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TOXIKON FINAL GLP REPORT: 06-4898-G1

CLASS VI TEST – USP

Test Article
Padprinting Ink Series 711-8005 black

Author
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Final Report Date
November 2, 2006

COMPLIANCE
21 CFR, Part 58
Good Laboratory Practice for Non–Clinical Laboratory Studies

MANAGEMENT OF THE STUDY

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TABLE OF CONTENTS

STUDY SUMMARY

The USP 0.9% Sodium Chloride for Injection (NaCl), Cottonseed Oil (CSO), 1 in 20 Ethanol in NaCl (EtOH), and Polyethylene Glycol 400 (PEG) extracts of the test article and the test article, Padprinting Ink Series 711-8005 black, did not produce a biological response following intramuscular implantation in rabbits, intracutaneous injection in rabbits, or systemic injection in mice. Therefore, the test article meets the requirements of the USP guidelines, for Class VI Plastics – 50 °C.

QUALITY ASSURANCE STATEMENT

This study was conducted in compliance with U.S. Food and Drug Administration regulations set forth in 21 CFR, Part 58.

The sections of the regulations not performed by or under the direction of Toxikon Corporation, exempt from this Good Laboratory Practice Statement, included characterization and stability of the test article and its mixture with carriers, 21 CFR, Parts 58.105 and 58.113.

The Quality Assurance Unit conducted inspections on the following dates. The findings were reported to the Study Director and to Toxikon's Management.

INSPECTIONS	DATE OF INSPECTION	DATE REPORTED STUDY DIRECTOR	DATE REPORTED MANAGEMENT
EXTRACTION	10/12/06	10/12/06	10/12/06
RAW DATA	11/02/06	11/02/06	11/02/06
FINAL REPORT	11/02/06	11/02/06	11/02/06

Christopher Mucci, B.S.
Quality Assurance

11/02/06
Date

STUDY DIRECTOR SIGNATURE AND VERIFICATION DATES

This study meets the technical requirements of the protocol. The study also meets with the requirements of the Good Laboratory Practice Regulations, 21 CFR, Part 58, with the exemptions as stated in the Quality Assurance Statement.

Protocol Number:	MTP/VIVO/005–06/000
Study Director:	Jianxun Xie, Ph.D.
Company:	Toxikon Corporation
Signature:	
Date:	11/02/06
Study Supervisor:	Shirley Lister, B.S., LATG

VERIFICATION DATES:

Protocol Effective Date:	08/02/06
Test Article Receipt:	09/29/06
Project Log Date:	09/29/06
Extraction Dates:	10/09/06 – 10/12/06
Technical Initiation:	10/12/06
Technical Completion:	10/19/06

1.0 PURPOSE

The purpose of the study was to determine the biological response of animals to direct and indirect contact with the test article or injection of the test article extract.

2.0 REFERENCES

The study was conducted based upon the following references:

2.1 United States Pharmacopeia 29, National Formulary 24, 2006. <88> Biological Reactivity Tests, *In Vivo*.

2.2 Draize Scale for Scoring Skin Reactions, Draize, J.H. "Dermal Toxicity", Appraisal of the Safety of Chemicals in Foods, Drugs and Cosmetics – Dermal Toxicity, pp. 49–52. Association of Food and Drug Officials of the United States, Topeka, Kansas, 1965.

2.3 ISO/IEC 17025, 2005, General Requirements for the Competence of Testing and Calibration Laboratories.

3.0 COMPLIANCE

The study conformed to the current FDA 21 CFR, Part 58 – Good Laboratory Practice for Non–Clinical Laboratory Studies.

4.0 IDENTIFICATION OF TEST AND CONTROL ARTICLES

The Sponsor supplied the following information on a test requisition form or other correspondence, wherever applicable (excluding confidential or trade secret information). The Sponsor was responsible for all test article characterization data as specified in the GLP regulations.

