

BASF

Abteilung Toxikologie
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ki-db; 2238/P2

MAY 22 1992

REPORT

Study of the Dermal Irritation of

UVINUL T 150

in Guinea Pigs

Application to the intact skin
over 4 weeks

Project No.: 42H0755/90083

VOLUME I OF III

Report section and Tables

Testing facility:

Department of Toxicology of
BASF Aktiengesellschaft
D-W6700 Ludwigshafen/Rhein, FRG

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Report; Project No.: 42H0755/90083

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

Kirsch May 20, 1992
.....
Dr.med.vet. P. Kirsch

Pathology:

Müller May 20, 1992
.....
for Dr.med.vet. Chr. Gemhardt

Head of
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Hildebrand 21.5.92
.....
Dr.med.vet. B. Hildebrand

Report; Project No.: 42H0755/90083

GLP STATEMENT

Title: Report: Study of the Dermal Irritation of
Uvinul T 150 in Guinea Pigs.
Application to the intact skin over 4 weeks.

This study was conducted in accordance with "OECD Principles of Good Laboratory Practice" (Paris, 1981).

H. Albrecht
..... 21.5.92
(Head of Experimental Toxicology)

Kissel May 20, 1992
.....
(Study Director)

Report; Project No.: 42H0755/90083

**STATEMENT
OF THE QUALITY ASSURANCE UNIT**

Number of test substance: 90/755

Name of test substance: Uvinul T 150

Title: Report: Study of the Dermal Irritation
of Uvinul T 150 in Guinea Pigs.
Application to the intact skin over
4 weeks.

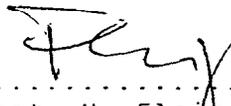
The Quality Assurance Unit inspected the study, audited the final report, and reported findings to the Study Director and to Management.

Phase of study/ inspection	Date of inspec- tion	Report to Study Di- rector and to Manage- ment
Protocol:	May 21, 1991	June 20, 1991
Conduct of study:	June 19, 1991 June 26, 1991	June 20, 1991 June 27, 1991
Audit of the report:	May 8, 1992	May 8, 1992

Remarks: Analytics was inspected independently by the Quality Assurance Unit of the analytical laboratory.

Ludwigshafen,

May 22, 1992


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

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1. **SUMMARY**

Uvinul T 150 was applied daily to the intact clipped left flank of 10 Pirbright White guinea pigs (5 male / 5 females) over a period of 4 weeks.

A concentration of 50% in polyethylenglycol DAB (Lutrol®) was chosen for the applications.

For comparison the solvent polyethylenglycol DAB (Lutrol®) was applied simultaneously to the right flank of each animal.

The applications were carried out at approximately the same time each day on the same skin area.

The test and control sites remained non-occluded. Skin findings were recorded daily immediately before each substance application as well as about 24 hours after the last application.

Photographs have been taken of the test material application sites immediately prior to treatment on days 0, 7, 14, 21 as well as about 24 hours after the last application (day 28).

The animals were carefully inspected immediately before each daily application and about 24 hours after the last application.

Body weight was determined weekly.

All animals were assessed by gross pathology examination.

Results:

Skin findings:	No signs of irritation could be observed at the application sites treated with test substance preparation or the solvent
Clinical signs:	All animals showed no abnormalities which could be related to the test substance application
Body weight:	The expected body weight gain has been observed in the course of the study
Mortality:	There were no deaths during the study period
Necropsy:	No gross lesions were noted in any of the animals during necropsy

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Conclusion:

Based on the results obtained during this dermal irritation study no irritating potential of Uvinul T 150 could be observed after 28 day repeated application to the intact skin of the guinea pig.

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2. **INTRODUCTION AND CHOICE OF CONCENTRATION**

The objective of the study was to determine a possible skin irritating potential of Uvinul T 150 after 28 day repeated application to the intact skin of the guinea pig.

Uvinul T 150 is used in commercial formulations in concentrations of maximal 10%.

Therefore a 50% suspension in polyethylenglycol DAB (Lutrol®)* was chosen for the applications in this test.

The study was carried out from May 29, 1991 to June 26, 1991 (beginning of application until necropsy).

* Lutrol® E 400 = polyethylenglycol DAB, BASF AG

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3. MATERIAL AND METHODS

3.1. TEST SUBSTANCE

ZST-Substance-No.: 90/755

Name of test substance: Uvinul T 150

Batch-No.: 18586/177, Batch 4,
Abt.-No. 19-0518

Date of manufacturing: September 20, 1990

Degree of purity: > 99%

Physical state/
appearance: Powder, slight yellow

Storage conditions: room temperature

Detailed information on the characterization of the test substance is included in the raw data.

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3.2. TEST ANIMALS

Male and female guinea pigs, Pirbright White, Dunkin Hartley HOE DHPK [SPF-LAC] Bö, supplied by Lippische Versuchstierzucht Hagemann GmbH & Co., KG, D-W4923 Extertal 1, FRG, which were free from any signs of disease, were used for the investigations.

Reasons for the selection:

The guinea pig is a frequently used animal for experiments on dermal irritation. Comprehensive experience with this animal species and strain is available. Moreover the guinea pig is recommended by OECD.

The guinea pigs were identified clearly by ear tag numbering.

3.3. HOUSING AND DIET

During the study period, the guinea pigs were housed singly in Makrolon cages type IV with bedding Granulat Typ 3/4 (staubfrei) supplied bei SSNIFF.

The cages with the test animals were placed on the racks in such a manner that uniform test conditions (supply air/waste air/light) were guaranteed.

The animals were housed in completely air-conditioned rooms in which central air conditioning ensured temperatures in the range 20 - 24°C and relative humidities in the range 30 - 70%.

The day/night rhythm was 12 hours (12 hours light from 6.00 a.m. - 6.00 p.m. and 12 hours dark from 6.00 p.m. - 6.00 a.m.).

There were no deviations from these ranges.

The animal room was completely disinfected using a disinfectant ("AUTEX" fully automatic, formalin-ammonia-based terminal disinfectant) before the start of the study. The floor and walls were cleaned three times a week with water containing about 2% Zephirol (supplied by Bayer AG).

The food received by the animals was standard Kliba maintenance diet for laboratory rabbits-guinea pigs, GLP 341 pellets, supplied by Klingentalmühle AG, CH-4303 Kaiser-augst, Switzerland; which was available ad libitum, as was drinking water. About 2 g of ascorbic acid per 10 l water was added twice a week.

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3.4. TEST GROUP AND CONCENTRATION

One test group with 5 males (animal No. 1 - 5) and 5 females (animal No. 6 - 10) was treated with test substance 50% in polyethylenglycol DAB (Lutrol®) and simultaneously with the vehicle polyethylenglycol DAB (Lutrol®).

3.5. ANALYSES

The analyses were carried out in the analytical laboratories of BASF Aktiengesellschaft (Dr. Thiele responsible).

3.5.1. Analyses of the test substance

The characterization of the test substance concerning degree of purity has been carried out prior to the start of the study. On completion of all tests the stability of the test substance will be verified by a repeated analysis. The result can be obtained from the sponsor (BASF AG).

To all appearances the test substance is a homogeneous slight yellow powder.

3.5.2. Analyses and preparation of test substance preparation

The stability of the test substance in polyethylenglycol DAB (Lutrol®) was verified over 24 hours by analysis. The test substance preparation was made up each workday immediately before application. For this purpose, the test substance and the carrier was weighed and subsequently mixed using an Ultraturrax. The suspension was kept homogeneously during the applications by means of a magnetic stirrer.

To verify the correctness of the concentration resp. the homogeneity of the test substance preparation, samples were sent to the analytical laboratory at the beginning of the study.

Detailed data may be found in the Supplement: Analyses of the test substance in the carrier.

3.5.3. Methods

A description of the methods is to be found in VOLUME III (Supplement) and with the raw data.

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3.5.4. Food analyses

The food used in the study was assayed for chemical and microbiological contaminants.

3.5.5. Drinking water analyses

The drinking water is regularly assayed for chemical contaminants by the municipal authorities of Frankenthal and the Technical Services of BASF Aktiengesellschaft as well as for the presence of germs by a contract laboratory.

3.5.6. Bedding analyses

The bedding is regularly assayed for contaminants (chlorinated hydrocarbons, heavy metals).

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3.6. EXPERIMENTAL PROCEDURE

The animals were supplied on May 22, 1991, and on the same day an 7-day adaptation period began, in which each animal was supplied with pelleted food and water ad libitum (about 2 g ascorbic acid per 10 l water was added twice a week).

The acclimatization period was followed by the daily application of 0.05 ml polyethylenglycol DAB (Lutrol®) (solvent control) on a marked skin area (2 cm x 2 cm; right flank) or of 0.05 ml Uvinul T 150 which was applied as a 50% suspension in polyethylenglycol DAB (Lutrol®) on a marked skin area (2 cm x 2 cm; left flank). The test and control sites remained non-occluded. The applications have been carried out once daily at approximately the same time each day on the same skin area for twenty-eight consecutive days.

After the 12, 16, 20 and 25th application, rests of test substance were removed immediately before repeated application with polyethylenglycol DAB (Lutrol®) in all animals.

The guinea pigs were clipped at least three times a week immediately before application. Only the first clipping was carried out at least 15 hours before the first application on the right and left flank.

The mean weight at the beginning of test substance application was

- 278 (260 - 297) g for males
- 281 (274 - 287) g for females.

The age of the animals at the beginning of test substance application was approximately

- 31 - 35 days for males
- 28 - 35 days for females

At the end of the 4-week application period, all animals were sacrificed after a fasting period (withdrawal of food of at least 16 hours).

The animals were anesthetized with CO₂ and killed by decapitation and bleeding.

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3.7. CLINICAL EXAMINATIONS

3.7.1. Skin findings, clinical signs and mortality

A check for any skin findings and a carefully inspection was carried out daily immediately before each substance application as well as about 24 hours after the last application.

A check for general observations and for dead or moribund animals was made twice a day (Monday to Friday) at the beginning and at the end of work and once on Saturdays, Sundays and on public holidays.

3.7.2. Body weight data

All animals were weighed once every week. The body weights were determined each time on the same day of week (exception: last weighing).

3.7.3. Photographs

In all animals photographs of the test material application sites have been taken prior to treatment on days 0, 7, 14, 21 and about 24 hours after the last application (day 28).

3.7.4. Irritation Indices

Daily Irritation Indices were calculated for each test and control material by adding together the scores for erythema and edema and dividing by the number of animals treated. Weekly Mean Irritation Indices were calculated from the seven Daily Indices of each week of treatment.

The maximum Weekly Mean Irritation Index used to arbitrarily classify the test and control materials according to the following table:

Maximum	Classification
0	Non-Irritant
> 0 < 0.5	Practically Non-Irritant
> 0.5 < 2.0	Slightly Irritant
> 2.0 < 5	Irritant
> 5 < 8	Very Irritant

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3.8. PATHOLOGY

For the description of methods, see VOLUME II (PATHOLOGY REPORT).

3.9. RETENTION OF RECORDS

The study protocol, the raw data, the reserve sample and the specimens, as well as the original of this report, will be stored at BASF Aktiengesellschaft for at least the period of time specified in the GLP regulations. The specimens will be retained for only as long as the quality of the material allows evaluation.

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4. RESULTS AND ASSESSMENT OF FINDINGS

4.1. ANALYSES

4.1.1. Analyses of the test substance

The analysis regarding the characterization of the test substance was carried out prior to the start of the study.

The degree of purity of the test substance was > 99%.

To all appearances the test substance is a homogeneous slight yellow powder.

On completion of all investigations, the stability of the test substance will be verified by a repeated analysis. The result can be obtained from the sponsor (BASF AG).

Details can be found in the raw data.

4.1.2. Analyses of test substance preparation

The stability of the test substance in polyethylenglycol DAB (Lutrol®) over a period of 24 hours was verified by analysis.

A concentration control analysis was performed. The concentrations found corresponds to about 98 - 100% of the expected ones.

The concentrations of the test substance in the samples analysed (3 samples) do not differ significantly indicating homogeneous distribution within the preparations.

Individual results are included in Volume III (Supplement): Analyses of the test substance in the carrier.

4.1.3. Food analyses

In view of the aim and duration of the study, the contaminants occurring in commercial food might not influence the results.

More details can be found in the archives of the Department of Toxicology.

4.1.4. Drinking water analyses

In view of the aim and duration of the study there are no special requirements exceeding the specification of drinking water.

More details can be found in the archives of the Department of Toxicology.

4.1.5. Bedding analyses

In view of the aim and duration of the study there are no special requirements exceeding the specification of a commercial grade monitored by the manufacturer.

More details can be found in the archives of the Department of Toxicology.

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4.2. CLINICAL EXAMINATIONS

The results of the study are to be found in the following Tables in the Annex:

	Table
Local skin findings	
- male animals	1 - 4
- female animals	5 - 8
Photographs	9 - 58
Body weight	
- male and female animals	59

Key to the abbreviations used in the tables resp. on the photographs

E = erythema RE. FL. = right flank NR. = animal number
 ED = edema LI. FL. = left flank

Assessment of skin findings
 (according to Draize, J.H. (1959): Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics. The Association of Food and Drug Officials of the United States Austin, Texas):

1. Erythema and eschar formation
 - a) No erythema = 0
 - b) Very slight erythema (barely perceptible)..... = 1
 - c) Well-defined erythema = 2
 - d) Moderate to severe erythema = 3
 - e) Severe erythema (beet redness) to slight eschar formation (injuries in depth) = 4

2. Edema formation
 - a) No edema = 0
 - b) Very slight edema (barely perceptible) = 1
 - c) Slight edema (edges of area well defined by definite raising) = 2
 - d) Moderate edema (raised approximately 1 mm) = 3
 - e) Severe edema (raised more than 1 mm and extending beyond the area of exposure) = 4

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4.2.1. Local skin findings
(Tables 1 - 8, Photographs Tables 9- 58)

No signs of irritation on the treated skin sites could be observed in both sexes. On account of these findings the calculation of the Irritation Indices have not been taken over in the report.

4.2.2. Clinical signs

No clinical signs of toxicity were observed in both sexes.

4.2.3. Body weight data
(Table 59)

During the entire treatment period the body weight gain did not appear to be affected by the test article treatment.

4.2.4. Mortality

There were no deaths during the study period.

4.3. PATHOLOGY

All pathology data are to be found in VOLUME II (PATHOLOGY REPORT).

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5. *DISCUSSION AND CONCLUSION*

In conclusion, it may be stated that the daily application of Uvinul T 150 to the clipped intact flank of the guinea pig over 4 weeks in a concentration of 50% in polyethylglycol DAB (Lutrol®) did not lead to any substance-induced findings.

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ANNEX:

Tables

Clinical Examinations

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TABLE: 9

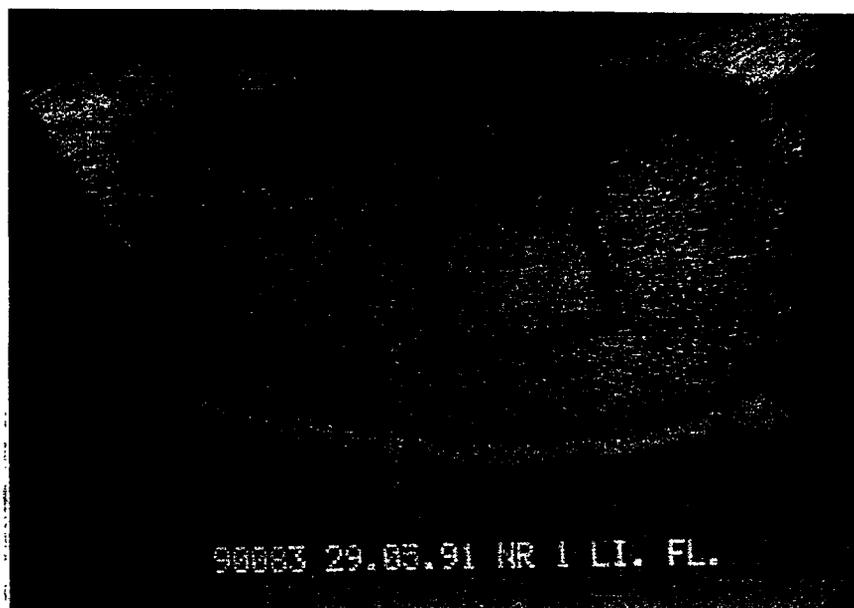
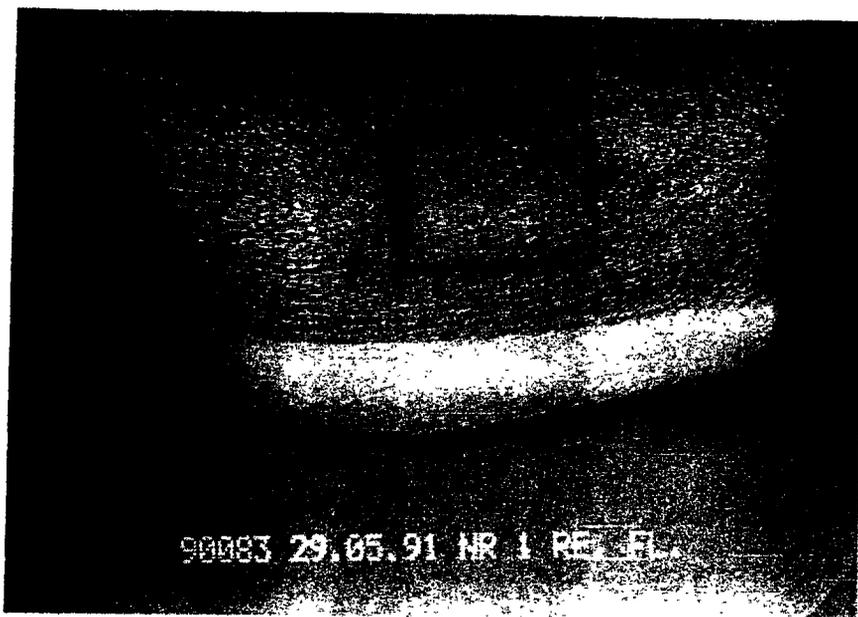
PHOTOGRAPHS

Animal No.: 1

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 10

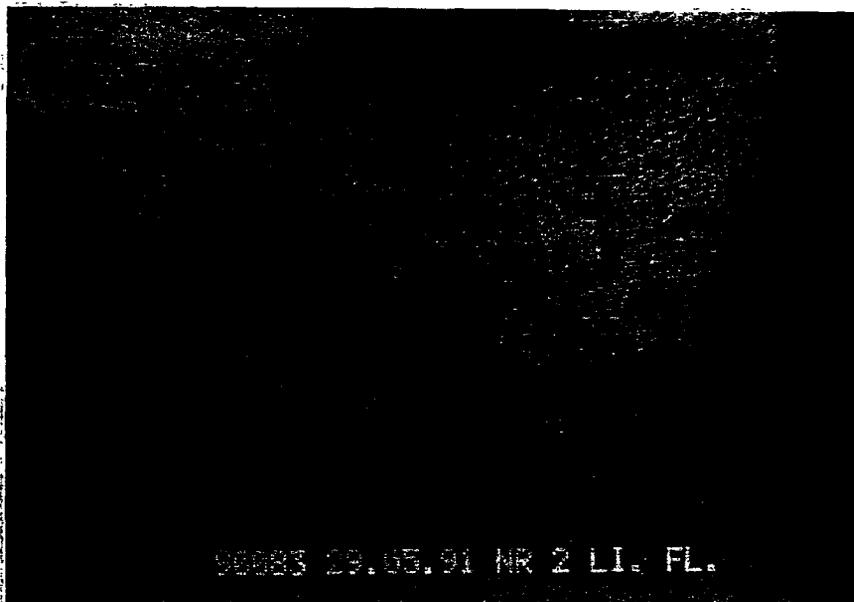
PHOTOGRAPHS

Animal No.: 2

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 11

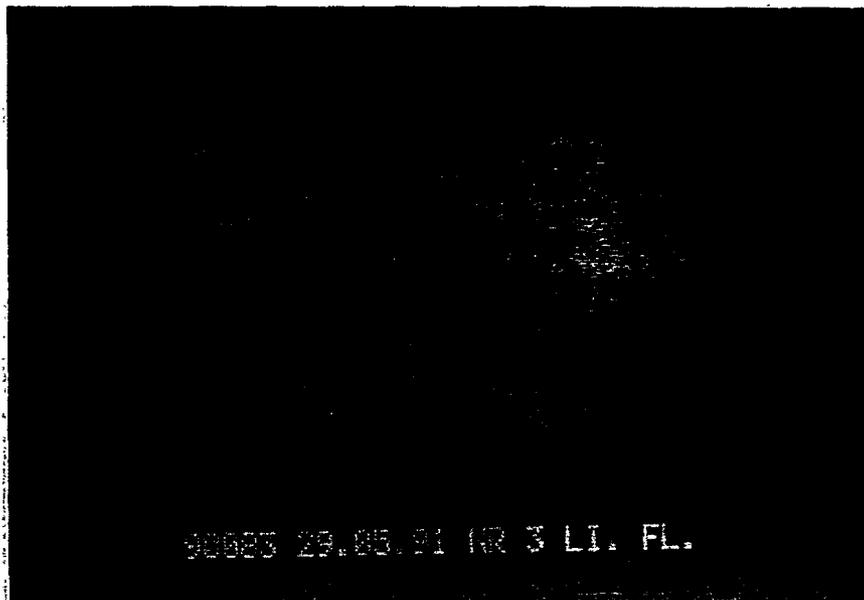
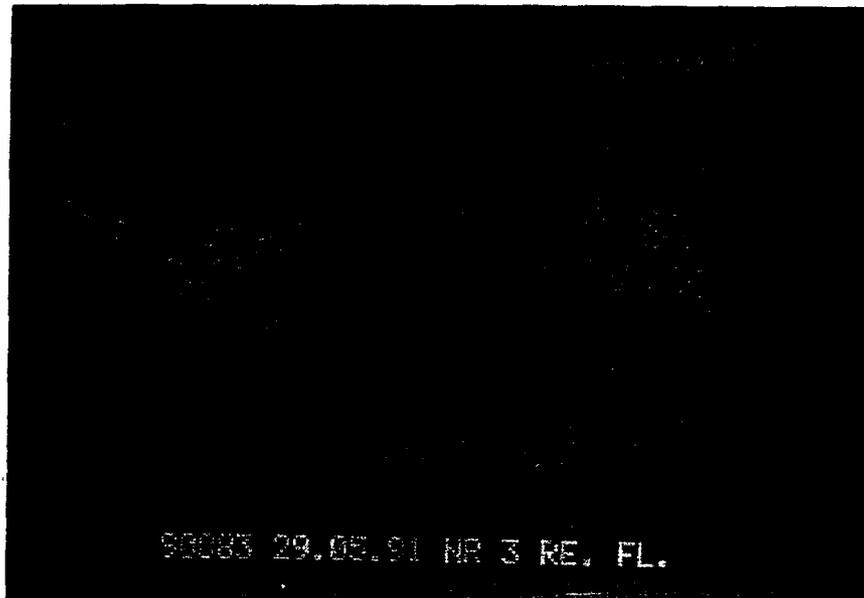
PHOTOGRAPHS

