FINAL STUDY REPORT

STUDY TITLE:	**ISO MEM Elution Assay With L-929 Mouse Fibroblast Cells**
PROTOCOL NUMBER:	140320-19
TEST ARTICLE IDENTIFICATION:	Part Description: SLR Size Electronics Cover with Zipper, Part Number: EC2800, Part Lot Number: 130911
PERFORMING LABORATORY:	WuXi AppTec 2540 Executive Drive St. Paul, MN 55120
SPONSOR:	Whitney Medical Solutions 6153C Mulford Street Niles, IL 60714
STUDY NUMBER:	194971
CLIENT MNEMONIC:	WMS01
RESULT SUMMARY:	The test article is considered **non-cytotoxic** under the conditions of this test.

QUALITY ASSURANCE UNIT SUMMARY

The objective of the Quality Assurance Unit is to monitor the conduct and reporting of nonclinical laboratory studies. This study has been performed under Good Laboratory Practice regulations (21 CFR part 58) and in accordance to standard operating procedures and a standard protocol. The Quality Assurance Unit maintains a copy of the study protocol and standard operating procedures and has inspected this study on the date(s) listed below. Each inspection was performed to assure the quality and integrity of the study.

Phase Inspected	Date	Study Director	Management
Reading Cells	12/17/13	12/18/13	01/06/14
Final Report	01/06/14	01/06/14	01/06/14

The findings of these inspections have been reported to management and the Study Director.

Quality Assurance Auditor: Michelle Abel Date: 01-07-14
Michelle Abel

GOOD LABORATORY PRACTICE STATEMENT

The study referenced in this report was conducted in compliance with U.S. Food and Drug Administration Good Laboratory Practice (GLP) regulations set forth in 21 CFR part 58.

The studies not performed by or under the direction of WuXi AppTec, are exempt from this Good Laboratory Practice Statement and include characterization and stability of the test compound(s)/test article.

Study Director: Date: 1/7/14
Ryan Koslofsky

Professional personnel involved:

Teri Tanquist, BS	Vice President of Process Improvement and Operations
Christine Olson, BS	Study Operations Director
Christine Bubendorf, BA	Associate Director of Operations
Ryan Koslofsky, MS	Study Director
Jean Mesarich, AA	Client Relations Manager

PURPOSE

The purpose of this study was to evaluate an extract of a test article for cytotoxicity to mammalian cells in culture by a method compliant with the requirements specified in ISO 10993-5:2009.

TEST FACILITY: WuXi AppTec
2540 Executive Drive
St. Paul, MN 55120

TEST ARTICLE RECEIVED:	12/09/13
INITIATION DATE:	12/11/13
COMPLETION DATE:	01/07/14

TEST ARTICLE IDENTIFICATION

Test Article Name:	Part Description: SLR Size Electronics Cover with Zipper, Part Number: EC2800, Part Lot Number: 130911
Lot #:	130911
Sterilization Method:	Radiation
Physical State:	Insoluble Material
Expiration Date:	Not Applicable
Storage Conditions:	Room Temperature
Intended Use/Application:	To be used to cover a variety of surgical and non-surgical equipment in various clinical settings.
Physical Description:	According to the Sponsor, the test article consisted of an LDPE Bag.

CHARACTERIZATION

The Sponsor was responsible for all test article characterization data as specified in the GLP regulations. The identity, strength, stability, purity, and chemical composition of the test article were solely the responsibility of the Sponsor. The Sponsor was responsible for supplying to the testing laboratory results of these determinations and any others that may have directly impacted the testing performed by the testing laboratory, prior to initiation of testing.

Furthermore, it was the responsibility of the Sponsor to ensure that the test article submitted for testing was representative of the final product that was subjected to materials characterization. Any special requirements for handling or storage were arranged in advance of receipt and the test article was received in good condition.

SAMPLE STORAGE

Upon receipt by the Sample Receiving Department, the test samples were placed in a designated, controlled access storage area ensuring proper temperature conditions. Test and control article storage areas are designed to preclude the possibility of mix-ups, contamination, deterioration or damage. The samples remained in the storage area until retrieved by the technician for sample preparation and/or testing.

SAFETY

Appropriate routine safety procedures were followed in handling the test article, unless more cautious procedures were specified by the Sponsor. All applicable WuXi AppTec safety policies and procedures were observed during the performance of the test.

EXPERIMENTAL DESIGN

Experimental Summary

The MEM elution assay evaluated the cytotoxic effects of the test article extracts on L-929 mouse fibroblast cells. The assay was conducted by extracting the test article and controls in E-MEM + 5% FBS for 24 ± 2 hours. The cultures were evaluated for cytotoxic effects by microscopic examination at 24, 48, and 72 ± 4 hours of incubation.

