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TOXIKON FINAL GLP REPORT: 09–5321–G1

CLASS VI TEST – USP
SYSTEMIC TOXICITY, INTRACUTANEOUS REACTIVITY, 2 WEEK MUSCLE IMPLANT – ISO

Test Article
LSR2050

Author
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Final Report Date
January 22, 2010

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

MANAGEMENT OF THE STUDY

Performing Laboratory
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Sponsor
Momentive Performance Materials
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Waterford, NY 1288

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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, following intracutaneous injection in rabbits and systemic injection in mice, and the test article, following implantation in rabbits, did not produce a biological response. Therefore, the test article, LSR2050, meets the requirements of the USP guidelines for Class VI Plastics – 70 °C, ISO 10993–11 guidelines for the Systemic Injection Test, ISO 10993–10 guidelines for the Intracutaneous Reactivity Test, and is classified as no reaction according to the ISO 10993–6 guidelines for the Implantation Test.

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.

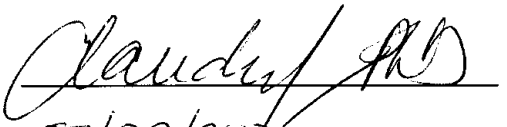
INSPECTIONS	DATE OF INSPECTION	DATE REPORTED STUDY DIRECTOR	DATE REPORTED MANAGEMENT
SACRIFICE	12/30/09	12/30/09	12/30/09
RAW DATA	01/22/10	01/22/10	01/22/10
FINAL REPORT	01/22/10	01/22/10	01/22/10

Ayomi Fernando, B.S.
Quality Assurance

01/22/10
Date

STUDY DIRECTOR SIGNATURE AND VERIFICATION DATES

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

Protocol Number:	PSW/VIVO/001–09/000
Study Director:	Claudine Kos, Ph.D.
Company:	Toxikon Corporation
Signature:	
Date:	07/22/2010
Study Supervisor:	Allan Sleger, A.S., LAT
Pathology Reviewer:	Ying Ping Yu, B.M.
Pathologist:	Alexander G. Richter, M.S., DVM, DACVP

VERIFICATION DATES:
The Study Initiation Date is the date the protocol is signed by the Study Director.

Test Article Receipt:	11/18/09
Project Log Date:	12/02/09
Study Initiation Date:	12/04/09
Extraction Dates:	12/22/09–12/23/09
Technical Initiation:	12/21/09
Technical Completion:	01/11/10
Histopathology Report:	01/18/10

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 32, National Formulary 27, 2009. <88> Biological Reactivity Tests, *In Vivo*.

2.2 ISO 10993–10, 2002, Biological Evaluation of Medical Devices – Part 10: Tests for Irritation and Delayed–Type Hypersensitivity, as amended 2006.

2.3 ISO 10993–11, 2006, Biological Evaluation of Medical Devices – Part 11: Tests for Systemic Toxicity.

2.4 ISO 10993–6, 2007, Biological Evaluation of Medical Devices – Part 6: Tests for Local Effects After Implantation.

2.5 ASTM F981–04, Standard Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Bone, 2004.

2.6 ASTM F763–04, Standard Practice for Short Term Screening of Implant Materials, 2004.

2.7 ISO 10993–12, 2007, Biological Evaluation of Medical Devices – Part 12: Sample Preparation and Reference Materials.

2.8 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: LSR2050
CAS/Code #: Not Supplied by Sponsor (N/S)
Lot/Batch #: 09B094 (WTFD)
Physical State: 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 (N/S)
Safety Precautions: Standard Laboratory Safety Precautions
Sponsor Note: LSR2050 (WTFD), press cure 10 min @ 175 C; post cure 4 hrs at 200 C)

4.2 Control Articles (Toxikon Supplied):

4.2.1 Negative Control Article Name: USP 0.9% Sodium Chloride for Injection (NaCl)
Toxikon QC #: CSC-09-10-011-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-09-11-006-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-08-12-008-VV; CSC-09-10-011-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-09-06-015-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

4.3 Reagent (Toxikon Supplied):

Reagent Name: Sterile Water for Injection (SWFI)
Toxikon QC #: CSC-09-09-004-VV
Physical State: Liquid
Color: Colorless
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 (females were non-pregnant and nulliparous)