Animal No.: 3

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 12

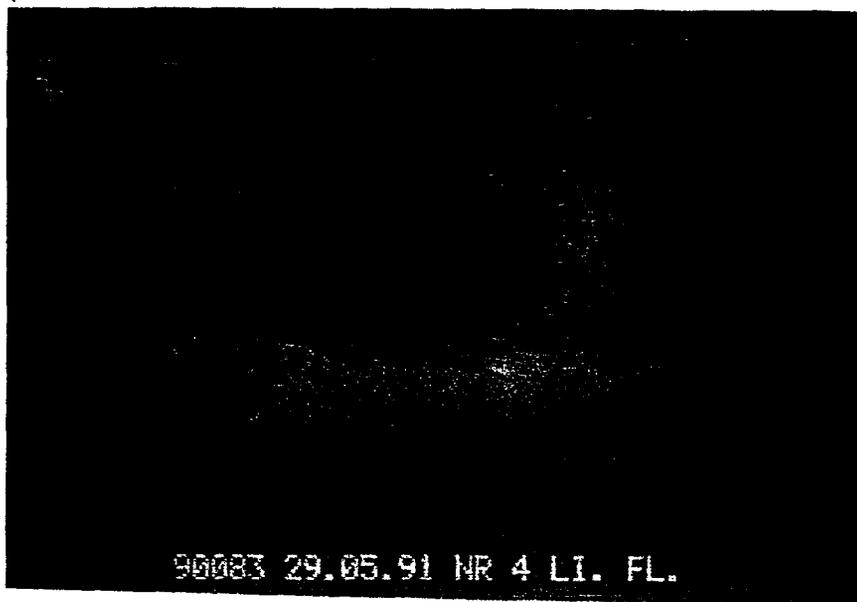
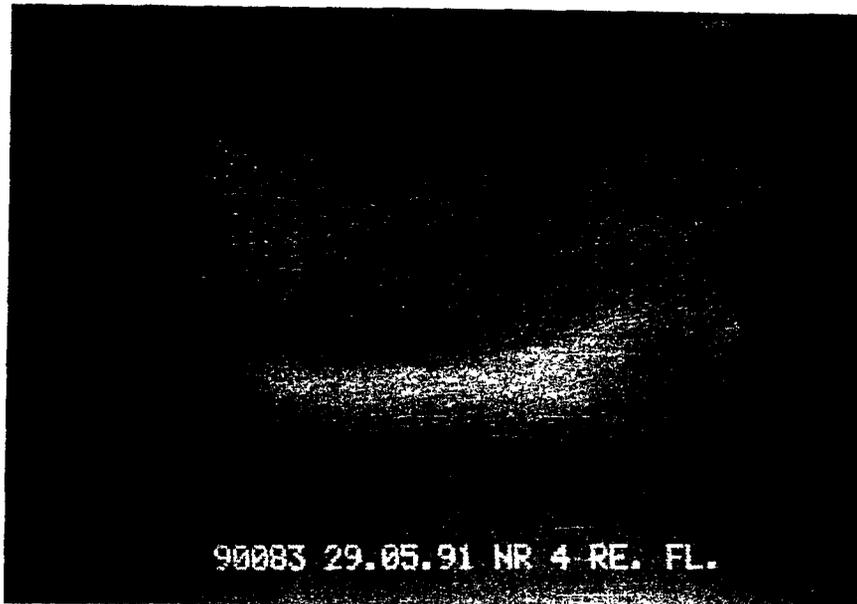
PHOTOGRAPHS

Animal No.: 4

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 13

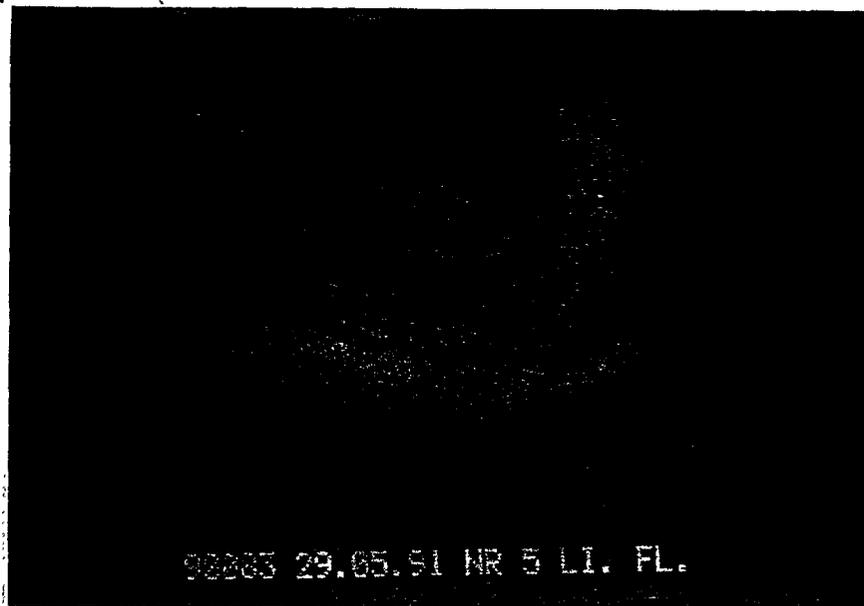
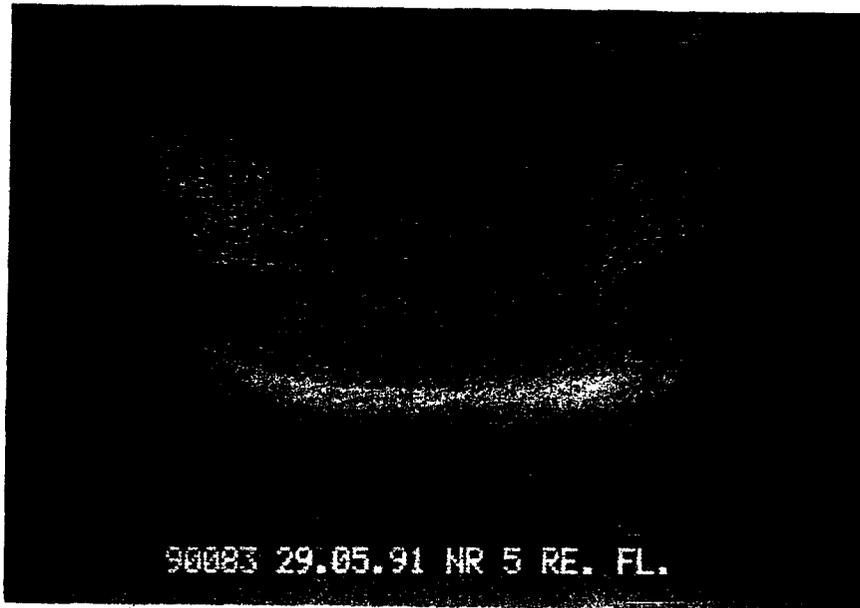
PHOTOGRAPHS

Animal No.: 5

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 14

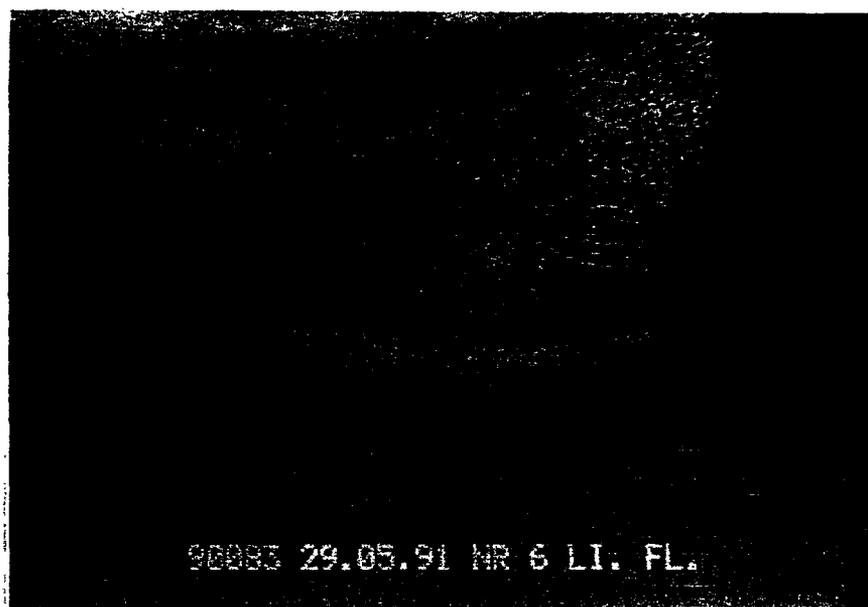
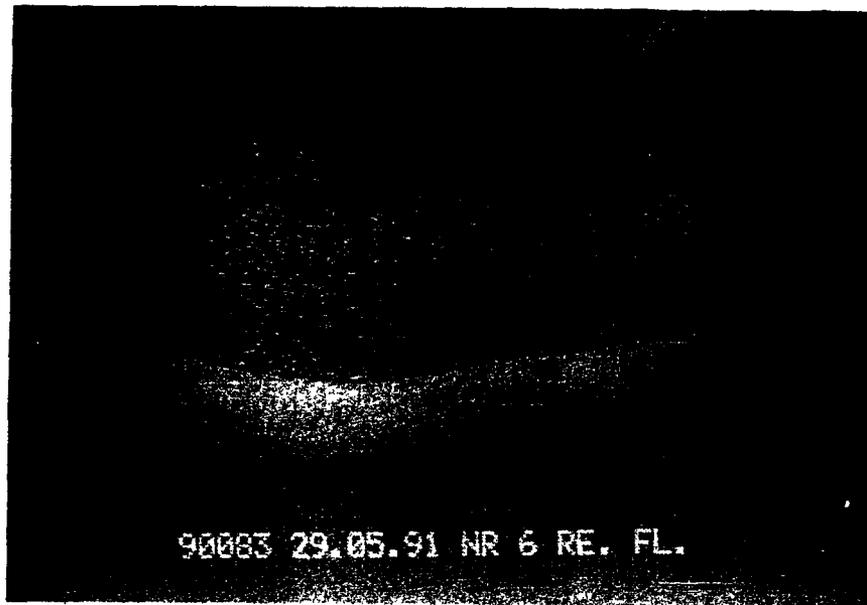
PHOTOGRAPHS

Animal No.: 6

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 15

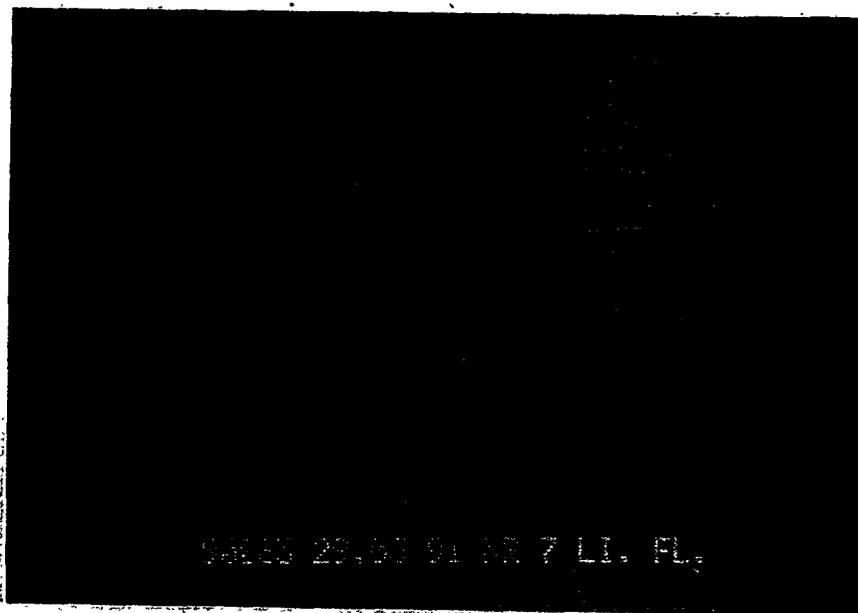
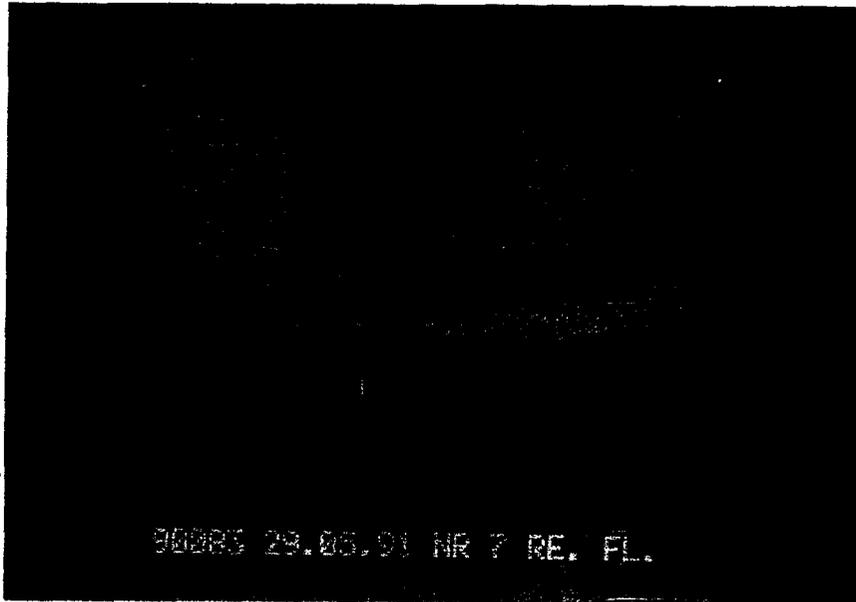
PHOTOGRAPHS

Animal No.: 7

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 16

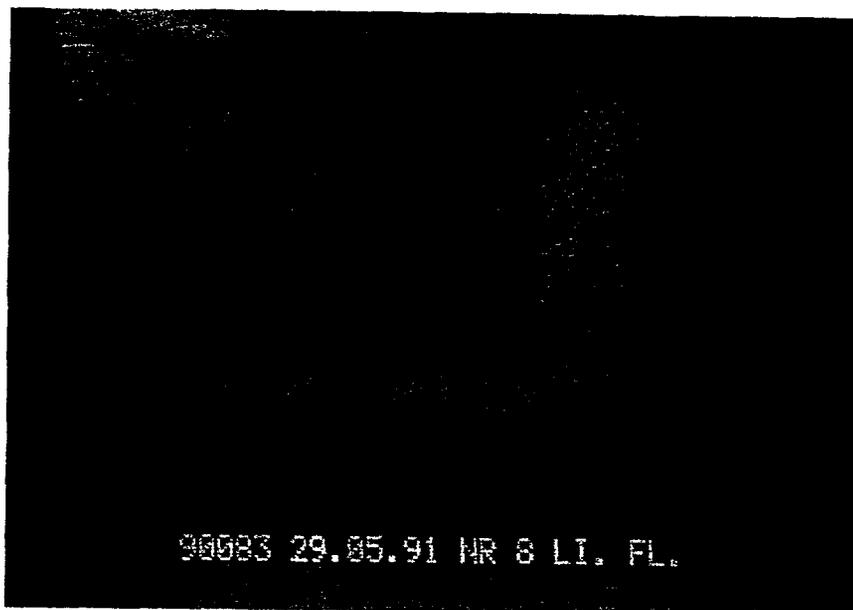
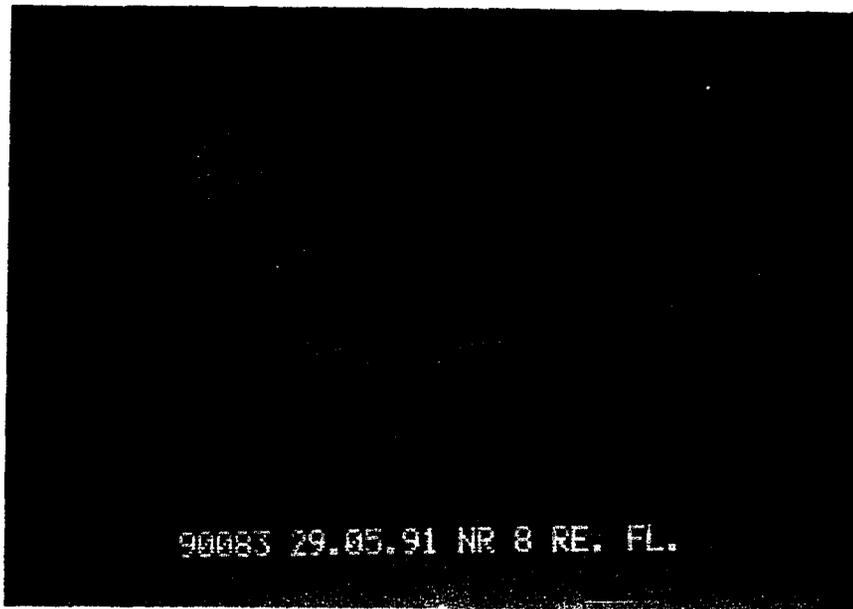
PHOTOGRAPHS

Animal No.: 8

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 17

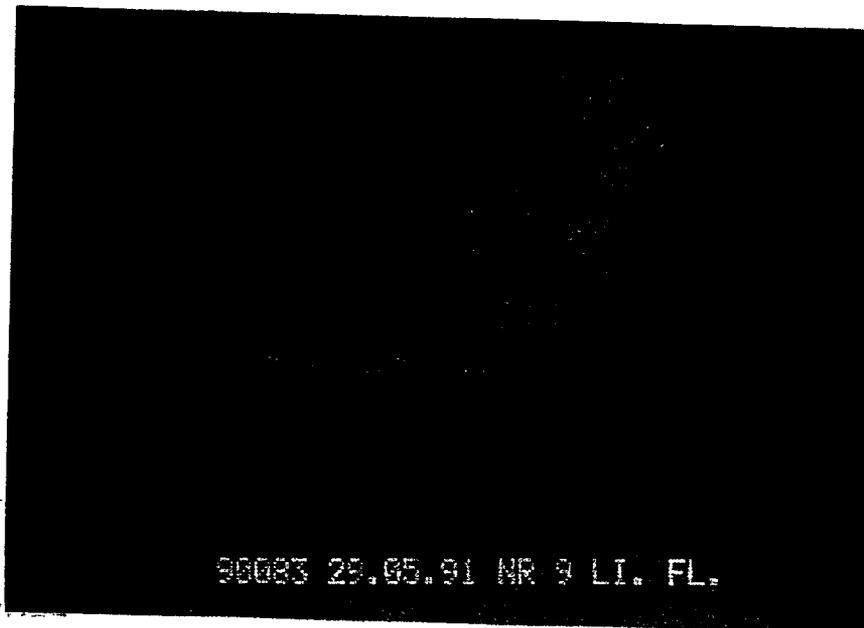
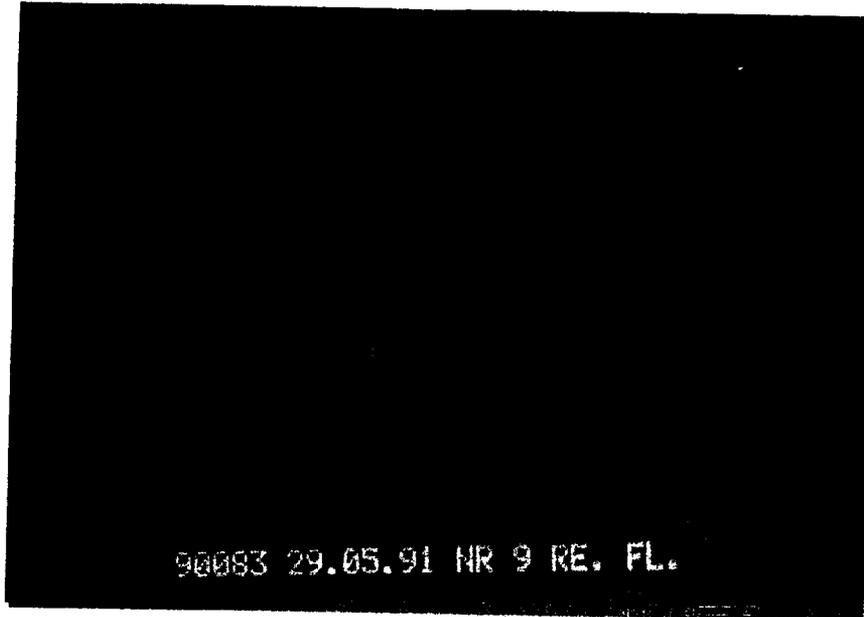
PHOTOGRAPHS

Animal No.: 9

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 18

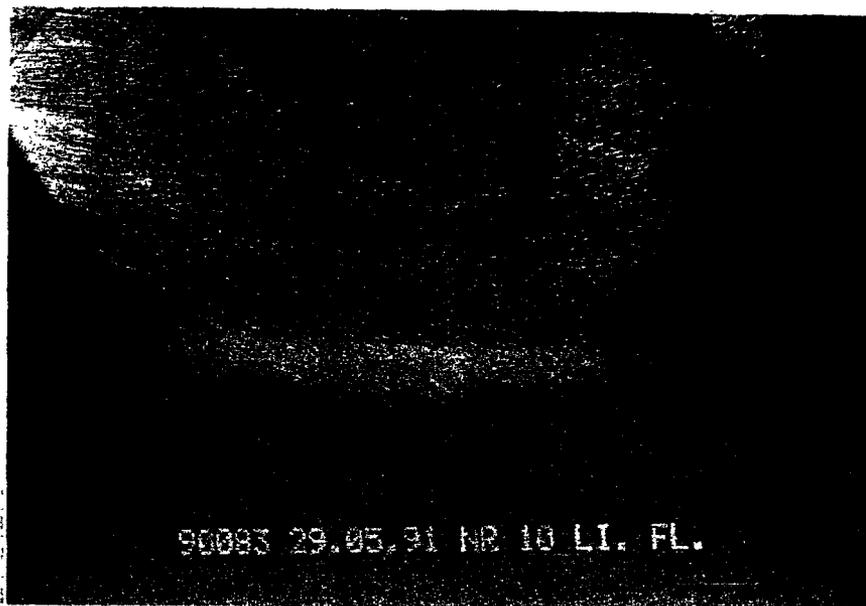
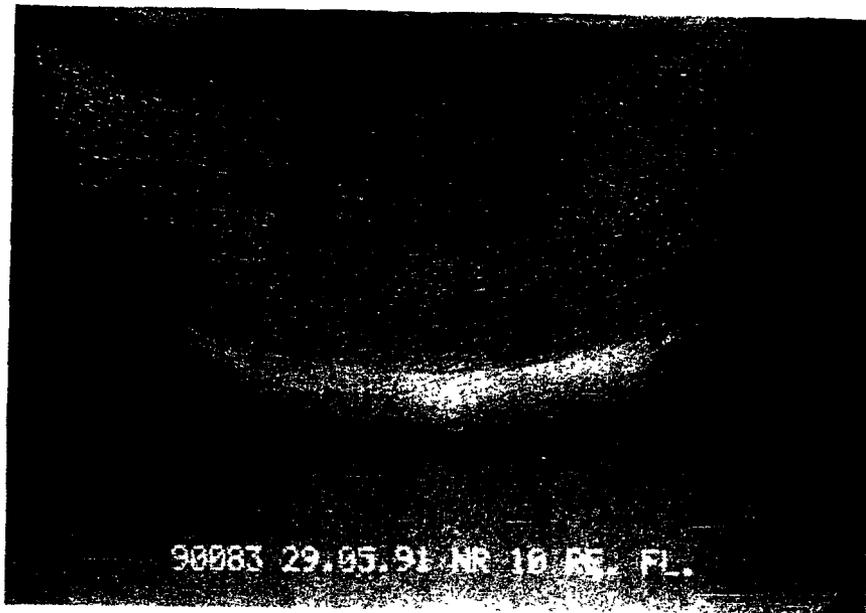
PHOTOGRAPHS