4.1 Test Article:

Test Article Name: Padprinting Ink Series 711-8005 black
CAS/Code #: ETO sterilised
Lot/Batch #: 050906
Physical State: Not Supplied by Sponsor (N/S)
Color: N/S
Expiration Date: N/S
Density: N/S
Stability: N/S
Solubility: N/S
pH: N/S
Storage Conditions: Room Temperature
Safety Precautions: Standard Toxikon Laboratory Safety Precautions

4.2 Control Articles (Toxikon Supplied):

4.2.1 Negative Control Article Name: USP 0.9% Sodium Chloride for Injection (NaCl)
Toxikon QC #: CSC-06-09-008-VV
Physical State: Liquid
Color: Colorless
Stability: Stable at Room Temperature
Storage Conditions: Room Temperature
Safety Precautions: Standard Laboratory Safety Precautions

4.2.2 Negative Control Article Name: Cottonseed Oil (CSO)
Toxikon QC #: CSC-06-04-007-VV
Physical State: Liquid
Color: Yellow
Stability: Stable at Room Temperature
Storage Conditions: Room Temperature
Safety Precautions: Standard Laboratory Safety Precautions

4.2.3 Negative Control Article Name: 1 in 20 Ethanol in NaCl (EtOH)
Toxikon QC #: CSC-06-03-003-VV; CSC-06-09-008-VV
Physical State: Liquid
Color: Colorless
Stability: Stable at Room Temperature
Storage Conditions: Room Temperature
Safety Precautions: Standard Laboratory Safety Precautions

4.2.4 Negative Control Article Name: Polyethylene Glycol 400 (PEG)
Toxikon QC #: CSC-05-10-029-VV
Physical State: Liquid
Color: Colorless
Stability: Stable at Room Temperature
Storage Conditions: Room Temperature
Safety Precautions: Standard Laboratory Safety Precautions

4.2.5 Negative Control Article Name: Negative Control High Density Polyethylene (Negative Control Plastic)
Toxikon QC #: CSC-04-05-009-CC
Physical State: Solid
Color: White
Storage Conditions: Room Temperature
Safety Precautions: Standard Laboratory Safety Precautions

5.0 IDENTIFICATION OF TEST SYSTEM

5.1 Animals Used in the Study:

5.1.1 Systemic Injection Test:

Number and Species: 40 Albino Swiss Mice (*Mus musculus*)

Sex: female

Weight/Age Range: 17.0 – 23.0 grams / at least 34 days old (adult)
weighed to the nearest 0.1 g

Health Status: healthy, not previously used in other experimental procedures

Animal Purchase: Harlan, Indianapolis, IN

Animal Identification: ear punch

5.1.2 Intracutaneous Injection and Implant Tests:

Number and Species: 6 New Zealand White rabbits (*Oryctolagus cuniculus*)

Sex: 3 males and 3 females

Weight/Age Range: 2.05 – 2.37 kilograms for Intracutaneous
3.24 – 3.35 kilograms for Implant Test
at least 10 weeks old (young adult)
weighed to nearest 10 g

Health Status: healthy, Intracutaneous animals not previously used in other experimental procedures, Implant animals previously used in other experimental procedures

Animal Purchase: Millbrook Breeding Labs, Amherst, MA

Animal Identification: ear marker

5.2 Animal Care and Maintenance:

5.2.1 Systemic Injection Test:

Animal Room Temperature: 68 ± 5 °F

Animal Room Relative Humidity: 30 – 70%

Air Exchanges per Hour: 10 to 15

Lights: 12–hour light/dark cycle, full spectrum fluorescent lights

Acclimation: minimum 3 days, under same conditions as for the actual test

Animal Selection: selected from larger pool and examined to ensure lack of adverse clinical signs

Housing: group housed (5 per cage of same sex)

Cages: polycarbonate

Bedding: hardwood chips, P.W.I. Industries, St–Hyacinthe, Quebec, Canada (contact)

Animal Rations: TEK 7012 Rodent Diet, Harlan Teklad, Madison, WI, *ad libitum*

Water: tap water, *ad libitum*

There were no known contaminants present in the feed, water, or bedding expected to interfere with the test data.

