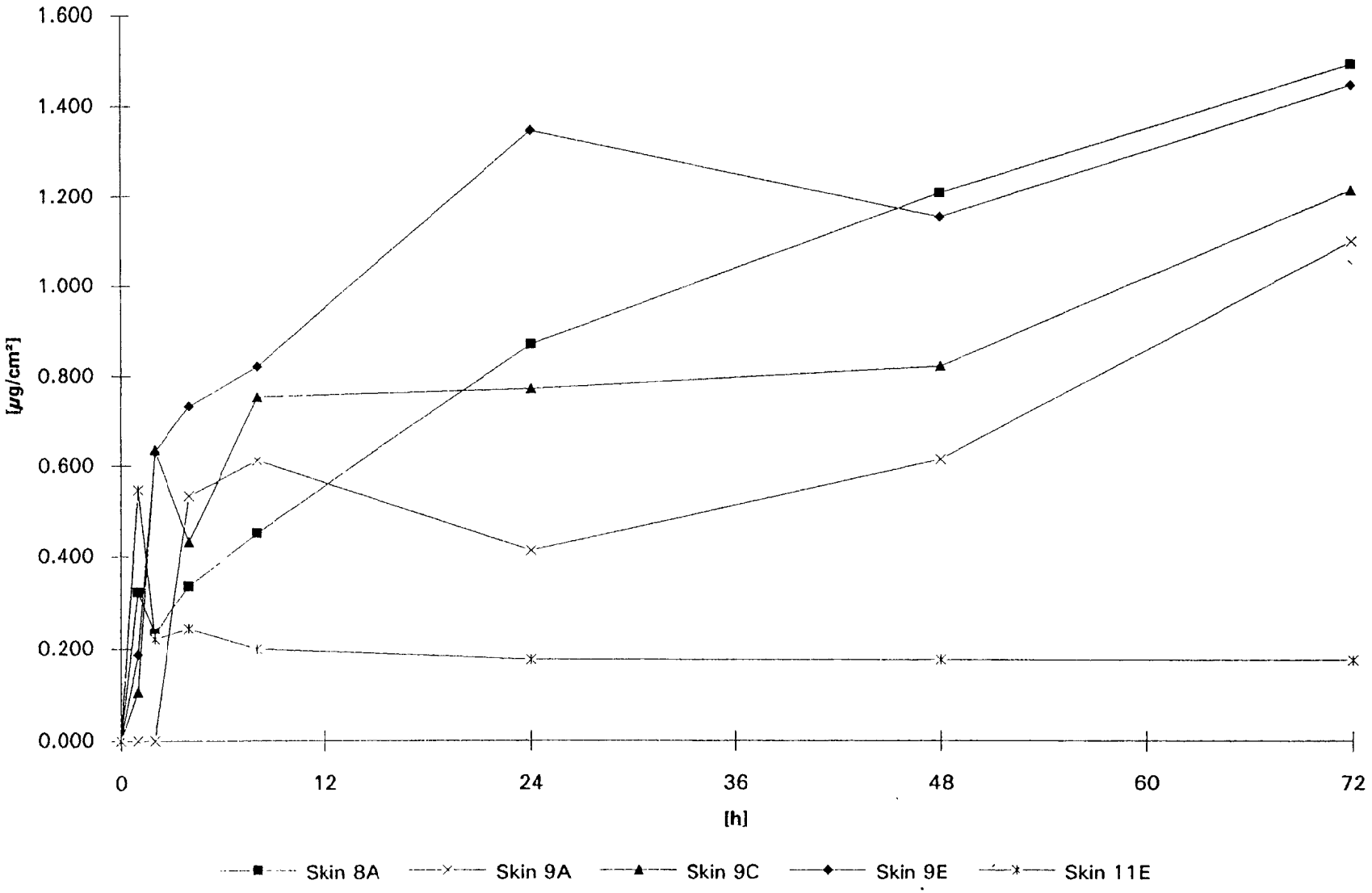
Time [h]	0	1	2	4	8	24	48	72
Skin Area	[µg/(cm² h)]							
8A	0.0000	0.3217	-0.0885	0.0506	0.0291	0.0262	0.0141	0.0119
9A	0.0000	*-	*-	0.1334	0.0197	-0.0125	0.0084	0.0203
9C	0.0000	0.1048	0.5299	-0.1011	0.0801	0.0011	0.0022	0.0163
9E	0.0000	0.1866	0.4427	0.0516	0.0221	0.0328	-0.0080	0.0122
11E	0.0000	0.5465	-0.3255	0.0110	-0.0108	-0.0015	0.0000	0.0000
Mean	0.0000	0.2899	0.1396	0.0291	0.0280	0.0092	0.0033	0.0122
Min	0.0000	0.1048	-0.3255	-0.1011	-0.0108	-0.0125	-0.0080	0 0000
Max	0.0000	0.5465	0.5299	0.1334	0.0801	0.0328	0.0141	0.0203