The test article was incubated in the appropriate volume of E-MEM + 5% FBS in a sterile vessel for 24 ± 2 hours at 37 ± 1 °C. At the end of the extraction period, the maintenance culture media was removed from test culture wells and replaced with 1 mL of test / control media. The positive control, test article extract, and control extracts were added at the same time to the culture plate in triplicate wells. The plates were then incubated for 72 ± 4 hours at 37 ± 1 °C in a humidified atmosphere of 5 ± 1% CO_2 in air. The cultures were evaluated for cytotoxic effects by microscopic examination at 24, 48, and 72 ± 4 hours of incubation.

Justification for Selection of the Test System
The MEM Elution Assay is one of several *in vitro* mammalian cell tests which have been used to screen materials for their potential cytotoxicity. The L-929 cell line has a history of use in assays of this type.

PROTOCOL AMENDMENTS/DEVIATIONS

Amendments
There were no amendments that occurred during the course of this study.

Deviations
During study initiation an outdated client protocol approval form was signed by the study director. The changes between versions 18 and 19 of the protocol were only for clarification of the positive control and cell growth incubation parameters. There were no changes in materials or methods used for testing and all of the correct parameters were used for testing, thus this deviation did not impact the interpretation of the study.

IDENTIFICATION OF TEST SYSTEM
Cultures of L-929 cells (mouse fibroblast) were obtained from American Type Culture Collection (ATCC # CCL-1). Mycoplasma-free cell lines were purchased from the vendor and kept frozen in the lab until used. To maintain the sensitivity, they are only sub-cultured for up to 15 passages and then discarded.

Cultures were grown and used as monolayers in disposable tissue culture labware at 37 ± 1 °C in a humidified atmosphere of 5 ± 1% CO_2 in air at WuXi AppTec. The media used for growth of cells is Eagle's minimal essential medium (E-MEM) supplemented with 5% (v/v) fetal bovine serum (FBS). The medium is also supplemented with the following: 2 mM L-glutamine, 10 mM HEPES, 0.01 mg/mL vancomycin, 0.01 mg/mL gentamicin, 1% 1000 units/mL penicillin, and 1% 2.50 µg/mL amphotericin B (Fungizone). WuXi AppTec has a long-standing history using antibiotics in culture medium. The use of antibiotics in culture media has not shown adverse effects when used for this assay; this is exhibited by the varying degrees of toxicity seen in the assay controls.

TEST ARTICLE PREPARATION
The test article, was cut for extraction, placed into an extraction vessel, and prepared at a ratio of 120 cm^2 to 20 mL of extraction vehicle.

Table 1: Test Article Record

Vehicle	Test Article Area (cm^2)	Vehicle Amount (mL)	Quantity of Test Article Used
E-MEM + 5% FBS	3909.00	651.5	1

CONTROL ARTICLE PREPARATION
A negative, positive, and cell control were run in parallel with the test article. A negative control (high density polyethylene (HDPE)) known to be non-toxic under the test conditions was prepared at a ratio of 60 cm^2 to 20 mL of extraction vehicle. A positive control (polyurethane film containing 0.1% zinc diethyldithiocarbamate (ZDEC)) known to be toxic under the test conditions was prepared at a ratio of 120 cm^2 to 20 mL of extraction vehicle. A cell control (E-MEM + 5% FBS) was incubated in parallel with the test sample and controls.

Table 2: Control / Cell Line Record

Control Identification	Class	Lot #	Supplier	Expiration
ZDEC	Positive Control	A-133	Hatano	03/2018
High Density Polyethylene (HDPE)	Negative Control	C-111	Hatano	08/2018
E-MEM + 5% FBS	Cell Control	LP112613S1	WXAT	12/24/13
L-929	Cell Line	L121213	ATCC	NA

NA = Not Applicable

EXTRACTION VEHICLE PREPARATION (E-MEM + 5% FBS)

Eagle's minimal essential medium (E-MEM), supplemented with 5% (v/v) fetal bovine serum (FBS), was used to extract the test article. The medium was also supplemented with the following: 2 mM L-glutamine, 10 mM HEPES, 0.01 mg/mL vancomycin, 0.01 mg/mL gentamicin, 1% 1000 units/mL penicillin, and 1% 2.50 µg/mL amphotericin B (Fungizone). The pH was confirmed to be 7.24.