Animal No.: 10

right and left flank

Date: May 29, 1991

(day 0)



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TABLE: 19

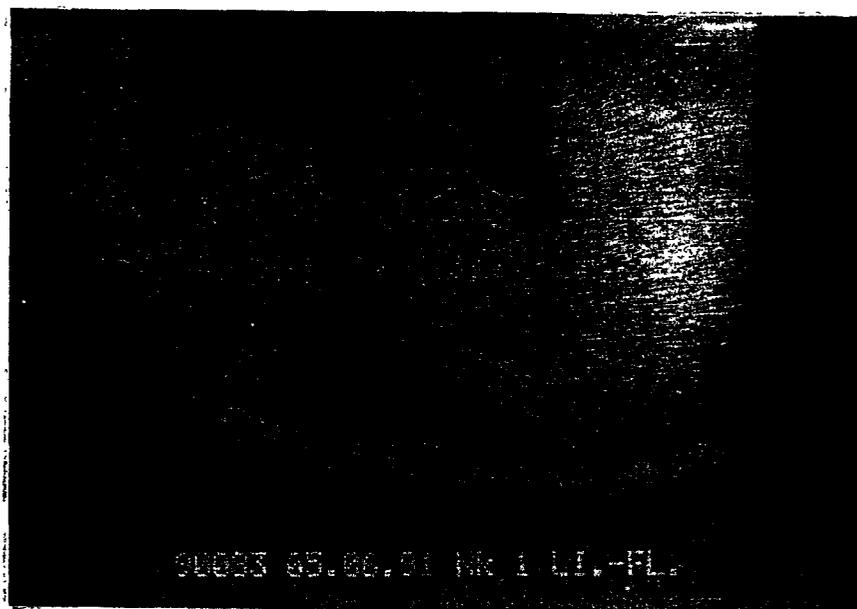
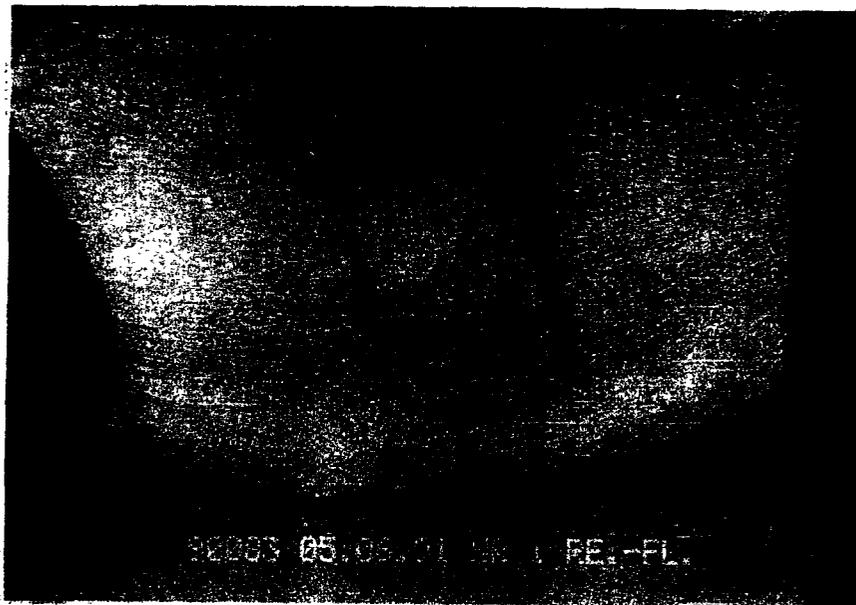
PHOTOGRAPHS

Animal No.: 1

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 20

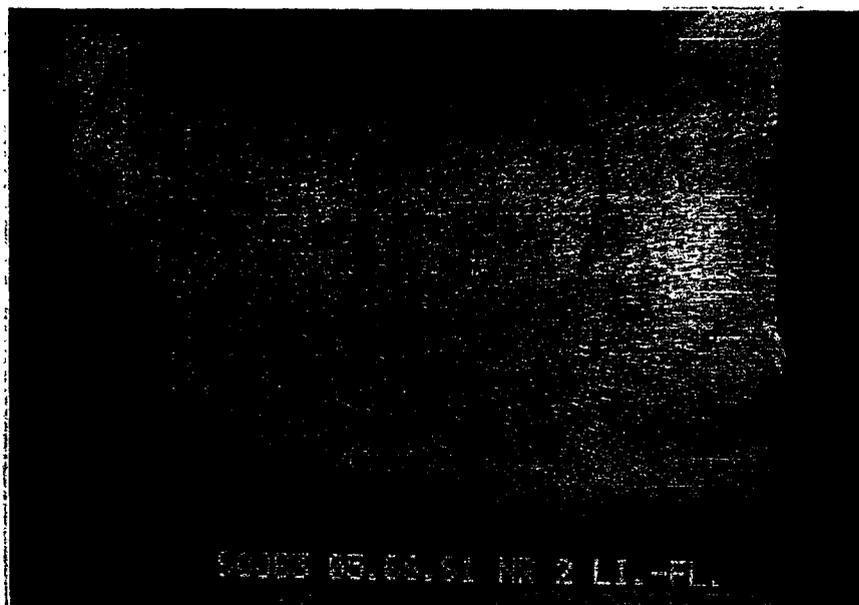
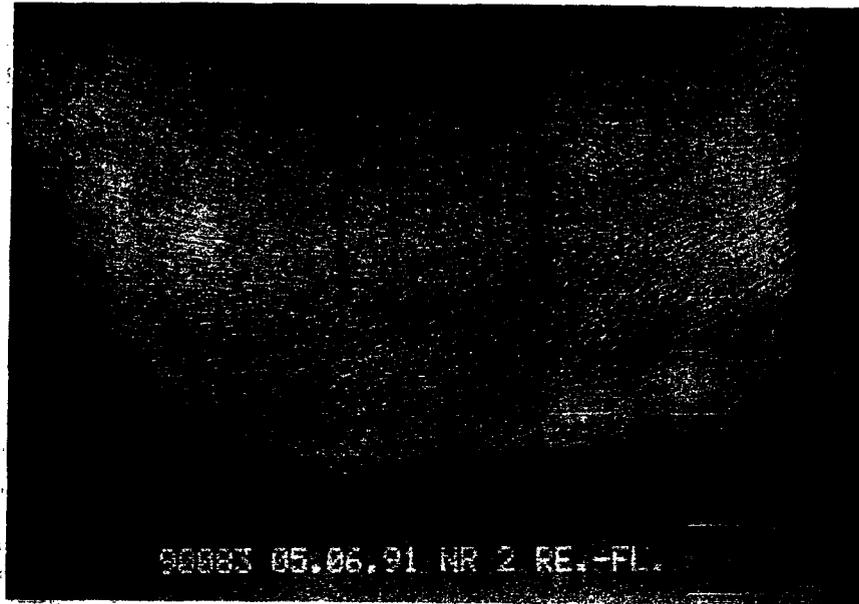
PHOTOGRAPHS

Animal No.: 2

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 21

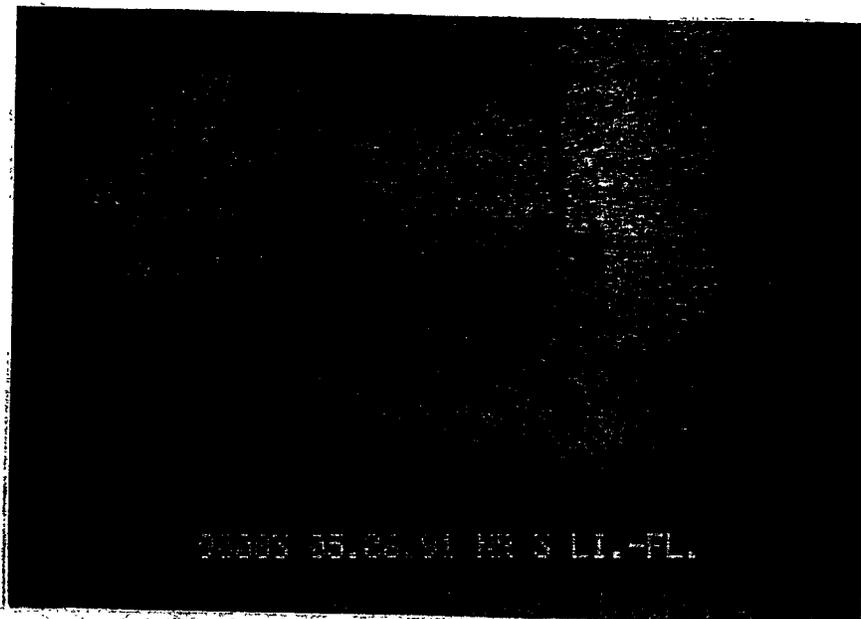
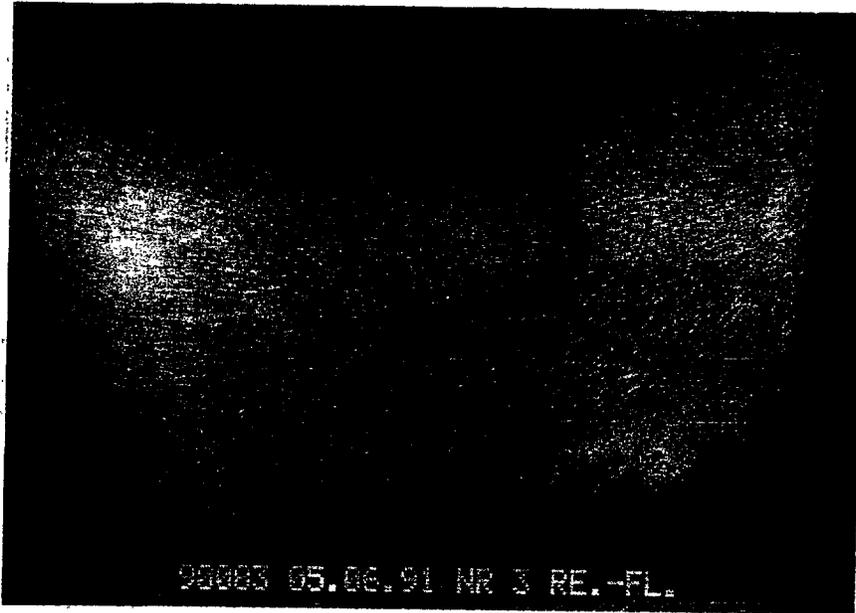
PHOTOGRAPHS

Animal No.: 3

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 22

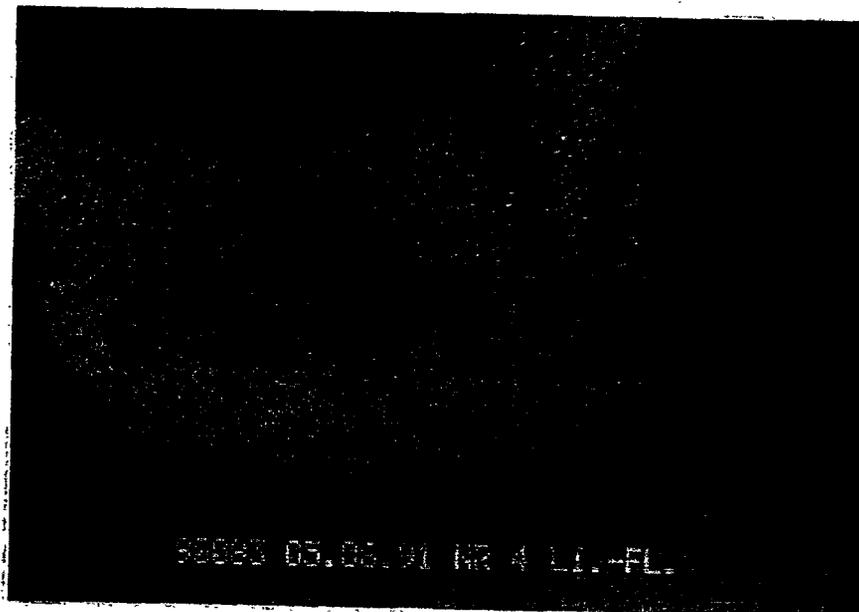
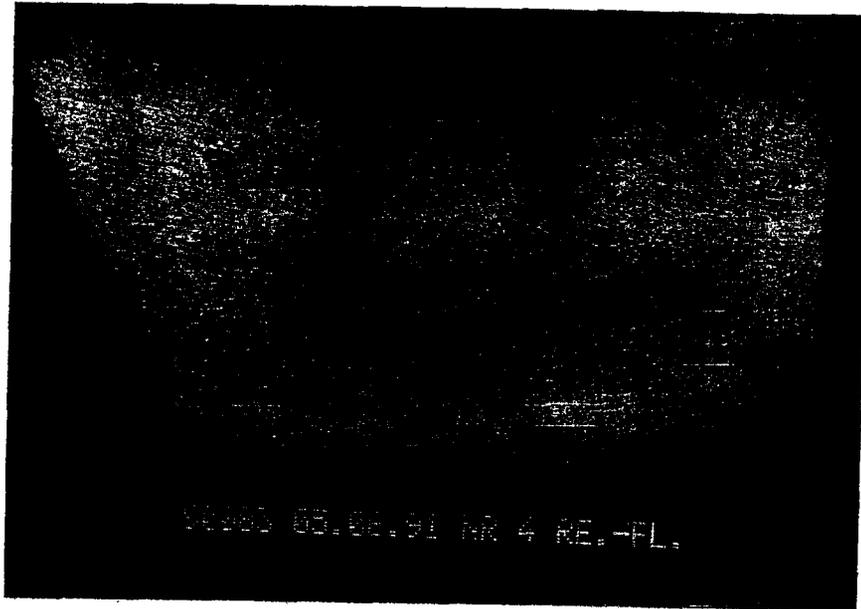
PHOTOGRAPHS

Animal No.: 4

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 23

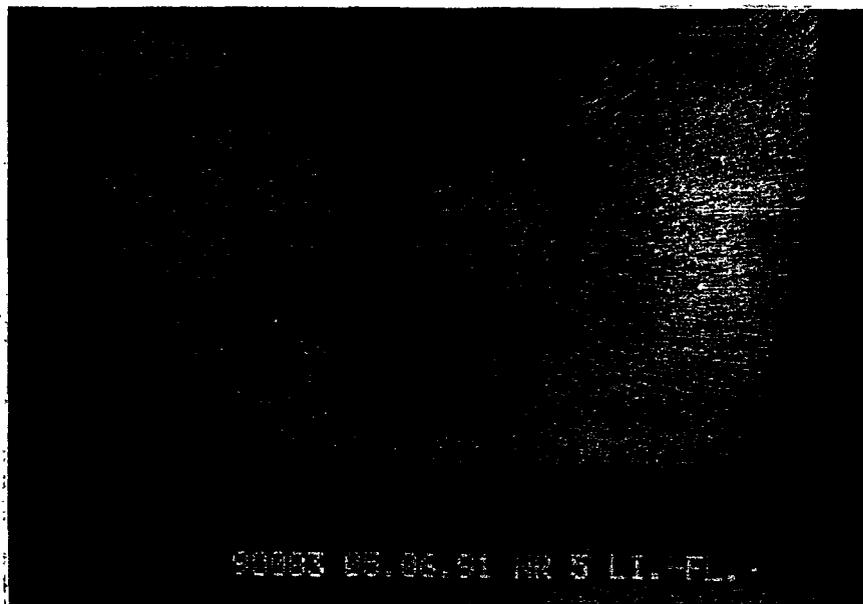
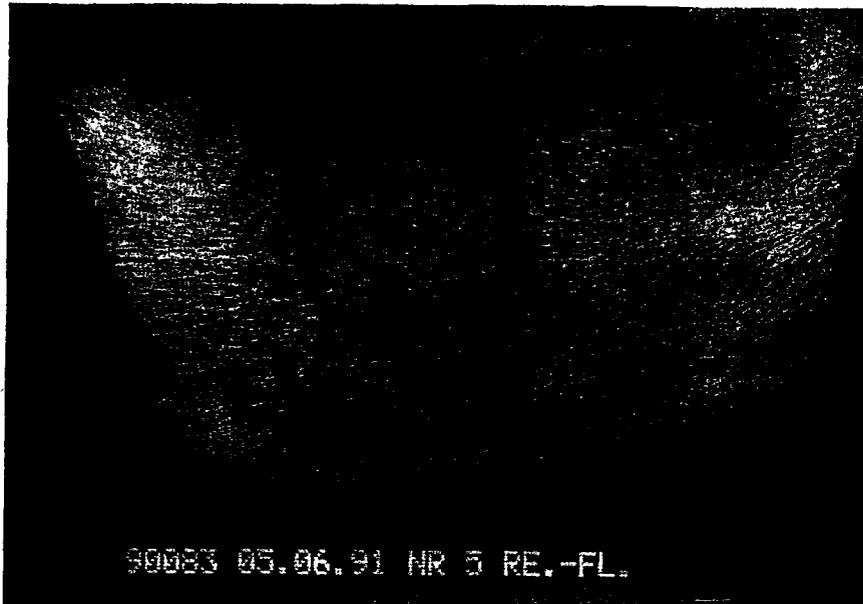
PHOTOGRAPHS

Animal No.: 5

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 24

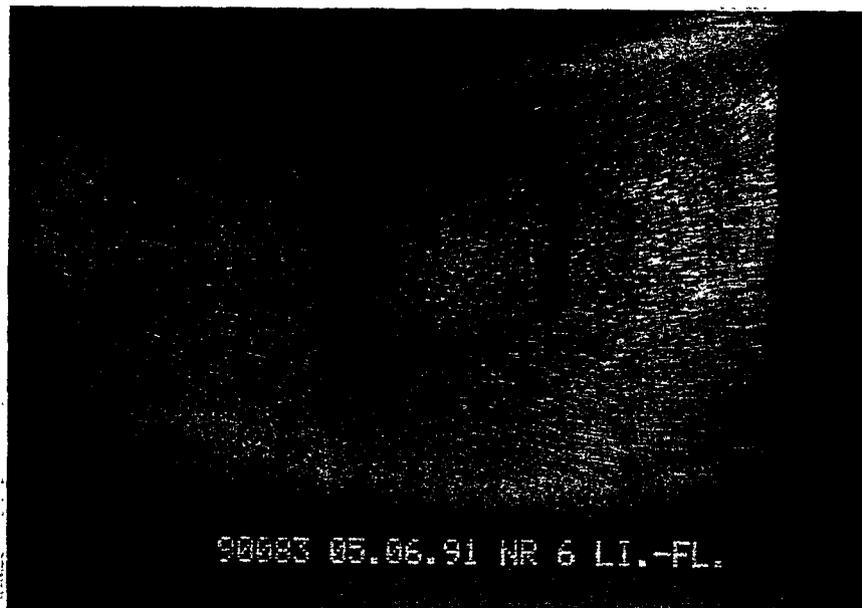
PHOTOGRAPHS

Animal No.: 6

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 25

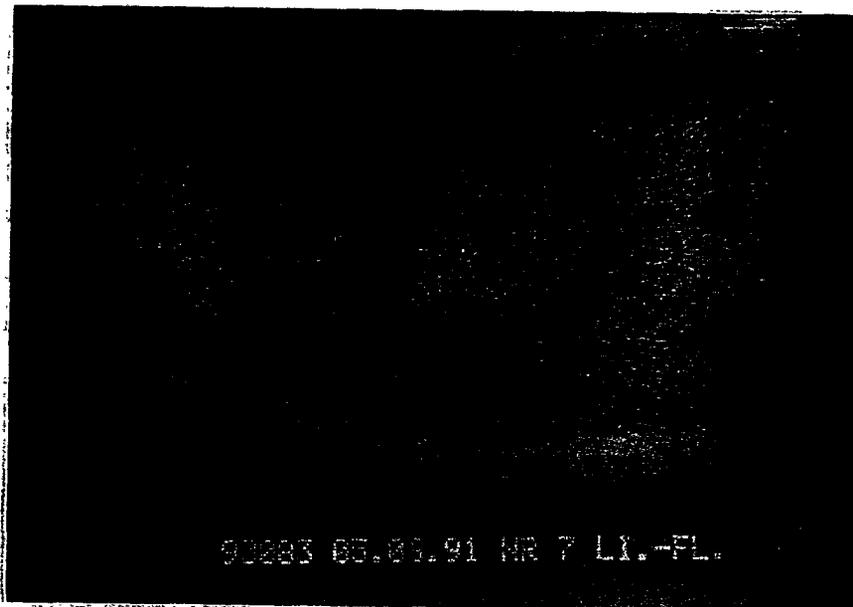
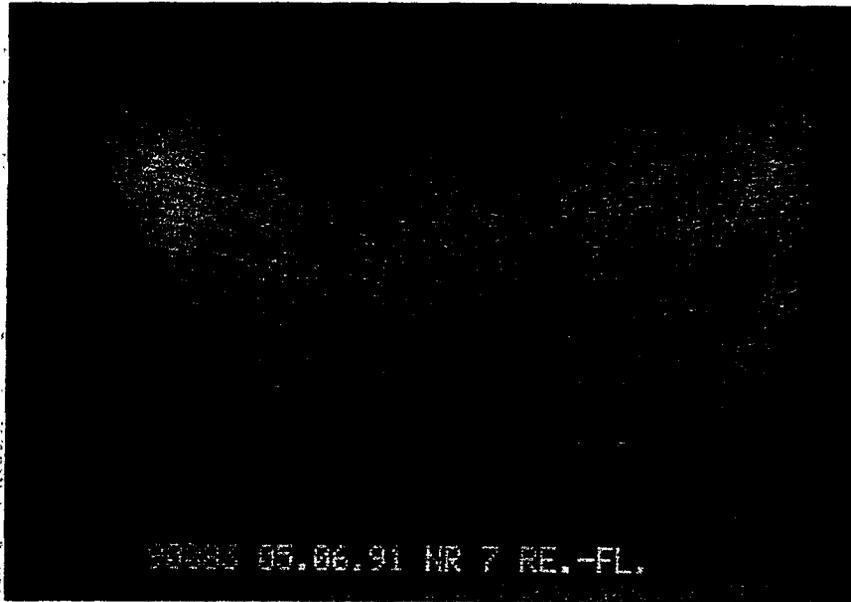
PHOTOGRAPHS

