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Institute Report No. 332

Approved

**Local Irritation Toxicity Study of
Hypertonic Saline/Dextran 70® and Constituents
in New Zealand White Rabbits**

**Gary M. Zaucha, DVM, CPT, VC
Denzil F. Frost, MS, DVM, CPT, VC
G. David Young, DVM, MAJ, VC
and
Don W. Korte, Jr., PhD, MAJ, MSC**

**MAMMALIAN TOXICOLOGY BRANCH
DIVISION OF TOXICOLOGY**

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December, 1988

Toxicology Series-244

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PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129**

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Local Irritation Toxicity Study of Hypertonic Saline/Dextran 70[®] and Constituents in New Zealand White Rabbits (Toxicology Series 244)--Zauch *et al*

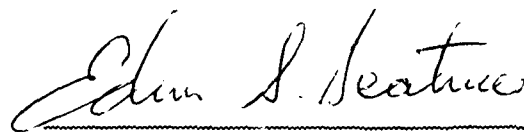
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In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. (AR 360-5)

 19 Dec 88

Edwin S. Beatrice (date)
COL, MC
Commanding

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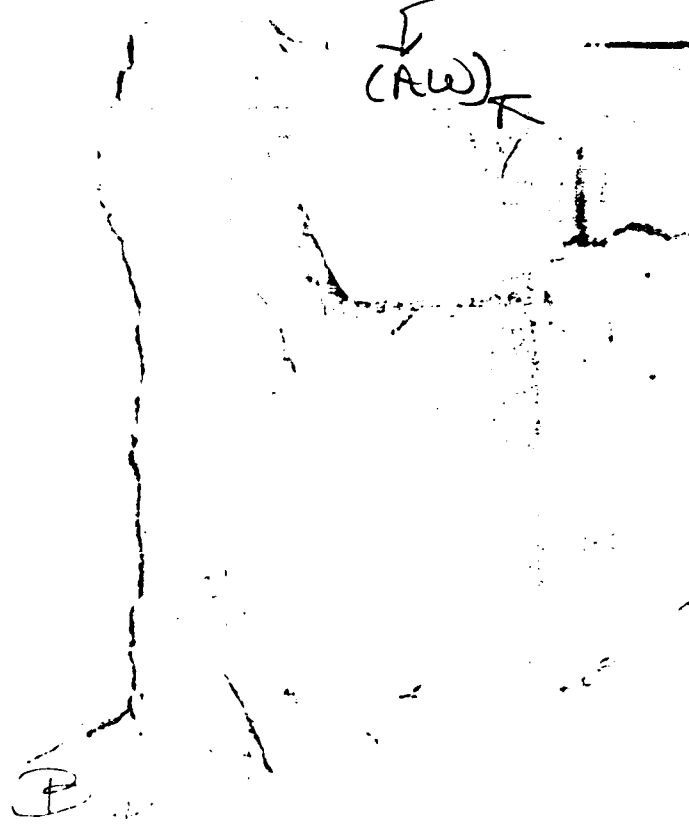
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high incidence of hematoma and bruise formation was observed at the intra-arterial sites (0.2 ml), but these changes were distributed equally among the four dosing solutions. No clinical signs were observed at the intramuscular injection sites (0.5 ml). Only transient injection bleb formation was observed at the subcutaneous sites (0.5 ml). The clinical observations following injection of the test substances were attributed to the perivascular leakage of blood subsequent to needle insertion. Designated subsets of the animals were submitted for necropsy at 4, 24, 48, and 72 hours after the injections for gross and microscopic evaluation of the injection sites. The pathologic findings were also consistent with leakage associated with needle insertion, and were of minimal clinical significance. These results suggest that hypertonic saline/dextran and its constituents are no more irritating than Ringer's lactate when administered by intravenous, paravenous, intra-arterial, intramuscular, or subcutaneous injection.

Keywords:

*Blood Substitutes
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ABSTRACT

The potential for local irritation following intravenous, paravenous, intra-arterial, intramuscular, and subcutaneous injections of hypertonic saline/Dextran 70® was evaluated with solutions of its major constituents, hypertonic saline (7.5%) and Dextran 70® (6%) in normal saline, in male New Zealand White rabbits. Ringer's lactate was also evaluated as a control. Animals were observed for signs of local irritation at 4, 24, 48, and 72 hours after the injections. Intravenous injections (0.5 ml) of hypertonic saline or Dextran 70® resulted in an increased incidence of bruises at the injection site relative to injections of hypertonic saline/Dextran 70® and Ringer's lactate. Paravenous injection (0.1 ml) resulted in the transient formation of injection blebs by all 4 dosing solutions and isolated bruising at the hypertonic saline, hypertonic saline/Dextran 70®, and Dextran 70® sites. A high incidence of hematoma and bruise formation was observed at the intra-arterial sites (0.2 ml), but these changes were distributed equally among the four dosing solutions. No clinical signs were observed at the intramuscular injection sites (0.5 ml). Only transient injection bleb formation was observed at the subcutaneous sites (0.5 ml). The clinical observations following injection of the test substances were attributed to the perivascular leakage of blood subsequent to needle insertion. Designated subsets of the animals were submitted for necropsy at 4, 24, 48, and 72 hours after the injections for gross and microscopic evaluation of the injection sites. The pathologic findings were also consistent with leakage associated with needle insertion, and were of minimal clinical significance. These results suggest that hypertonic saline/dextran and its constituents are no more irritating than Ringer's lactate when administered by intravenous, paravenous, intra-arterial, intramuscular, or subcutaneous injection.

Key Words: Local Irritation, Intravenous Injection, Paravenous Injection, Intra-arterial Injection, Intramuscular Injection, Subcutaneous Injection, Hypertonic Saline/Dextran 70®, Hypertonic Saline, Dextran 70®, New Zealand White Rabbits

PREFACE

TYPE REPORT: Local Irritation Toxicity GLP Study Report

TESTING FACILITY:

US Army Medical Research and Development Command
Letterman Army Institute of Research
Presidio of San Francisco, CA 94129-6800

SPONSOR:

US Army Medical Research and Development Command
Letterman Army Institute of Research
Presidio of San Francisco, CA 94129-6800

PROJECT DIRECTOR: Charles Wade, PhD

PROJECT/WORK UNIT/APC: 3S463807D836/087/TLRO

GLP STUDY NUMBER: 88004

STUDY DIRECTOR: Don W. Korte, Jr., PhD, MAJ, MSC
Diplomate, American Board of Toxicology

PRINCIPAL INVESTIGATOR: Gary M. Zaucha, DVM, CPT, VC

CO-PRINCIPAL INVESTIGATOR: Denzil F. Frost, MS, DVM, CPT, VC
Diplomate, American College of
Veterinary Preventive Medicine

PATHOLOGIST: G. David Young, DVM, MAJ, VC

DATA MANAGER: Yvonne C. LeTellier, BS

REPORT AND DATA MANAGEMENT: A copy of the final report,
study protocols, retired SOPs,
raw data, analytical and
stability data, and an aliquot
of the test compound will be
retained in the LAIR Archives.

TEST SUBSTANCE: Hypertonic Saline/Dextran 70®

INCLUSIVE STUDY DATES: 21 Apr 88 - 10 Jun 88

OBJECTIVE: The objective of this study was to determine
the local irritation potential of hypertonic
saline/Dextran 70® in male New Zealand White
Rabbits.

ACKNOWLEDGMENTS

SPC Dean K. Magnuson, BS, SPC Eric Dahlberg, BS, and SPC Vilmar O. L. Villa provided assistance in dose preparation and administration; SGT Tammie Heineman, SGT Barbara D. Green, and Richard Katona provided data collection, animal care, and facility management; and Synitha Fuller provided secretarial assistance.

SIGNATURES OF PRINCIPAL SCIENTISTS AND MANAGERS
INVOLVED IN THE STUDY

We, the undersigned, declare that GLP study number 88004 was performed under our supervision, according to the procedures described herein, and that this report is an accurate record of the results obtained.

Don W. Korte 14 Dec 88
DON W. KORTE, JR., PhD/DATE
MAJ, MSC
Study Director

Yvonne C. LeTellier 13 Dec 88
YVONNE C. LeTELLIER, BS/DATE
DAC
Data Manager

Gary M. Zaucha 13 Dec 88
GARY M. ZAUCHA, DVM/DATE
CPT, VC
Principal Investigator

Denzil F. Frost 13 Dec 88
DENZIL F. FROST, MS, DVM/DATE
CPT, VC
Co-Principal Investigator

Charles B. Clifford 13 Dec 88
CHARLES B. CLIFFORD, DVM, PhD/DATE
MAJ, VC
Pathologist



DEPARTMENT OF THE ARMY
LETTERMAN ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129-6800

REPLY TO
ATTENTION OF

SGRD-ULZ-QA

13 December 1988

MEMORANDUM FOR RECORD

SUBJECT: GLP Compliance for GLP Study 88004

1. This is to certify that in relation to LAIR GLP Study 88004, the following inspections were made:

27 January 1988	- Protocol Review
11 May 1988	- Animal Receipt/Room Inspection
07 June 1988	- Dosing
07 June 1988	- Necropsy (4-Hour)
08 June 1988	- Observations & Weighing
13 June 1988	- Histology

2. The institute report entitled "Local Irritation Toxicity Study of Hypertonic Saline/Dextran 70 and Constituents in New Zealand Rabbits," Toxicology Series 244, was audited on 21 November 1988.

Carolyn M. Lewis

CAROLYN M. LEWIS, MS
Diplomate, American Board of Toxicology
Chief, Quality Assurance

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Local Irritation Toxicity Study of Hypertonic
Saline/Dextran 70® and Constituents in New Zealand
White Rabbits -- Zaucha et al

INTRODUCTION

During conventional land warfare it has been estimated that 90% of the deaths occur either in the field or en route to a fixed medical treatment facility and that 50% of those deaths occur due to hemorrhage (1). Conventional treatment of hemorrhage has involved infusion of isotonic resuscitation fluids at volumes equivalent to two or three times the volume of blood lost (2). Supplying this volume of resuscitation fluid on the battlefield for treatment of multiple casualties is not feasible.

Hypertonic crystalloid solutions have been used for the past 70 years in the treatment of hemorrhage (3). However, the consensus has been that unless followed by replacement of the lost blood volume, the beneficial effects of treatment with hyperosmotic solutions are transient (4). Recently, the addition of a hyperoncotic colloid, 6% Dextran 70®, to the hypertonic crystalloid, 7.5% saline, has significantly extended 96-hour survival rates compared with those obtained with normal saline or 7.5% saline (5). If the effectiveness of this hypertonic saline/Dextran therapy is verified by clinical trial, it would be a significant advance in the treatment of blood loss due to traumatic injuries.

As with any new treatment regimen, there are potential risks. Low molecular weight dextran may cause bleeding abnormalities and phlebitis or interfere with the cross-matching of blood (6). Hypertonic solutions may cause neurologic abnormalities induced by the rapid increases in osmolalities (7-9) or cardiac arrhythmias induced by the hypokalemia associated with the rapid expansion of extracellular space (2, 10). Consequently, the Division of Toxicology, Letterman Army Institute of Research, was tasked to provide an acute and subchronic toxicity profile of the 7.5% hypertonic saline/6% Dextran 70® resuscitation fluid (HSD). This report describes the results of a local irritation study of HSD in male New Zealand White rabbits.

Objective of Study

The objective of this study was to determine the local irritation potential of hypertonic saline/Dextran 70® in male New Zealand White rabbits.

MATERIALS

Test Substance

Name: Hypertonic saline/Dextran 70®

LAIR Compound Code: TP96

Lot Number: NC 54845

Expiration Date: 31 December 1988

Composition per 100 ml: Dextran 70® 6 g
 sodium chloride 7.5 g
 water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
 Uppsala, Sweden

Test Substance Constituents

Name: Hypertonic saline (7.5%)

LAIR Compound Code: TP98

Lot Number: I 318712

Expiration Date: 31 December 1988

Composition per 100 ml: sodium chloride 7.5 g
 water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
 Uppsala, Sweden

Name: Dextran 70®

LAIR Compound Code: TP95

Lot Number: NE 54941

Expiration Date: 31 May 1989

Composition per 100 ml: Dextran 70® 6 g
 sodium chloride 0.9 g
 water for injection to 100 ml

Source: Pharmacia LEO Pharmaceuticals
 Uppsala, Sweden

Control

Name: Ringer's lactate

LAIR Compound Code: TP97

Lot Number: NC 54847

Expiration Date: 31 December 1988

Composition per 100 ml:	sodium chloride	600 mg
	potassium chloride	30 mg
	calcium chloride	
	dihydrate	20 mg
	sodium lactate	310 mg
	water for injection to	100 ml

Source: Pharmacia LEO Pharmaceuticals
Uppsala, Sweden

Other test substance information is presented in
Appendix A.

Animal Data

Twenty-six male New Zealand White rabbits (Elkhorn Rabbitry, 5265 Starr Way, Watsonville, CA 95076) were assigned to this study. They were identified individually with neck bands (E-Jay International Inc., P.O. Box 1835, Glendora, CA 91740). Two of the rabbits were utilized for quality control necropsy. The animal weights on receipt ranged from 2.0 to 2.6 kg. Additional animal data appear in Appendix B.

Husbandry

Study animals were individually housed in stainless steel, battery-type cages with screened bottoms, in racks equipped with automatically flushing dump tanks. The diet, fed at approximately 150 g per day (refilled each morning), consisted of Certified Purina® Rabbit Chow 5322 (Ralston Purina Company, St. Louis, MO); water, purified by reverse osmosis, was provided by continuous drip from a central line. The animal room temperature and humidity were continuously monitored by hygrothermograph. The temperature was maintained in a range from 20.0°C to 25.6°C, with a relative humidity range of 27 to 65%, with occasional spikes to as high as 84% during room cleaning. The photoperiod was 12 hours of light per day (0600 - 1800 hours).

METHODS

This study was conducted in accordance with FDA guidelines (11) and LAIR SOP-OP-STX-114, "Local Irritation Bioassay" (12).