TEST ARTICLE EXTRACTION

The extraction mixture and controls were then incubated for 24 ± 2 hours at 37 ± 1 °C. At the start of the extraction, the solutions appeared clear and free of particulates. The extracts were agitated during the course of the extraction period. At the end of the extraction period, the vessels were shaken well. The test article was observed after extraction to be intact with no macroscopically observable degradation and the extract was clear, normal in color, and particulate free. The extract was not filtered prior to use and was used immediately. See Tables 1-3.

Table 3: Extraction Record

Vehicle	Extraction Temperature (In)	Date/Time of Extraction Start	Extraction Temperature (Out)	Date/Time of Extraction End
E-MEM + 5% FBS	37.0 °C	12/15/13 1:28 pm	37.0 °C	12/16/13 1:12 pm

EXPERIMENTAL PROCEDURE

L-929 cells were plated at 2.5 x 10^4 cells/mL four days before use. Prior to dosing, the cell cultures were examined to ensure they had formed a nearly confluent monolayer and that they appeared uniform and viable.

The test article and controls were extracted with the appropriate amount of E-MEM + 5% FBS for 24 ± 2 hours at 37 ± 1 °C. At the end of the extraction period, the vessels were well shaken and the extraction media was used immediately. 1.0 mL aliquots of the test article and control extracts were plated in triplicate onto the cell line.

The cell cultures were incubated in a humidified atmosphere for 72 ± 4 hours. The monolayers were evaluated for cytotoxic effects at 24, 48, and 72 ± 4 hours. At each incubation period, the cell cultures were observed for signs of cytopathic effect (CPE) including lysis, crenation, plaques, and excessive rounding of cells.

TEST EVALUATION

Criteria for evaluating cytotoxicity included morphologic changes in cells, such as granulation, crenation, or rounding, and loss of viable cells from the monolayer by lysis or detachment. The validity of the test requires that negative control cultures maintain a healthy normal appearance throughout the duration of the test. Degrees of toxicity were scored as described in Table 4.

Table 4: Scoring

Grade	Reactivity	Conditions of all Cultures
0	None	Discrete intracytoplasmic granules; no cell lysis, no reduction of cell growth
1	Slight	Not more than 20% of the cells are round, loosely attached, and without intracytoplasmic granules, or show changes in morphology; occasional lysed cells are present; only slight growth inhibition observable.
2	Mild	Not more than 50% of the cells are round, devoid of intracytoplasmic granules, no extensive cell lysis; not more than 50% growth inhibition observable.
3	Moderate	Not more than 70% of the cell layers contain rounded cells or are lysed; cells layers not completely destroyed, but more than 50% growth inhibition observable.
4	Severe	Nearly complete or complete destruction of the cell layers

According to ISO guidelines, current revision, test articles scoring '0', '1', or '2' will be considered **'non-cytotoxic'**. Test articles scoring '3' or '4' will be considered **'cytotoxic'**.

VALIDITY CRITERIA
Validity of the assay and the test article result was based upon the criteria listed below and scientific judgment.

The negative and cell control should display no cytotoxic reaction. The positive control should display a moderate to severe cytotoxic reaction, a score of '3' or '4'.

METHOD FOR CONTROL OF BIAS: Not applicable.

DATA ANALYSIS: Not applicable.

STATISTICAL METHODS: None used.

RECORD RETENTION
An exact copy of the original final report and all raw data pertinent to this study will be stored by WuXi AppTec. It was the responsibility of the Sponsor to retain a sample of the test article.

COMPLIANCE

GLP Status: The study was conducted under GLP compliance (FDA, 21 CFR, Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies). The study was inspected during at least one phase and the final report was audited by the WuXi AppTec Quality Assurance unit.

International Standards
This study was performed in compliance with the following international standards:

ISO 10993-5:2009 Biological Evaluation of Medical Devices, Part 5: Tests for *In Vitro* Cytotoxicity

ISO 10993-12:2012 Biological Evaluation of Medical Devices, Part 12: Sample Preparation and Reference Materials

TEST ARTICLE DISPOSITION
Unused test samples remain in the storage area until all testing is completed. Once completed, the remaining samples were discarded or returned as requested by the Sponsor.

RESULTS

The negative and cell control were considered '0', the cells did not display a cytotoxic response. The positive control displayed a severe cytotoxic reaction, resulting in a score of '4'. Therefore, the test system was responding normally and met the criteria for a valid assay. See Table 5.

In this assay, the test article did not induce cytotoxicity. No abnormal events such as pH change or debris were noted.