Animal No.: 7

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 26

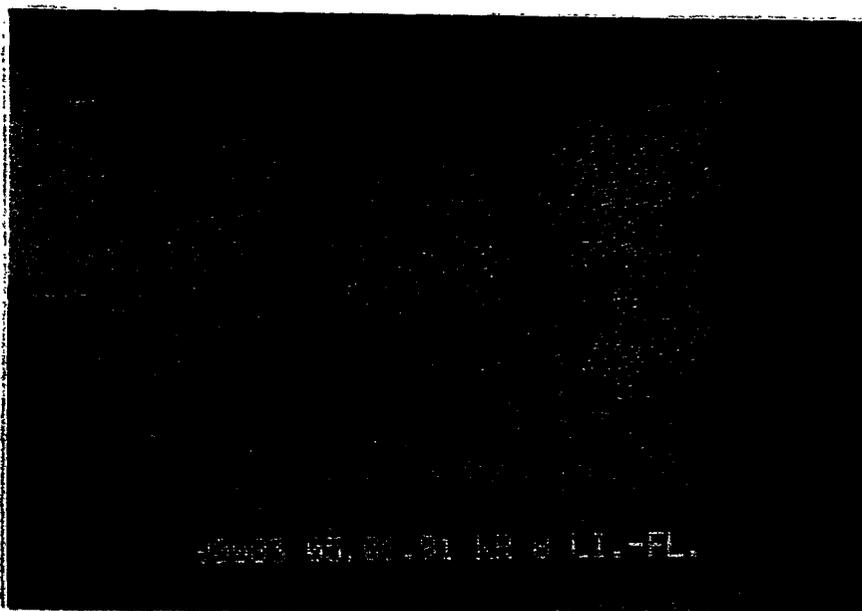
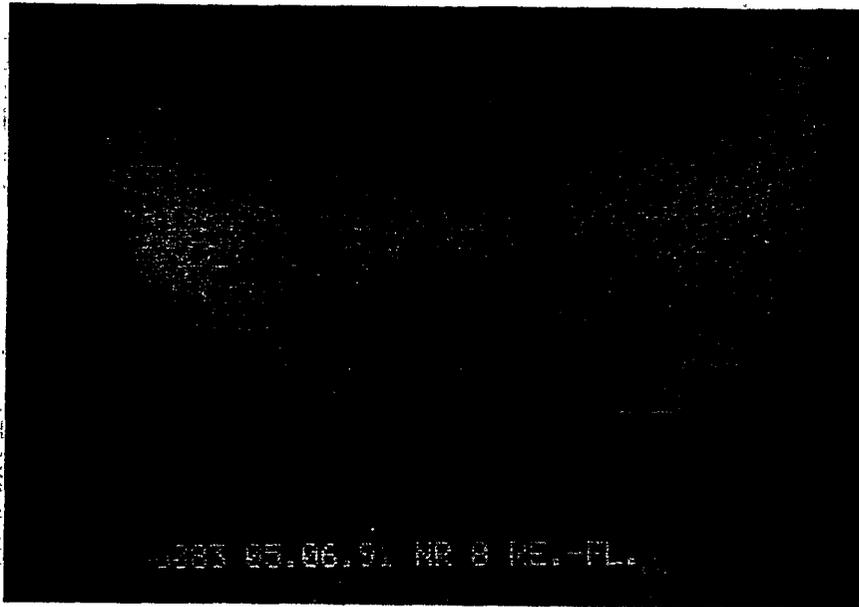
PHOTOGRAPHS

Animal No.: 8

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 27

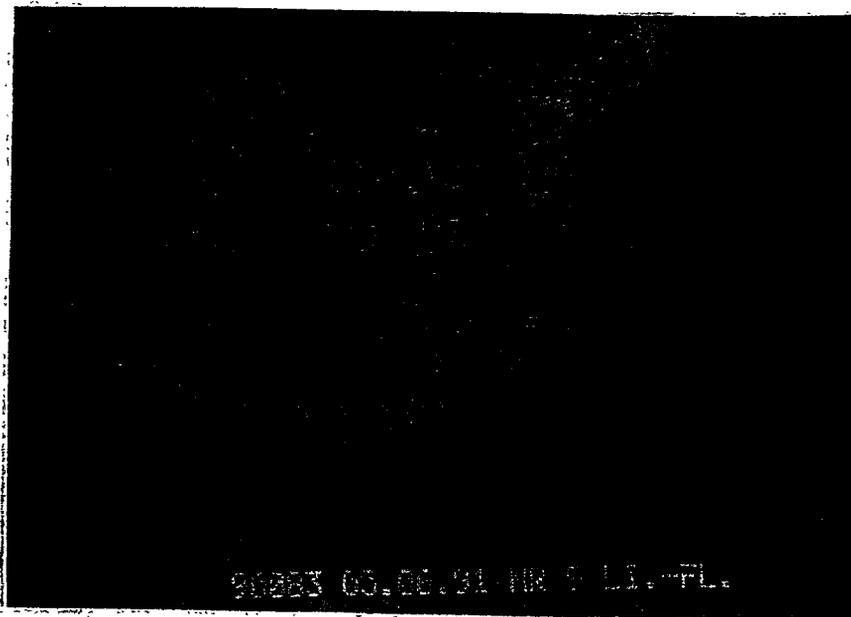
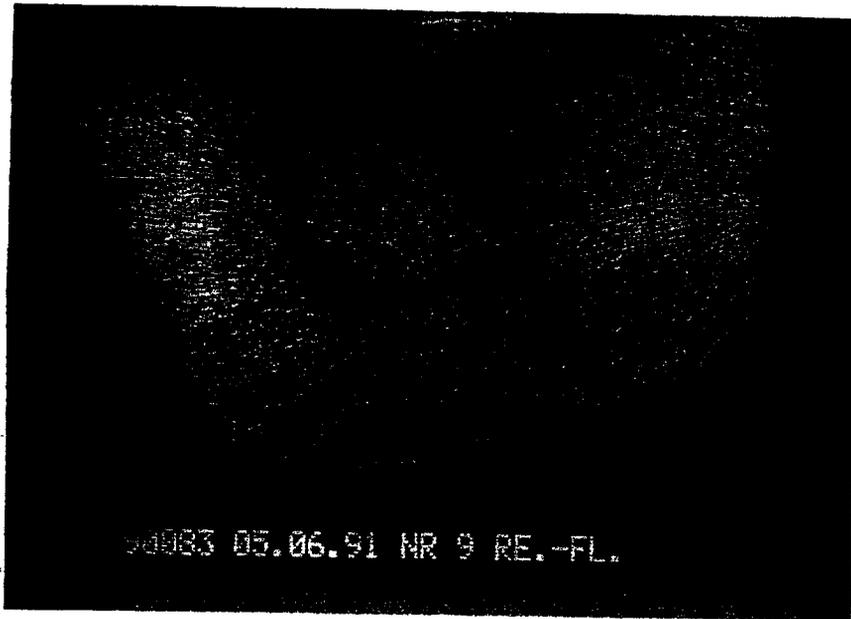
PHOTOGRAPHS

Animal No.: 9

right and left flank

Date: June 5, 1991

(day 7)



Report: Project No.: 42H0755/90083

TABLE: 28

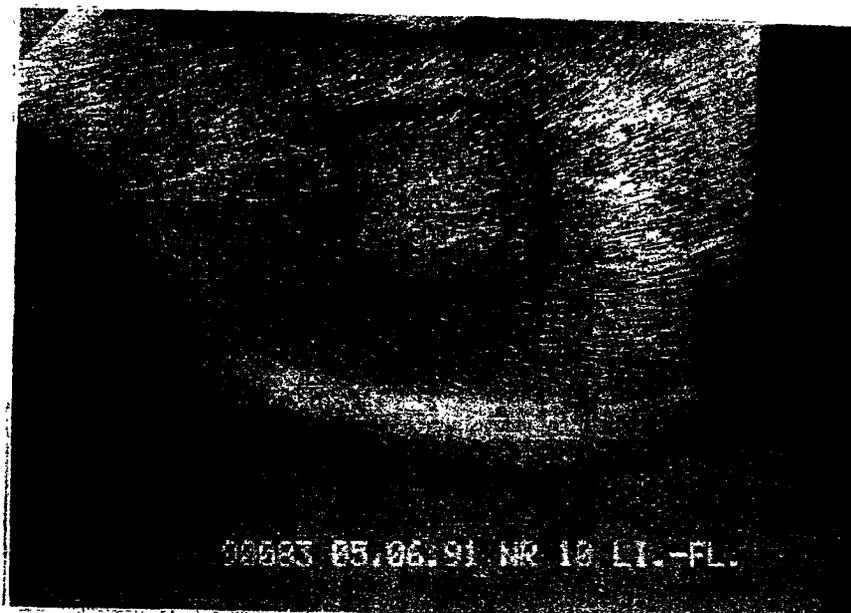
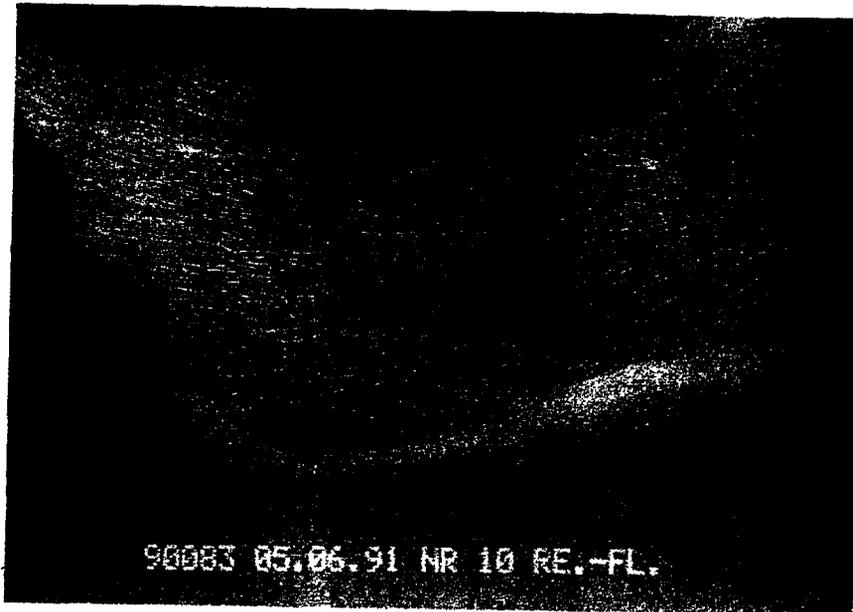
PHOTOGRAPHS

Animal No.: 10

right and left flank

Date: June 5, 1991

(day 7)



Report; Project No.: 42H0755/90083

TABLE: 29

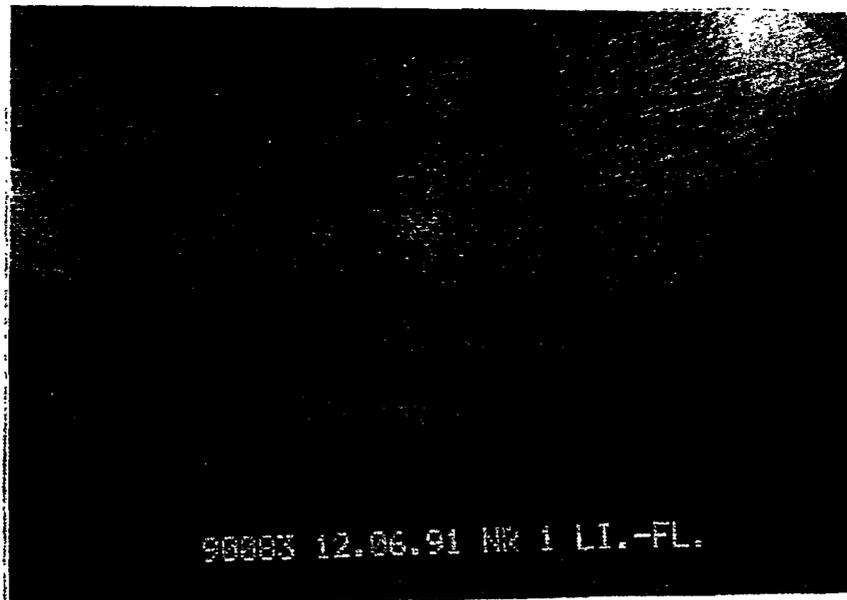
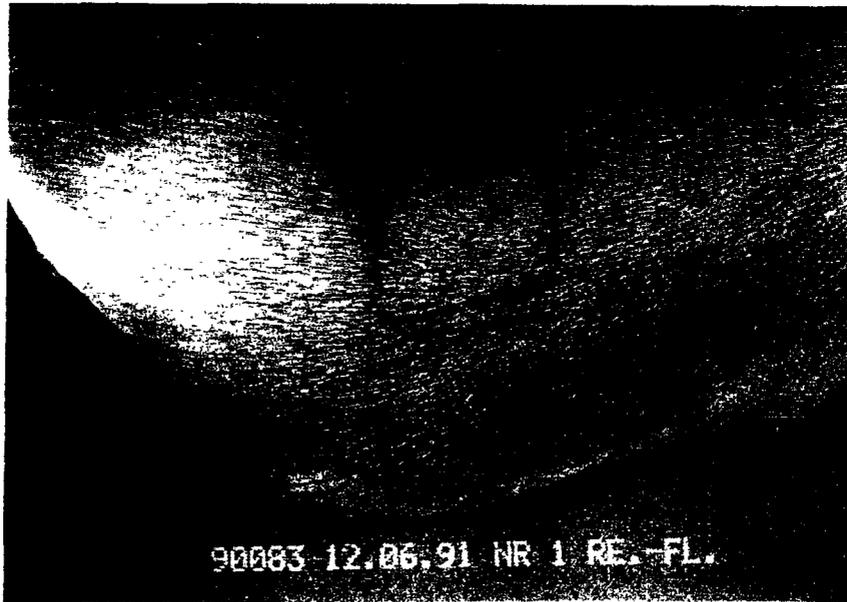
PHOTOGRAPHS

Animal No.: 1

right and left flank

Date: June 12, 1991

(day 14)



Report: Project No.: 42H0755/90083

TABLE: 30

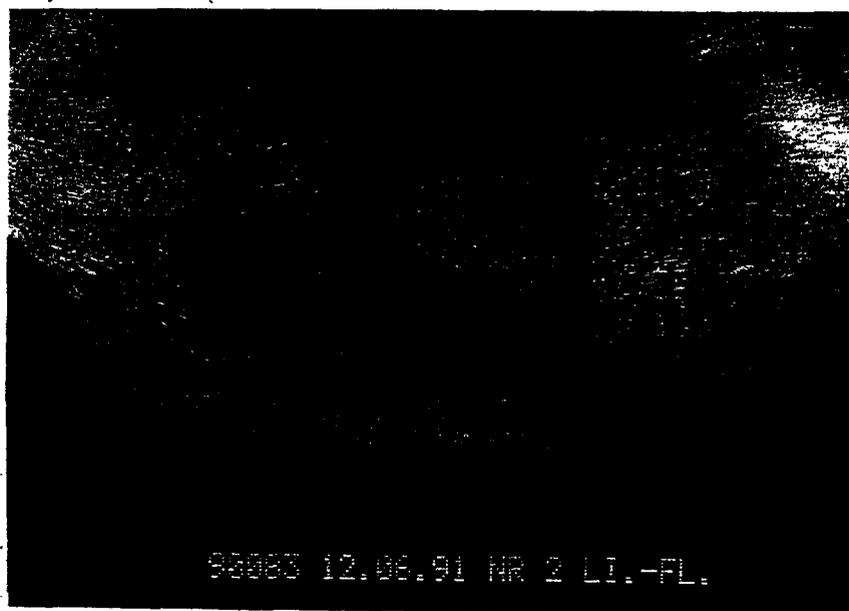
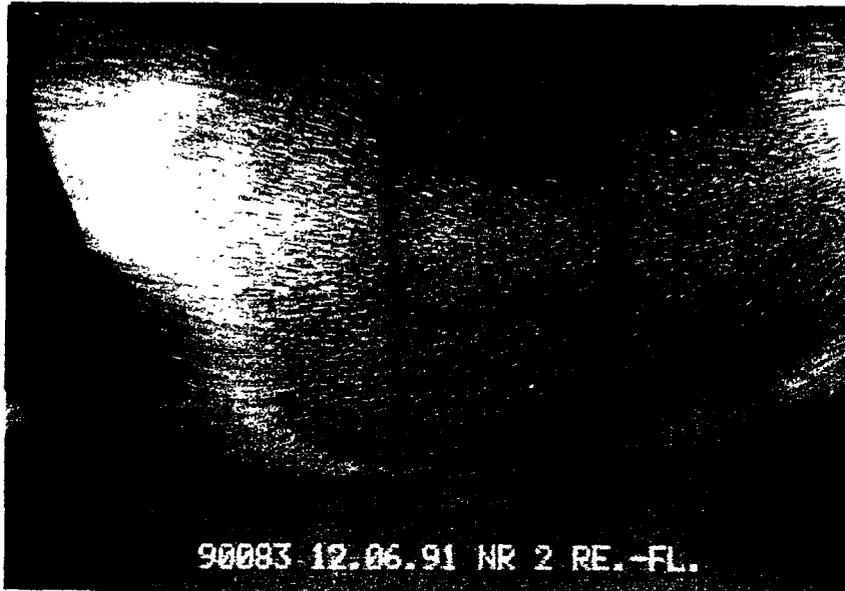
PHOTOGRAPHS

Animal No.: 2

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 31

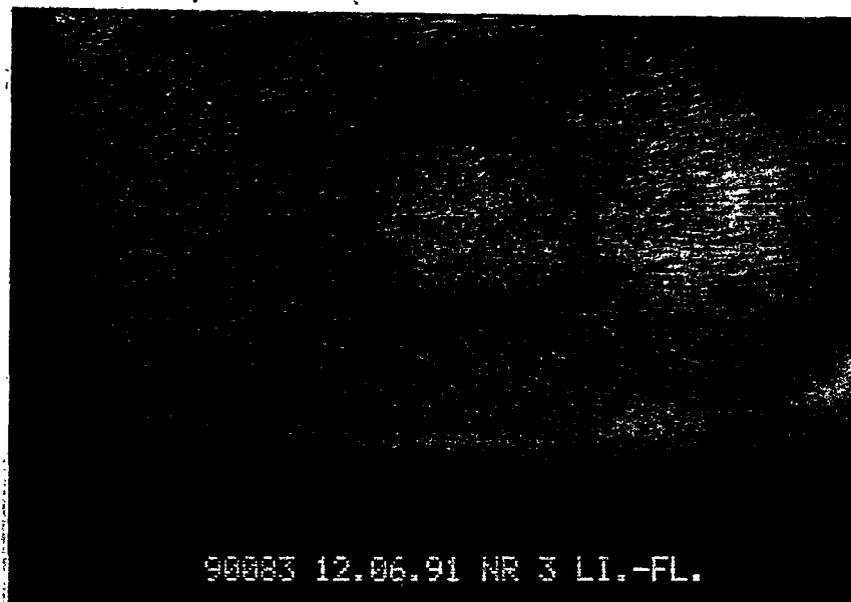
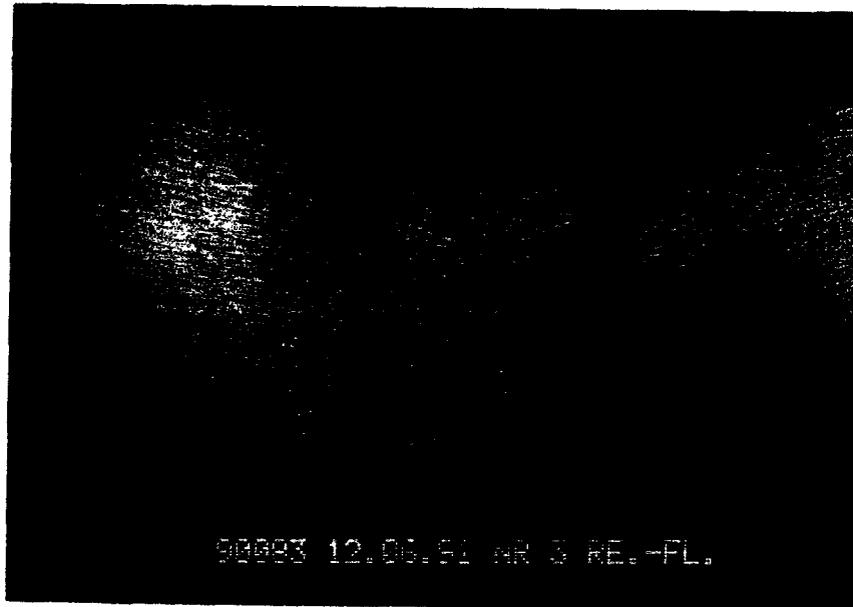
PHOTOGRAPHS

Animal No.: 3

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 32

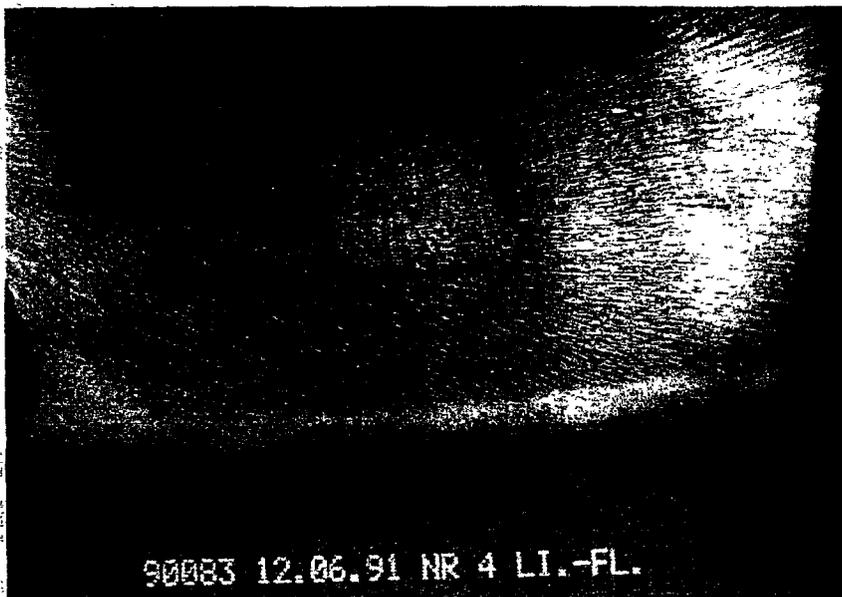
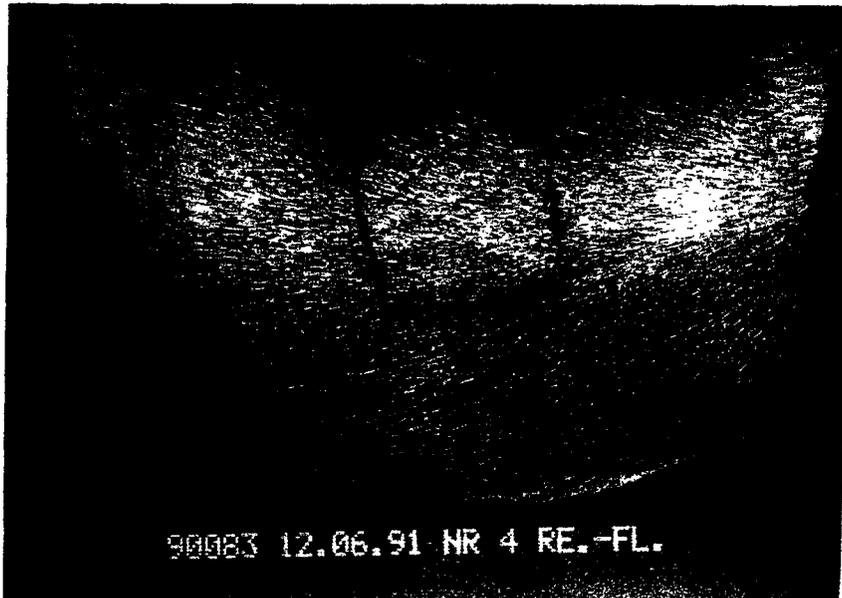
PHOTOGRAPHS