Weight/Age Range: 17.0 – 22.9 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 Laboratories, Indianapolis, IN

Animal Identification: ear punch

Acclimation: minimum 5 days, under same conditions as for the actual test

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

5.1.2 Intracutaneous Injection and Implant Tests:

Number and Species: 9 New Zealand White rabbits (*Oryctolagus cuniculus*)

Sex: 4 males and 5 females (females were non-pregnant and nulliparous)

Weight/Age Range: 2.34 – 2.55 kilograms for Intracutaneous
3.04 – 3.55 kilograms for Implant Test
at least 10 weeks old (young adult)
weighed to nearest 10 g

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

Animal Purchase: Covance Laboratories, Madison, WI (Intracutaneous)
Millbrook Breeding Labs, Amherst, MA (Implant)

Animal Identification: ear marker

Acclimation: minimum 5 days, under same conditions as for the actual test

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

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: a minimum of 10 changes per hour

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

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 Laboratories, 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: a minimum of 10 changes per hour

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

Housing: individually housed

Cages: suspended stainless steel

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

Animal Rations: TEK Hi–Fiber Rabbit Diet 2031, Harlan Laboratories, 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 Mice were used in this study because they have historically been used in systemic safety evaluation studies and the guidelines have no alternative (non–animal) methods. Animals were treated by intravenous and intraperitoneal routes. The animal species, number, and route of test article administration were recommended by both the USP and the ISO 10993–11 guidelines.

6.2 New Zealand White rabbits were used in this study because they have been historically used in intracutaneous and implantation safety evaluation studies and the guidelines have no alternative (non–animal) methods. Animals were treated by Intracutaneous Injections and Intramuscular Implantation. The animal species, number, and route were recommended by the USP, ISO 10993–6 and ISO 10993–10 guidelines.

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 Test and Control Extracts:

7.1.1.1 The test article (60 cm^2) was combined with 20 mL of vehicle at a ratio of 3 cm^2 per 1 mL per ISO 10993–12 and USP guidelines. The test article was separately extracted in NaCl, CSO, EtOH, and PEG at 70 ± 2 °C for 24 ± 2 hours for the Systemic Injection and Intracutaneous Injection tests.

7.1.1.2 Prior to extraction, the test article was washed two times with 70 mL of SWFI. The test article sample prepared for extraction with CSO was dried at 50 ± 2 °C for 1 ± 0.1 hour.

7.1.1.3 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.

7.1.1.4 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.

7.1.1.5 The Systemic Injection and Intracutaneous tests were performed using the same extracts. The test article appeared unchanged by the extraction procedure. It was not degraded or deformed. The extract was clear and free from particulates. Each extract was agitated vigorously prior to administration. All other test article preparation was as specified by the Sponsor.

7.1.2 Test and Control Implants:

7.1.2.1 All apparatus strips were prepared according to the ISO 10993–6 and USP guidelines. The test article (Sponsor–supplied) was cut to measure approximately 1 mm in diameter and 10 mm in length with rounded cross section and rounded ends. It was the Sponsor's responsibility to ensure that the test article was manufactured, processed, cleaned of contaminants, and sterilized by the methods intended for the final end use product. The test article was sterilized by dipping in 70% ethanol.

7.1.2.2 The control strips were Negative Control Plastic cut to measure approximately 1 mm in diameter by 10 mm in length and were sterilized by dipping in 70% ethanol.

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:

7.2.3.1 Two rabbits were used for the USP Implant Test and three rabbits were used for the ISO Implant Test.

7.2.3.2 Each animal was weighed prior to implantation.

7.2.3.3 On the day of the test, the dorsal side of the animals was clipped free of fur and loose hair was removed by means of vacuum.

7.2.3.4 Each animal was appropriately anesthetized. Prior to implantation, the area was swabbed with a surgical preparation solution.

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	2 mL/minute
CSO	Intraperitoneal	50 mL	—
EtOH	Intravenous	50 mL	2 mL/minute
PEG	Intraperitoneal	10 g	—

7.3.2 Intracutaneous Injection Test:

7.3.2.1 A volume of 0.2 mL of each test article extract 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 other sites on the other side of each rabbit, 0.2 mL of the corresponding control article was injected.