Table 5: Results

Test Article and Controls	Sample Extract		Cytotoxicity Score		
	Size	(mL)	24 Hours	48 Hours	72 Hours
Test Article	3909.00 cm^2	651.5	0/0/0	0/0/0	0/0/0
Positive Control	60.0 cm^2	10.0	4/4/4	4/4/4	4/4/4
Negative Control	30.0 cm^2	10.0	0/0/0	0/0/0	0/0/0
Cell Control	NA	10.0	0/0/0	0/0/0	0/0/0

NA = Not Applicable

ANALYSIS AND CONCLUSION

The test article scored '0' at 24, 48, and 72 ± 4 hours and is considered **non-cytotoxic** under the conditions of this test.

REFERENCES

U.S. Pharmacopeia, Section 87, current revision.

WuXi AppTec Reference Library Contents, Form ALS-4650-1

WuXi AppTec SOP: MED-8750, Minimum Essential Medium (MEM) Elution Assay

FINAL STUDY REPORT

STUDY TITLE:	**ISO Intracutaneous Reactivity Test**
PROTOCOL NUMBER:	9107015-5
TEST ARTICLE IDENTIFICATION:	Part Description: SLR Size Electronics Cover with Zipper Part Number: EC2800 Part Lot Number: 130911
PERFORMING LABORATORY:	WuXi AppTec 2540 Executive Drive St. Paul, MN 55120
SPONSOR:	Whitney Medical Solutions 6153C West Mulford St. Niles, IL 60714
STUDY NUMBER:	194973
CLIENT MNEMONIC:	WMS01
RESULT SUMMARY:	The requirements of the ISO Intracutaneous Reactivity Test **have been met** by the test article.

QUALITY ASSURANCE UNIT SUMMARY

The objective of the Quality Assurance Unit is to monitor the conduct and reporting of nonclinical laboratory studies. This study has been performed under Good Laboratory Practices regulations (FDA, 21 CFR, Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies) and in accordance to standard operating procedures and a standard protocol. The Quality Assurance Unit maintains copies of study protocols and standard operating procedures and has inspected this study on the dates listed below. Studies are inspected at time intervals to assure the quality and integrity of the study.

Phase Inspected	Date	Study Director	Management
Dosing	12/20/13	12/24/13	12/26/13
Final Report	12/26/13	12/26/13	12/26/13

The findings of these inspections have been reported to management and the Study Director.

Quality Assurance Auditor: Sandra Deane Date: 12/27/13

GOOD LABORATORY PRACTICES STATEMENT

The study referenced in this report was conducted in compliance with U.S. Food and Drug Administration Good Laboratory Practice (GLP) regulations set forth in 21 CFR Part 58.

The studies not performed by or under the direction of WuXi AppTec are exempt from this Good Laboratory Practice Statement and include characterization and stability of the test compound(s)/test article.

Study Director: John Ball Date: 12/27/13

Professional Personnel Involved:

Teri Tanquist, BS	Vice President of Process Improvement and Operations
Christine Olson, BS	Study Operations Director
Roxanne Miller, AA, CVT	Director, In-Life Operations
John Ball, BA, CVT	Associate Study Director
Jean Mesarich, AA	Client Relations Manager

PURPOSE
The purpose of this test was to determine if any chemicals that may leach or be extracted from the test article were capable of causing local irritation in the dermal tissues of rabbits.

TEST FACILITY: WuXi AppTec
2540 Executive Drive
St. Paul, MN 55120

DATE SAMPLE RECEIVED: 12/09/13
STUDY INITIATION DATE: 12/11/13
STUDY COMPLETION DATE: 12/27/13

TEST ARTICLE IDENTIFICATION:

Test Article Name:	Part Description: SLR Size Electronics Cover with Zipper Part Number: EC2800 Part Lot Number: 130911
Lot/Batch #:	130911
Sterilization Method:	Radiation
Physical State:	Insoluble Material
Expiration Date:	Not Applicable
Storage Conditions:	Room Temperature
Intended Use/Application:	To be used to cover a variety of surgical and non-surgical equipment in various clinical settings.
Physical Description:	According to the Sponsor, the test article consisted of LDPE Bag.

CHARACTERIZATION
The Sponsor was responsible for all test article characterization data as specified in the GLP regulations. The identity, strength, stability, purity, and chemical composition of the test article were solely the responsibility of the Sponsor. The Sponsor was responsible for supplying to the testing laboratory results of these determinations and any others that may have directly impacted the testing performed by the testing laboratory, prior to initiation of testing.

Furthermore, it was the responsibility of the Sponsor to ensure that the test article submitted for testing was representative of the final product that was subjected to materials characterization. Any special requirements for handling or storage were arranged in advance of receipt and the test article was received in good condition.