Animal No.: 4

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 33

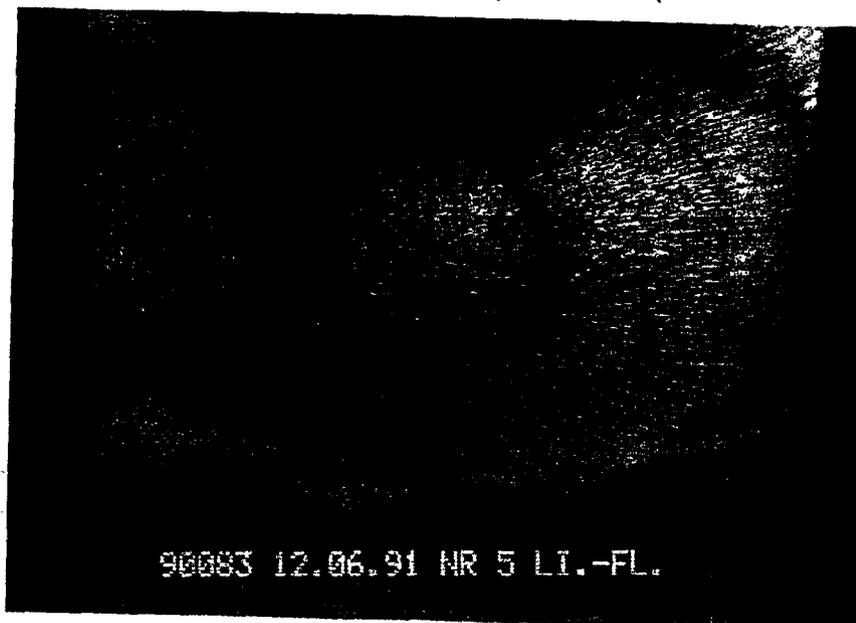
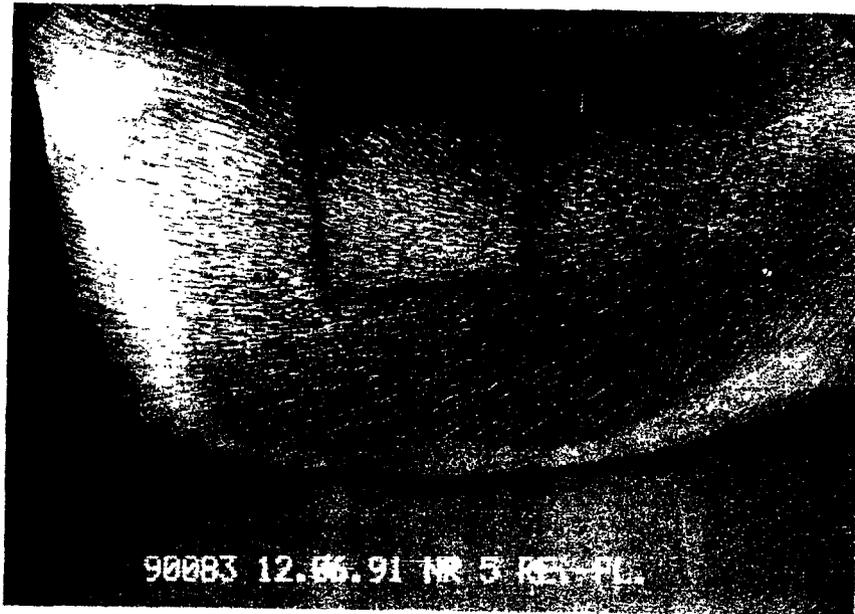
PHOTOGRAPHS

Animal No.: 5

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 34

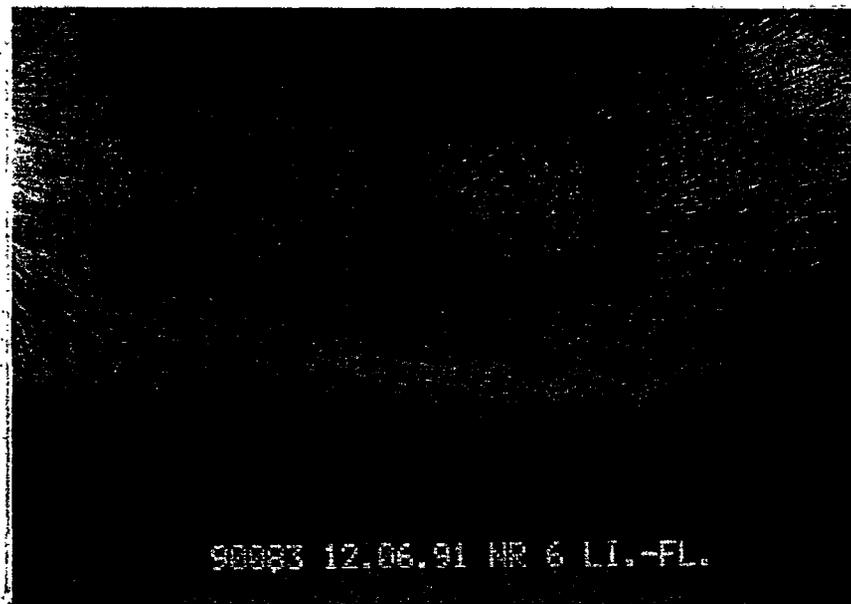
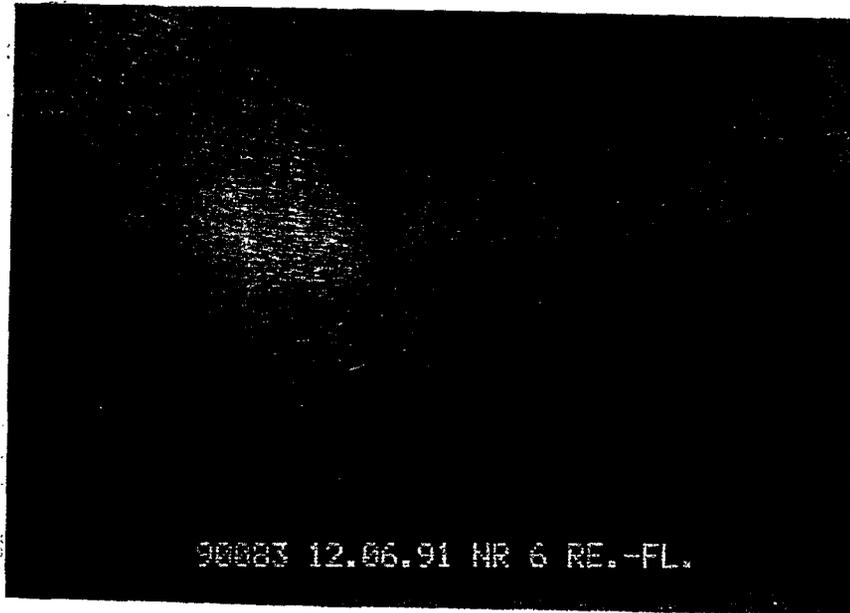
PHOTOGRAPHS

Animal No.: 6

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 35

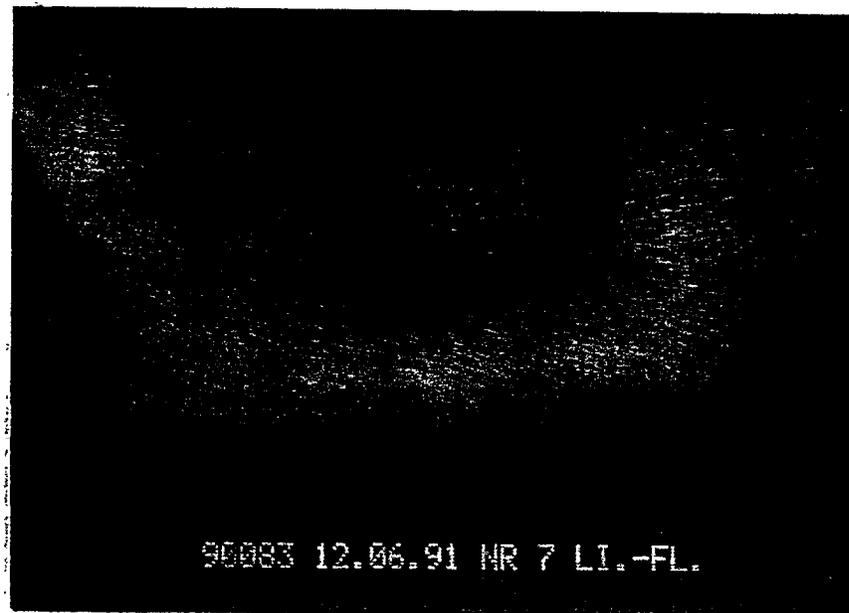
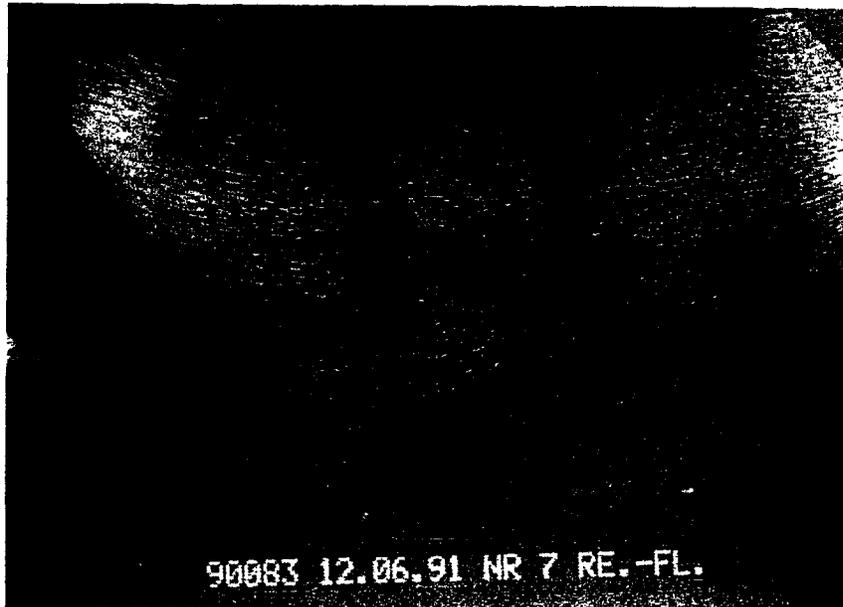
PHOTOGRAPHS

Animal No.: 7

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 36

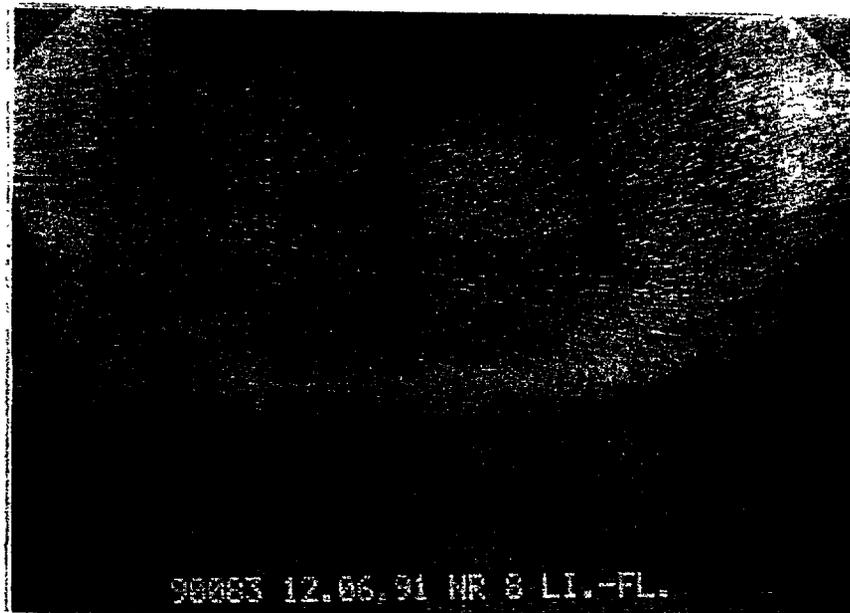
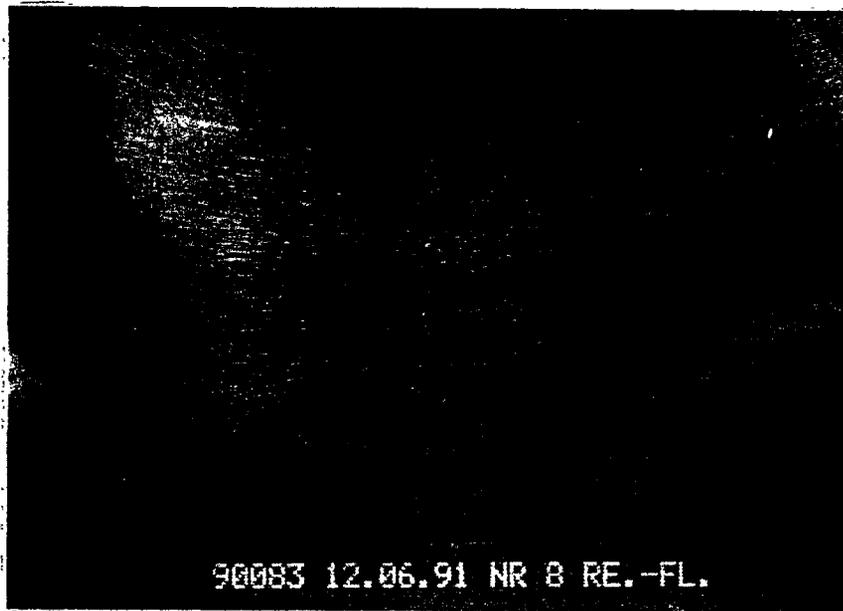
PHOTOGRAPHS

Animal No.: 8

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 37

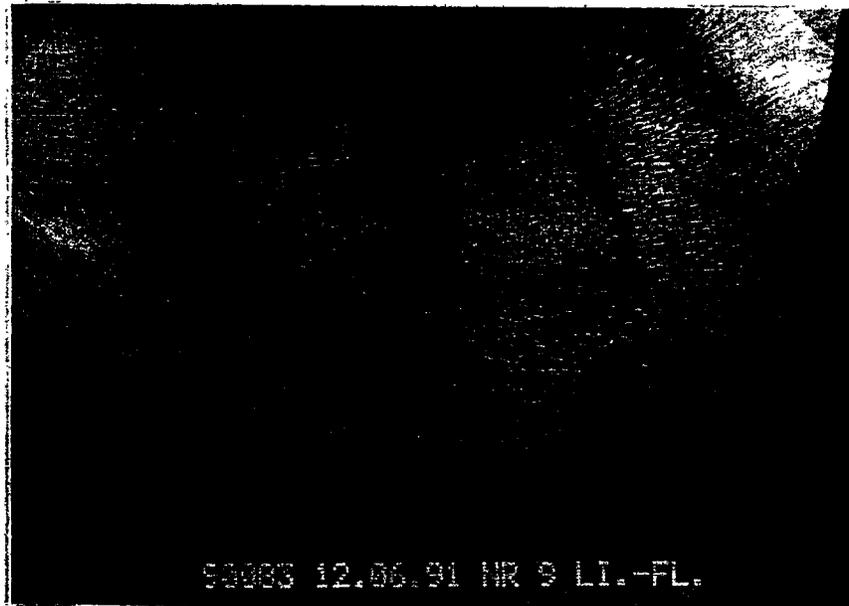
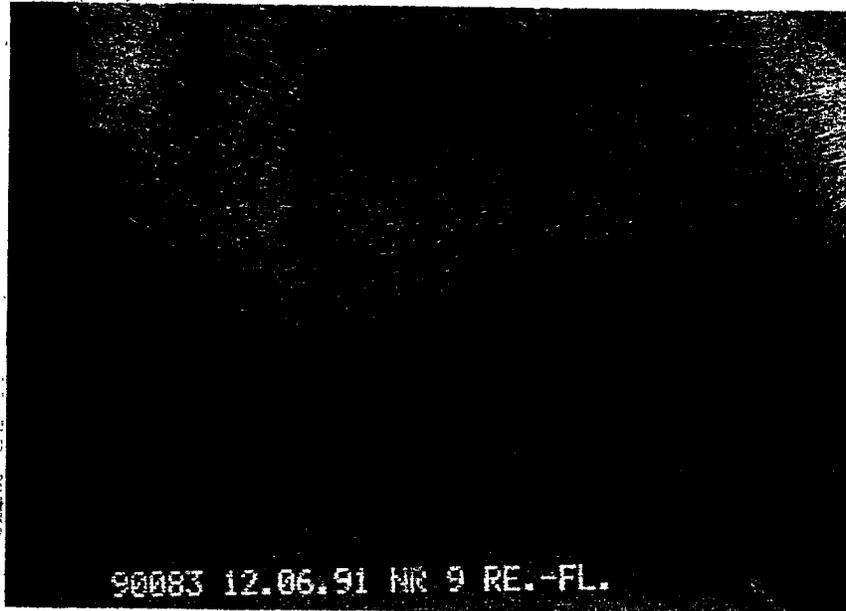
PHOTOGRAPHS

Animal No.: 9

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 38

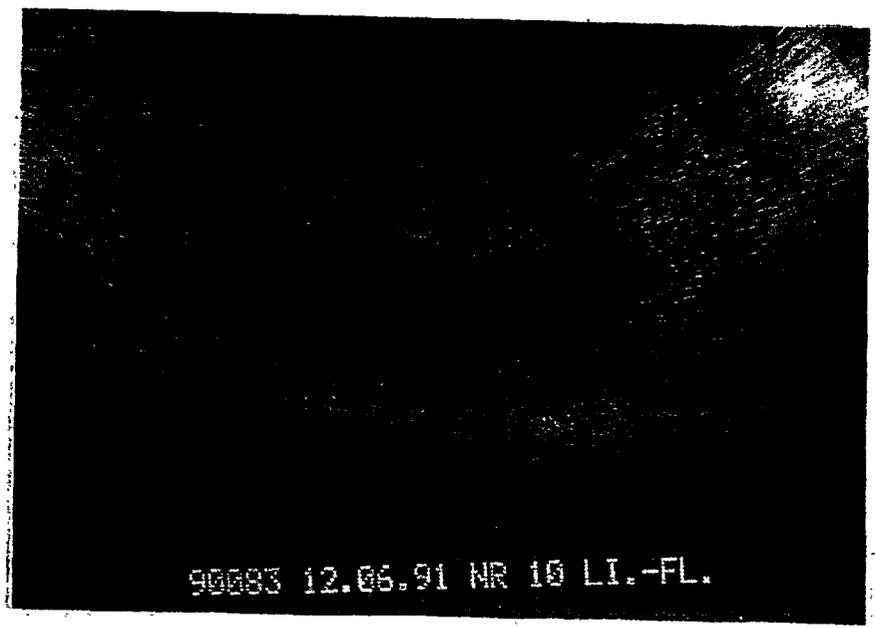
PHOTOGRAPHS

Animal No.: 10

right and left flank

Date: June 12, 1991

(day 14)



Report; Project No.: 42H0755/90083

TABLE: 39

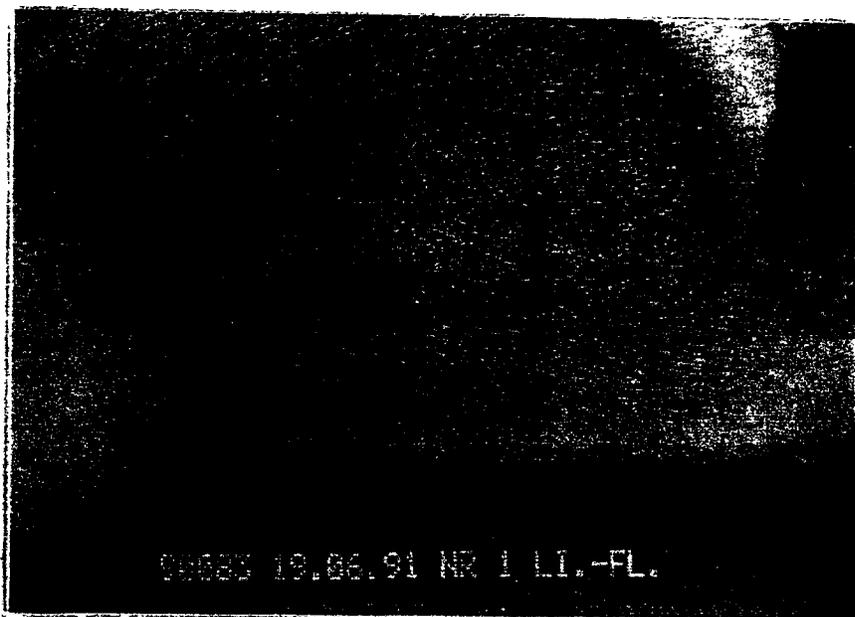
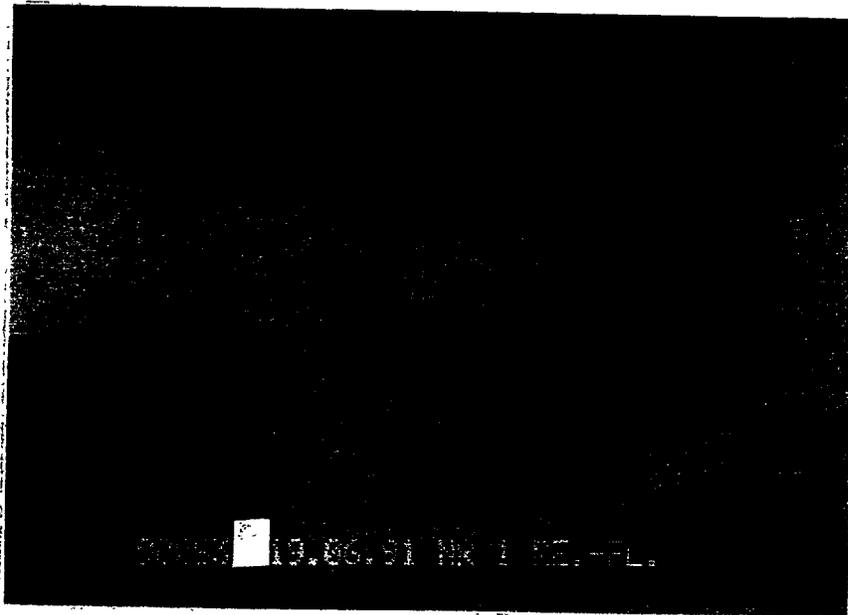
PHOTOGRAPHS