* = not considered for calculations

Cumulative Amount of Uvinul T 150 (Low Dose)



Cumulative Amount of Uvinul T 150 (High Dose)



Uvinul T 150 / 5 % Sunscreen Formulation

Balance: Parafilm

Project No.: 62V0398/943005

Extinction Fact.: 0.130842

Solvent: Dioxan/Ethanol/Aqua bidest. 50:25:25

Low dose: Samples 6A, 7C, 8B, 9D, 11F

High dose: Samples 8A, 9A, 9C, 9E, 11E

Skin	Sample No.	Amount before Dilution [g]	Addition of Solvent [g]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/g]	Amount in Sample Uvinul T 150 [µg]	[%dose]	Mean [%dose]	SDEV
6A	/1	0.244	1.974	0.024	1	0.183	0.362	0.011		
7C	/1	-	1.883	0.065	1	0.497	0.936	0.028		
8B	/1	-	1.941	0.123	1	0.940	1.825	0.059	0.063	0.079
9D	/1	-	1.961	0.030	1	0.229	0.449	0.015		
11F	/1	-	1.901	0.456	1	3.485	6.625	0.201		
8A	/1	-	1.926	0.026	1	0.199	0.383	0.001		
9A	/1	-	1.944	0.101	1	0.772	1.500	0.005		
9C	/1	-	1.923	0.020	1	0.153	0.294	0.001	0.005	0.006
9E	/1	-	2.016	0.030	1	0.229	0.462	0.001		
11E	/1	-	1.844	0.322	1	2.461	4.537	0.015		

Uvinul T 150 / 5 % Sunscreen Formulation

Balance: Swab

Project No.: 62V0398/943005

Extinction Fact.: 0.008146

Solvent: Dioxan

Low dose: Samples 6A, 7C, 8B, 9D, 11F

High dose: Samples 8A, 9A, 9C, 9E, 11E

Skin	Sample No.	Amount before Dilution [g]	Addition of Solvent [g]	E 309	Dilution Factor	Concentration Formulation [µg/g]	Amount in Sample Formulation [µg]	Uvinul T 150 [µg]	Uvinul T 150 [%dose]	Mean [%dose]	SDEV
6A	/2	0.256	5.154	0.109	40	535.232	2758.479	154.475	83.590		
7C	/2	-	15.494	0.306	1	37.564	582.012	32.593	17.637		
8B	/2	-	13.731	0.072	20	176.774	2427.194	135.923	78.297	56.844	39.785
9D	/2	-	14.639	0.079	20	193.960	2839.364	159.004	94.645		
11F	/2	-	15.437	0.175	1	21.483	331.636	18.572	10.050		
8A	/2	-	15.016	0.483	20	1185.858	17806.845	997.183	59.356		
9A	/2	-	14.486	0.510	40	2504.297	36275.988	2031.455	117.779		
9C	/2	-	15.776	0.422	40	2072.183	32691.168	1830.705	106.486	77.424	46.257
9E	/2	-	13.624	0.467	40	2293.150	31242.793	1749.596	98.870		
11E	/2	-	15.494	0.073	10	89.615	1388.470	77.754	4.628		