SAMPLE STORAGE
Upon receipt by the Sample Receiving Department, the test samples were placed in a designated, controlled access storage area ensuring proper temperature conditions. Test and control article storage areas are designed to preclude the possibility of mix-ups, contamination, deterioration or damage. The samples remained in the storage area until retrieved by the technician for sample preparation and/or testing.

SAFETY
Appropriate routine safety procedures were followed in handling the test article, unless more cautious procedures were specified by the Sponsor. All applicable WuXi AppTec safety policies and procedures were observed during the performance of the test.

EXPERIMENTAL DESIGN

Experimental Summary

The study was conducted in accordance with ISO 10993-10: 2010 Standard, Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Skin Sensitization, Pages 11-14. Each rabbit received five sequential 0.2 mL intracutaneous injections along either side of the dorsal mid-line, with the test article solution on one side and the concurrent vehicle control on the other. The irritation reaction of the test article solutions were compared to vehicle controls and recorded over a 72-hour period according to the standard ISO irritation scoring system.

Justification for Selection of the Test System

This test method and species have historically been used to assess the potential of the material under test to produce intradermal irritation to help determine biocompatibility of materials used in medical devices. The animal species, number and route of test article administration were as recommended in ISO 10993-10.

Institutional Animal Care and Use Committee (IACUC)

The protocol and any amendments or procedures involving the care or use of animals on this study were reviewed and approved by WuXi AppTec's IACUC prior to the initiation of such procedures.

IACUC Protocol / Effective Date: 07-122C / June, 2013

PROTOCOL AMENDMENTS/DEVIATIONS

There were no amendments or deviations that occurred during the course of this study.

TEST SYSTEM

Species/Strain: All of the animals used for this study were albino rabbits (*Oryctolagus cuniculus*) / New Zealand White strain.

Source: Animals were obtained from Bakkom Rabbitry, a previously approved vendor of commercial laboratory animals.

Sex: Both male and female animals were used. Females used were nulliparous and non-pregnant.

Weight Range: Animals weighed between 2.6 – 2.9 kilograms at the experimental start of the study.

Age: The rabbits were approximately 13 weeks of age at the start of the study.

Number: A total of three animals were used for this study.

Animal Identification: Individual animals were identified per WuXi AppTec SOP: ILS-0112.

HUSBANDRY

Receipt: Animals were received on 12/03/13 according to WuXi AppTec SOP: ILS-0092. The animals were acclimated for a minimum of 5 days under the same conditions as the actual test.

Housing: Animals were individually housed in stainless steel caging. Housing dimensions complied with NIH and AAALAC International guidelines for this species.

Environment: The environmental conditions in the animal rooms were maintained according to WuXi AppTec SOP: ILS-0018. The temperature and photo-period were set to meet the AAALAC International recommendations for this species. The laboratory and animal rooms were maintained as limited-access facilities.

Diet: Animals were supplied with certified commercial feed, *ad libitum*. There were no known contaminants present in the feed expected to interfere with the test results. Feed analysis results are available and archived by WuXi AppTec.

Water: Potable water was supplied from the local municipal water supply, *ad libitum*. There were no known contaminants present in the water expected to interfere with the test results. Periodic analysis of the water is conducted and the results are archived by WuXi AppTec.

TEST AND CONTROL MATERIAL PREPARATION

The test article was cut for extraction, placed into extraction vessels and prepared at a ratio of 120 cm^2 to 20 mL of extraction vehicle.

Table 1: Test Article Record

Extract Vehicle	Test Article Area (cm^2)	Vehicle Amount (mL)	Number of Test Article Devices Used per Vessel
0.9% Normal Saline (NS)	3909.00	651.5	1
Sesame Oil (SO)	3909.00	651.5	1

Test Article Extraction: The extraction mixtures and corresponding control blanks were incubated for 72 ± 2 hours at 50 ± 2 °C. At the start of the extraction, the solutions appeared clear and free of particulates. The extracts were agitated during the course of the extraction period. At the end of the extraction period, the vessels were shaken well and the liquid aseptically decanted into a sterile vessel. The test article was observed after the SO extraction to be intact with no macroscopically observable degradation and the SO extracts were normal in color, clear in transparency and free of particulates. The test article was observed after the NS extraction to appear discolored and the NS extract had a pink tint in color, was clear in transparency, and free of particulates. After decanting, the extracts were not filtered prior to use. The extracts were maintained at room temperature and used within 24 hours of preparation. See Tables 1-3.