Group Assignment/Acclimation

Since animals were to be terminated at four different time intervals following dosing, they were randomized into four groups of 6 animals each. Each group was further divided into 2 subgroups (a & b) of 3 animals each. Allocation was accomplished using a computer-based, stratified, weight-biased method. The XYBION Path/Tox AESLCT Animal Allocation Program was used in conjunction with a VAX 750 Computer.

The study animals were acclimated for 46 days before the day of dosing. During this period they underwent a 10 day treatment of sulfaquinoxaline in the drinking water for coccidiosis, were checked daily for signs of illness, and weighed weekly.

Dose Levels, Preparation, and Analysis

The local irritation potential following intravenous, paravenous, intra-arterial, intramuscular, and subcutaneous injections for 2 of the 4 intravenous formulations was evaluated in each animal, 1 solution being injected on the right side and 1 solution on the left (Table 1). The following dose levels were used: intravenous, 0.5 ml at a rate of 0.1 ml/10 seconds; paravenous, 0.1 ml in 10 seconds; intra-arterial, 0.2 ml at a rate of 0.1 ml/10 seconds; intramuscular, 0.5 ml in 10 seconds; and subcutaneous, 0.5 ml in 10 seconds. Solutions were used as supplied by the manufacturer, Pharmacia LEO Pharmaceuticals. Analysis of the dosing solutions was provided by Pharmacia LEO Pharmaceuticals. Additional chemical data are presented in Appendix A.

Test Procedures

The potential for local irritation of hypertonic saline/Dextran 70® (HSD) was evaluated in parallel with solutions of its major constituents, hypertonic saline (HS, 7.5%) and Dextran 70® (DEX 70, 6%) in normal saline, with Ringer's lactate (LRS) serving as the control. The dosing solutions were administered at the following injection sites: intravenous via the marginal ear vein as close to the tip of

Table 1
DOSE GROUPS

Group	Right Side	Left Side
4-hr sacrifice		
1a	HSD	Ringer's lactate
1b	hypertonic saline	Dextran 70®
24-hr sacrifice		
2a	HSD	Ringer's lactate
2b	hypertonic saline	Dextran 70®
48-hr sacrifice		
3a	HSD	Ringer's lactate
3b	hypertonic saline	Dextran 70®
72-hr sacrifice		
4a	HSD	Ringer's lactate
4b	hypertonic saline	Dextran 70®

the ear as feasible, paravenous immediately medial to the marginal ear vein approximately 1 inch proximal to the intravenous site, intra-arterial via the central artery of the ear near the base of the ear, intramuscular in the lateral compartment of the thigh (*m. vastus lateralis*), and subcutaneous in the dorsolateral thoracic region immediately caudal to the scapula. The hair on the injection sites was clipped with Oster clippers (Oster model A5, size 40 blade, Sunbeam Corporation, Milwaukee, WI 53217) on the day before dosing. Injections were made using tuberculin syringes (Becton Dickinson & Co., Rutherford, NJ 07070, Lot No. 7H355) and 23-gauge, 3/4-inch needles (manufactured by Nipro Medical Industries LTD., Tokyo, Japan, for Philadelphia Biologics Center, 1015 Chestnut Street, Philadelphia, PA 19107, Lot No. 82H31G). A 12-inch length of PE-50 polyethylene tubing (Clay Adams, Division of Becton Dickinson & Co., Parsippany, NJ 07054, Lot No. 93131, exp. date 6/92) was used to attach a s cond, hubless needle to the needle on the syringe to facilitate completion of the intravascular injections. Immediately following the injection, digital pressure was

Procedure

Application of the ink was made around each injection site with a marker of indelible ink.

Quarantine and

Animals were quarantined immediately after the injections on Day 0, and then at least twice during the 72-day period. Clinical signs were accomplished in the following manner: 1, 4, 24, 48, and 72 hours after the injections were recorded upon receipt of the animals during the quarantine and observation period, and at necropsy. Gross and microscopic findings of the injection sites and adjacent tissues were recorded.

Necropsy

Within the 72-day study period, all animals were submitted for necropsy. Following sacrifice by barbiturate overdose, animals in Group 1 were submitted for necropsy 4 hours after completion of the injections, Group 2 was submitted to necropsy 24 hours after the injections, Group 3 was submitted to necropsy 48 hours after the injections, and Group 4 was submitted 72 hours after the injections.

Statistical Analysis

Clinical signs were tabulated by groups. The means and standard errors for the body weights for each group were calculated. The body weight data was subjected to a one-way analysis of covariance using dosing weight as the covariate and dose group as the factor of interest for each sacrifice day (12). Gross and microscopic pathology findings were described for each animal and tabulated by groups.

Duration of Study

Appendix C is a complete listing of historical events.

Changes/Deviations

Due to the short duration of the study and the need to keep the animals' ears free of extraneous marks, study animals were identified by neck bands rather than by ear tattoo.

Body weight determinations scheduled for 6 June 1988 were performed on 7 June 1988.

Coccidiosis was diagnosed during the quarantine period (13 May 1988). A 0.1% solution of sulfaquinoxaline (MSD AG Vet, Division of Merck Co., Inc., Lot No. EZA-715) in the drinking water was administered from 13 May 1988 to 22 May 1988 to all study animals.

Group 1a (HSD right side and LRS left side) had only 2 animals instead of 3 because animal 88F00114 died on 5 Jun 88, 2 days prior to dosing.

The area around each injection site was marked with ink immediately after completion of each injection rather than at the time of shaving of the sites.

It is believed that these changes had no adverse effects on the results of this study.

Storage of Raw Data and Final Report

A copy of the final report, study protocol, raw data, retired SOPs, and an aliquot of the test compound will be retained in the Letterman Army Institute of Research Archives.

RESULTS

Clinical Observations

The clinical observations included bruises, hematomas, subcutaneous blebs, nodules, and erythema of the injection sites.

The most frequently observed sign at the intravenous injection site was the presence of bruises (18 of 46). The greatest incidence of bruising was observed at the HS and DEX 70 sites (7 of 12 and 5 of 12, respectively). Bruises developed within 24-48 hours and appeared to decrease in size over time. Hematomas were observed at the HS and DEX 70 sites (1 of 12 and 2 of 12, respectively) 4 hours after injection. The hematomas resolved into bruises by 24 hours.

The most frequently observed sign at the paravenous injection site was the presence of injection blebs (6 of 46) immediately following injection. The majority of blebs resolved within 4 hours without residual effects. Bruising was observed at the HS, HSD, and DEX 70 sites (2 of 12, 1 of 11, and 1 of 12, respectively). The majority of the bruises

Results of Study

were observed by 24 hours. The persistence of bruising did not appear to be compound related.

Hematoma formation occurred at the intra-arterial sites (37 of 46 sites) and at equal frequency among dosing solutions. Hematomas were observed immediately following injection at all dosing sites, with 5 of 37 animals having hematomas at the intra-arterial sites. Bruising was observed at the intra-arterial sites by 4 hours after dosing (34 of 46 sites). Bruising was not compound related. The formation of indurated nodule formation was observed at the intra-arterial sites. The nodules were observed at 72 hours and were formed as a result of the resolution of bruises. The presence of nodules could not be correlated to a specific dosing solution. One incidence of myeloma was observed in the LRS group.

No clinical signs were observed at the intramuscular injection sites.

Injection blebs were observed at the subcutaneous injection sites (11 of 46) immediately following injection, with the majority being observed at the HS and DEX 70 sites (5 of 12 at each respective site). All blebs had resolved by 24 hours.

Table 2 contains a summary of clinical observations. Appendix D contains individual animal histories.

Body Weights

Animal body weights were not significantly ($p \leq 0.05$) affected by dosing. Table 3 presents the mean body weights by group. Appendix E contains individual weight tables.

Necropsy Findings

No gross or microscopic pathological lesions attributable to the test compound or its constituents were reported. The Veterinary Pathologist's report is presented in Appendix F.

Table 2
INJECTION SITE EVALUATION*

Time (hours)	HSD				LRS				HS				DEX 70					
	H	B	L	N	E	n	H	B	L	N	E	n	H	B	L	N	E	n
Intravenous																		
0	-	-	-	-	-	11	-	-	-	-	-	11	1	-	-	-	-	12
4	-	-	-	-	-	11	-	-	-	-	-	11	1	3	-	-	-	12
24	-	1	-	-	-	9	-	1	-	-	-	9	-	5	-	-	-	9
48	-	1	-	-	-	6	-	3	-	-	-	6	-	3	-	-	-	6
72	-	1	-	-	-	3	-	-	-	-	-	3	-	1	-	-	-	3
Incidence§-	3	-	-	-	-	11	-	3	-	-	-	11	1	7	-	-	-	12
													2	5	-	-	-	12

* Clinical Observation Key

Values indicate incidence of observed sign.

H = hematoma

B = bruise

L = bleb

N = nodule

E = erythema

n = number of animals in group

§ = total number of injection sites exhibiting the sign at least once during the study period.

Table 2 (cont.): INJECTION SITE EVALUATION

Time (hours)	HSD			LRS			HS			DEX 70		
	H	B	L	H	B	L	H	B	L	H	B	L
	n	E	n	n	E	n	n	E	n	n	E	n
Intramuscular												
0	-	-	-	-	-	-	-	-	-	-	-	-
	11			11			12			12		
4	-	-	-	-	-	-	-	-	-	-	-	-
	11			11			12			12		
24	-	-	-	-	-	-	-	-	-	-	-	-
	9			9			9			9		
48	-	-	-	-	-	-	-	-	-	-	-	-
	6			6			6			6		
72	-	-	-	-	-	-	-	-	-	-	-	-
	3			3			3			3		
Total	-	-	-	-	-	-	-	-	-	-	-	-
	11			11			12			12		
Subcutaneous												
0	-	-	2	-	-	11	-	-	5	-	-	12
	11			11			12			12		
4	-	-	1	-	-	11	-	-	1	-	-	12
	11			11			12			12		
24	-	-	-	-	-	9	-	-	-	-	-	9
	9			9			9			9		
48	-	-	-	-	-	6	-	-	-	-	-	6
	6			6			6			6		
72	-	-	-	-	-	3	-	-	-	-	-	3
	3			3			3			3		
Total	-	-	2	-	-	11	-	-	5	-	-	12
	11			11			12			12		

MEMORANDUM FOR THE DIRECTOR, FBI (100-371101)

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DISCUSSION

The clinical observations following the intravenous, intramuscular, intra-arterial, intramuscular, and subcutaneous injections of hypertonic saline/dextran, hypertonic saline, Dextran 70[®], and Ringer's lactate could all be attributed to the perivascular leakage of blood subsequent to needle insertion. Following intravenous injection of HS and DEX 70, bleeding was observed at an increased incidence relative to injections of HSD or LRS. However, the majority of bruises had resolved by 72 hours in those animals observed through the 72-hour study period. The increased incidence of signs at the intra-arterial sites was due to the greater arterial blood pressure relative to the pressure at other injection sites, which resulted in increased extravasation of blood following intra-arterial injections. The occurrence of blebs following subcutaneous and paravenous injections were considered normal sequela to injection technique. None of the test solutions caused clinical signs following intramuscular injection.

The myofibrillar muscle degeneration and associated inflammation observed grossly and microscopically at necropsy were the consequence of either hemorrhage or the introduction of foreign material, i.e. fur, introduced as a result of needle insertion. The muscle degeneration and inflammation were considered to be of little clinical significance and were expected to heal with no residual morphological or functional alteration.

These results suggest that hypertonic saline/dextran and its constituents are no more irritating than Ringer's lactate when administered by injection.

CONCLUSION

Under the conditions, hypertonic saline/Dextran 70[®], and its constituents, hypertonic saline and Dextran 70[®], were no more irritating than Ringer's lactate under the conditions of this study.

RECEIVED

TO THE HONORABLE SECRETARY OF THE
NAVY
WASHINGTON, D. C.

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REFERENCES (cont.)

12. Local Irritation Bioassay. LAIR Standard Operating Procedure OP-STX-114, Letterman Army Institute of Research, Presidio of San Francisco, CA, 5 February 1988.
13. Dixon DJ, ed. BMDP statistical software. Berkeley: University of California Press, 1981: 555-573.

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Page 1004. Individual Animal Histories.....	24
Page 1005. Individual Body Weights.....	49
Page 1006. Pathology Report.....	51

Appendix A: CHEMICAL DATA



Pharmacia

CERTIFICATE OF ANALYSIS 1988-12-19

Product

6 % DEXTRAN 70 IN 7.5 %
SODIUM CHLORIDE INJECTION

Charge No. NC 54845

Inherent viscosity	27 ml/g
Absorbance (375 nm, 10 mm)	0,006
pH	4,6
Heavy metals	< 5 ppm
Sodium chloride	74,7 g/1000 ml
Dextran 70	60 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

Pharmacia AB
Analytical Chemistry Department

Pharmacia (Signed 1988)

Elisabet Fransson
Elisabet Fransson

Postal address	Telephone	Cables	Telex	Telecopier
Pharmacia AB				
S-751 82 Uppsala	Nat 018 18 30 03	pharmacia	78027	Nat 018 15 41 35
Sweden	Int +46 18 18 30 00	uppsala	pharmup s	Int +46 18 15 41 35

Appendix A (cont.): CHEMICAL DATA



Pharmacia

Product

CERTIFICATE OF ANALYSIS

7.5 % SODIUM CHLORIDE

Charge No. 11-18

Identification	passed test
Absorbance	0.000
pH	6.0
Heavy metals	< 5 ppm
Sodium chloride	75.0 g/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for biological trials.