7.3.3 USP Implant Test:
Four strips 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 were implanted in the contralateral muscle of each animal.

7.3.4 ISO Implant Test:
Six strips of the test article were implanted into each of the paravertebral muscles of each rabbit, approximately 2.5 cm from the midline and parallel to the spinal column and approximately 2.5 cm from each other. The test article strips were implanted on one side of the spine. In a similar fashion, six negative control strips were implanted in the contralateral muscle of each animal. A total of at least ten test article strips and ten control strips are required for evaluation.

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 24, 48, and 72 ± 2 hours after injection.

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 immediately after injection and at 24, 48, and 72 hours after injection of the test article. Observations were scored according to the Classification System for Scoring Skin Reactions (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 for the USP implant test and a period of 2 weeks for the ISO implant test.

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 Gross Observations:
The paravertebral muscles in which the test or control articles were implanted were excised *in toto* from each animal. The muscle tissue was removed by carefully slicing around the implant sites with a scalpel and lifting out the tissue. The excised implant tissues were examined grossly. For the ISO Implant Test, excessively invasive procedures that may have disrupted the integrity of the tissue for histopathological evaluation were not used. The tissues for histopathological assessment were placed in properly labeled containers containing 10% neutral buffered formalin. The axillary lymph nodes were examined with no findings and were not collected.

7.4.3.6 USP Macroscopic Evaluation:
The area of the tissue surrounding the center portion of each implant strip was examined macroscopically using a magnifying lens. Hemorrahaging, 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.

7.4.3.7 ISO Histopathology:

7.4.3.7.1 Following fixation in formalin, each of the implant sites was excised from the larger mass of tissue. The implant site, containing the implanted material, was examined macroscopically, aided by a magnifying glass if needed. Each site was examined for signs of inflammation, encapsulation, hemorrhaging, necrosis, and discoloration using the following scale:

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

7.4.3.7.2 The presence, form, and location of the implant material were recorded. The implant material was noted to appear unchanged. Photographs of the sites were taken and retained as part of the raw data and microscopic results were reported.

7.4.3.7.3 After macroscopic observation, the implant material was removed and a slice of tissue containing the implant site was processed. Histologic slides of hematoxylin and eosin stained sections were prepared by Toxikon.

7.4.3.7.4 The slides were evaluated and graded by light microscopic examination.

7.4.3.8 ISO Pathological Assessment:

7.4.3.8.1 The following categories of biological reaction were assessed by microscopic observation and the responses graded according to the following tables for each implant site:

TABLE 1
Inflammatory Responses

Cell Type/Response	Score				
	0	1	2	3	4
Polymorphonuclear Cells	0	Rare, 1–5/phf[a]	5–10/phf	Heavy Infiltrate	Packed
Lymphocytes	0	Rare, 1–5/phf	5–10/phf	Heavy Infiltrate	Packed
Plasma Cells	0	Rare, 1–5/phf	5–10/phf	Heavy Infiltrate	Packed
Macrophages	0	Rare, 1–5/phf	5–10/phf	Heavy Infiltrate	Packed
Giant Cells	0	Rare, 1–2/phf	3–5/phf	Heavy Infiltrate	Sheets
Necrosis	0	Minimal	Mild	Moderate	Severe

[a] phf = per high powered (400 ×) field.

TABLE 2
Healing Responses

Cell Type/Response	Score				
	0	1	2	3	4
Neovascularisation	0	Minimal capillary, proliferation, focal, 1–3 buds	Groups of 4–7 capillaries with supporting fibroblastic structures	Broad band of capillaries with supporting structures	Extensive band of capillaries with supporting fibroblastic structures
Fibrosis	0	Narrow band	Moderately thick band	Thick band	Extensive band
Fatty Infiltrate	0	Minimal amount of fat associated with fibrosis	Several layers of fat and fibrosis	Elongated and broad accumulation of fat cells about the implant site	Extensive fat completely surrounding the implant

7.4.3.8.2 The relative size of the involved area was scored by assessing the width of the area from the implant/tissue interface to unaffected areas which have the characteristics of normal tissue and normal vascularity. Relative size of the involved area was scored using the following scale:

0 = 0 mm, No site
1 = up to 0.5 mm, Very slight
2 = 0.6–1.0 mm, Mild
3 = 1.1–2.0 mm, Moderate
4 = > 2.0 mm, Severe

8.0 EVALUATION CRITERIA

8.1 Systemic Injection Test:
The test is considered negative if none of the animals injected with the test article shows 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 10% body weight loss, 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 should be conducted using an additional 3 rabbits. On the repeat test, the requirements of the test will be 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:

8.3.1 USP 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 do 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 do not exceed 1.0, for not more than one of four test article strips.