Animal No.: 1

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 40

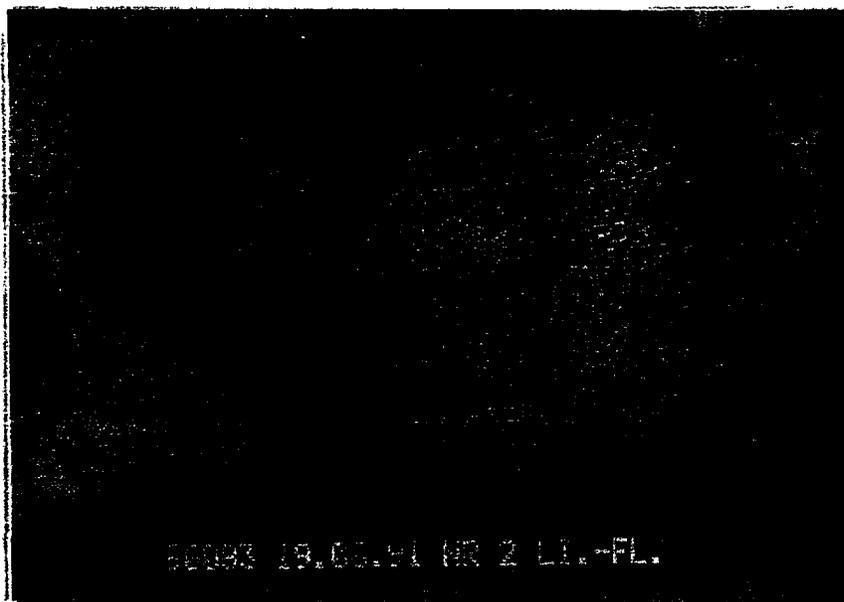
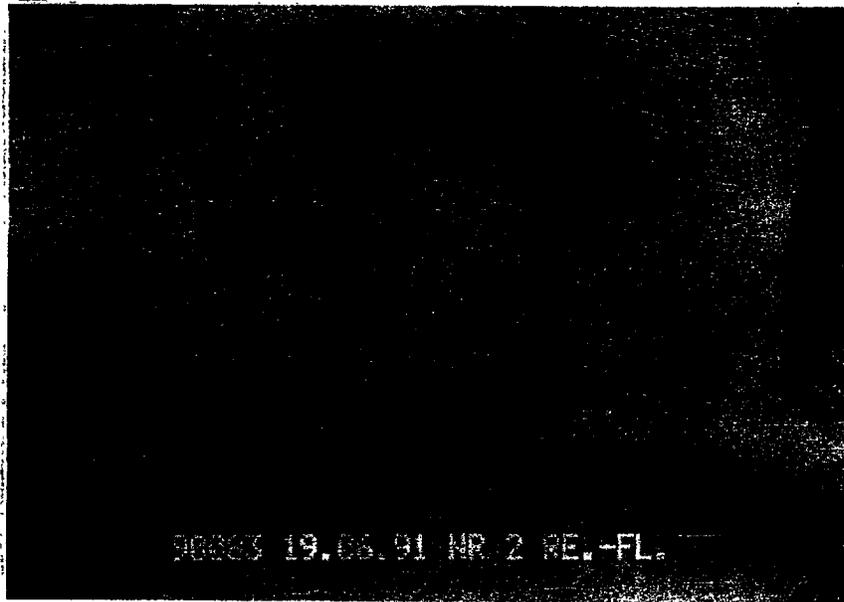
PHOTOGRAPHS

Animal No.: 2

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 41

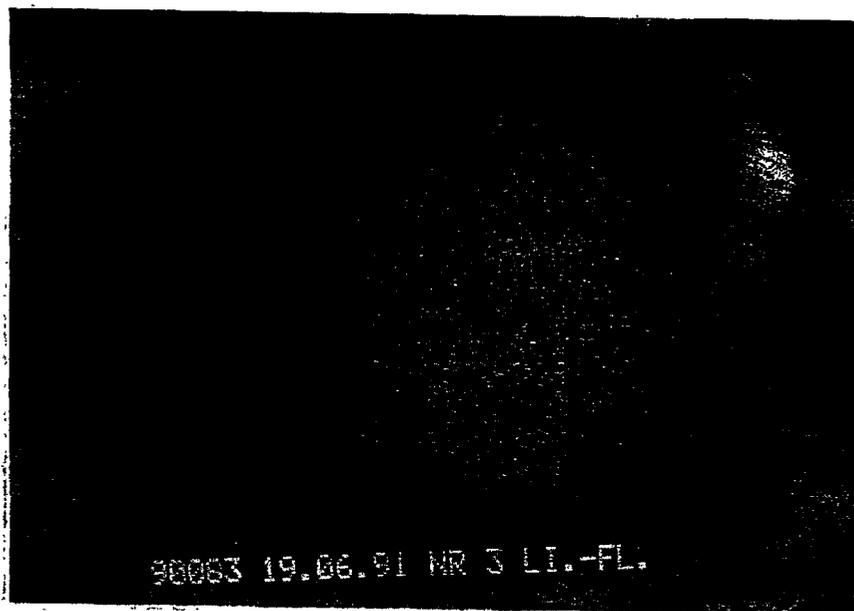
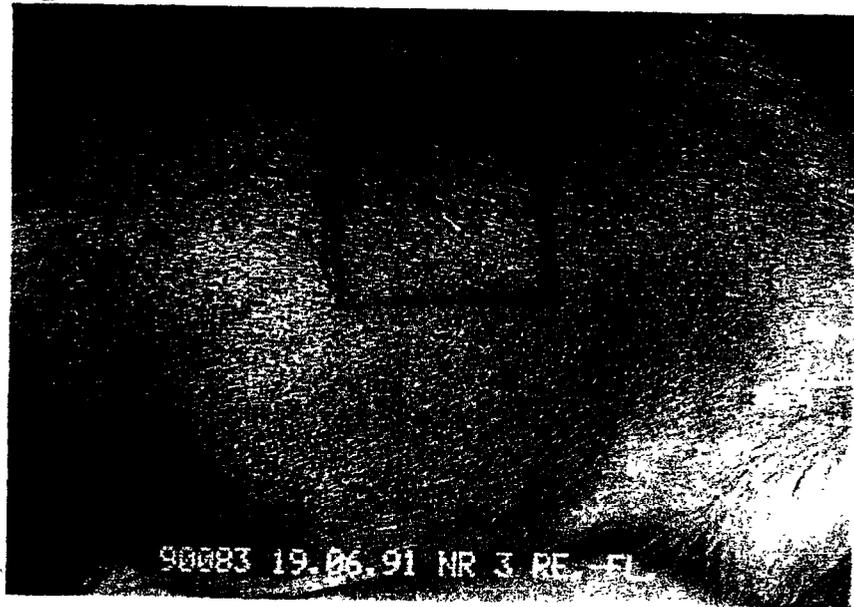
PHOTOGRAPHS

Animal No.: 3

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 42

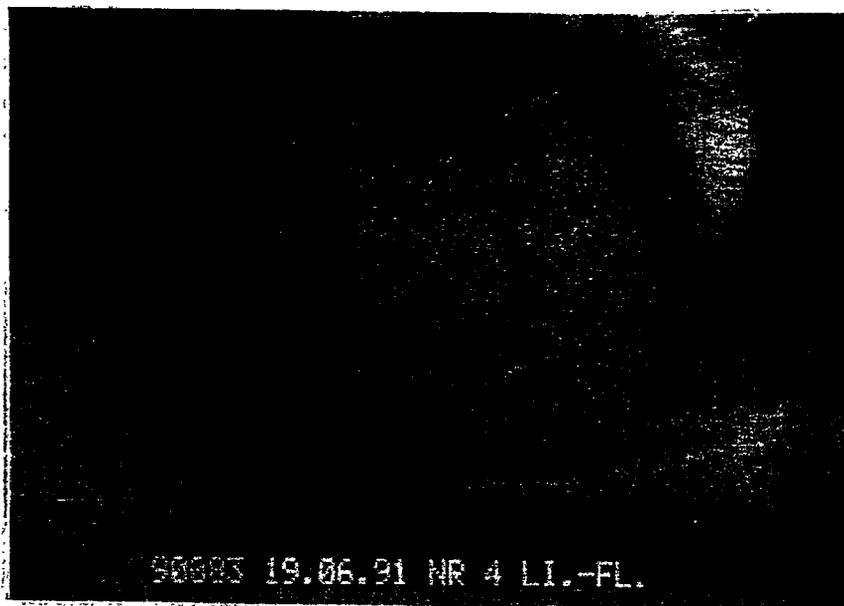
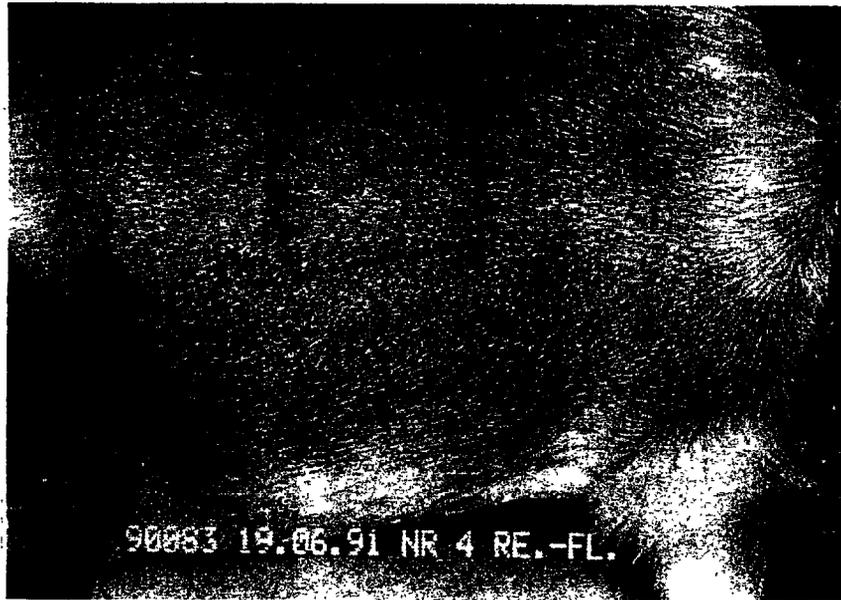
PHOTOGRAPHS

Animal No.: 4

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 43

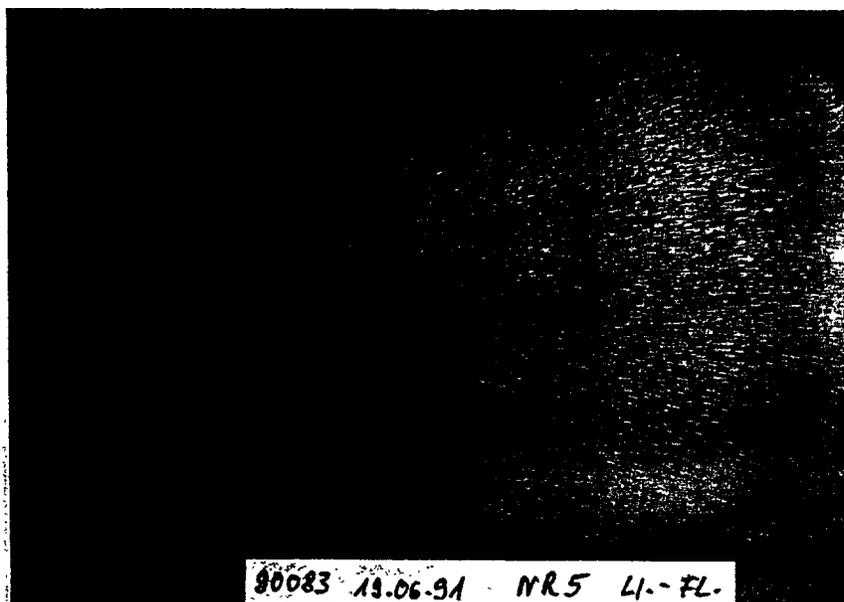
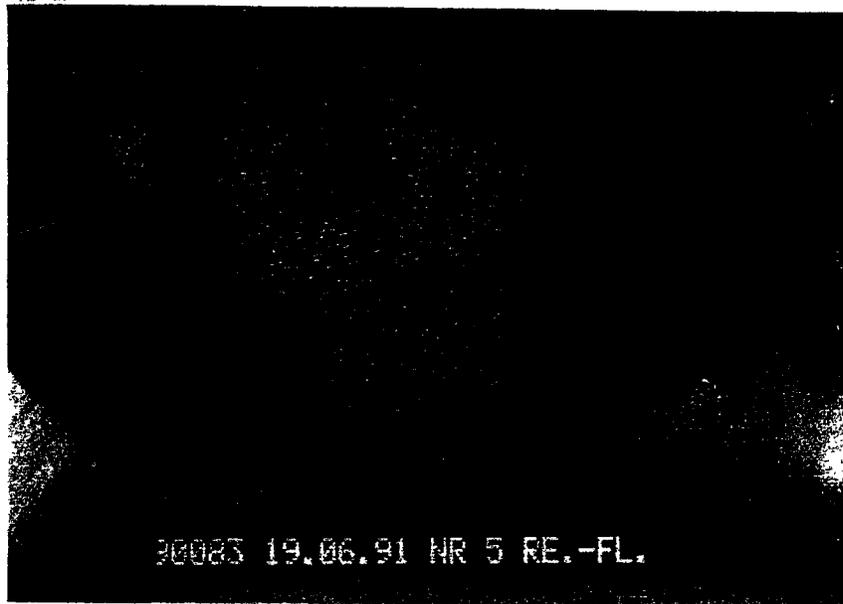
PHOTOGRAPHS

Animal No.: 5

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 44

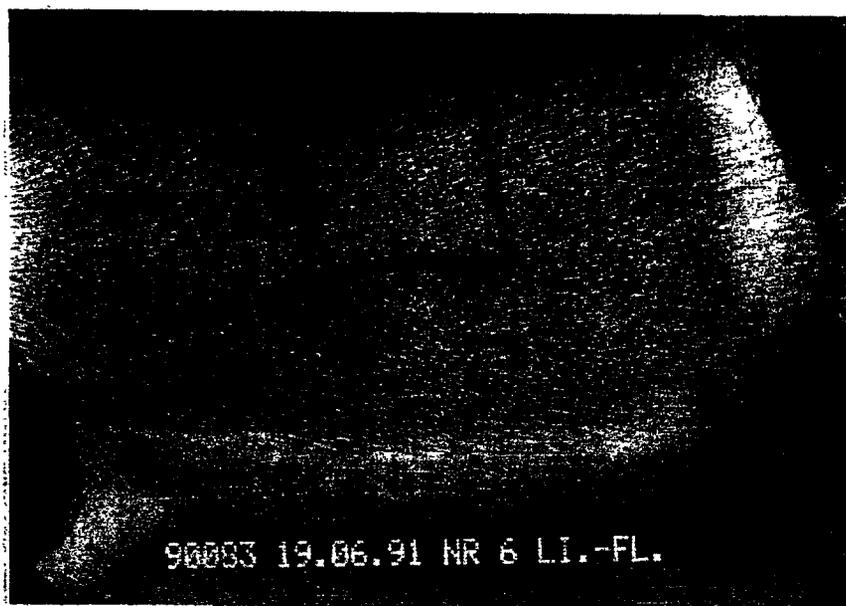
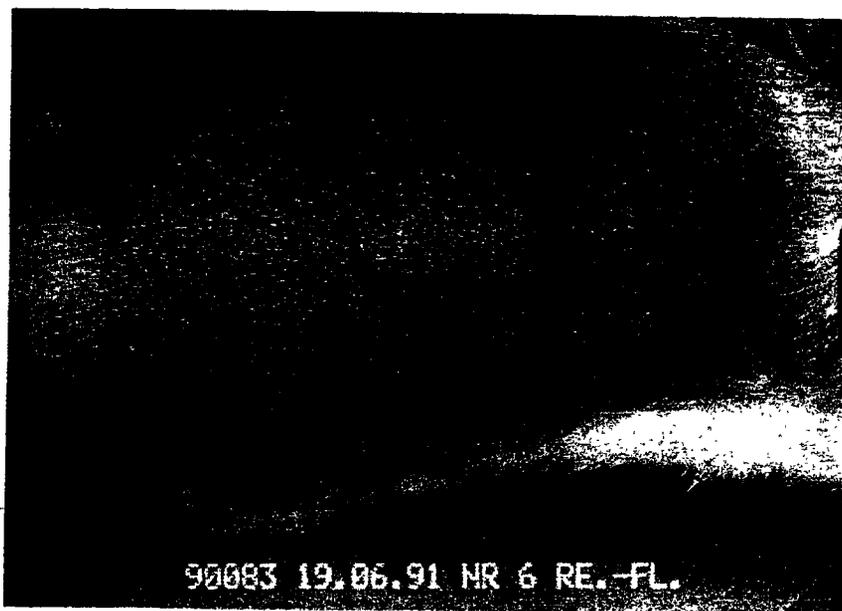
PHOTOGRAPHS

Animal No.: 6

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 45

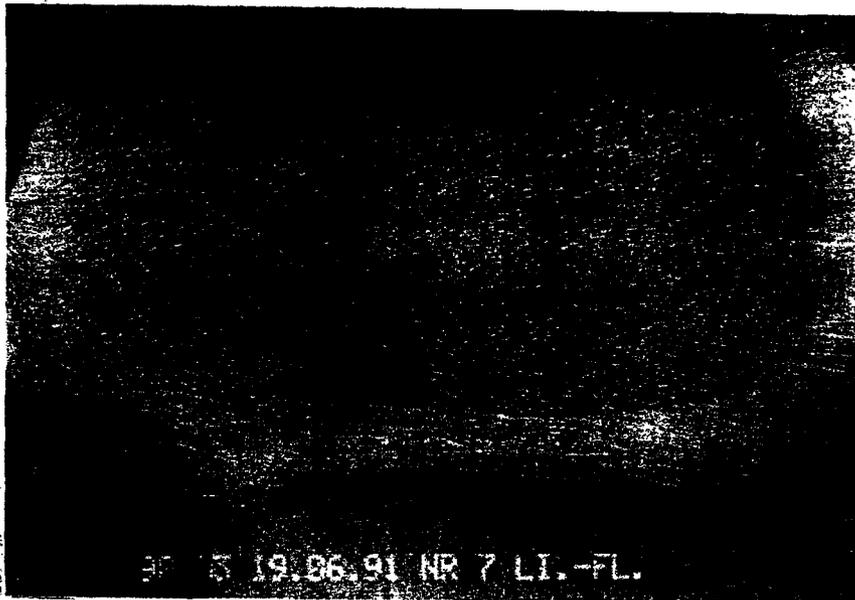
PHOTOGRAPHS

Animal No.: 7

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 46

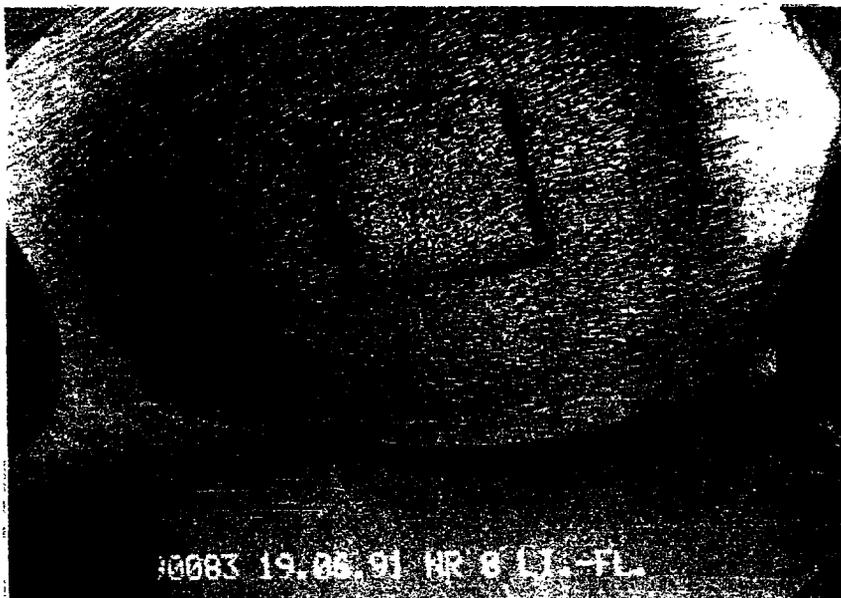
PHOTOGRAPHS

Animal No.: 8

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 47

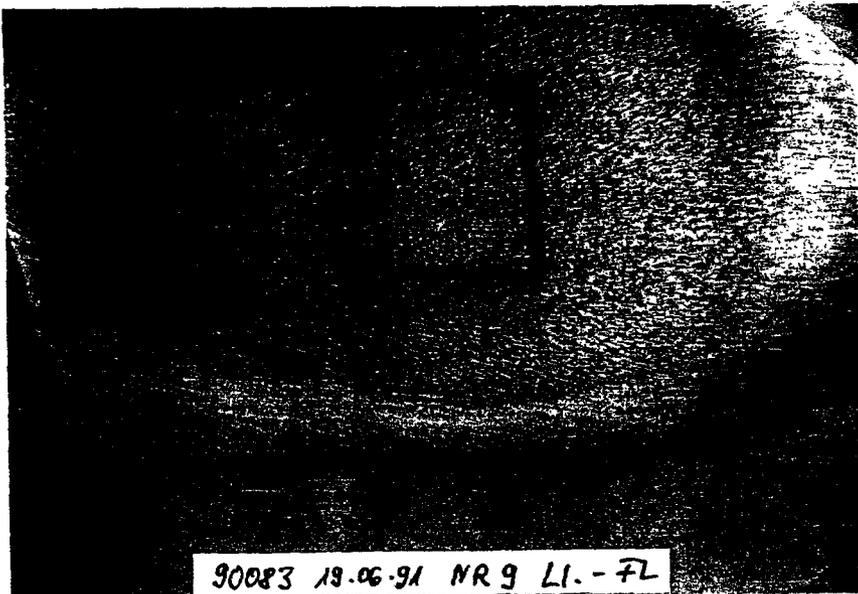
PHOTOGRAPHS

Animal No.: 9

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 48

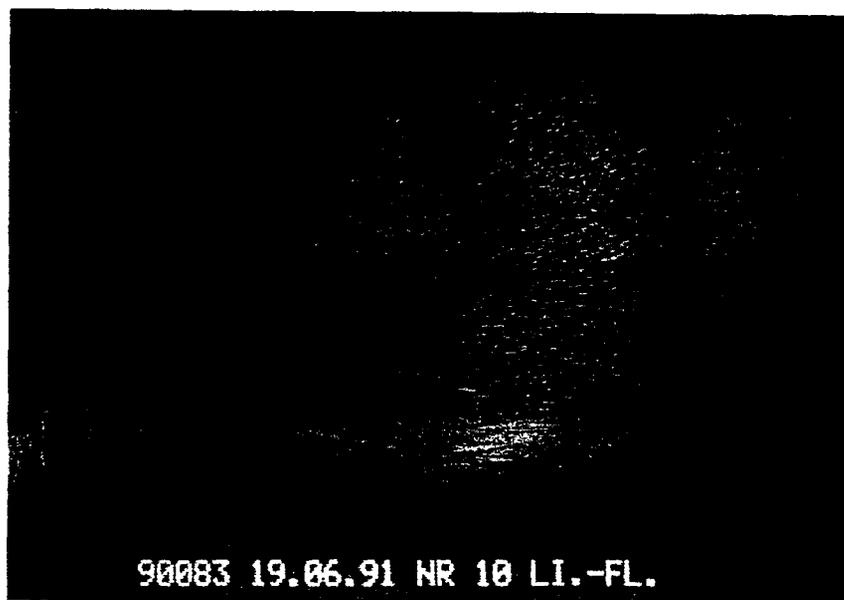
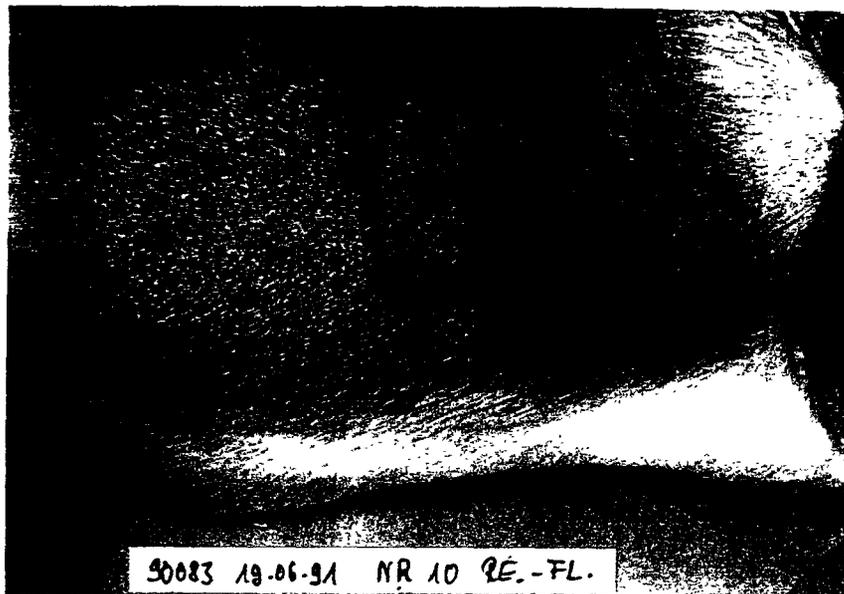
PHOTOGRAPHS