Uvinul T 150 / 5 % Sunscreen Formulation

Balance: Donor Chamber Wash

Project No.: 62V0398/943005

Extinction Fact.: 0.130842

Solvent: Dioxan/Ethanol/Aqua bidest. 50:25:25

Low dose: Samples 6A, 7C, 8B, 9D

High dose: Samples 8A, 9A, 9C, 9E

Skin	Sample No.	Amount before Dilution [g]	Addition of Solvent [g]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/g]	Amount in Sample Uvinul T 150 [µg]	[%dose]	Mean [%dose]	SDEV
6A	/3	1.825	-	0.072	2	1.101	2.009	0.061		
7C	/3	1.870	-	0.206	2	3.149	5.889	0.178	0.125	0.049
8B	/3	1.818	-	0.152	2	2.323	4.223	0.136		
9D	/3	1.782	-	0.139	2	2.125	3.787	0.126		
8A	/3	1.864	-	0.578	10	44.175	82.342	0.274		
9A	/3	1.846	-	0.683	10	52.200	96.361	0.313	0.221	0.092
9C	/3	1.839	-	0.234	10	17.884	32.889	0.107		
9E	/3	1.700	-	0.461	10	35.233	59.896	0.190		

Uvinul T 150 / 5 % Sunscreen Formulation

Balance: Donor Chamber Wash

Project No.: 62V0398/943005

Extinction Fact.: 0.008146

Solvent: Dioxan

Low dose: Sample 11F

High dose: Sample 11E

Skin	Sample No.	Amount before Dilution [g]	Addition of Solvent [g]	E 309	Dilution Factor	Concentration Formulation [µg/g]	Amount in Sample Formulation [µg]	Uvinul T 150 [µg]	[%dose]
11F	/3	7.080	-	0.161	20	395.286	2798.625	156.723	84.807
11E	/3	7.116	-	0.326	80	3201.571	22782.382	1275.813	75.941

Uvinul T 150 / 5 % Sunscreen Formulation

Balance: Receptor Chamber Wash

Project No.: 62V0398/943005

Extinction Fact.: 0.130842

Solvent: Dioxan/Ethanol/Aqua bidest. 50:25:25

Low dose: Samples 6A, 7C, 8B, 9D, 11F

High dose: Samples 8A, 9A, 9C, 9E, 11E

Skin	Sample No.	Amount before Dilution [g]	Addition of Solvent [g]	E 309	Dilution Factor	Concentration Uvinul T 150 [µg/g]	Amount in Sample Uvinul T 150 [µg]	[%dose]	Mean [%dose]	SDEV
6A	/5	1.761	-	0.014	2	0.214	0.377	0.011		
7C	/5	2.530	-	0.002	2	0.031	0.078	0.002		
8B	/5	2.033	-	0.000	2	0.000	0.000	0.000	0.006	0.007
9D	/5	1.837	-	0.002	2	0.031	0.057	0.002		
11F	/5	2.407	-	0.014	2	0.214	0.515	0.016		
8A	/5	1.497	-	0.000	2	0.000	0.000	0.000		
9A	/5	1.876	-	0.000	2	0.000	0.000	0.000		
9C	/5	1.771	-	0.000	2	0.000	0.000	0.000	0.000	0.000
9E	/5	1.873	-	0.000	2	0.000	0.000	0.000		
11E	/5	1.618	-	0.000	2	0.000	0.000	0.000		