8.3.2 ISO Bioreactivity Rating:

8.3.2.1 For each implanted site, a total score is determined. The inflammatory responses are totaled for each site and weighted by a factor or two (2). The healing responses are totaled separately. Inflammatory and healing responses are then added together resulting in a total score for each site. The average score of the test sites for each animal is compared to the average score of the control sites for that animal. The average difference between test and controls for all animals is calculated and the initial Bioreactivity Rating is assigned as follows:

0 – 2.9	No Reaction*
3.0 – 8.9	Slight Reaction
9.0 – 15.0	Moderate Reaction
> 15	Severe Reaction

* A negative calculation is reported as zero (0).

8.3.2.2 Modification of the Rating:
The pathology observer reviews the calculated level of bioreactivity. Based on the observation of all factors (e.g. relative size, pattern of response, inflammatory vs. resolution), the pathology observer may revise the Bioreactivity Rating. Justification for the modification to the rating is presented in the narrative report (Appendix II).

8.3.2.3 A descriptive narrative report regarding the biocompatibility of the test material is provided by the pathology observer (Appendix II).

8.4 Class VI Requirements:
The test article satisfies the requirements of the USP guidelines for the 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 (Table 3):

9.1.1 Animal Weights:
All test and control animals increased in weight.

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

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

9.2 Intracutaneous Test (Tables 4 and 5):

9.2.1 Animal Weights:
All of the animals increased in weight.

9.2.2 Clinical Observations:
There were no significant signs of erythema or edema observed at any of the test or control article sites.

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

9.3 USP Implant Test (Tables 4 and 6):

9.3.1 Animal Weights:
Both animals increased in weight.

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.

9.3.3 Per USP guidelines, 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.

9.4 ISO Implant Test (Tables 4, 7, and 8)

9.4.1 Animal Weights:
All of the animals increased in weight.

9.4.2 Clinical Observations:
There were no overt signs of toxicity noted in any animal.

9.4.3 Implantation Site Observations (Macroscopic) (ISO 10993–6):
Macroscopic evaluation of the test article implant sites indicated no significant signs of inflammation, encapsulation, hemorrhage, necrosis, or discoloration at the 2 week time period.

9.4.3 Implantation Site Observations (Microscopic):
Microscopic evaluation of the test article implant sites indicated no significant signs of inflammation, fibrosis, hemorrhage, or necrosis as compared to the control article sites. The Bioreactivity Rating for the 2 week time period (average of three animals) was 1.2, indicating no reaction.

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, following intracutaneous injection in rabbits and systemic injection in mice, and the test article, following implantation in rabbits, did not produce a biological response. Therefore, the test article, LSR2050, meets the requirements of the USP guidelines for Class VI Plastics – 70 °C, ISO 10993–11 guidelines for the Systemic Injection Test, ISO 10993–10 guidelines for the Intracutaneous Reactivity Test, and is classified as no reaction according to the ISO 10993–6 guidelines for the Implantation Test.

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 used and unused test article shall be disposed of by Toxikon.

12.0 CONFIDENTIALITY AGREEMENT

Per corporate policy, confidentiality shall be maintained in general, and in specific accordance with any relevant agreement specifically executed between Toxikon and the Sponsor.

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, 2006, Biological Evaluation of Medical Devices – Part 2: Animal Welfare Requirements.