Pharmacia AB
Analytical Chemistry Department

Elisabet Fransson
Elisabet Fransson

Postal address
Pharmacia AB
S-751 82 Uppsala
Sweden

Telephone
Nat 018 16 30 00
Int +46 18 16 30 00

Cables
pharmacia
Uppsala

Telex
20 022
PHARMAB S

File number
Date 1981-11-18
Lab. No. 11-18

Appendix A (cont.): CHEMICAL DATA



Pharmacia

Certificate of analysis

Name: **MACRODEX** 60 mg/ml in Normal saline

Item No.: 10-4510-00

Lot No.: NE 54941

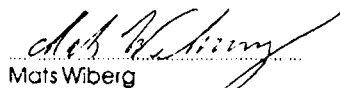
Test		Result	Tolerance limit	Method
Inherent viscosity	ml/g	26	25 - 28	03700
Colour		0.01	Max. 0.04	03811
pH		4.9	4.0 - 7.0	USP XX p. 968
Heavy metals ppm		< 5	Max. 5	USP XX p. 909
Assay for				
- sodium chloride	g/1000ml	8.88	8.10 - 9.90	02355
- dextran 70	g/1000ml	59	54 - 66	02356
Sterility		Passed test	To pass test	02885
Pyrogens		Passed test	To pass test	02983

The identity is assured through strict adherence to established GMP rules throughout the manufacturing procedures.

Released for sale: 1987-05-25

Pharmacia AB

Quality Control Department



Mats Wiberg

M09

Pharmacia AB
S-751 82 UPPSALA
Sweden

Telephone
Nat 018 - 163000
Int +46 18 163000

Telex
76027 pharmus

Telefax
Nat 018 - 154135
Int +46 18 154135

Appendix A (cont.): CHEMICAL DATA



Pharmacia

CERTIFICATE OF ANALYSIS 1989-12-10

Product

LACTATED RINGER'S INJECTION

Charge No. NC 54847

pH	5,8
Heavy metals	< 5 ppm
Sodium	127 mmol/1000 ml
Potassium	3,91 mmol/1000 ml
Calcium	1,30 mmol/1000 ml
Chloride	105,5 mmol/1000 ml
Lactate	27,2 mmol/1000 ml
Particulate matter	passed test
Sterility	passed test
Pyrogens	passed test

Released for clinical trials.

Pharmacia AB
Analytical Chemistry Department

450/1
Pharmacia Upplands 1988

Elisabet Fransson
Elisabet Fransson

Postal address
Pharmacia AB
S-751 82 Uppsala
Sweden

Telephone
Net 018-16 30 00
Int +46 18 16 30 00

Cables
pharmacia
uppsala

Telex
76027
pharmup s

Telecopier
Net 018-16 41 36
Int +46 18 16 41 35

Appendix B: ANIMAL DATA

Species: *Cyctolagus cuniculus*

Strain: New Zealand White

Source: Elkhorn Rabbitry
5265 Starr Way
Watsonville, CA 95076

Sex: Male

Date of birth: 21 Jan 88
22 Jan 88
1 Feb 88
5 Feb 88

Animal handling: Weight bias, stratified animal
allocation (KYBION Medical Systems PATH/TOX AESLCT Animal
Allocation program)

Animals in each group:	1a	2
	1b	3
	2a	3
	2b	3
	3a	3
	3a	3
	4a	3
	4b	3

Condition of animals at start of study: Normal

Body weight range at dosing: 2.4 - 3.9 kg

Identification procedures: Neck band

Animal conditioning: Quarantine/acclimation 21 April 1988
to 5 June 1988

Justification: The laboratory rabbit is the standard
laboratory model for local irritation studies and is accepted
by all regulatory agencies.

Appendix C: HISTORICAL LISTING OF STUDY EVENTS

<u>Date</u>	<u>Event</u>
21 Apr 88	Animals arrived at LAIR. They were observed for illness and caged in the GLP Suite. Twenty-six animals were assigned to the study.
22, 29 Apr, 6, 13, 20, 27 May, 3, 7 Jun 88	Animals were weighed.
22 Apr 88 - 9 Jun 88	Animals were observed twice daily.
2 May 88	Quality control animals were submitted for necropsy.
6 Jun 88	Animals were randomized into groups.
6 Jun 88	Animals were shaved.
7 Jun 88	Animals were dosed between 0900 and 1230 hours. Observations and inspection of injection sites were conducted immediately after dosing and four hours later. Group 1 animals were weighed and submitted for necropsy four hours after dosing was completed.
8 Jun 88	Animals were observed in a.m. and p.m. for clinical signs. Injection sites were inspected 24 hours after dosing was completed. Group 2 animals were weighed and submitted for necropsy 24 hours after dosing was completed.
9 Jun 88	Animals were observed in a.m. and p.m. for clinical signs. Injection sites were inspected 48 hours after dosing was completed. Group 3 animals were weighed and submitted for necropsy 48 hours after dosing was completed.

Appendix C (cont.): HISTORICAL LISTING
OF STUDY EVENTS

<u>Date</u>	<u>Event</u>
16 Jun 88	Animals were observed in a.m. and p.m. for clinical signs. Injection sites were inspected 72 hours after dosing was completed. Group 4 animals were weighed and submitted for necropsy 72 hours after dosing was completed.

Appendix D: INDIVIDUAL ANIMAL HISTORIES

Clinical Observation Severity Code

<u>Severity</u>	<u>Lesion Size (mm)</u>
1	≤ 3
2	4 - 6
3	7 - 9
4	10 - 12
5	> 12

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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PRINTED: 23-NOV-88
PAGE: 1

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00095	DAY OF DEATH: 1	STATUS: NORMAL, EUTHANIZED	CLINICAL OBSERVATIONS	TERMINAL BODY WEIGHT: 3.4 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:07	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	13:06	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	2

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

PRINTED: 23-NOV-88
 PAGE: 2

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00114	DAY OF DEATH: -2	STATUS: FOUND DEAD	CLINICAL OBSERVATIONS	TERMINAL BODY WEIGHT:	SEVERITY
DATE	DAY/WEEK OF STUDY	TIME OF DAY	OBSERVATIONS AND COMMENTS		
05-JUN-88	-2/-1	08:00	NONE		

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

PRINTED: 23 NOV 88
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STUDY START DATE: 07 JUN 88

ANIMAL: 88F00109	DAY OF DEATH: 1	STATUS: NORMAL, EUTHANIZED	CLINICAL OBSERVATIONS AND COMMENTS	TERMINAL BODY WEIGHT: 3.4 (KGS)	SEVERITY
DATE	DAY/WEEK OF STUDY	TIME OF DAY			
07 JUN 88	1/1	11:08	LEFT INTRA-ARTERIAL SITE / HEMATOMA		2
07 JUN 88	1/1	13:12	LEFT INTRA-ARTERIAL SITE / HEMATOMA		1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
PAGE: 4

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00101	DAY OF DEATH: 1	STATUS: NORMAL, EUTHANIZED	CLINICAL OBSERVATIONS	TERMINAL BODY WEIGHT: 2.9 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:11	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	13:20	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	3
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	2

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

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STUDY START DATE: 07 JUN 88

ANIMAL: 88F00110	DAY OF DEATH: 1	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.5 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	SEVERITY
07 JUN 88	1/1	11:14	1
07 JUN 88	1/1	14:03	2
CLINICAL OBSERVATIONS AND COMMENTS			
LEFT INTRA-ARTERIAL SITE / HEMATOMA			
RIGHT INTRA-ARTERIAL SITE / HEMATOMA			
LEFT INTRAVENOUS SITE / HEMATOMA			
LEFT INTRA-ARTERIAL SITE / HEMATOMA			

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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STUDY START DATE: 07-JUN-88

ANIMAL: 88F00108	DAY OF DEATH: 1	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.6 (KGS)	
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:30	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT PARAVENOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB LEFT PARAVENOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT INTRAVENOUS SITE / HEMATOMA LEFT INTRA-ARTERIAL SITE / HEMATOMA	4 1 3 4 1 4 1 1
07-JUN-88	1/1	13:32		

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
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STUDY START DATE: 07-JUN-88

ANIMAL: 88F00107	DAY OF DEATH: 2	STATUS: NORMAL, EUTHANIZED	CLINICAL OBSERVATIONS	TERMINAL BODY WEIGHT: 3.7 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:33	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	14:30	RIGHT INTRA-ARTERIAL SITE / BRUISE	2
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
			RIGHT INTRA-ARTERIAL SITE / BRUISE	1
08-JUN-88	2/1	10:37	RIGHT INTRA-ARTERIAL SITE / BRUISE	2
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00104	DAY OF DEATH: 2	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.4 (KGS)
DATE	DAY/WEEK OF STUDY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:36 LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	3 2 4
07-JUN-88	1/1	14:31 RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	3 3
08-JUN-88	2/1	12:48 LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	3 5 3

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00100	DAY OF DEATH: 2	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.7 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS
07-JUN-88	1/1	11:39	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE
07-JUN-88	1/1	14:32	
08-JUN-88	2/1	10:33	
			SEVERITY
			3
			2
			3
			3
			5
			4
			5
			4

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

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ANIMAL: 88F00111 DAY OF DEATH: 2 STATUS: NORMAL, EUTHANIZED STUDY START DATE: 07-JUN-88 TERMINAL BODY WEIGHT: 3.4 (KGS)

DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:42	NORMAL / NO SIGNIFICANT FINDINGS	-
07-JUN-88	1/1	14:47	RIGHT INTRAVENOUS SITE / BRUISE	2
			LEFT INTRAVENOUS SITE / BRUISE	1
08-JUN-88	2/1	10:45	RIGHT INTRAVENOUS SITE / BRUISE	1
			LEFT INTRAVENOUS SITE / BRUISE	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00093	DAY OF DEATH: 2	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.2 (KGS)	
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	11:45	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRAVENOUS SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRAVENOUS SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRAVENOUS SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	2 1 1 2 1 1 1 1 1 1 2 1
07-JUN-88	1/1	14:49		
08-JUN-88	2/1	10:47		

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00094	DAY OF DEATH: 2	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.1 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS
07-JUN-88	1/1	11:47	RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT PARAVENOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE
07-JUN-88	1/1	14:50	
08-JUN-88	2/1	10:49	

SEVERITY

2
1
1
2
1
1
1
1
1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
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STUDY START DATE: 07-JUN-88

ANIMAL: 88F00092	DAY OF DEATH: 3	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.4 (KGS)	
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:45	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:31	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	5
08-JUN-88	2/1	10:53	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	5
09-JUN-88	3/1	12:24	RIGHT INTRA-ARTERIAL SITE / BRUISE	4
			LEFT INTRA-ARTERIAL SITE / HEMATOMA / BRUISE	2
				4

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
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STUDY START DATE: 07-JUN-88

ANIMAL: 88F00105	DAY OF DEATH: 3	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.8 (KGS)	
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:46	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:32	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
08-JUN-88	2/1	10:53	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
08-JUN-88	2/1	10:53	LEFT INTRA-ARTERIAL SITE / BRUISE	5
09-JUN-88	3/1	12:27	RIGHT INTRA-ARTERIAL SITE / BRUISE	3
09-JUN-88	3/1	12:27	RIGHT INTRAVENOUS SITE / BRUISE	2
09-JUN-88	3/1	12:27	LEFT INTRA-ARTERIAL SITE / BRUISE	1
09-JUN-88	3/1	12:27	LEFT INTRAVENOUS SITE / BRUISE	2
09-JUN-88	3/1	12:27	LEFT INTRA-ARTERIAL SITE / BRUISE	1
09-JUN-88	3/1	12:27	LEFT INTRAVENOUS SITE / BRUISE	5

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
PAGE: 15

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00112	DAY OF DEATH: 3	STATUS: NORMAL, EUTHANIZED	CLINICAL OBSERVATIONS AND COMMENTS	TERMINAL BODY WEIGHT: 3.1 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:47	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:36	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
08-JUN-88	2/1	10:53	RIGHT INTRA-ARTERIAL SITE / BRUISE	2
08-JUN-88	2/1	12:28	LEFT INTRA-ARTERIAL SITE / BRUISE	2
09-JUN-88	3/1		RIGHT INTRA-ARTERIAL SITE / BRUISE	1
09-JUN-88	3/1		LEFT INTRA-ARTERIAL SITE / BRUISE	1
09-JUN-88	3/1		LEFT INTRAVENOUS SITE / BRUISE	1
09-JUN-88	3/1		LEFT INTRA-ARTERIAL SITE / BRUISE	1

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
PAGE: 16

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00102	DAY OF DEATH: 3	STATUS: NORMAL, EUTHANIZED	CLINICAL OBSERVATIONS AND COMMENTS	TERMINAL BODY WEIGHT: 3.4 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:54	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	2
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:38	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	4
08-JUN-88	2/1	11:09	RIGHT INTRA-ARTERIAL SITE / BRUISE	3
			RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	1
09-JUN-88	3/1	12:36	LEFT INTRA-ARTERIAL SITE / BRUISE	2
			RIGHT INTRA-ARTERIAL SITE / BRUISE	2
			RIGHT INTRA-ARTERIAL SITE / BRUISE	2
			LEFT INTRA-ARTERIAL SITE / BRUISE	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	2

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
PAGE: 17

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00099	DAY OF DEATH: 3	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.5 (KGS)	
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS & COMMENTS	SEVERITY
07-JUN-88	1/1	12:56	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE	3 1 2 1 5 3 1 4 1 4 1 3
07-JUN-88	1/1	16:39		
08-JUN-88	2/1	11:05		
09-JUN-88	3/1	12:32		

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

PRINTED: 23-NOV-88
 PAGE: 18

ANIMAL: 88F00115 DAY OF DEATH: 3 STATUS: NORMAL, EUTHANIZED STUDY START DATE: 07-JUN-88 TERMINAL BODY WEIGHT: 3.1 (KGS)

DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:57	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:48	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
08-JUN-88	2/1	11:06	LEFT INTRA-ARTERIAL SITE / BRUISE	5
			RIGHT INTRA-ARTERIAL SITE / BRUISE	3
09-JUN-88	3/1	12:33	LEFT INTRA-ARTERIAL SITE / BRUISE	3
			RIGHT INTRA-ARTERIAL SITE / BRUISE	4
			LEFT INTRA-ARTERIAL SITE / BRUISE	5

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23 NOV 88
PAGE: 19

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00091	DAY OF DEATH: 4	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.7 (KGS)	
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:48	RIGHT INTRA-ARTERIAL SITE / HEMATOMA LEFT PARAVENOUS SITE / SUBCUTANEOUS BLEB	1
07-JUN-88	1/1	16:58	LEFT INTRA-ARTERIAL SITE / HEMATOMA RIGHT INTRA-ARTERIAL SITE / BRUISE	1
08-JUN-88	2/1	10:54	LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE	1
09-JUN-88	3/1	12:29	LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE	3
10-JUN-88	4/1	13:42	LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / NODULE LEFT INTRA-ARTERIAL SITE / NODULE	5