BASF
Abteilung Toxikologie
Department of Toxicology

Uvinul T 150 / 5 % Sunscreen Formulation

Balance: Epidermis

Project No.: 62V0398/943005

Extinction Fact.: 0.008146

Solvent: Dioxan

Low dose: Samples 6A, 7C, 8B, 9D, 11F

High dose: Samples 8A, 9A, 9C, 9E, 11E

Skin	Sample No.	Amount before Dilution [g]	Addition of Solvent [g]	E 309	Dilution Factor	Concentration Formulation [µg/g]	Amount in Sample Formulation [µg]	Uvinul T 150 [µg]	Uvinul T 150 [%dose]	Mean [%dose]	SDEV
6A	/6	0.057	5.150	0.119	10	146.084	752.303	42.129	22.797		
7C	/6	0.091	10.211	0.262	10	321.630	3284.263	183.919	99.523		
8B	/6	0.046	9.989	0.151	10	185.367	1851.706	103.696	59.732	48.413	33.075
9D	/6	0.036	10.131	0.102	10	125.215	1268.589	71.041	42.286		
11F	/6	0.072	10.269	0.464	1	56.960	584.899	32.754	17.724		
8A	/6	0.056	10.073	0.611	10	750.061	7554.993	423.080	25.183		
9A	/6	0.033	9.962	0.098	10	120.304	1198.509	67.117	3.891		
9C	/6	0.037	10.091	0.233	10	286.030	2886.357	161.636	9.402	9.018	9.433
9E	/6	0.038	10.119	0.115	10	141.174	1428.479	79.995	4.521		
11E	/6	0.033	10 521	0.486	1	59.661	627.707	35.152	2.092		

Summary Table: Recovery of Uvinul T 150 in Receptor Chamber at 72 Hours Post Application

Skin	Dose	Cumulated Amount (without Background) [µg]	[%dose]	Mean [%dose]	SDEV
6A	low	5.696	3.08		
7C	low	6.647	3.60		
8B	low	5.822	3.35	2.50	1.23
9D	low	2.961	1.76		
11F	low	1.304	0.71		
8A	high	4.691	0.28		
9A	high	3.457	0.20		
9C	high	3.815	0.22	0.20	0.10
9E	high	4.545	0.26		
11E	high	0.551	0.03		

Summary Table: Total Recovery of Uvinul T 150

Skin	Dose	Recovery* [%dose]	Mean [%dose]	SDEV
6A	low	109.60		
7C	low	120.97		
8B	low	141.58	124.90	14.59
9D	low	138.84		
11F	low	113.50		
8A	high	85.09		
9A	high	122.19		
9C	high	116.22	102.01	17.83
9E	high	103.84		
11E	high	82.71		

* Sum of Parafilm, Swab, Donor Chamber Wash. Cumulative Amount in Receptor Chamber without Background. Receptor Chamber Wash and Epidermis

	Regression	low dose
0.0000	0.0000	
1.0000	0.3370	
2.0000	0.3700	
4.0000	0.4570	
8.0000	0.5950	0.5950
24.0000		0.8360
48.0000		1.0930
72.0000		1.4290

Plot 1
Order 1

Curve 1:
column 1 column 2:

Coefficien	
b[0]	0.1727
b[1]	0.0597
r ²	0.7329

Function V

x	f(x)
0.0000	0.1727
0.4000	0.1966
0.8000	0.2205
1.2000	0.2443
1.6000	0.2682
2.0000	0.2921
2.4000	0.3160
2.8000	0.3399
3.2000	0.3637
3.6000	0.3876
4.0000	0.4115
4.4000	0.4354
4.8000	0.4593
5.2000	0.4831
5.6000	0.5070
6.0000	0.5309
6.4000	0.5548
6.8000	0.5787
7.2000	0.6025
7.6000	0.6264
8.0000	0.6503

Curve 2:
column 1 column 3:

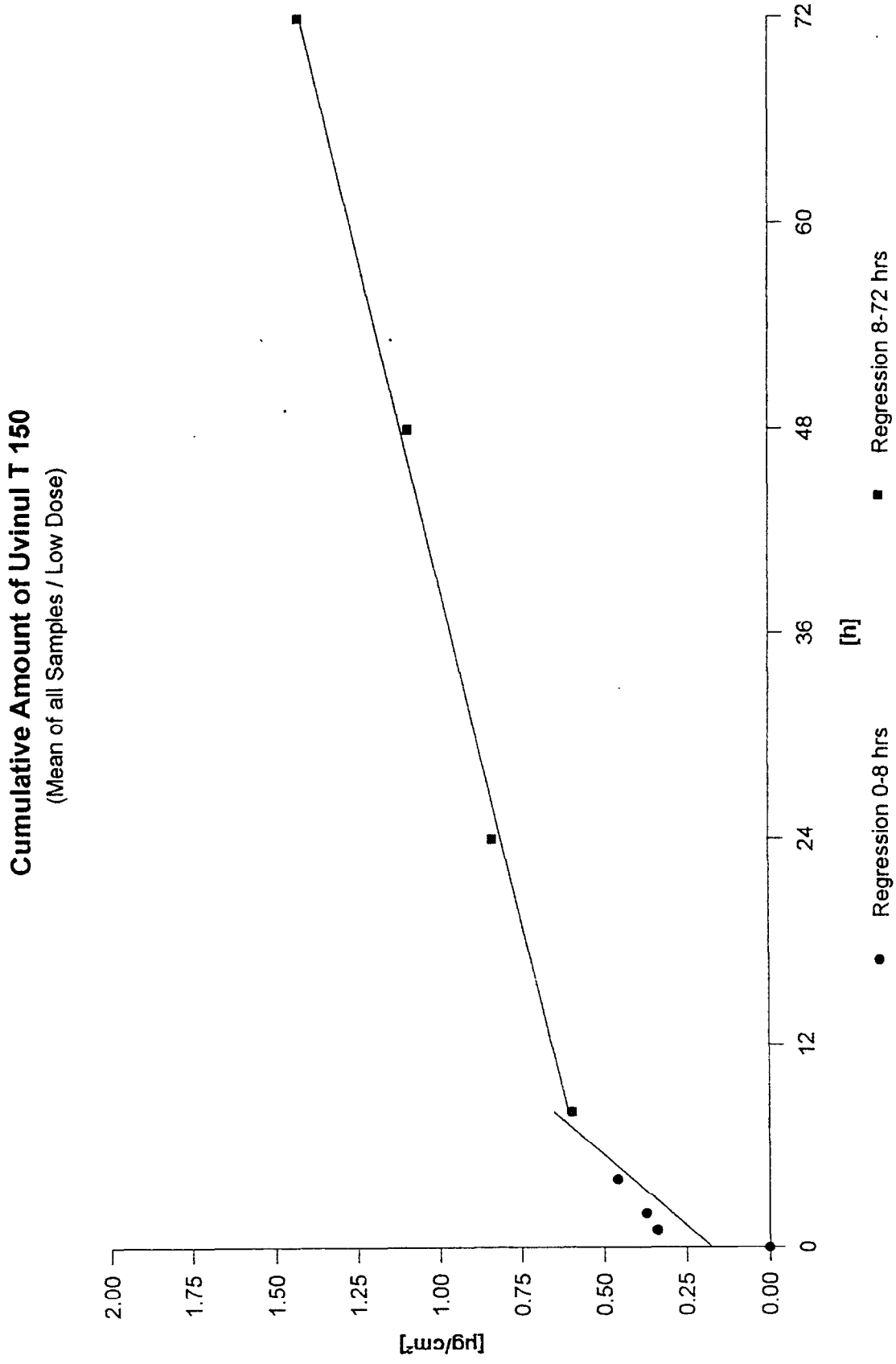
Coefficien	
b[0]	0.5042
b[1]	0.0127
r ²	0.9964

Function V

x	f(x)
8.0000	0.6061
11.2000	0.6468
14.4000	0.6876
17.6000	0.7284
20.8000	0.7691
24.0000	0.8099
27.2000	0.8507
30.4000	0.8914
33.6000	0.9322
36.8000	0.9730
40.0000	1.0137
43.2000	1.0545
46.4000	1.0953
49.6000	1.1360
52.8000	1.1768
56.0000	1.2176
59.2000	1.2583
62.4000	1.2991
65.6000	1.3398
68.8000	1.3806
72.0000	1.4214

slope (= b [1]) curve 1 = 0.0597

slope (= b [1]) curve 2 = 0.0127


Cumulative Amount of Uvinul T 150
(Mean of all Samples / Low Dose)
[µg/cm²]
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
60
72
[h]
Regression 0-8 hrs
Regression 8-72 hrs