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

TABLE 3
Systemic Injection Test:
Animal Weights and Clinical Observations

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

Group	Animal #	Sex	Dose (mL)	Body Weight (g)					Signs of Toxicity*
				Day 0 12/23/09	Day 1 12/24/09	Day 2 12/25/09	Day 3 12/26/09	Weight Change	
NaCl Test 50 mL/kg	1	Female	0.9	17.6	18.1	18.4	18.9	1.3	None
	2	Female	0.9	17.7	18.3	19.3	20.5	2.8	None
	3	Female	1.1	22.2	22.9	23.4	24.6	2.4	None
	4	Female	0.9	18.1	19.4	19.8	20.6	2.5	None
	5	Female	1.0	19.1	20.4	21.6	22.2	3.1	None
NaCl Control 50 mL/kg	6	Female	1.1	22.0	23.1	24.5	25.3	3.3	None
	7	Female	1.1	21.2	22.5	23.0	23.7	2.5	None
	8	Female	0.9	18.3	18.9	19.7	20.9	2.6	None
	9	Female	1.0	20.5	20.9	21.3	21.6	1.1	None
	10	Female	0.9	18.3	18.7	19.2	20.5	2.2	None
CSO Test 50 mL/kg	11	Female	0.9	18.8	19.3	20.0	21.2	2.4	None
	12	Female	1.0	20.1	20.5	21.7	22.4	2.3	None
	13	Female	0.9	17.3	18.0	18.3	19.3	2.0	None
	14	Female	0.9	18.9	19.0	19.7	20.6	1.7	None
	15	Female	1.1	22.3	23.6	24.0	24.3	2.0	None
CSO Control 50 mL/kg	16	Female	1.1	21.7	22.1	22.9	23.6	1.9	None
	17	Female	1.0	20.4	21.2	22.4	22.9	2.5	None
	18	Female	1.1	22.9	23.8	24.7	25.6	2.7	None
	19	Female	0.9	17.1	18.0	18.7	19.6	2.5	None
	20	Female	1.1	22.8	23.6	24.0	25.1	2.3	None
EtOH Test 50 mL/kg	21	Female	1.0	19.6	20.1	21.3	22.4	2.8	None
	22	Female	1.1	21.4	22.8	24.0	24.4	3.0	None
	23	Female	0.9	18.6	19.8	21.0	22.3	3.7	None
	24	Female	1.1	21.3	22.0	22.3	23.4	2.1	None
	25	Female	0.9	17.7	18.6	19.1	20.2	2.5	None
EtOH Control 50 mL/kg	26	Female	0.9	17.0	17.5	18.1	19.1	2.1	None
	27	Female	0.9	17.8	18.7	20.0	21.3	3.5	None
	28	Female	1.1	22.4	23.2	24.6	25.9	3.5	None
	29	Female	1.0	20.3	21.1	21.4	21.7	1.4	None
	30	Female	0.9	17.8	18.4	19.6	20.7	2.9	None
PEG Test 10 g/kg	31	Female	1.0	20.3	20.9	21.7	23.1	2.8	None
	32	Female	1.1	22.1	23.2	23.9	24.8	2.7	None
	33	Female	1.1	21.4	22.8	23.1	24.4	3.0	None
	34	Female	0.9	17.9	19.1	19.4	20.0	2.1	None
	35	Female	0.9	17.7	18.5	19.2	20.0	2.3	None
PEG Control 10 g/kg	36	Female	1.0	20.2	21.3	21.8	22.9	2.7	None
	37	Female	1.1	21.5	22.7	23.5	24.2	2.7	None
	38	Female	0.9	17.7	18.0	19.1	20.3	2.6	None
	39	Female	0.9	18.0	19.4	20.7	21.0	3.0	None
	40	Female	0.9	18.7	20.1	20.9	21.2	2.5	None

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

TABLE 4
Intracutaneous Injection and Implant Tests: Animal Weights and Clinical Observations

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

Group	Animal #	Sex	Body Weight (kg)			Signs of Toxicity*
			Day 0 12/23/09	Day 3 12/26/09	Weight Change	
NaCl & CSO	91777	Male	2.34	2.42	0.08	None
	91778	Female	2.55	2.62	0.07	None
EtOH & PEG	91779	Male	2.38	2.45	0.07	None
	91780	Female	2.48	2.50	0.02	None
Group	**Animal #**	**Sex**	**Body Weight (kg)**			**Signs of Toxicity***
			Day 0 12/23/09	**Day 7 12/30/09**	**Weight Change**	
USP Implant (7 Days)	91621	Male	3.04	3.07	0.03	None
	91623	Male	3.18	3.29	0.11	None
Group	**Animal #**	**Sex**	**Body Weight (kg)**			**Signs of Toxicity***
			Day 0 12/23/09	**Day 14 01/06/10**	**Weight Change**	
ISO Implant (2 Weeks)	B90401	Female	3.40	3.84	0.44	None
	B90402	Female	3.30	3.72	0.42	None
	B90403	Female	3.55	3.57	0.02	None

* Summary of Clinical Observations, Day 0 through Day 3, excluding skin reactions for the Intracutaneous Injection Test, Day 0 through Day 7 for the Implant Test (USP), and Day 0 through Day 14 for the Implant Test (ISO).