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

PRINTED: 23-NOV-88
PAGE: 20

STUDY START DATE: 07-JUN-88

ANIMAL: 88f00096		DAY OF DEATH: 4	STATUS: NORMAL, EUTHANIZED		TERMINAL BODY WEIGHT: 2.6 (KGS)	
DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS		SEVERITY	
07-JUN-88	1/1	12:49	RIGHT PARAVENOUS SITE / SUBCUTANEOUS BLEB		1	
07-JUN-88	1/1	17:00	RIGHT INTRA-ARTERIAL SITE / HEMATOMA		1	
08-JUN-88	2/1	10:59	LEFT INTRA-ARTERIAL SITE / BRUISE		4	
09-JUN-88	3/1	12:29	RIGHT INTRA-ARTERIAL SITE / ERYTHEMA		1	
10-JUN-88	4/1	13:45	LEFT INTRA-ARTERIAL SITE / BRUISE		4	
			RIGHT INTRA-ARTERIAL SITE / ERYTHEMA		1	
			LEFT INTRA-ARTERIAL SITE / BRUISE		5	
			NONE		1	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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ANIMAL: 88F00106 DAY OF DEATH: 4 STATUS: NORMAL, EUTHANIZED STUDY START DATE: 07-JUN-88 TERMINAL BODY WEIGHT: 4.0 (KGS)

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004

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DATE	DAY/WEEK OF STUDY	TIME OF DAY	C L I N I C A L OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:49	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	17:01	LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
			RIGHT PARAVENOUS SITE / BRUISE	5
			RIGHT INTRA-ARTERIAL SITE / BRUISE	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	4
08-JUN-88	2/1	11:00	RIGHT PARAVENOUS SITE / BRUISE	5
			RIGHT INTRA-ARTERIAL SITE / BRUISE	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	4
09-JUN-88	3/1	12:30	RIGHT PARAVENOUS SITE / BRUISE	5
			RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	1
10-JUN-88	4/1	13:49	RIGHT INTRA-ARTERIAL SITE / BRUISE	4
			RIGHT INTRA-ARTERIAL SITE / BRUISE	3
			RIGHT INTRA-ARTERIAL SITE / BRUISE	3
			RIGHT INTRA-ARTERIAL SITE / NODULE	1
			LEFT INTRA-ARTERIAL SITE / BRUISE	3
10-JUN-88	4/1	14:00	LEFT INTRA-ARTERIAL SITE / NODULE	1
			NONE	

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

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PRINTED: 23-NOV-88
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00103		DAY OF DEATH: 4	STATUS: NORMAL, EUTHANIZED	TERMINAL BODY WEIGHT: 3.2 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	C L I N I C A L O B S E R V A T I O N S	SEVERITY
07-JUN-88	1/1	12:58	RIGHT INTRA-ARTERIAL SITE / HEMATOMA	1
			LEFT INTRA-ARTERIAL SITE / HEMATOMA	1
07-JUN-88	1/1	16:52	RIGHT INTRAVENOUS SITE / BRUISE	1
			RIGHT INTRA-ARTERIAL SITE / BRUISE	3
			LEFT INTRA-ARTERIAL SITE / BRUISE	4
08-JUN-88	2/1	11:06	RIGHT INTRAVENOUS SITE / BRUISE	1
			RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	4
09-JUN-88	3/1	12:34	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	4
10-JUN-88	4/1	14:08	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	5

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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ANIMAL: 88F00116 DAY OF DEATH: 4 STATUS: NORMAL, EUTHANIZED STUDY START DATE: 07-JUN-88 TERMINAL BODY WEIGHT: 3.6 (KGS)

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004 PRINTED: 23-NOV-88
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DATE	DAY/WEEK OF STUDY	TIME OF DAY	CLINICAL OBSERVATIONS AND COMMENTS	SEVERITY
07-JUN-88	1/1	12:59	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	2
			RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB	2
07-JUN-88	1/1	16:53	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	4
08-JUN-88	2/1	11:07	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			LEFT INTRA-ARTERIAL SITE / BRUISE	5
09-JUN-88	3/1	12:34	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			RIGHT PARAVENOUS SITE / BRUISE	5
			RIGHT INTRA-ARTERIAL SITE / BRUISE	4
			LEFT INTRA-ARTERIAL SITE / BRUISE	1
10-JUN-88	4/1	14:10	RIGHT INTRA-ARTERIAL SITE / BRUISE	5
			RIGHT PARAVENOUS SITE / BRUISE	5
			RIGHT INTRA-ARTERIAL SITE / BRUISE	4
			LEFT INTRA-ARTERIAL SITE / BRUISE	5

Appendix D (cont.): INDIVIDUAL ANIMAL HISTORIES

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004

STUDY START DATE: 07-JUN-88

ANIMAL: 88F00098	DAY OF DEATH: 4	STATUS: NORMAL, EUTHANIZED	CLINICAL OBSERVATIONS	TERMINAL BODY WEIGHT: 3.2 (KGS)
DATE	DAY/WEEK OF STUDY	TIME OF DAY	SEVERITY	
07-JUN-88	1/1	13:00	LEFT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT PARAVENOUS SITE / SUBCUTANEOUS BLEB RIGHT INTRA-ARTERIAL SITE / HEMATOMA RIGHT SUBCUTANEOUS SITE / SUBCUTANEOUS BLEB RIGHT PARAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT PARAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRAVENOUS SITE / BRUISE LEFT PARAVENOUS SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE RIGHT PARAVENOUS SITE / BRUISE RIGHT INTRA-ARTERIAL SITE / BRUISE LEFT INTRA-ARTERIAL SITE / BRUISE NONE	2 2 1 2 1 1 4 2 1 1 5 1 1 1 1 4 5
07-JUN-88	1/1	16:55		
08-JUN-88	2/1	11:08		
09-JUN-88	3/1	12:35		
10-JUN-88	4/1	14:06		

Appendix E: BODY WEIGHTS (KG)

Animal	Group/ Subgroup	Day of Study									
		-46	-39	-32	-25	-18	-11	-4	0	1	2 3
88F00095	1/a	2.48	2.69	2.74	3.06	2.95	3.14	3.29	3.38		
88F00114	1/a	2.45	2.64	2.50	2.30	2.55	2.84	2.81			
88F00109	1/a	2.52	2.61	2.63	2.88	3.09	3.21	3.45	3.39		
Mean		2.48	2.65	2.62	2.75	2.86	3.06	3.18	3.39		
Std Dev		0.03	0.04	0.12	0.39	0.28	0.20	0.33	0.01		
SEM		0.02	0.02	0.07	0.23	0.16	0.11	0.19	0.01		
88F00107	2/a	2.48	2.63	2.77	3.16	3.23	3.50	3.62	3.67	3.65	
88F00104	2/a	2.10	2.50	2.54	2.75	2.96	3.16	3.27	3.29	3.36	
88F00100	2/a	2.53	2.85	2.77	3.06	3.16	3.46	3.67	3.63	3.71	
Mean		2.37	2.66	2.69	2.99	3.12	3.37	3.52	3.53	3.57	
Std Dev		0.24	0.18	0.13	0.21	0.14	0.19	0.22	0.21	0.19	
SEM		0.14	0.10	0.08	0.12	0.08	0.11	0.13	0.12	0.11	
88F00092	3/a	2.35	2.63	2.80	3.00	2.92	3.13	3.27	3.33		3.36
88F00105	3/a	2.26	2.45	2.58	2.98	3.11	3.53	3.62	3.68		3.76
88F00112	3/a	2.28	2.35	2.53	2.68	2.70	2.91	3.13	3.11		3.06
Mean		2.30	2.47	2.64	2.89	2.91	3.19	3.34	3.37		3.39
Std Dev		0.05	0.14	0.14	0.18	0.21	0.31	0.25	0.29		0.35
SEM		0.03	0.08	0.08	0.10	0.12	0.18	0.15	0.17		0.20
88F00091	4/a	2.30	2.50	2.70	2.88	3.07	3.39	3.40	3.60		3.66
88F00096	4/a	2.55	2.63	2.73	2.85	2.21	2.08	2.29	2.40		2.59
88F00106	4/a	2.46	2.78	2.86	3.21	3.39	3.67	3.84	3.89		3.99
Mean		2.44	2.64	2.76	2.98	2.89	3.05	3.18	3.30		3.41
Std Dev		0.13	0.14	0.08	0.20	0.61	0.85	0.80	0.79		0.73
SEM		0.07	0.08	0.05	0.12	0.35	0.49	0.46	0.46		0.42

Appendix E (cont.): BODY WEIGHTS (KG)

Animal	Group/ Subgroup	Day of Study										
		-46	-39	-32	-25	-18	-11	-4	0	1	2	3
88F00101	1/b	2.29	2.54	2.62	2.82	2.70	2.92	3.07	2.89			
88F00110	1/b	2.18	2.53	2.73	2.96	3.13	3.34	3.46	3.45			
88F00108	1/b	2.34	2.71	2.90	3.19	3.32	3.60	3.77	3.59			
Mean		2.27	2.59	2.75	2.99	3.05	3.29	3.43	3.31			
Std Dev		0.08	0.10	0.14	0.19	0.32	0.34	0.35	0.37			
SEM		0.05	0.06	0.08	0.11	0.18	0.20	0.20	0.21			
88F00111	2/b	2.28	2.65	2.79	2.80	3.00	3.24	3.40	3.38	3.38		
88F00093	2/b	2.15	2.41	2.36	2.52	2.73	2.92	3.11	3.16	3.21		
88F00094	2/b	2.30	2.16	2.53	2.78	2.38	2.62	2.88	3.05	3.09		
Mean		2.24	2.41	2.56	2.70	2.70	2.93	3.13	3.20	3.23		
Std Dev		0.08	0.25	0.22	0.16	0.31	0.31	0.26	0.17	0.15		
SEM		0.05	0.14	0.12	0.09	0.18	0.18	0.15	0.10	0.08		
88F00102	3/b	2.20	2.48	2.61	2.92	2.99	3.31	3.34	3.46	3.40		
88F00099	3/b	2.44	2.70	2.72	3.01	3.17	3.34	3.38	3.46	3.49		
88F00115	3/b	2.25	2.48	2.44	2.84	2.77	3.04	3.12	3.26	3.15		
Mean		2.30	2.55	2.59	2.92	2.98	3.23	3.28	3.39	3.35		
Std Dev		0.12	0.13	0.14	0.08	0.20	0.16	0.14	0.12	0.18		
SEM		0.07	0.07	0.08	0.05	0.12	0.10	0.08	0.07	0.10		
88F00103	4/b	2.02	2.35	2.48	2.68	2.88	3.08	3.14	3.26	3.23		
88F00116	4/b	2.60	2.74	2.79	2.64	2.92	3.20	3.34	3.49	3.57		
88F00098	4/b	2.53	2.75	2.86	2.93	2.87	3.06	3.19	3.20	3.21		
Mean		2.38	2.61	2.71	2.75	2.89	3.11	3.22	3.32	3.34		
Std Dev		0.32	0.23	0.20	0.16	0.03	0.08	0.10	0.15	0.20		
SEM		0.16	0.13	0.12	0.09	0.02	0.04	0.06	0.09	0.10		

Appendix F: PATHOLOGY REPORT

GLP STUDY 88004

Principal Investigator: CPT Gary Zaucha
Co-Principal Investigator: CPT Denzil Frost
Pathologist: MAJ David Young

I. INTRODUCTION

Study: Local Irritation Study
Test Compound: Hypertonic Saline/Dextran Solution (HSD)
Animal: Rabbit, New Zealand White, 2.5-3.5 kg, Male.

Usage Groups:

Group 1 (controls)	Lactated Ringers Solution
Group 2	Hypertonic Saline/Dextran Solution
Group 3	Hypertonic Saline
Group 4	Dextran 70®

II. SUMMARY OF PROCEDURES:

Euthanasia: Ketamine, IM followed by Sodium
Pentobarbital, IC
Fixative: 10% Neutral Buffered Formalin
Histopathology: Routine
Other Procedures: Gross observation and measurement of
injection sites.

III. GROSS FINDINGS: Measurements of the injection sites were made at necropsy. The sites were scored on the area (in cm²) of observable/palpable skin blebbing or displacement. The grading criteria are as listed in Table 1. The incidence summary of all gross findings is listed in Table 2.

IV. MICROSCOPIC FINDINGS: Tissues saved for microscopic evaluation from all groups were skin sections from the 5 injection sites and muscle from site 5 (thigh) which exhibited gross changes. Three sections of skin from each injection site was taken; one from the actual site of injection and sections 1 cm distal and 1 cm proximal to the injection sites. All 3 sections per site were evaluated and grading was based on the most severely affected section.

Table 3 lists the incidence summary (with percentages) for microscopic observation for all animals. Table 4 contains the incidence summary of non-neoplastic graded microscopic diagnoses evaluated using the Kolmogorov-Smirnov

Appendix F (cont.): PATHOLOGY REPORT

two-tailed test. This analysis revealed no significant difference from controls at the 0.05 level. Annex A lists the body weight, gross findings and microscopic diagnoses for each individual animal in all groups.

The most common lesion noted in both control and experimental groups was hemorrhage, frequently with an associated acute to subacute dermatitis. Minimal to mild skeletal muscle degeneration was occasionally present, primarily in the thoracic and thigh injection sites, with an infrequent minimal acute myositis. The inflammation, and to a lesser degree, the muscle degenerative changes appear to be a consequence of the hemorrhage or from foreign material (i.e., fur) in the dermis as a result of the injection. All hemorrhage and associated inflammation were likely to resolve without permanent morphologic or functional alteration.