The laboratory and animal rooms were maintained as limited–access facilities.

5.2.2 Intracutaneous Injection and Implant Tests:

Animal Room Temperature: 68 ± 5 °F

Animal Room Relative Humidity: 30 – 70%

Air Exchanges per Hour: 10 to 15

Lights: 12–hour light/dark cycle, full spectrum fluorescent lights

Acclimation: minimum 3 days, under same conditions as for the actual test

Animal Selection: selected from larger pool and examined to ensure lack of adverse clinical signs

Housing: individually housed

Cages: suspended stainless steel

Bedding: hardwood chips, P.W.I. Industries, St–Hyacinthe, Quebec, Canada (non–contact)

Animal Rations: TEK 8630 Rabbit Diet, Harlan Teklad, Madison, WI, *ad libitum*

Water: tap water, *ad libitum*

There were no known contaminants present in the feed, water, or bedding expected to interfere with the test data.

The laboratory and animal rooms were maintained as limited–access facilities.

6.0 JUSTIFICATION OF TEST SYSTEM AND ROUTE OF ADMINISTRATION

6.1 Albino mice and rabbits were used in this study because they have historically been used in USP Class VI tests and the guidelines have no alternative (non–animal) methods. The species and number of animals used in this study were recommended by the USP guidelines.

6.2 Systemic injection in mice, intracutaneous injection, and intramuscular implantation in rabbits are recommended by the USP guidelines for Class VI tests.

6.3 The test article was exposed to the test system directly and through solvents compatible with the test system.

7.0 EXPERIMENTAL DESIGN AND DOSAGE

7.1 Preparation of Test and Control Articles:

7.1.1 Systemic and Intracutaneous Testing Preparation:

7.1.1.1 Properly prepared test articles were extracted at a ratio of 120 cm^2 per 20 mL at 50 ± 2 °C for 72 ± 2 hours.

7.1.1.2 Properly prepared test articles were placed in separate extraction bottles, and to each bottle the appropriate medium was added. The extraction medium completely covered the test article.

7.1.1.3 Each extracting medium (control article) was prepared for parallel treatments and comparisons. Each control article was prepared in the same manner as the test article.

7.1.1.4 The Systemic Injection and Intracutaneous tests were performed using the same extracts. Each extract was agitated vigorously prior to administration. All other test article preparation was as specified by the Sponsor.

7.1.2 Implant Testing Preparation:
The test and control articles were cut into strips measuring 1 mm × 10 mm. The test and control article strips were sterilized by dipping in 70% ethanol prior to implantation.

7.2 Pre–Dose Procedure:

7.2.1 Systemic Injection Test:

7.2.1.1 Acclimated animals were weighed prior to dosing.

7.2.1.2 For the Systemic Injection Test, the PEG test article extract and the corresponding control were diluted with NaCl to obtain PEG concentration of approximately 200 mg/mL.

7.2.2 Intracutaneous Injection Test:

7.2.2.1 On the day of the test, the animals were weighed and clipped free of fur on the dorsal side.

7.2.2.2 For the Intracutaneous Test, the PEG test article extract and the corresponding control were diluted with NaCl to obtain PEG concentration of approximately 120 mg/mL.

7.2.3 Implant Test:
Two rabbits were used for the Implantation Test. On the day of the test, the animals were weighed and the skin on both sides of the spinal column was clipped free of fur. Each animal was anesthetized to prevent muscular movement.

7.3 Dose Administration:

7.3.1 Systemic Injection Test:
Groups of 5 animals were injected with either the test article extract or the corresponding control article extract in the same amounts and by the same routes set forth below:

Extract	Route	Dose/kg	Injection Rate
NaCl	Intravenous	50 mL	0.1 mL/second
CSO	Intraperitoneal	50 mL	—
EtOH	Intravenous	50 mL	0.1 mL/second
PEG	Intraperitoneal	10 g	—

7.3.2 Intracutaneous Injection Test:

7.3.2.1 A volume of 0.2 mL of each test article was injected intracutaneously at five sites on one side of each of two rabbits. More than one test article extract was used per rabbit.