Table 2: Extraction Record

Vehicle	Extraction Temperature (In)	Date/Time of Extraction Start	Extraction Temperature (Out)	Date/Time of Extraction End
NS	50.4 °C	12/17/13 8:29 am	50.4 °C	12/20/13 6:38 am
SO	50.4 °C	12/17/13 8:29 am	50.4 °C	12/20/13 6:38 am

Table 3: Vehicle Record

Vehicle Identification	Lot #	Supplied By	Expiration
NS	J3P440	Braun	05/2016
SO	2CJ0092	Spectrum	05/14/2014

SELECTION OF ANIMALS

Animals were randomly placed in cages upon receipt, and were placed on study as available. Any animals considered unsuitable due to poor health, abraded skin or outlying body weight were excluded from the study.

ANIMAL PREPARATION

Each animal was weighed and the weight recorded prior to test injection. The fur of the animals was clipped on both sides of the spinal column to expose a sufficient sized area for injection.

TEST ARTICLE ADMINISTRATION

The two test article extracts and the two vehicle controls were each injected into three rabbits. Each rabbit received five sequential 0.2 mL intracutaneous injections of the test article extract on the right side of the vertebral column and similarly the control vehicle on the left side. The second test and control extract injections were parallel and distal to the first injection sites. (See Figure 1.)

CONTROL		HEAD	TEST		
	Control Vehicle #2	Control Vehicle #1	Test Extract #1	Test Extract #2	
0.2 mL Control Vehicle Injected	1	1	1	1	0.2 mL Test Article Extract Injected
	2	2	2	2	
	3	3	3	3	
	4	4	4	4	
	5	5	5	5	
		TAIL			

Figure 1: Injection Sites on Rabbits

OBSERVATIONS AND SCORING

The animals were observed daily for abnormal clinical signs. The appearance of each injection site was noted immediately post injection and at 24 ± 2, 48 ± 2, and 72 ± 2 hours. The tissue reactions were rated for gross evidence of erythema and edema. The intradermal injection of SO frequently elicits an inflammatory response. SO erythema scores ≤ 2 are considered normal. A well-defined positive response is characterized by a score equal to or greater than 2. Table 4 was used to score the reactions.

Table 4: Dermal Observation Scoring

Erythema	Edema
0 = No erythema	0 = No edema
1 = Very slight erythema (barely perceptible)	1 = Very slight edema (barely perceptible)
2 = Well defined erythema	2 = Well defined edema (edges of area well-defined by definite raising)
3 = Moderate to severe erythema	3 = Moderate edema (raised ~1 mm)
4 = Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4 = Severe edema (raised > 1 mm and extending beyond area)

TERMINATION

All animals were euthanized according to WuXi AppTec SOP: ILS-0230 with a sodium pentobarbital based solution after the 72-hour observations were recorded.

EVALUATION CRITERIA

According to ISO 10993:10 test criteria, if the difference between the average scores for the extract of the test article and the vehicle control is less than or equal to 1.0, the test article is considered to have met the requirements of the test.

ASSAY VALIDITY

Final evaluation of the validity of the assay and test article results was based upon scientific judgment.

METHOD FOR CONTROL OF BIAS: Not applicable.

DATA ANALYSIS: See calculations section.

STATISTICAL METHODS: None used.

RECORD RETENTION: An exact copy of the original final report and all raw data pertinent to this study will be stored by WuXi AppTec. It was the responsibility of the Sponsor to retain a sample of the test article.

COMPLIANCE

Animal Welfare

WuXi AppTec maintains the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International accreditation. All applicable portions of the study also conformed to the following regulations and guidelines regarding animal care and welfare:

- NIH guidelines as reported in the "Guide for the Care and Use of Laboratory Animals," National Research Council of the National Academies, eighth edition, 2011;
- (OPRR), "Public Health Service Policy on Humane Care and Use of Laboratory Animals," Health Research Extension Act of 1985 (Public Law 99-158), Revised 1986.
- USDA, Department of Agriculture, Animal and Plant Health Inspection Service, 9 CFR, Parts 1, 2, and 3, Animal Welfare, Final Rule 1989.
- WuXi AppTec Policy on Humane Care.

International Standards

The study was also in compliance with the following international standards:

ISO 10993-10: 2010 Standard, Biological Evaluation of Medical Devices, Part 10: Tests for Irritation and Skin Sensitization, Pages 11-14.

ISO 10993-12:2012 Biological Evaluation of Medical Devices, Part 12: Sample Preparation and Reference Materials

TEST ARTICLE DISPOSITION: Unused test samples remain in the storage area until all testing is completed. Once completed, the remaining samples were discarded or returned as requested by the Sponsor.