V. SUMMARY COMMENTS: Dermal and subcutaneous hemorrhage occurred frequently without significant differences in all groups. Acute to subacute inflammation, occurring with less frequency, was also present in all groups and was a direct and expected response to hemorrhage. Moderate acute inflammation was almost always associated with fragments of fur displaced within the dermis. Although not evident from the appendices, subjectively the acute inflammatory responses were predominantly seen in the 4 and 24 hour interim sacrifice animals and the subacute inflammation was primarily in the older lesions (48 and 72 hours). Skeletal muscle degeneration, sporadically found in all groups, may have been an incidental finding; those associated with an acute myositis were most likely related to the inflammatory aspects of hemorrhage. Ulcerative dermatitis was an occasional focal lesion indicating the actual epidermal site of injection.

All of the hemorrhage, muscle degeneration and associated inflammation were of unlikely clinical significance and would be expected to heal with no residual morphological or functional alteration.

Appendix F (cont.): PATHOLOGY REPORT

Other lesions present in the lung, digestive tract, lymph nodes and ears were incidental findings and, while they may reflect a concurrent bacterial or parasitic infection, had little to no relationship to the skin and muscle changes.

Chas 3 Clipp's DVM PhD

for G. DAVID YOUNG, DVM
MAJ, VC
Division of Pathology

19 August 1988/dbj

Appendix F (cont.): PATHOLOGY REPORT

TABLE 1

Grading Criteria for Gross Finding at Injection Sites

- 1 = 0-0.9 cm²
- 2 = 1.0-1.9 cm²
- 3 = 2.0-2.9 cm²
- 4 = $\geq$ 3.0 cm²

GLP 88004

GLOSSARY OF MICROSCOPIC FINDINGS

SKIN

1. **Hemorrhage** - Variable amounts of red blood cells (RBCs) present within the dermis and/or subcutaneous tissue. Occasional white blood cells (heterophils and monocytes) were scattered among the RBCs. Occasionally associated with the hemorrhagic sites were foci of collagen degradation and infrequent segmental fibrinoid necrosis of the muscular artery wall (site of intra-arterial injection). The degree of hemorrhage was graded on the basis of relative amount of RBCs, expansion of tissue and obliteration of normal skin cytoarchitecture. Severity-grading criteria are as follows:

- 1 = Scattered individual to small aggregates of RBCs coursing between and mildly separating collagen fibers. (Trace)
- 2 = Slightly larger aggregates to islands of RBCs dissecting the dermal collagen and/or subcutaneous tissue, often in a linear fashion, with expansion of the tissue. No to little obliteration of tissue was present. (Mild)
- 3 = Lakes of RBCs that expand dermis and subcutis, often with a bulge in the skin surface contour. Notable cytoarchitectural obliteration was present. Edema, evidenced by clear spaces and widening of collagen/connective tissue fibers, was present. (Moderate)

Appendix F (cont.): PATHOLOGY REPORT

Diffuse RBCs with prominent dermal and/or subcutaneous expansion and obliteration, often present along the entire width of the section. In sections with a tunica muscularis, the hemorrhage was often transmural, extending from dermis to subcutis. (Marked)
Severe. (Not observed in this study)

Dermatitis - Presence of inflammatory cells within the dermis and/or subcutaneous tissue. Almost always this inflammation was present with hemorrhage and in greater amount than seen with the hemorrhage alone. The inflammatory infiltrate was primarily of two distinct types and divided into acute and subacute responses.

a. Acute - The inflammatory cells consisting predominantly (and often exclusively) of heterophils. Grading was based on the relative numbers of cells present.

- 1 - Scattered cells within and adjacent to sites of hemorrhage. Heterophils were occasionally observed within vascular lumina, often margined against the endothelium. (Trace)
- 2 - Prominent numbers of cells, often forming small clusters with the dermis and/or subcutis. (Mild)
- 3 - Numerous cells within the dermis and/or subcutis, forming aggregates (microabscesses) up to 1 mm in diameter. Multiple fragments of fur were consistently present within these aggregates. (Moderate)
- 4 - Diffuse infiltration of cells within the dermis and/or subcutis with the complete obliteration of normal structures. (Marked)
- 5 - Severe (Not observed in this study)

b. Subacute - The presence of inflammatory cells including lymphocytes, plasma cells, macrophages and small heterophils. These infiltrates were almost always present in association with resolving hemorrhage. Grading was based on the subjective numbers of cells present.

Appendix F (cont.): PATHOLOGY REPORT

- 1 = Presence of a few mononuclear cells within the dermis and/or subcutis. (Trace)
- 2 = Prominent cell infiltration of the dermis and/or subcutis. (Mild)
- 3 = Diffuse infiltration of the dermis and/or subcutis. (Moderate)
- 4 = Diffuse infiltrate with destruction of dermal and/or subcutaneous structures. (Marked)
- 5 = Severe (Not observed in this study)

3. Superficial ulcerative dermatitis - This lesion was focally present on the skin surface and consists of an ulcerative, often penetrating lesion with destruction of the epidermis and coagulative necrosis of the superficial dermis (consistent with a needle puncture of the skin). Some sections contained a variably thickened zone of necrotic cellular debris and keratin overlying the ulcer. There was no adjacent inflammation in the epidermis or dermis. Coded as present.

4. Mononuclear cell infiltration - The presence of lymphocytes, plasma cells and macrophages within the dermis. These cells occasionally surrounded adnexa with minimal destruction or obliteration. There was no associated epidermal infiltration nor any adjacent hemorrhage. This minimal infiltration was restricted to the region of the tail tip. Coded as present.

5. Acute folliculitis/perifolliculitis - This minimal and focal lesion consisted of acute inflammation and necrosis of the base of hair follicles and the immediately adjacent dermal tissue. The inflammatory cell infiltrate was composed primarily of heterophils and lymphocytes. Coded as present.

SKELETAL MUSCLE

1. Acute myositis - This was acute inflammation of skeletal muscle. Muscle fibers were separated by infiltration of heterophils and fewer macrophages and lymphocytes. Most cases contained hemorrhage that separated larger muscle bundles and individual muscle fibers. In the more severe cases there was coagulative necrosis of muscle fibers and phagocytosis of the necrotic cellular debris. Criteria for grading severity were based on subjective count of inflammatory cells and the degree of necrosis.

Appendix F (cont.): PATHOLOGY REPORT

- 1 - Minimal detectable infiltration of heterophils. (Trace)
- 2 - Mild infiltration of heterophils and few macrophages. (Mild)
- 3 - Prominent heterophilic infiltration with minimal necrosis of skeletal muscle. (Moderate)
- 4 - Diffuse heterophilic infiltration and necrosis of muscle. (Marked)
- 5 - Severe (Not observed in this study)

Myocyte degeneration - This lesion consists of pale, clear cells (macrophages, satellite cells) and a scant eosinophilic coagulum completely filling and obscuring individual skeletal muscle fibers. There was usually little or no myocyte degeneration and rarely were other inflammatory cells present. The foci of degeneration were often multiple and random within the muscle bundle. This lesion was coded as present when it constituted a significant histological feature.

III

Subacute fibrinous pleuritis - This moderate inflammatory lesion consisted of a diffuse and moderate thickening of the pulmonary pleura by a zone of loosely arrayed fibrin and connective tissue with scattered neovascularization and diffuse infiltration of variable numbers of heterophils, lymphocytes, plasma cells and macrophages. At the junction of pulmonary parenchyma and the thickened pleura were numerous lymphocyte-filled small lymphatic channels. The underlying pulmonary interstitial tissue was mildly thickened and congested with occasional alveoli containing fibrin and edema. This lesion, present in a single animal, is most consistent with a bacterial infection, most likely *Pasteurella multocida*. Coded as present.

IV

Abscessation - A single mandibular lymph node was enlarged and filled by variable numbers of heterophils, lymphocytes, plasma cells and macrophages. Within the node was a large focus of degenerative heterophils mixed with cellular necrotic debris which expanded and disrupted the affected lymphoid tissue (abscess). This lesion was surrounded by a minimally compressed zone of connective and a minimal fibrous response. This lesion is most consistent with a bacterial infection, probably *Pasteurella multocida*. Coded as present.

Appendix F (cont.): PATHOLOGY REPORT

CECUM

1. **Mucous cell hyperplasia** - The epithelium contained random and scattered mucous cells. Cecal crypts were diffusely lined by similar cells. The lamina propria contained moderate numbers of plasma cells and few macrophages and lymphocytes. Coded as present.
2. **Plasmacytic infiltration** - This lesion consisted of diffuse and moderate infiltration of the lamina propria by numerous plasma cells and few lymphocytes and macrophages. No epithelial changes were present.
3. **Typhlitis** - This single lesion of the sacculus rotundus of the rabbit cecum consisted of a diffuse expansion of the lamina propria with numerous macrophages, heterophils with fewer lymphocytes and plasma cells. Crypts contained moderate cellular debris, degenerating heterophils and clumps of eosinophilic fibrillar material. Within the lymphoid tissue of this tissue, there was a single abscess that obliterated the follicle. Coded as present.

EAR

Fibrinocellular exudate (Acariasis) - Debris removed from the ear canal consisted of abundant fibrinocellular exudate with numerous scattered cross-sections of mites (probably *Pcoroptes cuniculi*). Coded as present.

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INCIDENCE SUMMARY REPORT FOR GROSS NECROPSY OBSERVATIONS
 STUDY NUMBER: 88004P
 REPORT INCLUDES ALL SCHEDULED DEATHS
 STUDY START DATE: 07-JUN-88

PRINTED: 14-DIC-88
 PAGE: 1

ACUTE/PRIMARY SKIN IRRITATION

--- MALES ---

CTLS	2	3	4
11	11	12	12

CECUM

PARASITIC INFESTATION	4	4	6	6
DISTENDED, CONTENTS GASEOUS	1	1	0	0
INFLAMMATION	1	1	0	0
TOTAL:	6	6	6	6

EAR

OTITIS EXTERNA	1	1	1	1
TOTAL:	1	1	1	1

LYMPH NODES

ABCESS(ES)	0	0	1	1
TOTAL:	0	0	1	1

LUNGS

PNEUMONIA	0	0	1	1
TOTAL:	0	0	1	1

SKIN

HEM EAR ART	10	11	12	11
HEM EAR DIST	3	3	6	4
HEM EAR PROX	1	4	7	3
HEM THORAX	2	2	5	2
HEM THIGH	2	4	4	3
ALOPECIA	1	1	1	1
FOLLICULITIS	0	0	1	1
TOTAL:	19	25	36	25

SKELETAL MUSCLE

HEM THORAX	0	0	0	1
HEM THIGH	3	5	5	2
TOTAL:	3	5	5	3

THYMUS

GENERALIZED ATROPHY	1	1	0	0
TOTAL:	1	1	0	0

Table 2

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP
 INCIDENCE SUMMARY (WITH PERCENTAGES) FOR MICROSCOPIC OBSERVATIONS
 STUDY NUMBER: 88004P
 ALL DIAGNOSES
 PRESDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE
 PRINTED: 14-DEC-88
 PAGE: 1

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

NOTES: ANIMALS = ALL SCHEDULED SACRIFICED ANIMAL
 CONTROLS FROM GROUP(S): 1

-- AN I M A L S A F F E C T E D --

ANIMAL SEX:

DOSAGE GROUP:

NO. IN GROUP:

T I S S U E S W I T H D I A G N O S E S

SK EAR DIST NUMBER EXAMINED:

HEMORRHAGE

ACUTE DERMATITIS

ULCERATIVE DERMATITIS

SUBACUTE DERMATITIS

SK EAR PROX NUMBER EXAMINED:

HEMORRHAGE

ACUTE DERMATITIS

ULCERATIVE DERMATITIS

MONONUCLEAR CELL INFILTRATION

SUBACUTE DERMATITIS

SK EAR ARTERY NUMBER EXAMINED:

HEMORRHAGE

ACUTE DERMATITIS

ULCERATIVE DERMATITIS

CTL	1	2	3	4
12	11	11	12	12
12	5	7	7	10
12	45%	64%	58%	83%
1	1	2	3	6
9%	18%	25%	50%	
0	1	0	0	0
0%	9%	0%	0%	
3	1	1	1	0
27%	9%	8%	0%	
11	11	12	12	12
8	10	9	8	
73%	91%	75%	67%	
5	3	5	5	
45%	27%	42%	42%	
0	0	1	0	
0%	0%	8%	0%	
0	0	2	0	
0%	0%	17%	0%	
1	3	2	0	
9%	27%	17%	0%	
11	11	12	12	
9	10	12	12	
82%	91%	100%	100%	
4	5	8	7	
36%	27%	57%	50%	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP
 INCIDENCE SUMMARY (WITH PERCENTAGES) FOR MICROSCOPIC OBSERVATIONS
 STUDY NUMBER: 88004P
 ALL DIAGNOSES
 STUDY START DATE: 07-JUN-88
 PRINTED: 14-DEC-88
 PAGE: 2

ACUTE/PRIMARY SKIN IRRITATION

-- ANIMALS AFFECTED --

NOTES: ANIMALS = ALL SCHEDULED SACRIFICED ANIMAL
 CONTROLS FROM GROUP(S): 1

ANIMAL SEX: CTLS 2 3 4
 DOSAGE GROUP: 12 12 12 12
 NO. IN GROUP:

T I S U E S W I T H D I A G N O S E S

SK THORAX NUMBER EXAMINED:
 HEMORRHAGE

ACUTE DERMATITIS

ACUTE MYOSITIS

ACUTE FOLLICULITIS/PERIFOLLICULITIS

SKELETAL MUSCLE DEGENERATION

ULCERATIVE DERMATITIS

SK THIGH NUMBER EXAMINED:
 HEMORRHAGE

ACUTE DERMATITIS

ACUTE MYOSITIS

SKELETAL MUSCLE DEGENERATION

ULCERATIVE DERMATITIS

EAR DEBRIS NUMBER EXAMINED:
 FIBRINOCELLULAR EXUDATE

Table 3 (cont.)