7.3.2.2 At five sites on the other side of each rabbit, 0.2 mL of the corresponding control article was injected.

7.3.3 Implant Test:
Four samples of the test article were implanted into the paravertebral muscle on one side of the spine of each of two rabbits (2.5 to 5.0 cm from the midline, parallel to the spinal column and about 2.5 cm from each other). In a similar fashion, two strips of the Negative Control Plastic was implanted in the contra–lateral muscle of each animal.

7.4 Post–Dose Procedure:

7.4.1 Systemic Injection Test:

7.4.1.1 The animals were observed for clinical signs immediately after injection, 4 hours after injection, and at 24, 48, and 72 ± 2 hours after injection. Observations conducted included all clinical and toxicologic signs.

7.4.1.2 The animals were weighed at the end of the observation period.

7.4.1.3 Animals were sacrificed by carbon dioxide inhalation.

7.4.2 Intracutaneous Injection Test:

7.4.2.1 The injection sites on each animal were observed for signs of erythema and edema 24, 48, and 72 hours after injection of the test article. Observations were scored according to the Draize Scale for Scoring Skin Reactions (see Appendix I). Observations conducted also included all clinical signs.

7.4.2.2 All average erythema and edema scores for the test and control sites at 24, 48, and 72 hours were totaled separately and divided by 12 (2 animals × 3 scoring periods × 2 scoring categories) to determine the overall mean score for the test article versus the corresponding control article.

7.4.2.3 Animals were weighed at the end of the observation period.

7.4.2.4 The animals were returned to the general colony.

7.4.3 Implant Test:

7.4.3.1 The animals were maintained for a period of 7 days.

7.4.3.2 The animals were observed daily for this period to ensure proper healing of the implant sites and for clinical signs of toxicity. Observations included all clinical manifestations.

7.4.3.3 At the end of the observation period, the animals were weighed. Each animal was sacrificed by an injectable barbiturate.

7.4.3.4 Sufficient time was allowed to elapse for the tissue to be cut without bleeding.

7.4.3.5 The area of the tissue surrounding the center portion of each implant strip was examined macroscopically using a magnifying lens. Hemorrhaging, necrosis, discolorations, and infections were scored using the following scale:

0 = Normal
1 = Mild
2 = Moderate
3 = Severe

Encapsulation, if present, was scored by first measuring the width of the capsule (the distance from the periphery of the implant to the periphery of the capsule) rounded to the nearest 0.1 mm. The encapsulation was scored as follows:

Capsule Width	Score
None	0
Up to 0.5 mm	1
0.6 to 1.0 mm	2
1.1 to 2.0 mm	3
Greater than 2.0 mm	4

The differences between the average scores for the test article and control article implant sites were calculated.

8.0 EVALUATION CRITERIA

8.1 Systemic Injection Test:
The test is considered negative if none of the animals injected with the test article show a significantly greater biological reaction than the animals treated with the control article.

If two or more mice die, or show signs of toxicity such as convulsions or prostration, or if three or more mice lose more than 2 g of body weight, the test article does not meet the requirements of the test. If any animal treated with a test article shows only slight signs of biological reaction, and not more than one animal shows gross signs of biological reaction or dies, a repeat test is conducted using groups of 10 mice. On the repeat test, all 10 animals must not show a significantly greater biological reaction than the animals treated with the control article.

8.2 Intracutaneous Injection Test:
The requirements of the test are met if the difference between the test article and control article mean reaction scores (erythema/edema) is 1.0 or less.

If at any observation point, the average reaction to the test article sites is questionably greater than the corresponding control article sites, a repeat for the particular test article extract/solution is conducted using an additional 3 rabbits. On the repeat test, the requirements of the test is met if the difference between the test article and control article mean reaction scores (erythema/edema) is 1.0 or less.