TABLE 5
Intracutaneous Test:
Skin Reaction Scores

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

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
91777	NaCl	0 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
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91778	NaCl	0 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
		72 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				

† = Immediately after injection, not used for the evaluation criteria.
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–6	T–7	T–8	T–9	T–10	C–6	C–7	C–8	C–9	C–10
91777	CSO	0 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
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91778	CSO	0 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
		72 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				

† = Immediately after injection, not used for the evaluation criteria.
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 5
Intracutaneous Test:
Skin Reaction Scores (Cont.)

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

EtOH Extract

Animal #	Vehicle	Time	Site Numbers Scoring (ER/ED)									
			T–11	T–12	T–13	T–14	T–15	C–11	C–12	C–13	C–14	C–15
91779	EtOH	0 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
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91780	EtOH	0 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
		72 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				

† = Immediately after injection, not used for the evaluation criteria.
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–16	T–17	T–18	T–19	T–20	C–16	C–17	C–18	C–19	C–20
91779	PEG	0 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
		72 hours	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0	0/0
91780	PEG	0 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
		72 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				

† = Immediately after injection, not used for the evaluation criteria.
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 6
USP Implant Test:
Macroscopic Observations
7 Days

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

Animal #: 91621

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 #: 91623

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

TABLE 7
ISO Implant Test:
Macroscopic Observations
2 Weeks

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

Animal #: B90401

Tissue Site	T1	T2	T3	T4	T5	T6	Test Average	C1	C2	C3	C4	C5	C6	Control Average
Inflammation	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Encapsulation	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Necrosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Discoloration	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0		0	0	0	0	0	0	

Animal #: B90402

Tissue Site	T1	T2	T3	T4	T5	T6	Test Average	C1	C2	C3	C4	C5	C6	Control Average
Inflammation	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Encapsulation	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Necrosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Discoloration	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0		0	0	0	0	0	0	

Animal #: B90403

Tissue Site	T1	T2	T3	T4	T5	T6	Test Average	C1	C2	C3	C4	C5	C6	Control Average
Inflammation	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Encapsulation	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hemorrhage	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Necrosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Discoloration	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0		0	0	0	0	0	0	

T = Test
C = Control

Grading Scale

0 = no reaction
1 = mild reaction
2 = moderate reaction
3 = severe reaction

TABLE 8
Microscopic Observations
2 Week Implantation

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

Animal #: B90401

Categories of Reaction	Test Sites						Control Sites					
	T1	T2	T3	T4	T5	T6	C1	C2	C3	C4	C5	C6
Foreign Debris	0	0	0	0	0	0	0	0	0	0	0	0
Rel. Size	1	1	1	1	1	1	1	1	1	1	0	1
*Polymorphs	2	1	1	2	1	1	1	1	1	1	1	1
*Lymphocytes	0	0	0	0	0	0	0	0	0	0	0	0
*Plasma Cells	0	0	0	0	0	0	0	0	0	0	0	0
*Macrophages	2	1	1	2	1	1	1	1	1	1	1	1
*Giant Cells	0	0	0	0	0	0	0	0	0	0	0	0
*Necrosis	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal (x2)	**8**	**4**	**4**	**8**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**
*Neovascularisation	1	1	1	1	1	1	1	0	1	0	1	1
*Fibrosis	1	1	1	1	1	1	1	1	1	1	1	1
*Fatty Infiltrate	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal (x1)	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**1**	**2**	**1**	**2**	**2**
TOTAL	**10**	**6**	**6**	**10**	**6**	**6**	**6**	**5**	**6**	**5**	**6**	**6**

Animal Test Score (Average of Totals) = 7.3
Animal Control Score (Average of Totals) = 5.7

Animal Score (Average Test Score - Average Control Score) = 1.6

* Used in calculation of Bioreactivity Rating.