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH DIV OF RES SUPP, PATH SERV GP
 INCIDENCE SUMMARY (WITH PERCENTAGES) FOR MICROSCOPIC OBSERVATIONS
 STUDY NUMBER: 88004P
 PRINTED: 14-DEC-88
 PAGE: 3
 PRESIDIO OF SAN FRANCISCO, CA 94129
 ALL DIAGNOSES
 RABBIT/NEW ZEALAND WHITE
 STUDY START DATE: 07-JUN-88

T I S S U E S	W I T H	D I A G N O S E S	A N I M A L S		A F F E C T E D
			CTLS	MALES	
LUNG			12	12	12
			12	12	12
			0	0	1
			0	0	1
			0%	0%	100%
			0	0	1
			0	0	1
			0%	0%	100%
			2	5	2
			2	4	1
			100%	80%	50%
			2	2	0
			100%	40%	0%
			2	4	0
			100%	80%	0%
			2	2	0
			2	2	0
			100%	100%	0%
			1	1	0
			50%	50%	0%
			1	1	0
			50%	50%	0%
			0	0	0

NOTES: ANIMALS = ALL SCHEDULED SACRIFICED ANIMAL
 CONTROLS FROM GROUP(S): 1
 ANIMAL SEX:
 DOSAGE GROUP:
 NO. IN GROUP:
 SUBACUTE FIBRINOUS PLEURITIS
 LUNG
 Lymph Node
 Abscessation
 SK. MUSCLE THIGH
 Hemorrhage
 ACUTE MYOSITIS
 SKELETAL MUSCLE DEGENERATION
 CECUM
 MUCOUS CELL HYPERPLASIA
 PLASMACYTIC INFILTRATION
 TYPHLITIS
 SKIN (DORSUM)

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INCIDENCE SUMMARY OF MICROSCOPIC OBSERVATIONS
 STUDY NUMBER: 88004P
 NONNEOPLASTIC GRADED DIAGNOSES
 STUDY START DATE: 07-JUN-88

PRINTED: 14-DEC-88
 PAGE: 1

ACUTE/PRIMARY SKIN IRRITATION		ACUTE/PRIMARY SKIN IRRITATION	
CONTROLS FROM GROUP(S): 1		CONTROLS FROM GROUP(S): 1	
T I S S U E S W I T H D I A G N O S E S		T I S S U E S W I T H D I A G N O S E S	
SK EAR DIST		SK EAR DIST	
HEMORRHAGE	11	HEMORRHAGE	11
ACUTE DERMATITIS	5	ACUTE DERMATITIS	5
SUBACUTE DERMATITIS	3	SUBACUTE DERMATITIS	3
SK EAR PROX	11	SK EAR PROX	11
HEMORRHAGE	8	HEMORRHAGE	8
ACUTE DERMATITIS	5	ACUTE DERMATITIS	5
SUBACUTE DERMATITIS	1	SUBACUTE DERMATITIS	1
SK EAR ARTERY	11	SK EAR ARTERY	11
HEMORRHAGE	9	HEMORRHAGE	9
ACUTE DERMATITIS	4	ACUTE DERMATITIS	4
SUBACUTE DERMATITIS	1	SUBACUTE DERMATITIS	1
SK THORAX	11	SK THORAX	11
HEMORRHAGE	3	HEMORRHAGE	3
ACUTE DERMATITIS	0	ACUTE DERMATITIS	0
ACUTE MYOSITIS	0	ACUTE MYOSITIS	0
SK THIGH	11	SK THIGH	11
HEMORRHAGE	1	HEMORRHAGE	1
ACUTE DERMATITIS	0	ACUTE DERMATITIS	0
ACUTE MYOSITIS	1	ACUTE MYOSITIS	1
EAR DEBRIS	1	EAR DEBRIS	1
LUNG	0	LUNG	0
LYMPH NODE	0	LYMPH NODE	0
SK. MUSCLE THIGH	2	SK. MUSCLE THIGH	2
HEMORRHAGE	2	HEMORRHAGE	2
ACUTE MYOSITIS	2	ACUTE MYOSITIS	2
CECUM	2	CECUM	2
SKIN (DORSUM)	0	SKIN (DORSUM)	0

NOTE: ENTRIES FLAGGED WITH A - (MINUS) ARE SIGNIFICANTLY DIFFERENT FROM CONTROL AT THE 0.05 LEVEL USING THE KOLMOGOROV-SMIRNOV TWO TAILED TEST.

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH		INDIVIDUAL ANIMAL DATA DUMP TABLE		PRINTED: 14-DEC-88
DIV OF RES SUPP, PATH SERV GP		STUDY NUMBER: 88004P		PAGE: 1
PRESIDIO OF SAN FRANCISCO, CA 94129		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION
RABBIT/NEW ZEALAND WHITE		STATUS: FINAL SACRIFICE		TERMINAL BODY WEIGHT: 3.7 (KGS)
ANIMAL: 88F0091L	DAY OF DEATH: 4	<< GROSS OBSERVATIONS >>		
(SEVERITY)KEYWORDS		GROSS FREE-TEXT COMMENTS		
SKIN		ANTERIOR DORSAL THORAX		
		<< NECROPSY MEMOS >>		
TISSUE		NO NECROPSY MEMOS RECORDED ON ANIMAL		
		<< PATHOLOGY OBSERVATIONS >>		
TISSUE		DISTRIBUTION (SEVERITY)		HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX		NOT SPECIFIED(MODERATE)		ACUTE DERMATITIS
SK EAR ARTERY		NOT SPECIFIED(PRESENT)		ULCERATIVE DERMATITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 2

ANIMAL: 88F0092L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN

(MILD)HEM EAR ART
(TRACE)HEM EAR DIST

CECUM

(MARKED)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX	NOT SPECIFIED(TRACE)		HEMORRHAGE	
SK EAR ARTERY	NOT SPECIFIED(MODERATE)		HEMORRHAGE	
SK THIGH	NOT SPECIFIED(PRESENT)		SKELETAL MUSCLE DEGENERATION	
CECUM	NOT SPECIFIED(PRESENT)		MUCOUS CELL HYPERPLASIA PLASMACYTIC INFILTRATION	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 3

ANIMAL: 88F0095L DAY OF DEATH: 1 STATUS: INTERJM SACRIFICE 1 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS
SKIN (MILD)HEM EAR ART
(MILD)HEM THIGH
EAR (MILD)OTITIS EXTERNA

<< NECROPSY MEMOS >> NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	<< PATHOLOGY OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	DISTRIBUTION (SEVERITY)	
SK EAR PROX	NOT SPECIFIED(TRACE)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MILD)	HEMORRHAGE
SK THORAX	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
EAR DEBRIS	NOT SPECIFIED(MODERATE)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(PRESENT)	FIBRINOCELLULAR EXUDATE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

ANIMAL: 88F0096L DAY OF DEATH: 4 STATUS: FINAL SACRIFICE STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 STUDY NUMBER: 88004P TERMINAL BODY WEIGHT: 2.6 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART

THYMUS (MODERATE)GENERALIZED ATROPHY

CECUM (MILD)DISTENDED, CONTENTS GASEOUS
 (MILD)INFLAMMATION MULTIPLE WHITE SPOTS

TISSUE << NECROPSY MEMOS >> NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST NOT SPECIFIED(TRACE) SUBACUTE DERMATITIS

CECUM NOT SPECIFIED(PRESENT) MUCOUS CELL HYPERPLASIA
 NOT SPECIFIED(PRESENT) TYPHLITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
 PAGE: 5

ANIMAL: 88F0100L DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.7 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN
 (MODERATE)HEM EAR ART
 (MILD)HEM THIGH

SKELETAL MUSCLE

TISSUE << NECROPSY MEMOS >>
 NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MARKED)	HEMORRHAGE
SK THIGH	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(MILD)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(MILD)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

PRINTED: 14-DEC-88
PAGE: 6

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PREFSIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

ANIMAL: 88F0104L DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

<< GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

TISSUE (SEVERITY)KEYWORDS

SKIN
(TRACE)HEM THIGH
(MILD)HEM THORAX
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX
(MILD)HEM EAR ART

<< NECROPSY MEMOS >>
NECROPSY MEMOS

TISSUE

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR PROX

NOT SPECIFIED(MILD)
NOT SPECIFIED(TRACE)

HEMORRHAGE
ACUTE DERMATITIS

SK EAR ARTERY

NOT SPECIFIED(MODERATE)
NOT SPECIFIED(TRACE)

HEMORRHAGE
ACUTE DERMATITIS

SK THORAX

NOT SPECIFIED(TRACE)

HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 7

ANIMAL: 88F0105L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.8 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART (TRACE)HEM EAR DIST (MILD)HEM THORAX (MILD)HEM THIGH (MARKED)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >> NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)	HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(TRACE)	SUBACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MILD)	HEMORRHAGE
SK THORAX	NOT SPECIFIED(MODERATE)	SUBACUTE DERMATITIS
	NOT SPECIFIED(TRACE)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	SUBACUTE DERMATITIS
	NOT SPECIFIED(TRACE)	HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GRP
PESICIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 8

STUDY START DATE: 07-JUN-88
ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 4.0 (KGS)

STATUS: FINAL SACRIFICE

ANIMAL: 8801061 DAY OF DEATH: 4

ACUTE/PRIMARY SKIN IRRITATION

STATUS: FINAL SACRIFICE

ANIMAL: 8801061 DAY OF DEATH: 4

TERMINAL BODY WEIGHT: 4.0 (KGS)

STATUS: FINAL SACRIFICE

ANIMAL: 8801061 DAY OF DEATH: 4

ACUTE/PRIMARY SKIN IRRITATION

STATUS: FINAL SACRIFICE

ANIMAL: 8801061 DAY OF DEATH: 4

<< NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MILD)		HEMORRHAGE	
	NOT SPECIFIED(TRACE)		SUBACUTE DERMATITIS	
SK EAR PROX	NOT SPECIFIED(TRACE)		HEMORRHAGE	
	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS	
SK EAR ARTERY	NOT SPECIFIED(MILD)		HEMORRHAGE	
	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESTON OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 8801 P

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ANIMAL: 8801071 DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.7 (KGS)

ISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

CECUM (MARKED)PARASITIC INFESTATION HEAVY INFESTATION OF WHIPWORMS

SKIN (TRACE)HEM EAR ART

ISSUE << NECROPSY MEMOS >>
 NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

ISSUE << PATHOLOGY OBSERVATIONS >>
 HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST NOT SPECIFIED(TRACE) HEMORRHAGE

SK EAR PROX NOT SPECIFIED(TRACE) HEMORRHAGE

SK EAR ARTERY NOT SPECIFIED(MODERATE) HEMORRHAGE
 NOT SPECIFIED(PRESENT) ULCERATIVE DERMATITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 880042

PRINTED: 14-DEC-88
PAGE: 10

STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 58F0109L DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1 TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
DISTRIBUTION (SEVERITY) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR PROX NOT SPECIFIED(MILD) HEMORRHAGE
NOT SPECIFIED(TRACE) ACUTE DERMATITIS

SK EAR ARTERY NOT SPECIFIED(MODERATE) HEMORRHAGE
NOT SPECIFIED(TRACE) ACUTE DERMATITIS

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Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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STUDY START DATE: 07-JUN-88
STUDY NUMBER: 88004P
PRINTED: 14-DEC-88
PAGE: 11

ANIMAL: 88F0112L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.1 (KGS)

TISSUE (SEVERITY)KEYWORDS GROSS OBSERVATIONS
SKIN (TRACE)HEM EAR ART
SKELETAL MUSCLE (MILD)HEM THIGH
CECUM (MILD)PARASITIC INFESTATION

TISSUE
NO NECROPSY MEMOS RECORDED ON ANIMAL
GROSS OBSERVATIONS
GROSS FREE-TEXT COMMENTS

TISSUE DISTRIBUTION (SEVERITY) OBSERVATIONS
SK EAR DIST NOT SPECIFIED(TRACE)
SK EAR ARTERY NOT SPECIFIED(TRACE)
SK. MUSCLE THIGH NOT SPECIFIED(MODERATE)
NOT SPECIFIED(TRACE)
NOT SPECIFIED(TRACE)
NOT SPECIFIED(PRESENT)

HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
HEMORRHAGE
ACUTE DERMATITIS
HEMORRHAGE
HEMORRHAGE
ACUTE MYOSITIS
SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 98004P

PRINTED: 14-DEC-88
PAGE: 12

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F011-L DAY OF DEATH: -2 STATUS: FOUND DEAD TERMINAL BODY WEIGHT: 3.2 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

NO GROSS OBSERVATIONS RECORDED ON ANIMAL

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

WHOLE BODY

This animal died before the start of the study, and was not included in any data tabulation.