RESULTS

Clinical Observations

None of the animals on study showed abnormal clinical signs during the 24, 48, and 72 hour observation periods.

Dermal Observations

There were no significant dermal reactions observed at the injected test and control sites on the rabbits at the 24, 48, and 72 hour observation periods.

Calculations

After the 72 ± 2 hour observation period, all erythema grades plus edema grades 24 ± 2, 48 ± 2, and 72 ± 2 hour were totaled separately for each test sample or control for each individual animal. To calculate the score of a test sample or control on each individual animal, each of the totals was divided by 15 (three scoring time points x five test or control sample injection sites). To determine the overall mean score for each test sample and each corresponding control, the scores were added for the three animals and divided by three. The final test sample score was obtained by subtracting the score of the control from the test sample score. The results are presented in Tables 6 and 7.

Positive Control

A positive control was completed on 11/08/13 (See Table 5 for individual animal scores). WuXi AppTec completes positive controls at least every 6 months as required per ISO guidelines. The methods for the positive control assay are performed similar to the Experimental Summary above, except that the test and control solutions are dosed neat and not extracted. A solution of 0.15% sodium laurel sulfate (dissolved in 0.9% normal saline) is used as the test solution and 0.9% normal saline is used as the control. After the 72 hour test period all rabbits elicited a positive reactivity response and the comparative result of the positive control assay was greater than 1.0, indicating a positive response.

Table 5: Dermal Observations – Dermal Scores

Rabbit # 32639	Control Scores						Test Scores					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	1	1	1	1	1	0
Site 2	0	0	0	0	0	0	1	1	1	1	1	1
Site 3	0	0	0	0	0	0	2	1	1	1	1	1
Site 4	0	0	0	0	0	0	1	1	1	1	1	1
Site 5	0	0	0	0	0	0	2	1	1	1	1	1
Total	0		0		0		12		10		9	
Rabbit # 32640	**Control Scores**						**Test Scores**					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	1	1	1	1	1	0
Site 2	0	0	0	0	0	0	1	1	1	1	2	1
Site 3	0	0	0	0	0	0	1	1	1	1	2	1
Site 4	0	0	0	0	0	0	1	1	1	1	2	1
Site 5	0	0	0	0	0	0	1	1	1	1	2	1
Total	0		0		0		10		10		13	
Rabbit # 32643	**Control Scores**						**Test Scores**					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	2	1	1	1	1	1
Site 2	0	0	0	0	0	0	2	1	1	1	1	1
Site 3	0	0	0	0	0	0	2	1	1	1	1	1
Site 4	0	0	0	0	0	0	2	1	1	1	1	0
Site 5	0	0	0	0	0	0	2	1	1	1	1	0
Total	0		0		0		15		10		8	

Rabbit #	Control Scores (Total ER & ED)			Test Scores (Total ER & ED)		
32639	0	0	0	12	10	9
32640	0	0	0	10	10	13
32643	0	0	0	15	10	8

Rabbit #	Total / 15	Total / 15
32639	0	2.1
32640	0	2.2
32643	0	2.2
Average (Total / 3)	0 / 3 = 0	6.5 / 3 = 2.2

Comparative Results (Average Test – Average Control)	2.2 – 0 = **2.2**

ER=Erythema ED=Edema

Table 6: Dermal Observations – 0.9% Normal Saline

Rabbit # 33810	Control Scores						Test Scores					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	0	0	0	0	0	0
Site 2	0	0	0	0	0	0	0	0	0	0	0	0
Site 3	0	0	0	0	0	0	0	0	0	0	0	0
Site 4	0	0	0	0	0	0	0	0	0	0	0	0
Site 5	0	0	0	0	0	0	0	0	0	0	0	0
Total	0		0		0		0		0		0	
Rabbit # 33817	**Control Scores**						**Test Scores**					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	0	0	0	0	0	0
Site 2	0	0	0	0	0	0	0	0	0	0	0	0
Site 3	0	0	0	0	0	0	0	0	0	0	0	0
Site 4	0	0	0	0	0	0	0	0	0	0	0	0
Site 5	0	0	0	0	0	0	0	0	0	0	0	0
Total	0		0		0		0		0		0	
Rabbit # 33811	**Control Scores**						**Test Scores**					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	0	0	0	0	0	0
Site 2	0	0	0	0	0	0	0	0	0	0	0	0
Site 3	0	0	0	0	0	0	0	0	0	0	0	0
Site 4	0	0	0	0	0	0	0	0	0	0	0	0
Site 5	0	0	0	0	0	0	0	0	0	0	0	0
Total	0		0		0		0		0		0	