TABLE 8
Microscopic Observations (Cont.)
2 Week Implantation

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

Animal #: B90402

Categories of Reaction	Test Sites						Control Sites					
	T1	T2	T3	T4	T5	T6	C1	C2	C3	C4	C5	C6
Foreign Debris	0	0	0	0	0	0	0	0	0	0	0	0
Rel. Size	1	1	1	1	1	1	1	1	1	1	1	1
*Polymorphs	1	1	1	2	1	1	1	1	1	1	1	1
*Lymphocytes	0	0	0	0	0	0	0	0	0	0	0	0
*Plasma Cells	0	0	0	0	0	0	0	0	0	0	0	0
*Macrophages	1	1	1	2	1	1	1	1	1	1	1	1
*Giant Cells	0	0	0	0	0	0	0	0	0	0	0	0
*Necrosis	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal (x2)	**4**	**4**	**4**	**8**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**
*Neovascularisation	1	1	1	1	1	1	1	0	1	0	1	1
*Fibrosis	1	1	1	1	1	1	1	1	1	1	1	1
*Fatty Infiltrate	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal (x1)	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**1**	**2**	**1**	**2**	**2**
TOTAL	**6**	**6**	**6**	**10**	**6**	**6**	**6**	**5**	**6**	**5**	**6**	**6**

Animal Test Score (Average of Totals) = 6.7
Animal Control Score (Average of Totals) = 5.7

Animal Score (Average Test Score - Average Control Score) = 1.0

* Used in calculation of Bioreactivity Rating.

TABLE 8
Microscopic Observations (Cont.)
2 Week Implantation

Test Article: LSR2050

Lot/Batch #: 09B094 (WTFD)

Animal #: B90403

Categories of Reaction	Test Sites						Control Sites					
	T1	T2	T3	T4	T5	T6	C1	C2	C3	C4	C5	C6
Foreign Debris	0	0	0	0	0	0	0	0	0	0	0	0
Rel. Size	1	1	1	1	1	1	1	1	1	1	1	1
*Polymorphs	1	1	1	2	1	1	1	1	1	1	1	1
*Lymphocytes	0	0	0	0	0	0	0	0	0	0	0	0
*Plasma Cells	0	0	0	0	0	0	0	0	0	0	0	0
*Macrophages	1	1	1	2	1	1	1	1	1	1	1	1
*Giant Cells	0	0	0	0	0	0	0	0	0	0	0	0
*Necrosis	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal (x2)	**4**	**4**	**4**	**8**	**4**	**4**	**4**	**4**	**4**	**4**	**4**	**4**
*Neovascularisation	1	1	1	1	1	1	1	0	1	0	1	1
*Fibrosis	1	1	1	1	1	1	1	1	1	1	1	1
*Fatty Infiltrate	0	0	0	0	0	0	0	0	0	0	0	0
Subtotal (x1)	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**1**	**2**	**1**	**2**	**2**
TOTAL	**6**	**6**	**6**	**10**	**6**	**6**	**6**	**5**	**6**	**5**	**6**	**6**

Animal Test Score (Average of Totals) = 6.7
Animal Control Score (Average of Totals) = 5.7

Animal Score (Average Test Score - Average Control Score) = 1.0

* Used in calculation of Bioreactivity Rating.

Animal Number B90401 = 1.6
Animal Number B90402 = 1.0
Animal Number B90403 = 1.0

Bioreactivity Rating = 1.2 = No Reaction

APPENDIX I
Classification System 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 (injuries in depth)	4

Total possible erythema score = 4

Edema Formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges are 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

Total possible score for irritation = 8

APPENDIX II
Histopathology Report

APPENDIX III
Software Systems

Software	Use
Adobe Acrobat 8 Professional	Document preparation
DocuKnowledge 3.0	Lotus Domino–based document management system used for SOPs
Lotus Domino Rel. 5	Client–server application for sponsor, sample, test codes, and quotation management application databases
MS Office 2007 Small Business Suite	Business software (suite includes Word, Excel, PowerPoint, Outlook, Publisher, Office tools)
Rees CentronSQL System 2.0	Environmental monitoring and metrology system