Animal No.: 10

right and left flank

Date: June 19, 1991

(day 21)



Report; Project No.: 42H0755/90083

TABLE: 49

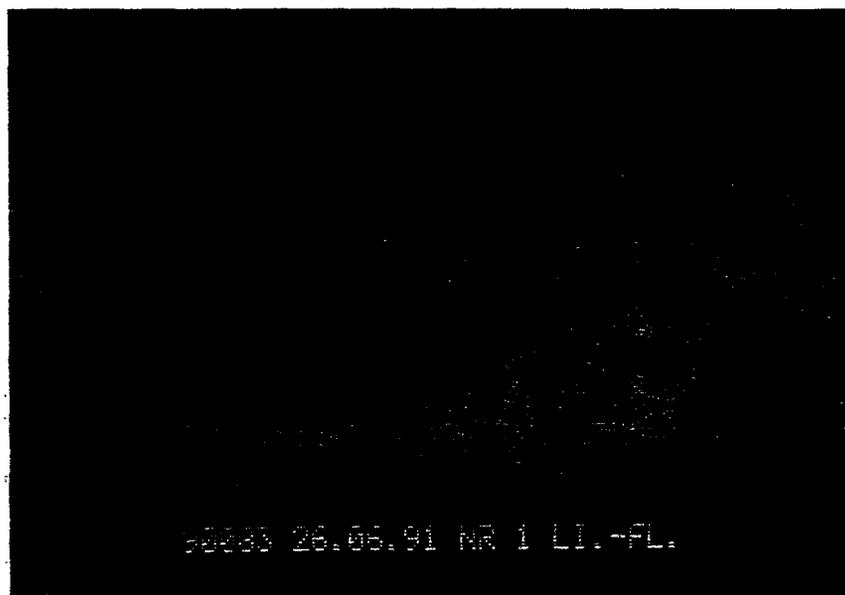
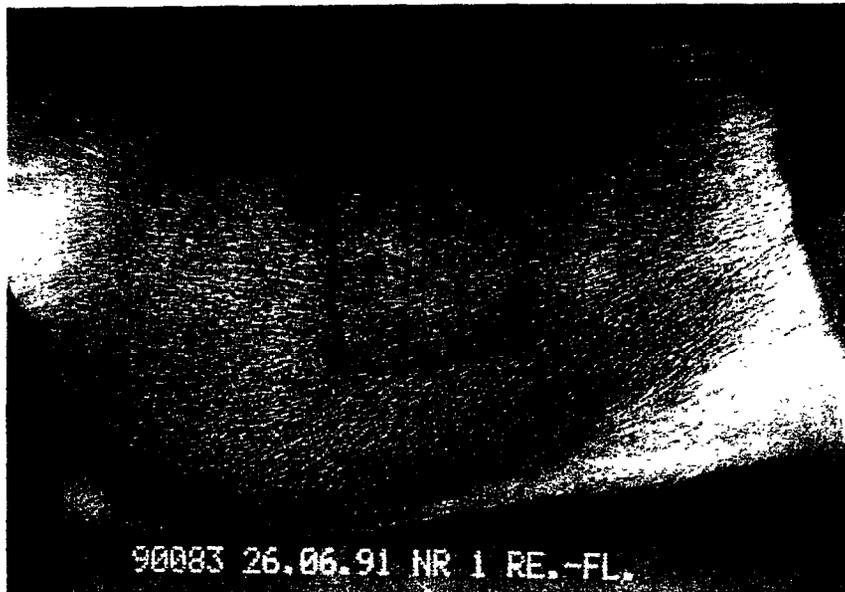
PHOTOGRAPHS

Animal No.: 1

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 50

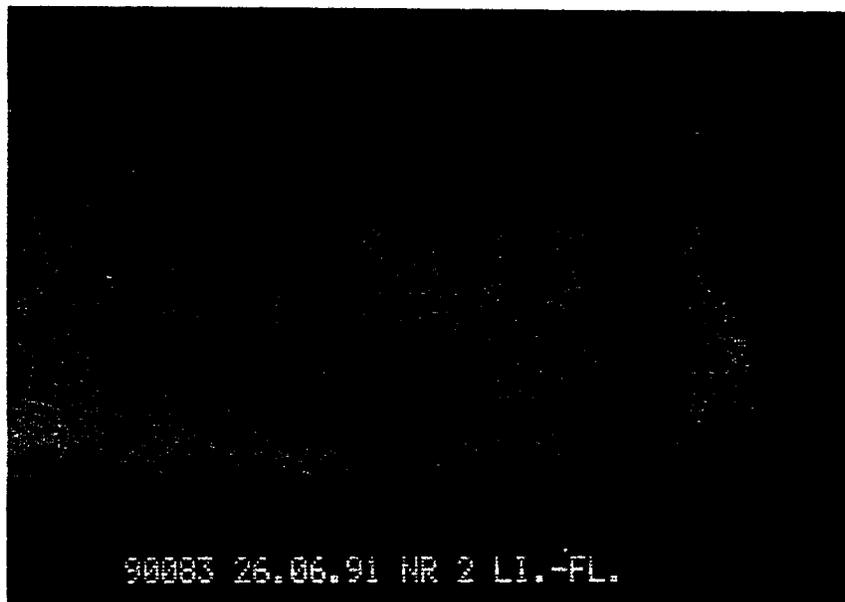
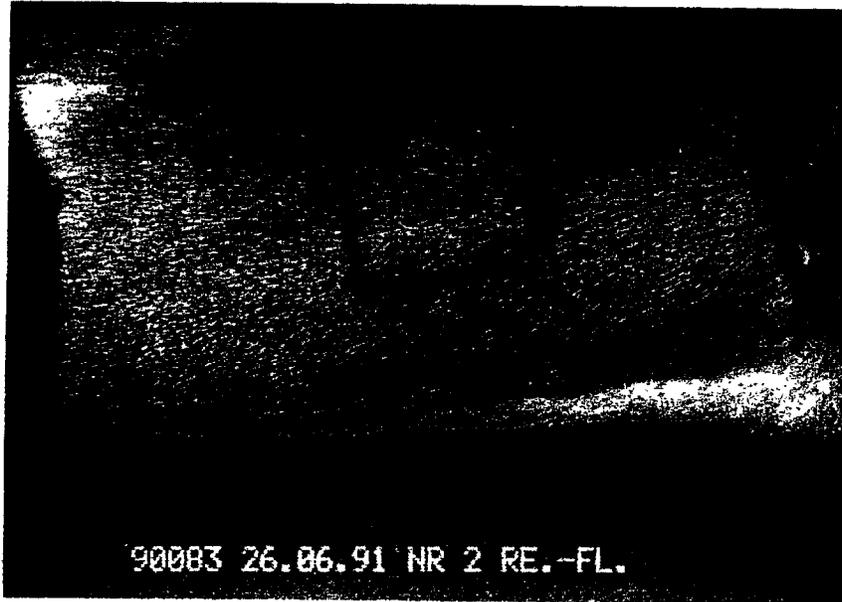
PHOTOGRAPHS

Animal No.: 2

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 51

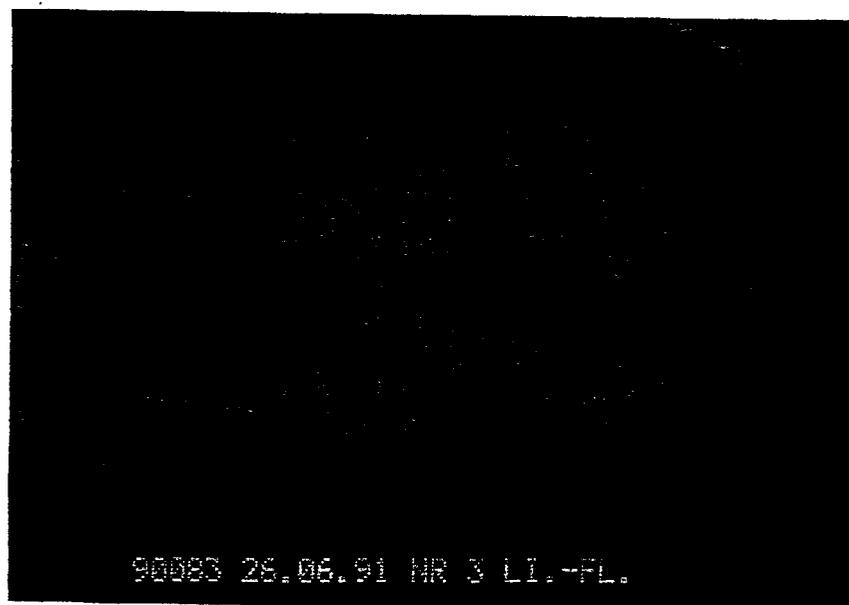
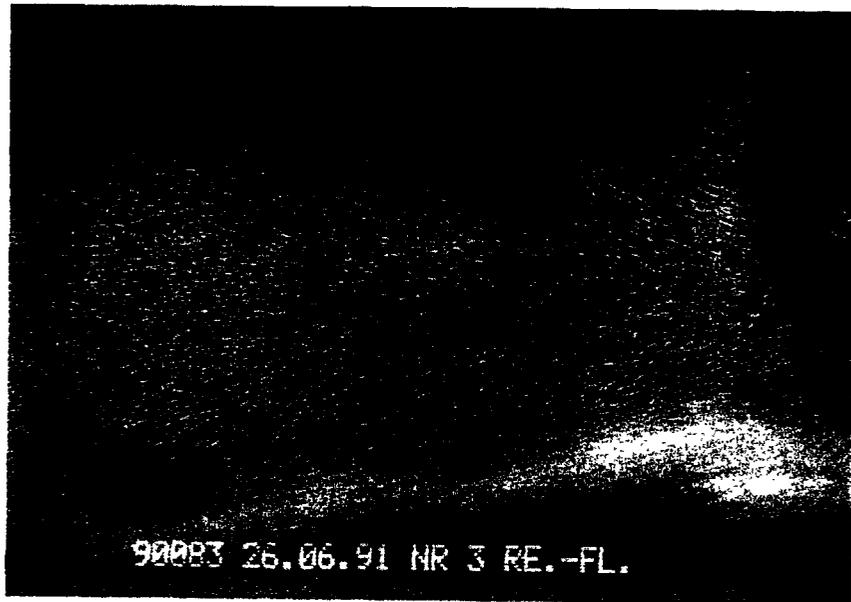
PHOTOGRAPHS

Animal No.: 3

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 52

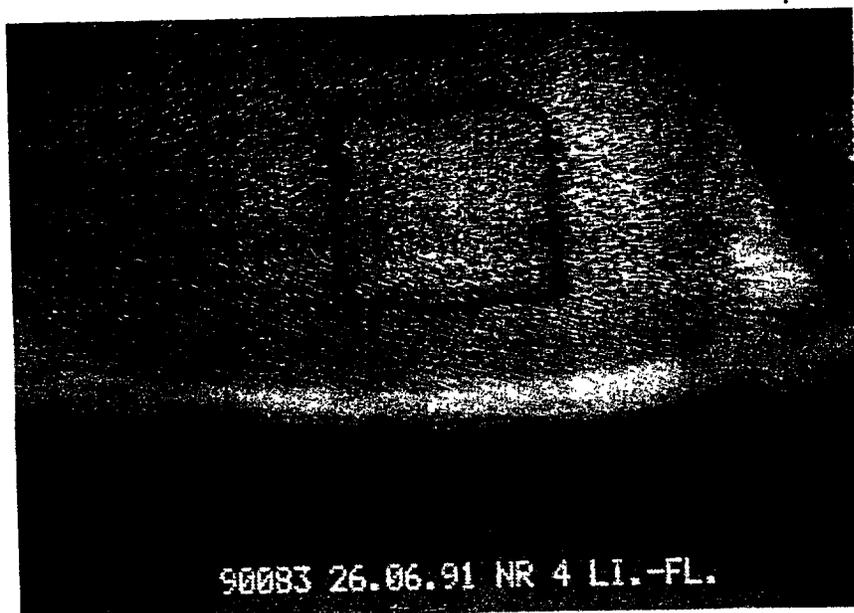
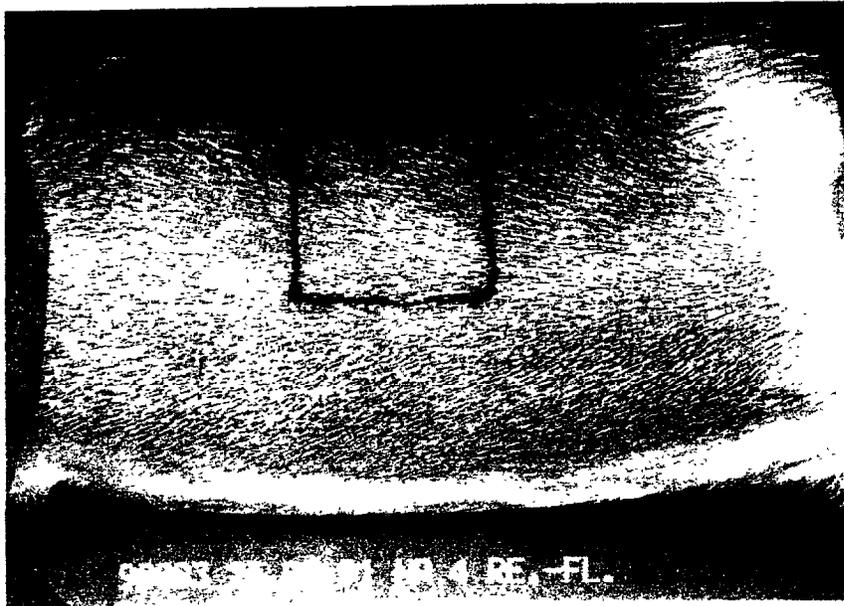
PHOTOGRAPHS

Animal No.: 4

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 53

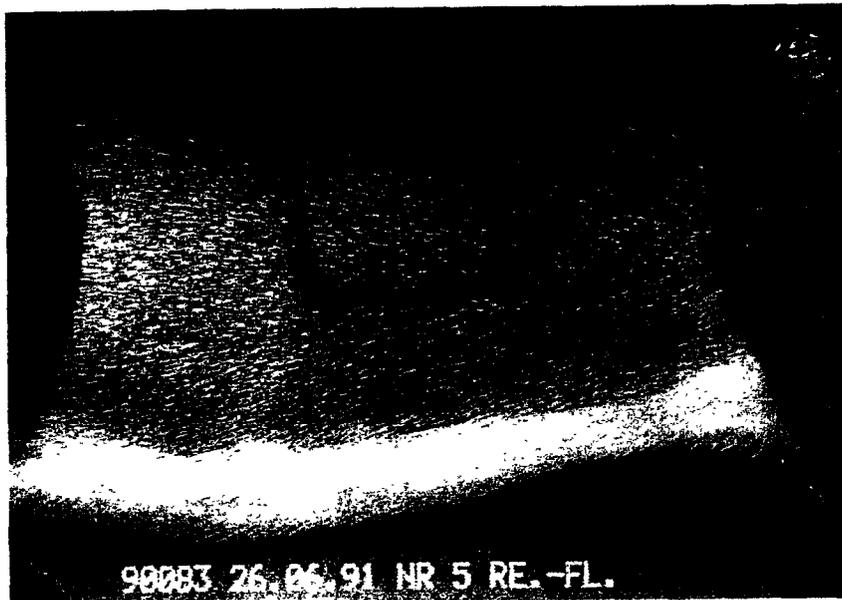
PHOTOGRAPHS

Animal No.: 5

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 54

PHOTOGRAPHS

Animal No.: 6

right and left flank

Date: June 26, 1991

(day 28)

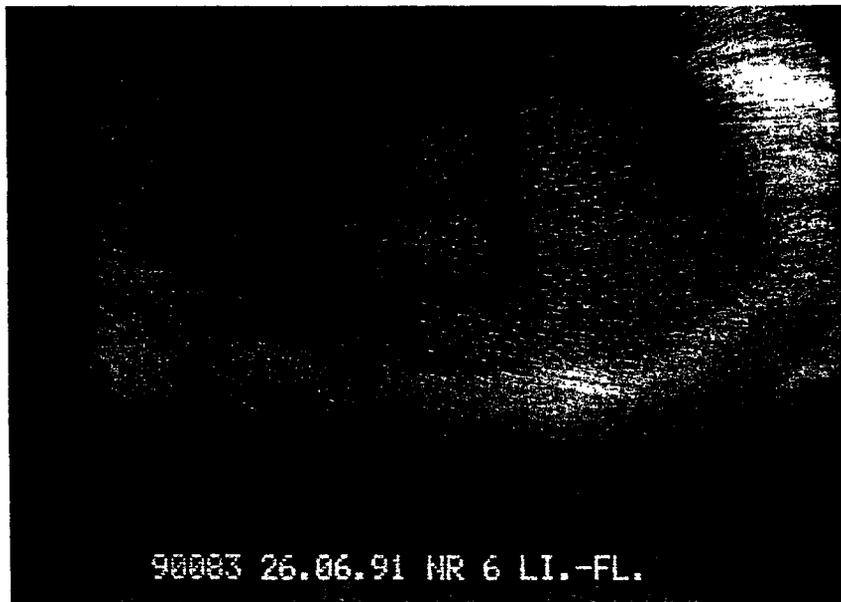
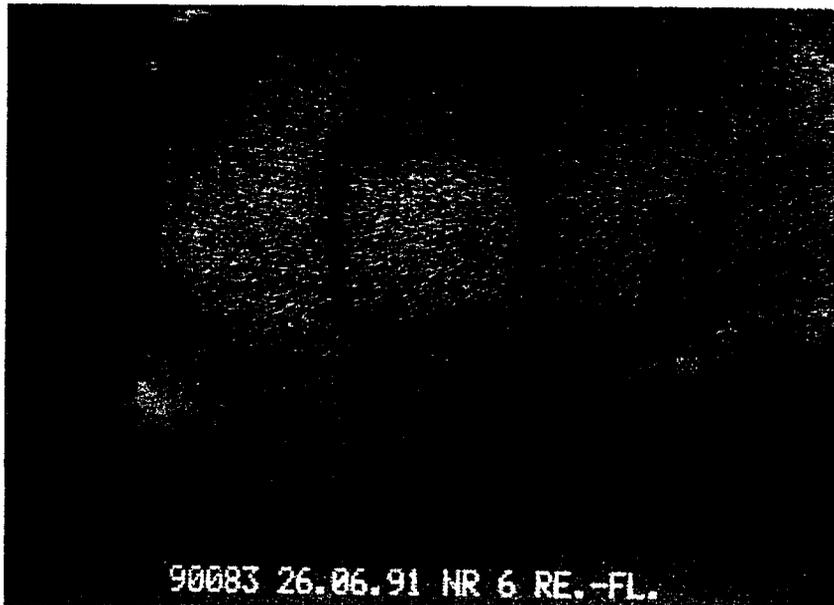


TABLE: 55

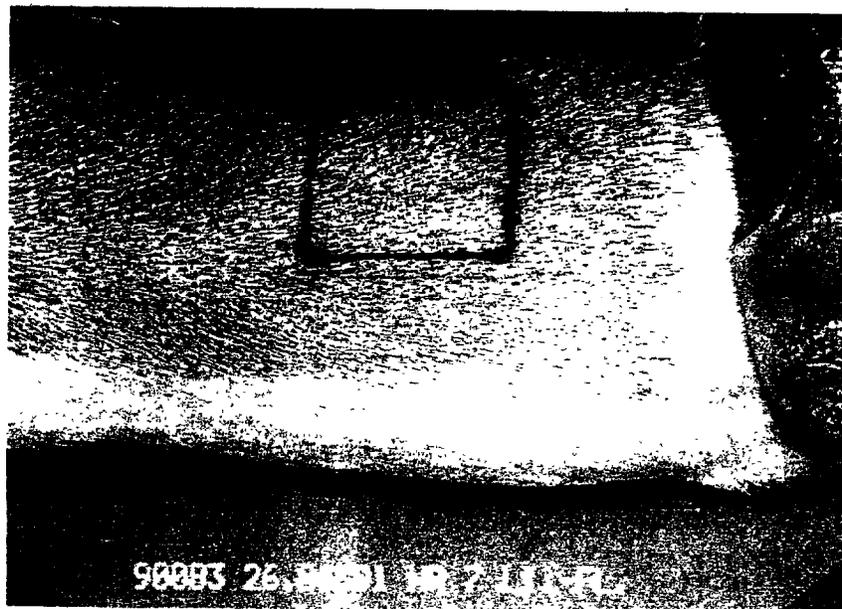
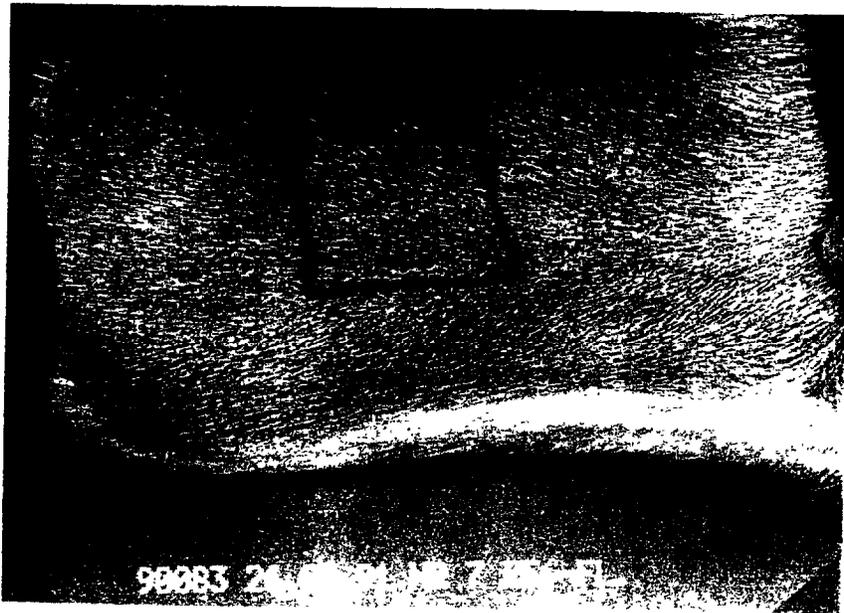
PHOTOGRAPHS