	Regression	high dose
0.0000	0.0000	
1.0000	0.2900	
2.0000	0.4300	
4.0000	0.4550	
8.0000	0.5670	0.5670
24.0000		0.7150
48.0000		0.7950
72.0000		1.0870

Plot 2
Order 1

Curve 1:
column 1 column 2:

Coefficien	
b[0]	0.1774
b[1]	0.0570
r^2	0.6818

Function V

x	f(x)
0.0000	0.1774
0.4000	0.2002
0.8000	0.2230
1.2000	0.2458
1.6000	0.2686
2.0000	0.2914
2.4000	0.3142
2.8000	0.3370
3.2000	0.3598
3.6000	0.3826
4.0000	0.4054
4.4000	0.4282
4.8000	0.4510
5.2000	0.4738
5.6000	0.4966
6.0000	0.5194
6.4000	0.5422
6.8000	0.5650
7.2000	0.5878
7.6000	0.6106
8.0000	0.6334

Curve 2:
column 1 column 3:

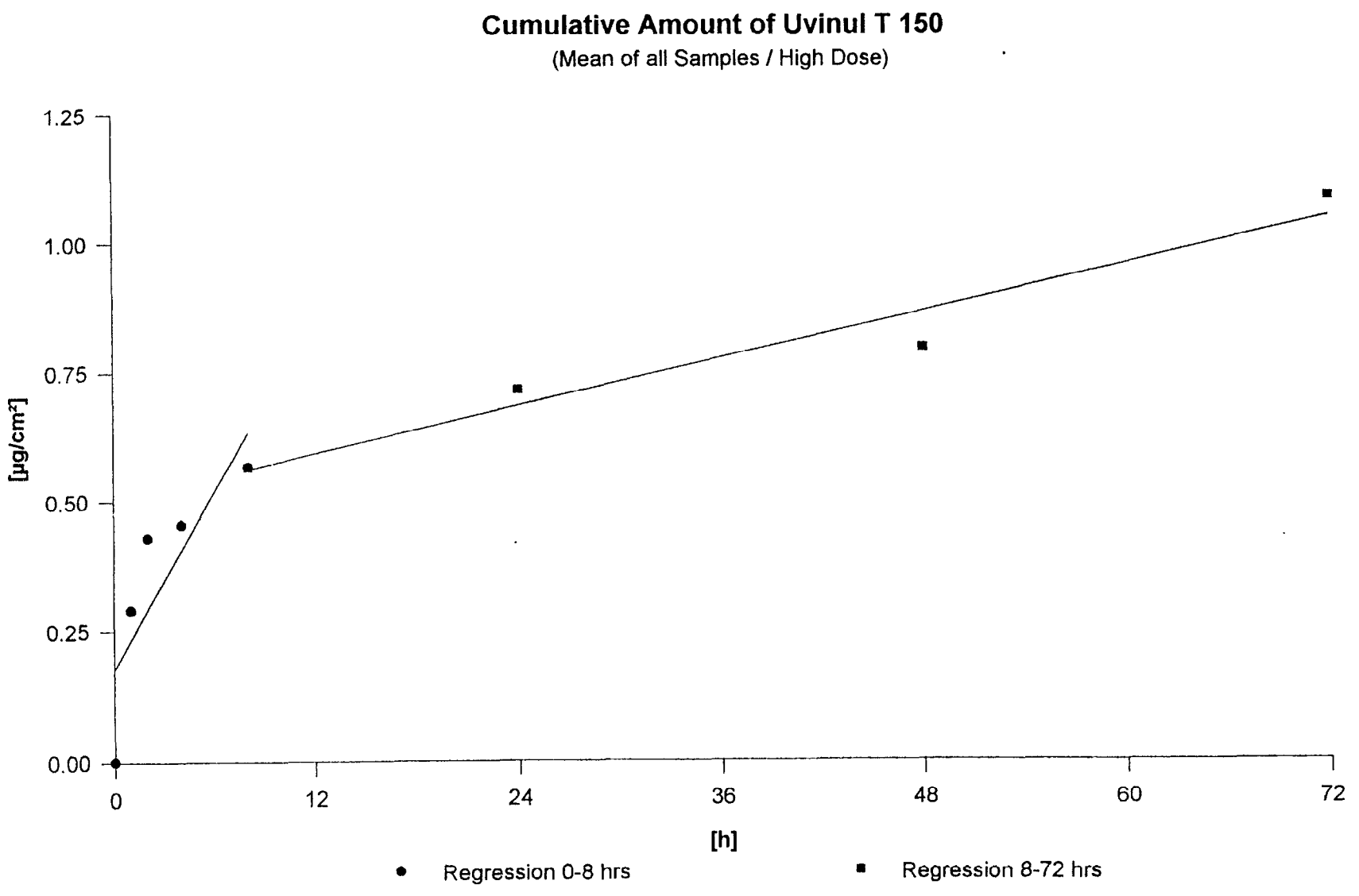
Coefficien	
b[0]	0.5020
b[1]	7.6054e-3
r^2	0.9475