8.3 Implant Test:
The test is considered negative if, in each rabbit, the difference between the average scores for each category of biological reaction for the test article and control article implant sites does not exceed 1.0; or if the difference between the mean scores for all categories of biological reaction for each test article and the average score for all categories for all the control implant sites does not exceed 1.0, for not more than one of four test article strips.

8.4 Class VI Requirements:
The test article satisfies the requirements of the USP Class VI test if the requirements described above are met.

8.5 The study and its design employ methodology to minimize uncertainty of measurement and control of bias for data collection and analysis.

9.0 RESULTS

9.1 Systemic Injection Test:

9.1.1 Animal Weights:
All of the test and control animals increased in weight (Table I).

9.1.2 Clinical Observations:
None of the test or control animals exhibited overt signs of toxicity at any of the observation points (Table I).

9.1.3 The test is considered negative because none of the animals injected with extracts of the test article showed a significantly greater biological reaction than the animals treated with the control articles.

9.2 Intracutaneous Injection Test:

9.2.1 Animal Weights:
All of the animals increased in weight (Table II).

9.2.2 Clinical Observations:
There were no overt signs of toxicity observed in any test or control animals (Table II).

9.2.3 The difference between the test article and control article mean reaction scores (erythema/edema) was less than 1.0. The test article meets the requirements of the Intracutaneous Test. (Table III)

9.3 Implant Test:

9.3.1 Animal Weights:
Both animals increased in weight (Table II).

9.3.2 Clinical Observations:
There were no overt signs of toxicity noted in either animal. Macroscopic evaluation of the test and control article implant sites showed no significant infection, encapsulation, hemorrhage, necrosis, or discoloration (Tables II and IV).

9.3.3 The test is considered negative, since in each rabbit the difference between the average scores for all of the categories of biological reaction for the test article and control article implant sites did not exceed 1.0, and the difference between the mean scores for all categories of biological reaction for all of the test article implant sites and the average score for all categories for all the control implant sites did not exceed 1.0. The test article meets the requirements of the Implantation Test (Table IV).

10.0 CONCLUSION

The USP 0.9% Sodium Chloride for Injection (NaCl), Cottonseed Oil (CSO), 1 in 20 Ethanol in NaCl (EtOH), and Polyethylene Glycol 400 (PEG) extracts of the test article and the test article, Padprinting Ink Series 711-8005 black, did not produce a biological response following intramuscular implantation in rabbits, intracutaneous injection in rabbits, or systemic injection in mice. Therefore, the test article meets the requirements of the USP guidelines, for Class VI Plastics – 50 °C.

11.0 RECORDS

11.1 Original raw data are archived at Toxikon Corporation.

11.2 A copy of the final report and any report amendments is archived at Toxikon Corporation.

11.3 The original final report, and a copy of any protocol amendments or deviations, is forwarded to the Sponsor.

11.4 All unused test article shall be disposed of by Toxikon, per Sponsor's request.

12.0 CONFIDENTIALITY AGREEMENT

Statements of confidentiality were as agreed upon prior to study initiation.

13.0 ANIMAL WELFARE STATEMENT

The Sponsor assured that, to the best of their knowledge, this study did not unnecessarily duplicate previous testing and that there were no non–animal alternatives acceptable for the evaluation of this test article as defined by the protocol.

No evidence of pain and suffering was reported to the Veterinarian and/or Study Director.

Toxikon strictly adhered to the following standards in maintaining the animal care and use program:

United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service, 9 CFR Ch. 1 (1/1/95 edition), Subchapter A–Animal Welfare.

"Guide for the Care and Use of Laboratory Animals," National Research Council, 1996. (NIH).

Office for Laboratory Animal Welfare (OLAW), "Public Health Service Policy on Humane Care and Use of Laboratory Animals," Health Research Extension Act of 1985 (Public Law 99–158 November 20, 1985), Reprinted 1996.

ISO 10993–2, 1992, Biological Evaluation of Medical Devices – Part 2: Animal Welfare Requirements.

Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC) International.