Animal No.: 7

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 56

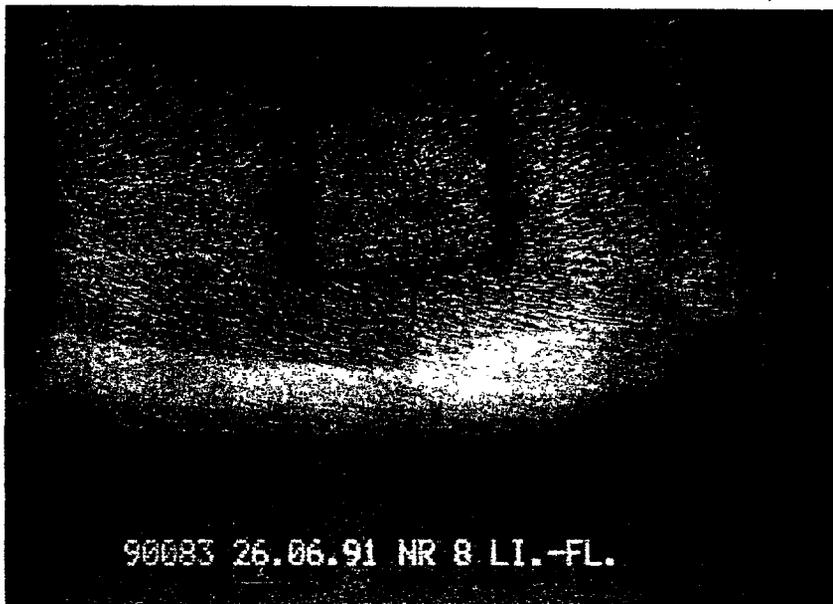
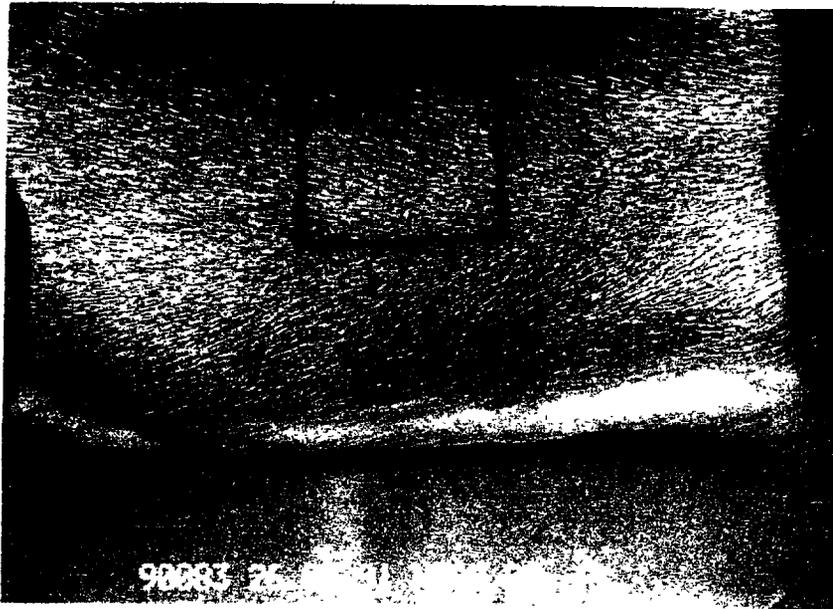
PHOTOGRAPHS

Animal No.: 8

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 57

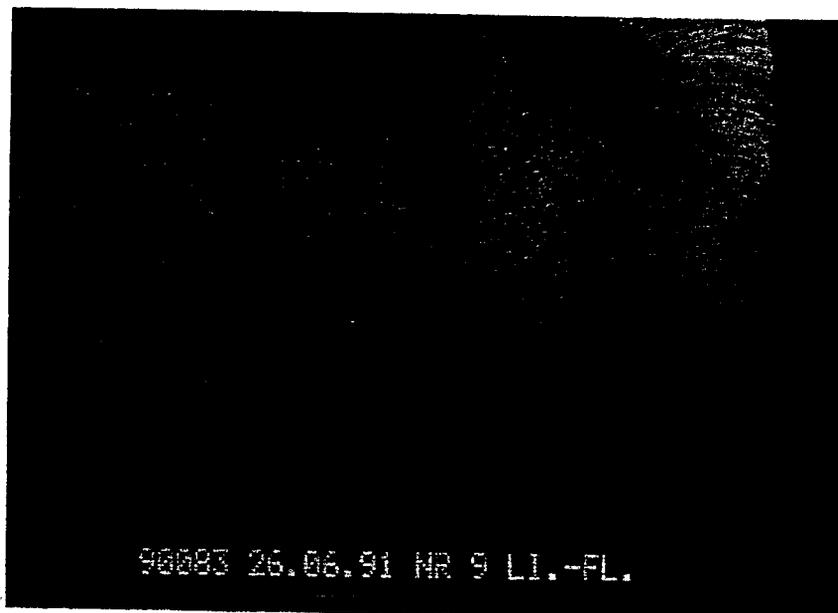
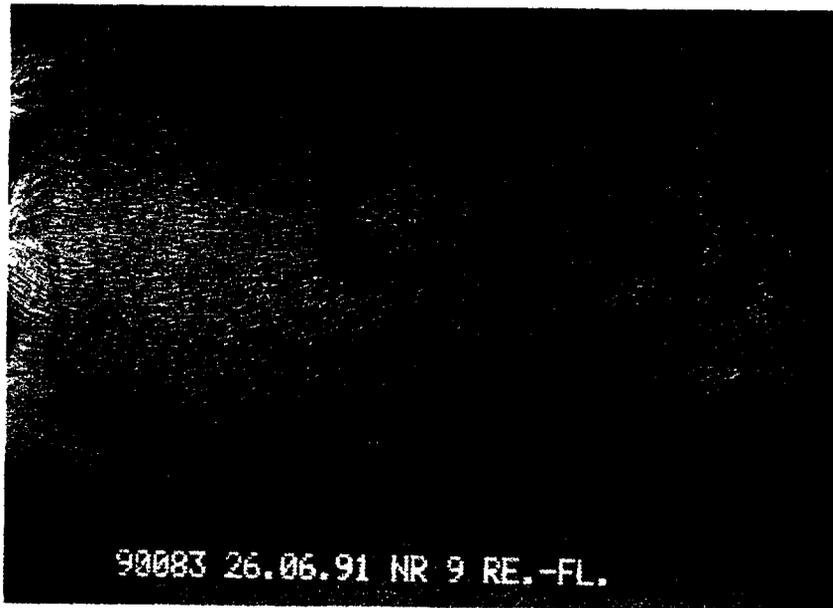
PHOTOGRAPHS

Animal No.: 9

right and left flank

Date: June 26, 1991

(day 28)



Report; Project No.: 42H0755/90083

TABLE: 58

PHOTOGRAPHS

Animal No.: 10

right and left flank

Date: June 26, 1991

(day 28)

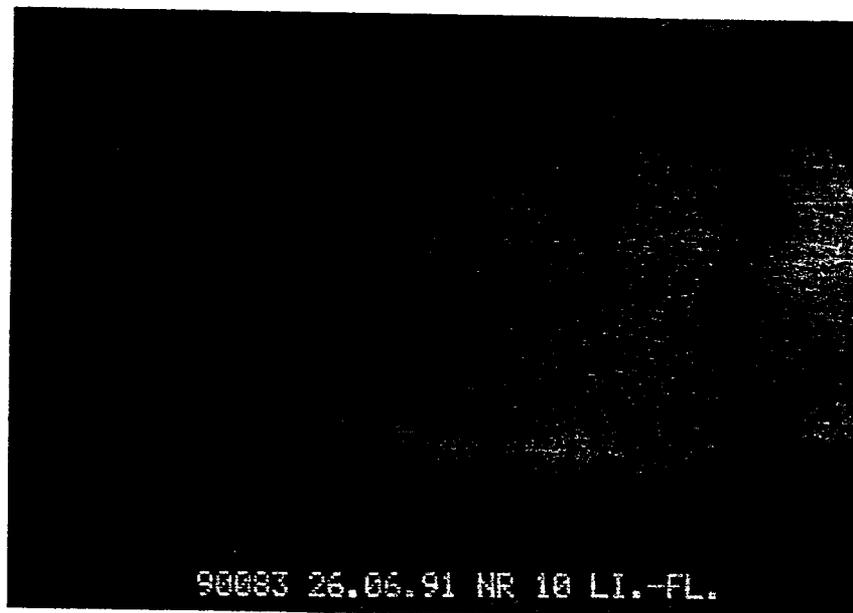
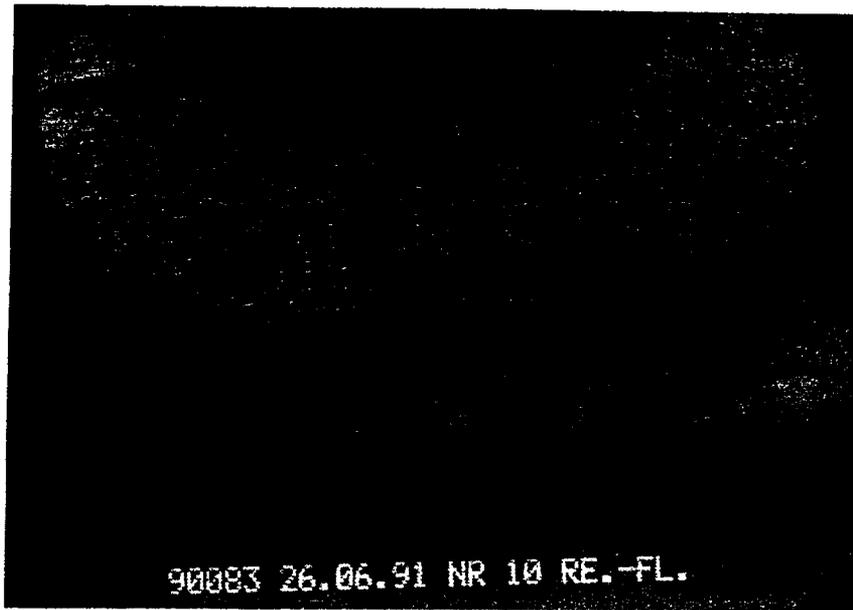


TABLE: 59

BODY WEIGHT DATA

Individual data listing with means

MALES

Animal No.	Body weight (g) after:				
	Day 0	Day 7	Day 14	Day 21	Day 27
1	297	341	384	409	448
2	267	313	348	391	413
3	290	351	417	506	568
4	260	313	358	401	439
5	274	304	352	383	395
Mean	278	324	372	418	453

FEMALES

Animal No.	Body weight (g) after:				
	Day 0	Day 7	Day 14	Day 21	Day 27
6	287	313	342	366	384
7	274	313	338	364	372
8	281	324	349	375	412
9	285	323	383	415	468
10	278	331	360	378	384
Mean	281	321	354	380	404

BASF

Abteilung Toxikologie
Department of Toxicology

D-W6700 Ludwigs-
hafen, FRG

ki-db; 2238-81

MAY 22 1992

REPORT

Study of the Dermal Irritation of

UVINUL T 150

in Guinea Pigs

Application to the intact skin
over 4 weeks

Project No.: 42H0755/90083

VOLUME II OF III

PATHOLOGY REPORT

Testing facility:

Department of Toxicology of
BASF Aktiengesellschaft
D-W6700 Ludwigshafen/Rhein, FRG

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BASF Department of Toxicology

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PATHOLOGY REPORT

42H0755/90083

UVINUL T 150, 4-Week Dermal Irritation
in Guinea Pigs

May/18/1992 DIMI
acopat system

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MATERIALS AND METHODS

The animals were sacrificed by decapitation under CO2 anesthesia. The exsanguinated animals were necropsied and assessed by gross pathology.

Subsequently the following organs or tissues were fixed in 4% formaldehyde solution:

- treated skin - untreated skin - gross lesions

No further investigations were performed.

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RESULTS

Weight Parameters

No weight parameters were determined.

Gross Lesions

No gross lesions were noted in any of the animals during necropsy.

Histopathology

No histopathologic investigations were performed.

LIST OF ABBREVIATIONS

F = female animals

F1 = final sacrifice groups

M = male animals

NAD = number of animals without gross lesions

Codes for the Status at Necropsy:

1 = planned sacrifice

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INCIDENCE OF GROSS LESIONS

Sacrifice group	F1		
Sex	M	F	
Dose group	1		
Animals	5	5	
	NAD	5	5

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SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	M
Dose group	1
Animal	1

General information

Status at necropsy: planned sacrifice
Date of death: Jun/26/1991
Day(s) after start exposure: 28
Day(s) after end exposure: 1
Sex: male
Dose group: Lutrol and Lutrol + UVINUL 50%
Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

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SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	M
Dose group	1
Animal	2

General information

Status at necropsy: planned sacrifice
 Date of death: Jun/26/1991
 Day(s) after start exposure: 28
 Day(s) after end exposure: 1
 Sex: male
 Dose group: Lutrol and Lutrol + UVINUL 50%
 Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

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in Guinea Pigs

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SINGLE ANIMAL SHEET

	Sacrifice group	F1
	Sex	M
	Dose group	1
	Animal	3

General information

Status at necropsy: planned sacrifice
Date of death: Jun/26/1991
Day(s) after start exposure: 28
Day(s) after end exposure: 1
Sex: male
Dose group: Lutrol and Lutrol + UVINUL 50%
Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	M
Dose group	1
Animal	4

General information

Status at necropsy: planned sacrifice

Date of death: Jun/26/1991

Day(s) after start exposure: 28

Day(s) after end exposure: 1

Sex: male

Dose group: Lutrol and Lutrol + UVINUL 50%

Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

BASF Department of Toxicology
PATHOLOGY REPORT
UVINUL T 150, 4-Week Dermal Irritation
in Guiana Pigs

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42H0755/90083
May/18/1992 DIMI
acopat system

SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	M
Dose group	1
Animal	5

General information

Status at necropsy: planned sacrifice
Date of death: Jun/26/1991
Day(s) after start exposure: 28
Day(s) after end exposure: 1
Sex: male
Dose group: Lutrol and Lutrol + UVINUL 50%
Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

UVINUL T 150, 4-Week Dermal Irritation
in Guiana Pigs

May/18/1992 DIMI
acopat system

SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	F
Dose group	1
Animal	6

General information

Status at necropsy: planned sacrifice
 Date of death: Jun/26/1991
 Day(s) after start exposure: 28
 Day(s) after end exposure: 1
 Sex: female
 Dose group: Lutrol and Lutrol + UVINUL 50%
 Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

UVINUL T 150, 4-Week Dermal Irritation
in Guinea Pigs

May/18/1992 DIMI
acopat system

SINGLE ANIMAL SHEET

	Sacrifice group	F1
	Sex	F
	Dose group	1
	Animal	7

General information

Status at necropsy: planned sacrifice
 Date of death: Jun/26/1991
 Day(s) after start exposure: 28
 Day(s) after end exposure: 1
 Sex: female
 Dose group: Lutrol and Lutrol + UVINUL 50%
 Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

PATHOLOGY REPORT

42H0755/90083

UVINUL T 150, 4-Week Dermal Irritation
in Guiana Pigs

May/18/1992 DIMI
acopat system

SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	F
Dose group	1
Animal	8

General information

Status at necropsy: planned sacrifice
Date of death: Jun/26/1991
Day(s) after start exposure: 28
Day(s) after end exposure: 1
Sex: female
Dose group: Lutrol and Lutrol + UVINUL 50%
Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	F
Dose group	1
Animal	9

General information

Status at necropsy: planned sacrifice
 Date of death: Jun/26/1991
 Day(s) after start exposure: 28
 Day(s) after end exposure: 1
 Sex: female
 Dose group: Lutrol and Lutrol + UVINUL 50%
 Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

SINGLE ANIMAL SHEET

Sacrifice group	F1
Sex	F
Dose group	1
Animal	10

General information

Status at necropsy: planned sacrifice
 Date of death: Jun/26/1991
 Day(s) after start exposure: 28
 Day(s) after end exposure: 1
 Sex: female
 Dose group: Lutrol and Lutrol + UVINUL 50%
 Sacrifice group: Final sacrifice group

Organ weights

No weight parameters required.

Macroscopy

Animal without particular findings.

BASF

Abteilung Toxikologie
Department of Toxicology

D-W6700 Ludwigs-
hafen, FRG

ki-db; 2238-82

MAY 22 1992

REPORT

Study of the Dermal Irritation of

UVINUL T 150

in Guinea Pigs

Application to the intact skin
over 4 weeks

Project No.: 42H0755/90083

VOLUME III OF III

SUPPLEMENT

Testing facility:

Department of Toxicology of
BASF Aktiengesellschaft
D-W6700 Ludwigshafen/Rhein, FRG

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Report; Project No.: 42H0755/90083

ANALYSES OF THE TEST SUBSTANCE IN THE CARRIER

- stability analysis in the carrier

Analytical report

Stability of Uvinul T 150 in Polyethylene Glycol

Anal.Nr. O/91/8410

- 1. Sender: Dr. Kirsch , ZST
- 2. ZST project no: 90/755 for 42 H 0755/90083
- 3. Test substance (name): Uvinul T 150
- 4. Batch number: 19-0518 / 09 / 1990
- 5. Carrier: polyethylen glycol (Lutrol ®)
- 6. Date of receipt of test substance: 20.02.91
- 7. Date of test mixture preparation: 12.03.91
- 8. Storage conditions of test substance before start of test: room temperature
- 9. Storage conditions of test mixture during test: room temperature

10. Analytical method:

- Apparatus: spectrophotometer
- Reagents: polyethylene glycole
dichloromethane
- Sample preparation: 1 g of test substance was mixed with 1 g of carrier. After storage the mixture was dissolved in dichloromethane and diluted to obtain an appropriate absorbance.
- Measuring parameters: cells: 1 cm quartz
wavelength: 308 nm
- Evaluation: The stability was monitored by measuring the spezific absorbance before and after storage.

11. Results:

sample no	given conc.	analytical results (E1%/cm)			
		starting value	time/day	value after	value after
1	50 %	1473	12.03.91	1483	24h
2	50 %	1474	12.03.91	1481	24h

12. Discussion of results:

The test substance is stable in the carrier for at least 24 hours.
The determinations were carried out according to GLP.
Retention of records: archive ZSZ, E 210

S Schmidt 20.03.1991
Signature; date(day.month.year)
(Dr. Schmidt)

ZSZ Analytik

(Analytical Laboratory ZSZ)

STATEMENT OF THE QUALITY ASSURANCE UNIT

ZSZ-No. (No. of analysis)

O/ 91/ 8410

ZST-No. (No. of tox.study/project)

90/ 755 for
42 H 0755/ 90083

Test substance : "Uvinul T 150"

Titel of report : Analytical Report
Stability of Uvinul T 150 in Polyethylene
Glycol.

Name of author : Dr.SCHMIDT

Date of report : 20.03.91 (dd.mm.yy)

The laboratories and the conduct of analytical studies are inspected in regular intervals. Besides these general inspections we inspected the following items concerning this special study.

Findings are reported to analytical study director and analytical management.

Inspection of ...	Date of inspection	Reported to study director and management
<u>Analytical report</u>	} 28.03.91	} 28.03.91
<u>Raw data</u>		

Ludwigshafen

H. W. Schnell
Dr. H. W. SCHNELL

28.03.91
(Date: dd.mm.yy)

Report; Project No.: 42H0755/90083

ANALYSES OF THE TEST SUBSTANCE IN THE CARRIER

- analytical check of the homogeneity
and the concentration in the carrier

Analytical Report
- Concentration control -

1. Sender: Fr. Remmele/H. Dr. Kirsch, ZST, Z 470
 2. ZST project no: 42 H 0755/90083
 3. Test substance (name): Uvinul T 150
 4. Batch number/Manufacturing date: 18586/177, Charge 4, Abl.-Nr. 19-0518
 5. Carrier: Polyethylene glycol (Lutrol E 400)
 6. Date of sample preparation,
time: 29.05.1991
 7. Date of receipt of test substance: 29.05.1991
 8. Storage conditions before start: samples 1, 2: room temperature
samples 3 - 5: freezer
 9. Storage conditions of test
mixture during test: room temperature
 10. Analytical method: HPLC with external standard
- Apparatus: Modular HPLC system for NP chromatography, iso-
cratic mobile phase und UV/VIS detection.
- Reagents: Solution of the test substance of known concen-
tration as standard (1 - 3 mg/100 ml), ethanol
(Merck), n-heptane (Merck), Lutrol E 400 (BASF).
- Sample preparation: The delivered samples (1 ml) were diluted with the
mobile phase in order to correspond with the
calibration range and afterwards injected to the
HPLC system.

Analytical Report
- Concentration control -

Measuring parameters: Column: Nucleosil CN
(5 μ m; 250 x 4 mm; M & N)
Mobile phase: 93 vol-% n-heptane,
7 vol-% ethanol
Flow: 1 ml/min
Injection volume: 20 μ l
Temperature: room temperature
Detection: UV/VIS; λ = 218 nm

Results:

sample no.	expected conc. (g/100 g)	date (d.m.y.) of anal. det.	anal. value (g/100 ml)	anal. value (g/100 ml)	mean value (g/100 ml)
3	50	09.07.1991	49.54	49.66	49.6
4	50	09.07.1991	50.70	49.05	49.9
5	50	09.07.1991	48.74	48.98	48.9

Discussion of results:

Supposed the test samples having a specified weight of 1 g/ml, the concentrations found correspond to about 98 - 100 % of the expected ones.

The concentrations of the test substance in the samples analysed (series 3 to 5) do not differ significantly indicating homogenous distribution within the preparations.

Analytical Report
- Concentration control -

The determinations were carried out according to GLP.
Retention of records: GLP archives, ZSZ, E 210

Dr. Euler *22.07.1991*
Signature date
(Dr. Euler) *Ma* (day, month, year)

STATEMENT OF THE QUALITY ASSURANCE UNIT

ZSZ-No (analysis)

0/ 91/ 30250 - 30253

ZSZ is the code of the analytical department of BASF, Ludwigshafen, Germany.
 ZSZ-No is the ZSZ-code of analysed sample(s).

ZST-No (substance)
 (project)

42 H 0755/90083

Test substance : Uvinul T 150

Title of report : Analytical Report:
 Concentration Control

Author / Stud.dir.: Dr.Euler

Date of report : 18.07.91 (dd.mm.yy)

Date of signature : 22.07.91 (dd.mm.yy)

The laboratories and the conduct of analytical studies are inspected in regular intervals. Besides these general inspections we inspected the following items concerning this special study. - Findings are reported to analytical study director and his management.

Inspection of	Date of inspection	Reported to study director and management
Raw data	} 29.07.91	} 29.07.91
Analytical report		

Ludwigshafen

POIGNÉE
 POIGNÉE C

29.07.91

(Date: dd.mm.yy)

(qstate_1;19.07.91)