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST				REQUIRED TISSUE NOT EXAMINED
SK EAR PROX				REQUIRED TISSUE NOT EXAMINED
SK EAR ARTERY				REQUIRED TISSUE NOT EXAMINED
SK THORAX				REQUIRED TISSUE NOT EXAMINED
SK THIGH				REQUIRED TISSUE NOT EXAMINED

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
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ANIMAL: 88F0091R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.7 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
 SKIN (TRACE)NEW EAR ART GROSS FREE-TEXT COMMENTS
 (MODERATE)ALOPECIA

ANTERIOR DORSAL THORAX

TISSUE << NECROPSY MEMOS >>
 NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
 SK EAR PROX DISTRIBUTION (SEVERITY) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
 NOT SPECIFIED(TRACE) HEMORRHAGE
 NOT SPECIFIED(TRACE) SUBACUTE DERMATITIS
 SK EAR ARTERY NOT SPECIFIED(TRACE) HEMORRHAGE
 NOT SPECIFIED(PRESENT) ULCERATIVE DERMATITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
 PAGE: 14

ANIMAL: 88F0092R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
 SKIN (MILD)HEM EAR ART GROSS FREE-TEXT COMMENTS
 (TRACE)HEM EAR PROX
 SKELETAL MUSCLE (MODERATE)HEM THIGH
 CECUM (MARKED)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >>
 NO NECROPSY MEMOS RECORDED ON ANIMAL
 NECROPSY MEMOS

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)	HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK THIGH	NOT SPECIFIED(TRACE)	SUBACUTE DERMATITIS
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)	HEMORRHAGE
CECUM	NOT SPECIFIED(MODERATE)	ACUTE DERMATITIS
	NOT SPECIFIED(TRACE)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION
	NOT SPECIFIED(TRACE)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION
	NOT SPECIFIED(PRESENT)	MUCOUS CELL HYPERPLASIA
	NOT SPECIFIED(PRESENT)	PLASMACYTIC INFILTRATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH		INDIVIDUAL ANIMAL DATA DUMP TABLE		PRINTED: 14-DEC-88
DIV OF RES SUPP, PATH SERV GP		STUDY NUMBER: 88004P		PAGE: 15
PRESIDIO OF SAN FRANCISCO, CA 94129		STUDY START DATE: 07-JUN-88		
RABBIT/NEW ZEALAND WHITE		ACUTE/PRIMARY SKIN IRRITATION		
ANIMAL: 88F0095R	DAY OF DEATH: 1	STATUS: INTERIM SACRIFICE 1	TERMINAL BODY WEIGHT: 3.4 (KGS)	
<< GROSS OBSERVATIONS >>				
TISSUE	(SEVERITY)KEYWORDS	GROSS FREE-TEXT COMMENTS		
SKIN	(MODERATE)HEM EAR ART (TRACE)HEM THORAX			
SKELETAL MUSCLE	(MILD)HEM THIGH			
EAR	(MILD)OTITIS EXTERNA			
<< NECROPSY MEMOS >>				
TISSUE	NECROPSY MEMOS			
NO NECROPSY MEMOS RECORDED ON ANIMAL				
<< PATHOLOGY OBSERVATIONS >>				
TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS		
SK EAR PROX	NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)	HEMORRHAGE ACUTE DERMATITIS		
SK EAR ARTERY	NOT SPECIFIED(MARKED) NOT SPECIFIED(MODERATE)	HEMORRHAGE ACUTE DERMATITIS		
SK THORAX		TISSUE IS MISSING		
SK THIGH	NOT SPECIFIED(MODERATE) NOT SPECIFIED(MILD) NOT SPECIFIED(MILD)	HEMORRHAGE ACUTE DERMATITIS ACUTE MYOSITIS		
EAR DEBRIS	NOT SPECIFIED(PRESENT)	FIBRINOCELLULAR EXUDATE		

Appendix F (cont.): PATHOLOGY REPORT

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INDIVIDUAL ANIMAL DATA DUMP TABLE
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ANIMAL: 88F0096R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 2.6 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART
THYMUS (MODEPATE)GENERALIZED ATROPHY
CECUM (MILD)DISTENDED, CONTENTS GASEOUS
(MILD)INFLAMMATION MULTIPLE WHITE SPOTS

TISSUE << NECROPSY MEMOS >> NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST NOT SPECIFIED(TRACE) SUBACUTE DERMATITIS
CECUM NOT SPECIFIED(PRESENT) MUCOUS CELL HYPERPLASIA
NOT SPECIFIED(PRESENT) TYPHLITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

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ANIMAL: 88F0100R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.7 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
(MODERATE)HEM EAR ART GROSS FREE-TEXT COMMENTS
SKIN (MILD)HEM THIGH

TISSUE << NECROPSY MEMOS >>
NO NECROPSY MEMOS RECORDED ON ANIMAL NECROPSY MEMOS

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK THORAX	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
SK. MUSCLE THIGH	NOT SPECIFIED(TRACE)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION
	NOT SPECIFIED(TRACE)	HEMORRHAGE
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

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ANIMAL: 88F0104R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN

(MILD)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX
(TRACE)HEM THIGH

TISSUE

NO NECROPSY MEMOS RECORDED ON ANIMAL

<< NECROPSY MEMOS >>
NECROPSY MEMOS

TISSUE

<< PATHOLOGY OBSERVATIONS >>
HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

NOT SPECIFIED(MILD)
NOT SPECIFIED(PRESENT)
NOT SPECIFIED(MILD)
NOT SPECIFIED(MODERATE)
NOT SPECIFIED(TRACE)
NOT SPECIFIED(PRESENT)
NOT SPECIFIED(TRACE)

HEMORRHAGE
ULCERATIVE DERMATITIS

SK EAR PROX

HEMORRHAGE

SK EAR ARTERY

HEMORRHAGE

SK THORAX

HEMORRHAGE

HEMORRHAGE
SKELETAL MUSCLE DEGENERATION

SK THIGH

HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

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PRESIDIO OF SAN FRANCISCO, CA 94129		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION
RABBIT/NEW ZEALAND WHITE		STATUS: INTERIM SACRIFICE 3		TERMINAL BODY WEIGHT: 3.8 (KGS)
ANIMAL: 88F0105R	DAY OF DEATH: 3			
<< GROSS OBSERVATIONS >>				
TISSUE	(SEVERITY)KEYWORDS	GROSS FREE-TEXT COMMENTS		
SKIN	(MILD)HEM EAR ART (TRACE)HEM EAR DIST (TRACF)HEM EAR PROX (MARKED)PARASITIC INFESTATION			
CECUM				
<< NECROPSY MEMOS >>				
TISSUE		NECROPSY MEMOS		
NO NECROPSY MEMOS RECORDED ON ANIMAL				
<< PATHOLOGY OBSERVATIONS >>				
TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS		
SK EAR DIST	NOT SPECIFIED(MILD)	HEMORRHAGE		
SK EAR PROX	NOT SPECIFIED(TRACE)	HEMORRHAGE		
SK EAR ARTERY	NOT SPECIFIED(TRACE)	SUBACUTE DERMATITIS		
SK. MUSCLE THIGH	NOT SPECIFIED(MARKED)	HEMORRHAGE		
	NOT SPECIFIED(TRACE)	SUBACUTE DERMATITIS		
	NOT SPECIFIED(MILD)	HEMORRHAGE		
	NOT SPECIFIED(TRACE)	ACUTE MYOSITIS		
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION		

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004p

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STUDY START DATE: 07-JUN-83 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0106R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE TERMINAL BODY WEIGHT: 4.0 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
DISTRIBUTION (SEVERITY) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX NOT SPECIFIED(MILD) HEMORRHAGE
NOT SPECIFIED(TRACE) SUBACUTE DERMATITIS
SK EAR ARTERY NOT SPECIFIED(MILD) HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

ANIMAL: 88F0107R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.7 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM THIGH

 (MILD)HEM EAR ART

SKELETAL MUSCLE (MILD)HEM THIGH

CECUM (MARKED)PARASITIC INFESTATION

 HEAVY INFESTATION WHIPWORMS

TISSUE << NECROPSY MEMOS >> NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST DISTRIBUTION (SEVERITY)

 NOT SPECIFIED(MILD)

 NOT SPECIFIED(TRACE)

SK EAR PROX

 NOT SPECIFIED(MILD)

 NOT SPECIFIED(TRACE)

SK EAR ARTERY

 NOT SPECIFIED(MODERATE)

SK THIGH

 NOT SPECIFIED(MILD)

SK. MUSCLE THIGH

 NOT SPECIFIED(MILD)

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88064P

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ANIMAL: 88F0109R DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN
(MILD)HEM EAR ART
(TRACE)HEM THIGH
(TRACE)HEM THORAX

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MILD) NOT SPECIFIED(TRACE)	HEMORRHAGE ACUTE DERMATITIS
SK EAR PROX	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)	HEMORRHAGE ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MARKED) NOT SPECIFIED(MODERATE) NOT SPECIFIED(PRESENT)	HEMORRHAGE ACUTE DERMATITIS ULCERATIVE DERMATITIS
SK THIGH	NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE) NOT SPECIFIED(TRACE)	HEMORRHAGE ACUTE DERMATITIS ACUTE MYOSITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

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ANIMAL: 88F0112R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

TERMINAL BODY WEIGHT: 3.1 (KGS)

<< GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

(SEVERITY)KEYWORDS

TISSUE

(MILD)HEM THIGH
(TRACE)HEM EAR ART

SKELETAL MUSCLE

CECUM

(MILD)PARASITIC INFESTATION

TISSUE

<< NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)	HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK THORAX	NOT SPECIFIED(PRESENT)	ULCERATIVE DERMATITIS
SK THIGH	NOT SPECIFIED(MILD)	HEMORRHAGE
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 880041P

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PAGE: 24

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0114R DAY OF DEATH: -2 STATUS: FOUND DEAD

TERMINAL BODY WEIGHT: ---

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

NO GROSS OBSERVATIONS RECORDED ON ANIMAL

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

WHOLE BODY

This animal died before the start of the study, and was not included in any data tabulation.

TISSUE << PATHOLOGY OBSERVATIONS >>

DISTRIBUTION (SEVERITY) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

REQUIRED TISSUE NOT EXAMINED

SK EAR PROX

REQUIRED TISSUE NOT EXAMINED

SK EAR ARTERY

REQUIRED TISSUE NOT EXAMINED

SK THORAX

REQUIRED TISSUE NOT EXAMINED

SK THIGH

REQUIRED TISSUE NOT EXAMINED

Appendix F (cont.): PATHOLOGY REPORT

ETERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 25

ANIMAL: 88F0093R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.2 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN
(TRACE)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX
(MODERATE)HEM THORAX
(MODERATE)HEM THIGH

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
SK THORAX	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(MARKED)	HEMORRHAGE
	NOT SPECIFIED(MILD)	ACUTE DERMATITIS
	NOT SPECIFIED(MILD)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION
SK THIGH	NOT SPECIFIED(MARKED)	HEMORRHAGE
	NOT SPECIFIED(MILD)	ACUTE DERMATITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
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ANIMAL: 88F0094R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.1 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS
SKIN
.....
(MILD)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX
(MILD)HEM THIGH
SKELETAL MUSCLE
.....
(TRACE)HEM THIGH
EAR
.....
(MILD)OTITIS EXTERNA

<< NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
DISTRIBUTION (SEVERITY) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX
.....
NOT SPECIFIED(MODERATE) HEMORRHAGE
NOT SPECIFIED(TRACE) ACUTE DERMATITIS
NOT SPECIFIED(PRESENT) MONONUCLEAR CELL INFILTRATION
SK EAR ARTERY
.....
NOT SPECIFIED(MARKED) HEMORRHAGE
NOT SPECIFIED(MILD) ACUTE DERMATITIS
SK THIGH
.....
NOT SPECIFIED(MILD) HEMORRHAGE
EAR DEBRIS
.....
NOT SPECIFIED(PRESENT) FIBRINOCELLULAR EXUDATE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 27

STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.2 (KGS)

ANIMAL: 83F0098R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN

(TRACE)HEM EAR ART
(TRACE)HEM EAR PROX
(MILD)FOLLICULITIS
(MILD)PARASITIC INFESTATION

SUB-MANDIBULAR

CECUM

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MILD)	HEMORRHAGE
SK THORAX	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 28

ANIMAL: 88F009R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.5 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN

(MILD)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX
(MILD)PARASITIC INFESTATION

CECUM

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
SK THORAX	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(MILD)	ACUTE DERMATITIS
	NOT SPECIFIED(MILD)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 29

ANIMAL: 88F0101R DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 2.9 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM THIGH
(MARKED)HEM EAR ART
SKELETAL MUSCLE (TRACE)HEM THIGH
LUNGS (MILD)PNEUMONIA
ADHERED TO RIB

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS	
SK EAR ARTERY	NOT SPECIFIED(MARKED) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS	
SK THIGH	NOT SPECIFIED(MODERATE) NOT SPECIFIED(TRACE)		HEMORRHAGE ACUTE DERMATITIS	
LUNG	NOT SPECIFIED(PRESENT)		SUBACUTE FIBRINOUS PLEURITIS Most consistent with Pasteurella infection	
SK. MUSCLE THIGH	NOT SPECIFIED(MILD)		HEMORRHAGE	

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 30

ANIMAL: 88F0102R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN

(MILD)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX

SKELETAL MUSCLE

(TRACE)HEM THIGH

CECUM

(MARKED)PARASITIC INFESTATION

TISSUE

<< NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(TRACE)	SUBACUTE DERMATITIS
SK THORAX	NOT SPECIFIED(MARKED)	HEMORRHAGE
	NOT SPECIFIED(MARKED)	HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 31

ANIMAL: 88F0103R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.2 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN (TRACE)HEM EAR ART
(TRACE)HEM EAR PROX

CECUM (MARKED)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)		
SK EAR PROX	NOT SPECIFIED(MODERATE)		SUBACUTE DERMATITIS
	NOT SPECIFIED(TRACE)		HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MILD)		SUBACUTE DERMATITIS
	NOT SPECIFIED(TRACE)		HEMORRHAGE
SK THIGH	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS
			HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
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ANIMAL: 88F0108R DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.6 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS
LYMPH NODES (MODERATE)ABCESS(ES) PASTEURELLA
SKIN (MARKED)HEM EAR ART
SKELETAL MUSCLE (MILD)HEM THIGH

<< NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)	HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
	NOT SPECIFIED(PRESENT)	ULCERATIVE DERMATITIS
SK THORAX	NOT SPECIFIED(MODERATE)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
	NOT SPECIFIED(MILD)	ACUTE MYOSITIS
	NOT SPECIFIED(PRESENT)	ACUTE FOLLICULITIS/PERIFOLLICULITIS
LYMPH NODE	NOT SPECIFIED(PRESENT)	ABSCESSATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

ANIMAL: 88F0110R DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

TERMINAL BODY WEIGHT: 3.5 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN (MILD)HEM EAR ART
 (TRACE)HEM THIGH
 (MARKED)HEM THORAX

TISSUE << NECROPSY MEMOS >> NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST NOT SPECIFIED(TRACE) HEMORRHAGE

SK EAR PROX NOT SPECIFIED(TRACE) HEMORRHAGE
 NOT SPECIFIED(TRACE) ACUTE DERMATITIS
 NOT SPECIFIED(PRESENT) ULCERATIVE DERMATITIS

SK EAR ARTERY NOT SPECIFIED(MODERATE) HEMORRHAGE
 NOT SPECIFIED(MODERATE) ACUTE DERMATITIS
 NOT SPECIFIED(PRESENT) ULCERATIVE DERMATITIS