TABLE I
Systemic Injection Test:
Animal Weights and Clinical Observations

Test Article: Padprinting Ink Series 711-8005 black

Lot/Batch #: 050906

Group	Animal #	Sex	Dose (mL)	Body Weight (g)			Signs of Toxicity*
				Day 0 10/12/06	Day 3 10/15/06	Weight Change	
NaCl Test 50 mL/kg	1	Female	0.9	17.7	19.9	2.2	None
	2	Female	1.0	20.3	21.8	1.5	None
	3	Female	0.9	17.0	19.6	2.6	None
	4	Female	1.1	22.8	24.4	1.6	None
	5	Female	1.1	21.1	23.6	2.5	None
NaCl Control 50 mL/kg	6	Female	1.1	21.3	23.7	2.4	None
	7	Female	1.0	20.2	22.0	1.8	None
	8	Female	1.0	19.8	21.7	1.9	None
	9	Female	1.0	20.3	22.9	2.6	None
	10	Female	0.9	17.1	18.5	1.4	None
CSO Test 50 mL/kg	11	Female	0.9	18.9	21.3	2.4	None
	12	Female	1.0	19.8	21.1	1.3	None
	13	Female	1.0	19.5	21.7	2.2	None
	14	Female	0.9	17.4	19.5	2.1	None
	15	Female	0.9	18.5	20.7	2.2	None
CSO Control 50 mL/kg	16	Female	0.9	17.8	20.5	2.7	None
	17	Female	0.9	17.6	19.3	1.7	None
	18	Female	0.9	18.7	20.5	1.8	None
	19	Female	1.0	19.7	21.0	1.3	None
	20	Female	1.0	20.7	22.0	1.3	None
EtOH Test 50 mL/kg	21	Female	1.1	22.6	24.2	1.6	None
	22	Female	1.0	19.7	21.5	1.8	None
	23	Female	0.9	17.3	19.2	1.9	None
	24	Female	0.9	17.0	18.4	1.4	None
	25	Female	1.0	20.9	22.7	1.8	None
EtOH Control 50 mL/kg	26	Female	1.1	21.8	24.4	2.6	None
	27	Female	0.9	17.5	19.4	1.9	None
	28	Female	1.1	21.7	24.2	2.5	None
	29	Female	1.0	19.2	21.0	1.8	None
	30	Female	1.1	22.5	25.1	2.6	None
PEG Test 10 g/kg	31	Female	0.9	18.0	20.6	2.6	None
	32	Female	1.0	19.3	20.9	1.6	None
	33	Female	1.1	21.3	23.7	2.4	None
	34	Female	1.1	23.0	24.6	1.6	None
	35	Female	0.9	18.5	20.0	1.5	None
PEG Control 10 g/kg	36	Female	1.0	20.1	22.5	2.4	None
	37	Female	1.0	19.5	22.0	2.5	None
	38	Female	1.1	22.2	24.7	2.5	None
	39	Female	1.0	20.4	23.1	2.7	None
	40	Female	1.1	21.5	23.9	2.4	None

* Summary of clinical observations - Immediately, 4, 24, 48, and 72 h, after injection.

TABLE II
Intracutaneous Injection and Implant Tests: Animal Weights and Clinical Observations

Test Article: Padprinting Ink Series 711-8005 white

Lot/Batch #: 050906

Group	Animal #	Sex	Body Weight (kg)			Signs of Toxicity*
			Day 0 10/12/06	Day 3 10/15/06	Weight Change	
NaCl & CSO	61464	Female	2.10	2.13	0.03	None
	61465	Male	2.30	2.34	0.04	None
EtOH & PEG	61466	Female	2.05	2.08	0.03	None
	61467	Male	2.37	2.38	0.01	None
Group	**Animal #**	**Sex**	**Body Weight (kg)**			**Signs of Toxicity***
			Day 0 10/12/06	**Day 7 10/19/06**	**Weight Change**	
Implant	61192	Female	3.35	3.48	0.13	None
	61193	Male	3.24	3.45	0.21	None

* Summary of Clinical Observations, Day 0 through Day 3, excluding skin reactions for the Intracutaneous Injection Test and Day 0 through Day 7 for the Implant Test.