Function V

x	f(x)
8.0000	0.5628
11.2000	0.5872
14.4000	0.6115
17.6000	0.6358
20.8000	0.6602
24.0000	0.6845
27.2000	0.7089
30.4000	0.7332
33.6000	0.7575
36.8000	0.7819
40.0000	0.8062
43.2000	0.8305
46.4000	0.8549
49.6000	0.8792
52.8000	0.9036
56.0000	0.9279
59.2000	0.9522
62.4000	0.9766
65.6000	1.0009
68.8000	1.0252
72.0000	1.0496

slope (= b [1]) curve 1 = 0.0570

slope (= b [1]) curve 2 = 7.6054e-3


Cumulative Amount of Uvinul T 150
(Mean of all Samples / High Dose)
1.25
1.00
0.75
0.50
0.25
0.00
[µg/cm²]
0
12
24
36
48
60
72
[h]
Regression 0-8 hrs
Regression 8-72 hrs

COSMETICON

SONNENSCHUTZCREME, TYP O/W REZEPT-NR. 53/013N

Eigenschaften

Feste, leicht verteilbare Creme. Hinterläßt ein angenehmes Hautgefühl.

	%	Rohstoff	Lieferant	CTFA
A	2.00	Cremophor A 6	(1)	Ceteareth-6 (and) Stearyl Alcohol
	2.00	Cremophor A 25	(1)	Ceteareth-25
	5.00	Dracorin 100 s.e.	(17)	Glyceryl Stearate (and) PEG-100 Stearate
	10.00	Iso-Adipat	(17)	Diisopropyl Adipate
	10.00	Miglyol 812	(11)	Caprylic/Capric Triglyceride
	5.00	Vaseline		Petrolatum White
	2.00	Stearinsäure	(27)	Stearic Acid
	5.00	Uvinul T 150	(1)	Octyl Triazone
B	0.30	Carbopol 934	(6)	Carbomer
	3.00	1,2-Propylenglykol USP	(1)	Propylene Glycol
	4.00	D-Panthenol 50 P	(1)	Panthenol (and) Propylene Glycol
	q.s.	Konservierungsmittel		
	50.30	Wasser dest.		Water
C	0.40	Triethanolamin	(1)	Triethanolamine
D	q.s.	Parfümöl		
	1.00	Vitamin-E-Acetat	(1)	Tocopheryl Acetate

Herstellung

Phase A und B getrennt auf ca. 80°C erwärmen.

Phase B in Phase A unter Homogenisieren einrühren.