SK THIGH NOT SPECIFIED(MILD) HEMORRHAGE
 NOT SPECIFIED(MILD) ACUTE DERMATITIS
 NOT SPECIFIED(MILD) ACUTE MYOSITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
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ANIMAL: 88F0111R DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

<< GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

TISSUE (SEVERITY)KEYWORDS
SKIN (TRACE)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM THORAX
SKELETAL MUSCLE (TRACE)HEM THIGH

<< NECROPSY MEMOS >>
NECROPSY MEMOS

TISSUE
NO NECROPSY MEMOS RECORDED ON ANIMAL

<< PATHOLOGY OBSERVATIONS >>
HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

TISSUE DISTRIBUTION (SEVERITY)

SK EAR DIST NOT SPECIFIED(MODERATE)
NOT SPECIFIED(TRACE)

SK EAR PROX NOT SPECIFIED(TRACE)
NOT SPECIFIED(TRACE)

SK EAR ARTERY NOT SPECIFIED(MILD)
NOT SPECIFIED(TRACE)

SK THORAX NOT SPECIFIED(PRESENT)

HEMORRHAGE
ACUTE DERMATITIS

HEMORRHAGE
ACUTE DERMATITIS

HEMORRHAGE
ACUTE DERMATITIS

SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

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ANIMAL: 88F0115R DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.1 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN

(TRACE)HEM EAR ART
(MILD)HEM THORAX

CECUM

(MODERATE)PARASITIC INFESTATION

TISSUE

<< NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
DISTRIBUTION (SEVERITY) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

NOT SPECIFIED(MILD)

HEMORRHAGE

SK EAR PROX

NOT SPECIFIED(MILD)

HEMORRHAGE

SK EAR ARTERY

NOT SPECIFIED(MILD)

HEMORRHAGE

SK THORAX

NOT SPECIFIED(MILD)

ACUTE MYOSITIS

NOT SPECIFIED(PRESENT)

SKELETAL MUSCLE DEGENERATION

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
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STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0116R DAY OF DEATH: 4 STATUS: FINAL SACRIFICE TERMINAL BODY WEIGHT: 3.6 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN

(TRACE)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX
(MILD)HEM THORAX
(MODERATE)ALOPECIA
(MILD)PARASITIC INFESTATION

CECUM

DORSAL ANTERIOR THORAX

TISSUE

<< NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

NOT SPECIFIED(MILD)

ACUTE DERMATITIS

SK EAR PROX

NOT SPECIFIED(PRESENT)

MONONUCLEAR CELL INFILTRATION

SK EAR ARTERY

NOT SPECIFIED(MODERATE)

HEMORRHAGE

NOT SPECIFIED(MILD)

ACUTE DERMATITIS

SK THORAX

NOT SPECIFIED(MILD)

HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
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ANIMAL: 88F0093L DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.2 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

SKIN

(TRACE)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX

TISSUE

NO NECROPSY MEMOS RECORDED ON ANIMAL

<< NECROPSY MEMOS >>
NECROPSY MEMOS

TISSUE

SK EAR DIST

DISTRIBUTION (SEVERITY) << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
NOT SPECIFIED(MODERATE)
NOT SPECIFIED(TRACE)
NOT SPECIFIED(MILD)
NOT SPECIFIED(MODERATE)
NOT SPECIFIED(TRACE)
NOT SPECIFIED(MILD)
NOT SPECIFIED(PRESENT)

SK EAR PROX

SK EAR ARTERY

SK THORAX

SK THIGH

HEMORRHAGE
ACUTE DERMATITIS
HEMORRHAGE
HEMORRHAGE
ACUTE DERMATITIS
ACUTE DERMATITIS
ULCERATIVE DERMATITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

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 PAGE: 38

ANIMAL: R00094L DAY OF DEATH: 2 STATUS: INTERIM SACRIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.1 (KGS)

<< GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

TISSUE (SEVERITY)KEYWORDS
 SKIN (TRACE)HEM EAR ART
 SKELETAL MUSCLE (TRACE)HEM THIGH
 EAR (MILD)OTITIS EXTERNA

<< NECROPSY MEMOS >>
 NECROPSY MEMOS

TISSUE
 NO NECROPSY MEMOS RECORDED ON ANIMAL

<< PATHOLOGY OBSERVATIONS >>
 HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

TISSUE	DISTRIBUTION (SEVERITY)	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MILD)	HEMORRHAGE
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
SK THIGH	NOT SPECIFIED(TRACE)	HEMORRHAGE
EAR DEBRIS	NOT SPECIFIED(PRESENT)	FIBRINOCELLULAR EXUDATE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
PRESIDIO OF SAN FRANCISCO, CA 94129
RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P
PRINTED: 14-DEC-88
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ANIMAL: 88F0098L DAY OF DEATH: 4 STATUS: FINAL SACRIFICE STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.2 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS

CECUM (MILD)PARASITIC INFESTATION
SKIN (MILD)FOLLICULITIS SUB-MANDIBULAR

TISSUE << NECROPSY MEMOS >>
NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	PATHOLOGY	OBSERVATIONS	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)			
	NOT SPECIFIED(MILD)			
SK EAR PROX	NOT SPECIFIED(MILD)			HEMORRHAGE ACUTE DERMATITIS
	NOT SPECIFIED(TRACE)			
SK EAR ARTERY	NOT SPECIFIED(TRACE)			HEMORRHAGE ACUTE DERMATITIS
	NOT SPECIFIED(TRACE)			
SK THIGH	NOT SPECIFIED(TRACE)			HEMORRHAGE HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 40

ANIMAL: 88F00099L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.5 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS
SKIN (MILD)HEM EAR ART
(TRACE)HEM EAR DIST
(TRACE)HEM EAR PROX
CECUM (MILD)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >> NECROPSY MEMOS
NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST NOT SPECIFIED(TRACE) HEMORRHAGE
SK EAR ARTERY NOT SPECIFIED(MILD) HEMORRHAGE
SK THORAX NOT SPECIFIED(MARKED) HEMORRHAGE
NOT SPECIFIED(TRACE) ACUTE DERMATITI

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 41

ANIMAL: 88F0101L DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 2.9 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS
SKIN (MODERATE)HEM EAR ART
(TRACE)HEM THIGH
LUNGS (MILD)PNEUMONIA ADHERED TO RIB

TISSUE << NECROPSY MEMOS >> NECROPSY MEMOS
NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MILD)	HEMORRHAGE	
SK EAR PROX	NOT SPECIFIED(MODERATE)	HEMORRHAGE	
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS	
SK EAR ARTERY	NOT SPECIFIED(MODERATE)	HEMORRHAGE	
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS	
LUNG	NOT SPECIFIED(PRESENT)	SUBACUTE FIBRINOUS PLEURITIS	Most consistent with Pasteurella infection

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

PRINTED: 14-DEC-88
PAGE: 42

ANIMAL: 88F0102L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
TERMINAL BODY WEIGHT: 3.4 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN (MILD)HEM EAR ART
CECUM (MARKED)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(TRACE)		HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(MODERATE)		ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS
	NOT SPECIFIED(MODERATE)		HEMORRHAGE
	NOT SPECIFIED(TRACE)		ACUTE DERMATITIS

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH		INDIVIDUAL ANIMAL DATA DUMP TABLE		PRINTED: 14-DEC-88
DIV OF RES SUPP, PATH SEKV GP		STUDY NUMBER: 88004P		PAGE: 43
PRESIOIO OF SAN FRANCISCO, CA 94129		STUDY START DATE: 07-JUN-88		ACUTE/PRIMARY SKIN IRRITATION
RABBIT/NEW ZEALAND WHITE		STATUS: FINAL SACRIFICE		TERMINAL BODY WEIGHT: 3.2 (KGS)
ANIMAL: 88F0103L	DAY OF DEATH: 4	<< GROSS OBSERVATIONS >>		
(SEVERITY)KEYWORDS		GROSS FREE-TEXT COMMENTS		
SKIN		(TRACE)HEM EAR ART		
CECUM		(MARKED)PARASITIC INFESTATION		
TISSUE		<< NECROPSY MEMOS >>		
NO NECROPSY MEMOS RECORDED ON ANIMAL		NECROPSY MEMOS		
TISSUE		<< PATHOLOGY OBSERVATIONS >>		
SK EAR ARTERY		HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS		
NOT SPECIFIED(TRACE)		HEMORRHAGE		
NOT SPECIFIED(MILD)		ACUTE DERMATITIS		

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
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 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
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ANIMAL: 88F0108L DAY OF DEATH: 1 STATUS: INTERIM SACRIFICE 1 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.6 (KGS)

<< GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

TISSUE (SEVERITY)KEYWORDS
 SKIN (TRACE)HEM EAR ART
 SKELETAL MUSCLE (MILD)HEM THIGH
 (TRACE)HEM THORAX
 LYMPH NODES (MODERATE)ABCESS(ES)
 PASTEURELLA

<< NECROPSY MEMOS >>
 NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

<< PATHOLOGY OBSERVATIONS >>
 HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

TISSUE DISTRIBUTION (SEVERITY)

SK EAR DIST	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
SK EAR PROX	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MILD)	HEMORRHAGE
	NOT SPECIFIED(TRACE)	ACUTE DERMATITIS
LYMPH NODE	NOT SPECIFIED(PRESENT)	ABSCESSATION

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STUDY START DATE: 07-JUN-88

ERVATIONS >>
GROSS FREE-TEXT COMMENTS

.. .. THIGH
(TRACE)HEM
(MARKED)HEM EAR ART

M E M O S
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE	DISTRIBUTION (SEVERITY)	<< PATHOLOGY	OBSERVATIONS >>	HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
SK EAR DIST	NOT SPECIFIED(MILD)			HEMORRHAGE
SK EAR PROX	NOT SPECIFIED(TRACE)			HEMORRHAGE
	NOT SPECIFIED(TRACE)			ACUTE DERMATITIS
SK EAR ARTERY	NOT SPECIFIED(MODERATE)			HEMORRHAGE
	NOT SPECIFIED(MODERATE)			ACUTE DERMATITIS
SK THORAX				TISSUE IS MISSING

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

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ANIMAL: 88F0111L DAY OF DEATH: 2 STATUS: INTERIM S/RIFICE 2 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.4 (KGS)

<< GROSS OBSERVATIONS >>
 GROSS FREE-TEXT COMMENTS

TISSUE (SEVERITY)KEYWORDS
 SKIN (TRACE)HEM EAR ART
 (TRACE)HEM EAR DIST
 (TRACE)HEM EAR PROX

<< NECROPSY MEMOS >>
 NECROPSY MEMOS

TISSUE
 NO NECROPSY MEMOS RECORDED ON ANIMAL

<< PATHOLOGY OBSERVATIONS >>
 HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

TISSUE DISTRIBUTION (SEVERITY)

SK EAR DIST NOT SPECIFIED(TRACE) HEMORRHAGE
 NOT SPECIFIED(TRACE) ACUTE DERMATITIS

SK EAR PROX NOT SPECIFIED(MILD) HEMORRHAGE

SK EAR ARTERY NOT SPECIFIED(MODERATE) HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
 DIV OF RES SUPP, PATH SERV GP
 PRESIDIO OF SAN FRANCISCO, CA 94129
 RABBIT/NEW ZEALAND WHITE

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INDIVIDUAL ANIMAL DATA DUMP TABLE
 STUDY NUMBER: 88004P

ANIMAL: 88F0115L DAY OF DEATH: 3 STATUS: INTERIM SACRIFICE 3 STUDY START DATE: 07-JUN-88 ACUTE/PRIMARY SKIN IRRITATION
 TERMINAL BODY WEIGHT: 3.1 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >> GROSS FREE-TEXT COMMENTS
 SKIN (TRACE)HEM EAR DIST (MILD)HEM THORAX (TRACE)HEM EAR ART (MODERATE)PARASITIC INFESTATION

TISSUE << NECROPSY MEMOS >> NECROPSY MEMOS
 NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >> HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS
 SK EAR DIST NOT SPECIFIED(MILD) HEMORRHAGE
 SK EAR PROX NOT SPECIFIED(MILD) HEMORRHAGE
 SK EAR ARTERY NOT SPECIFIED(MILD) HEMORRHAGE
 SK THORAX NOT SPECIFIED(TRACE) SUBACUTE DERMATITIS
 NOT SPECIFIED(MODERATE) HEMORRHAGE

Appendix F (cont.): PATHOLOGY REPORT

LETTERMAN ARMY INSTITUTE OF RESEARCH
DIV OF RES SUPP, PATH SERV GP
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RABBIT/NEW ZEALAND WHITE

INDIVIDUAL ANIMAL DATA DUMP TABLE
STUDY NUMBER: 88004P

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STUDY START DATE: 07-JUN-88

ACUTE/PRIMARY SKIN IRRITATION

ANIMAL: 88F0116L DAY OF DEATH: 4 STATUS: FINAL SACRIFICE TERMINAL BODY WEIGHT: 3.6 (KGS)

TISSUE (SEVERITY)KEYWORDS << GROSS OBSERVATIONS >>
GROSS FREE-TEXT COMMENTS

SKIN

(TRACE)HEM EAR ART
(TRACE)HEM THORAX
(TRACE)HEM THIGH
(MODERATE)ALOPECIA
(MILD)PARASITIC INFESTATION

DORSAL ANTERIOR THORAX

CECUM

TISSUE << NECROPSY MEMOS >>
NECROPSY MEMOS

NO NECROPSY MEMOS RECORDED ON ANIMAL

TISSUE << PATHOLOGY OBSERVATIONS >>
DISTRIBUTION (SEVERITY) HISTOPATHOLOGIC DIAGNOSES / SPECIAL HISTOLOGICAL COMMENTS

SK EAR DIST

NOT SPECIFIED(TRACE)

ACUTE DERMATITIS

SK EAR PROX

NOT SPECIFIED(TRACE)

HEMORRHAGE

SK EAR ARTERY

NOT SPECIFIED(MODERATE)

HEMORRHAGE

NOT SPECIFIED(MILD)

SUBACUTE DERMATITIS

SK THORAX

NOT SPECIFIED(TRACE)

HEMORRHAGE

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