TABLE III
Intracutaneous Test Draize Scores

Test Article: Padprinting Ink Series 711-8005 black

Lot/Batch #: 050906

NaCl Extract

Animal #	Vehicle	Time	Site Numbers Scoring (ER/ED)									
			T–1	T–2	T–3	T–4	T–5	C–1	C–2	C–3	C–4	C–5
61464	NaCl	24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
61465	NaCl	72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Total			0.0					0.0				

Overall Mean Score* for Test Article = 0.0
Overall Mean Score* for Control Article = 0.0
Difference between Test Article and Control Article Overall Mean Score = 0.0–0.0 = 0.0

CSO Extract

Animal #	Vehicle	Time	Site Numbers Scoring (ER/ED)									
			T–1	T–2	T–3	T–4	T–5	C–1	C–2	C–3	C–4	C–5
61464	CSO	24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
61465	CSO	72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Total			0.0					0.0				

Overall Mean Score* for Test Article = 0.0
Overall Mean Score* for Control Article = 0.0
Difference between Test Article and Control Article Overall Mean Score = 0.0–0.0 = 0.0

ER = Erythema; ED=Edema; T = Test Sites; C = Control Sites
* Overall Mean Score = Total erythema plus edema scores divided by 12
(2 animals × 3 scoring periods × 2 scoring categories)

TABLE III
Intracutaneous Test Draize Scores (Cont.)

Test Article: Padprinting Ink Series 711-8005 black

Lot/Batch #: 050906

EtOH Extract

Animal #	Vehicle	Time	Site Numbers Scoring (ER/ED)									
			T–1	T–2	T–3	T–4	T–5	C–1	C–2	C–3	C–4	C–5
61466	EtOH	24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
61467	EtOH	72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Total			0.0					0.0				

Overall Mean Score* for Test Article = 0.0
Overall Mean Score* for Control Article = 0.0
Difference between Test Article and Control Article Overall Mean Score = 0.0–0.0 = 0.0

PEG Extract

Animal #	Vehicle	Time	Site Numbers Scoring (ER/ED)									
			T–1	T–2	T–3	T–4	T–5	C–1	C–2	C–3	C–4	C–5
61466	PEG	24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
61467	PEG	72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		24 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
		48 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
Total			0.0					0.0				

Overall Mean Score* for Test Article = 0.0
Overall Mean Score* for Control Article = 0.0
Difference between Test Article and Control Article Overall Mean Score = 0.0–0.0 = 0.0

ER = Erythema; ED=Edema; T = Test Sites; C = Control Sites
* Overall Mean Score = Total erythema plus edema scores divided by 12
(2 animals × 3 scoring periods × 2 scoring categories)

TABLE IV
Implant Test:
Macroscopic Observations

Test Article: Padprinting Ink Series 711-8005 black

Lot/Batch #: 050906

Animal #: 61192

Tissue Site	T1	T2	T3	T4	Test Average	C1	C2	Control Average
Infection	0	0	0	0	0	0	0	0
Encapsulation	0	0	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0	0	0
Necrosis	0	0	0	0	0	0	0	0
Discoloration	0	0	0	0	0	0	0	0
Total	0	0	0	0		0	0	
Mean Score (total/5)	0	0	0	0		0	0	

Animal #: 61193

Tissue Site	T1	T2	T3	T4	Test Average	C1	C2	Control Average
Infection	0	0	0	0	0	0	0	0
Encapsulation	0	0	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0	0	0
Necrosis	0	0	0	0	0	0	0	0
Discoloration	0	0	0	0	0	0	0	0
Total	0	0	0	0		0	0	
Mean Score (total/5)	0	0	0	0		0	0	

T = Test
C = Control

APPENDIX I
Draize Scale for Scoring Skin Reactions

Erythema and eschar formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well–defined erythema	2
Moderate erythema	3
Severe erythema (beet redness) to slight eschar formation (preventing grading of erythema)	4

Total possible erythema score = 4

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

Total possible edema score = 4