Danach Phase C einrühren und kurz nachhomogenisieren.

Abkühlen auf ca. 40°C, Phase D zugeben, nochmals homogenisieren.

Viskosität: ca. 60 000 mPa s

pH - Wert: ca. 7

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Department of Toxicology
D-67056 Ludwigshafen, FRG

cp; 0107

AMENDMENT No. 1

to the Report:

Penetration of **Uvinul T 150** (5 % in a Sunscreen Formulation) through Human Epidermis in vitro.

Project No.: 62V0398/943005

This amendment contains 3 pages

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cp; 0118

AMENDMENT No. 2

to the Report:

Penetration of **Uvinul T 150** (5 % in a Sunscreen Formulation) through Human Epidermis in vitro.

Project No.: 62V0398/943005

This amendment contains 3 pages

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Abteilung Toxikologie
Department of Toxicology

STATEMENT

of the Quality Assurance Unit

Number of test substance:	94/398
Name of test substance:	Uvinul T 150 / 5% Sunscreen Formulation
Title:	Report: Penetration of **Uvinul T 150** (5 % in a Sunscreen Formulation) through Human Epidermis in vitro.

The Quality Assurance Unit audited the amendment dated March 17, 1995 to the report of Feb 27, 1995.

Date of audit: March 17, 1995

Ludwigshafen, March 17, 1995

Dr. med. Dr. rer. nat. R. Rossbacher
(Quality Assurance Unit)

Report, p. 17

Erroneously wrong figures were given for the amount of penetrated Uvinul T 150 at 24 hours post application in the conclusion. The last sentence of page 17 has therefore to be amended (amended figures in bold print):

5. **Conclusion**

Based on the findings of this study it can be calculated that approx. 0.1 % (= approx. **0.72** µg/cm²) of the applied Uvinul T 150 in the high dose level and approx. 1.5 % (= approx. **0.84** µg/cm²) of the low dose has penetrated the epidermis 24 hours after applicaton.

Report, p. 1

Therefore, the Recovery Data in the Summary also have to be amended as follows. Because all data are substantiated by measurement, the brackets are left out in order to avoid misunderstanding (amended parts in bold print):

1. **Summary**

Recovery of Uvinul T 150 in receptor fluid:

after 72 hours:	low dose:	approx. 2.5 % of the applied dose
	high dose:	approx. 0.2 % of the applied dose
after 24 hours:	low dose:	approx. **1.5** % of the applied dose
	high dose:	approx. 0.1 % of the applied dose

C. Pölloth March 17 1995
Study Director: Dr.med. C. Pölloth

STATEMENT

of the Quality Assurance Unit

Number of test substance:	94/398
Name of test substance:	Uvinul T 150 / 5% Sunscreen Formulation
Title:	Report: Penetration of **Uvinul T 150** (5 % in a Sunscreen Formulation) through Human Epidermis in vitro.

The Quality Assurance Unit audited the amendment dated May 03, 1995 to the report of Feb 27, 1995.

Date of audit: May 03, 1995

Ludwigshafen, May 03, 1995 .....J. Hajok.....
J. Hajok
(Quality Assurance Unit)

Further ecological information

Do not discharge product into natural waters without pretreatment (biological treatment plant).

COD-Value: 1 600 mg/g
Theoretical OD value: 2 394 mg/g

13. Disposal considerations

Product: Must be disposed of by special means, e.g. suitable incineration, in accordance with local regulations.

14. Transport information

Not classified as hazardous under transport regulations.

15. Regulatory information

Labelling according to EEC Directives

R53 - May cause long-term adverse effects in the aquatic environment.

S61 - Avoid release to the environment. Refer to special instructions/Safety data sheets.

National legislation/regulations

Water hazard class: WGK (1) (Germany) (BASF self-classification)

16. Other information

A backslash in the left hand margin indicates an amendment from the previous version.

The information contained herein is based on the present state of our knowledge and does not therefore guarantee certain properties. Recipients of our product must take responsibility for observing existing laws and regulations.