Rabbit #	Control Scores (Total ER & ED)			Test Scores (Total ER & ED)		
33810	0	0	0	0	0	0
33817	0	0	0	0	0	0
33811	0	0	0	0	0	0

Rabbit #	Total / 15	Total / 15
33810	0	0
33817	0	0
33811	0	0
Average (Total / 3)	0 / 3 = 0	0 / 3 = 0
Comparative Results (Average Test – Average Control)	0 – 0 = **0**	

ER=Erythema ED=Edema

Table 7: Dermal Observations – Sesame Oil

Rabbit # 33810	Control Scores						Test Scores					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	0	0	0	0	0	0
Site 2	0	0	0	0	0	0	0	0	0	0	0	0
Site 3	0	0	0	0	0	0	0	0	0	0	0	0
Site 4	0	0	0	0	0	0	0	0	0	0	0	0
Site 5	0	0	0	0	0	0	0	0	0	0	0	0
Total	0		0		0		0		0		0	
Rabbit # 33817	**Control Scores**						**Test Scores**					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	1	0	1	0	1	0	1	0	1	0	1	0
Site 2	1	0	1	0	1	0	1	0	1	0	1	0
Site 3	0	0	1	0	1	0	1	0	1	0	1	0
Site 4	0	0	0	0	1	0	1	0	1	0	1	0
Site 5	0	0	0	0	0	0	1	0	1	0	1	0
Total	2		3		4		5		5		5	
Rabbit # 33811	**Control Scores**						**Test Scores**					
	24 Hour		48 Hour		72 Hour		24 Hour		48 Hour		72 Hour	
	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED	ER	ED
Site 1	0	0	0	0	0	0	0	0	0	0	0	0
Site 2	0	0	0	0	0	0	0	0	0	0	0	0
Site 3	0	0	0	0	0	0	0	0	0	0	0	0
Site 4	0	0	0	0	0	0	0	0	0	0	0	0
Site 5	0	0	0	0	0	0	0	0	0	0	0	0
Total	0		0		0		0		0		0	

Rabbit #	Control Scores (Total ER & ED)			Test Scores (Total ER & ED)		
33810	0	0	0	0	0	0
33817	2	3	4	5	5	5
33811	0	0	0	0	0	0

Rabbit #	Total / 15	Total / 15
33810	0	0
33817	0.6	1
33811	0	0
Average (Total / 3)	0.6 / 3 = 0.2	1.0 / 3 = 0.3
Comparative Results (Average Test – Average Control)	0.3 – 0.2 = **0.1**	

ER=Erythema ED=Edema

ANALYSIS AND CONCLUSION

The test was considered valid based upon scientific judgment. The differences in the mean test and control scores of the extract dermal observations were **less than 1.0**, indicating that the requirements of the ISO Intracutaneous Reactivity Test **have been met** by the test article.

REFERENCES

U.S. Pharmacopeia, Section 88, current revision.

WuXi AppTec SOP: ALS-0260, Sample Extraction Procedures

WuXi AppTec Reference Library Contents, Form ALS-4650-1

WuXi AppTec SOP: ILS-0018, Environmental Conditions in the Animal Facility

WuXi AppTec SOP: ILS-0092, Placing Animal Orders and Receiving Shipments of Animals

WuXi AppTec SOP: ILS-0096, Intracutaneous Reactivity Positive Control

WuXi AppTec SOP: ILS-0100, ISO/USP/Japanese Intracutaneous Reactivity Test

WuXi AppTec SOP: ILS-0112, Animal Identification

WuXi AppTec SOP: ILS-0230, Euthanasia Procedures

WuXi AppTec SOP: ILS-0233, Proper Handling of Sick, Injured, and/or Moribund Animals

WuXi AppTec SOP: TRG-0300, Preparation of Biomaterials for Extraction

FINAL STUDY REPORT

STUDY TITLE:	**ISO Acute Systemic Injection Test**
PROTOCOL NUMBER:	901770-22
TEST ARTICLE IDENTIFICATION:	Part Description: SLR Size Electronics Cover with Zipper Part Number: EC2800, Part Lot Number: 130911 Lot # 130911
PERFORMING LABORATORY:	WuXi AppTec 2540 Executive Drive St. Paul, MN 55120
SPONSOR:	Whitney Medical Solutions 6153C West Mulford Street Niles, IL 60714
STUDY NUMBER:	194972
CLIENT MNEMONIC:	WMS01
RESULT SUMMARY:	The requirements of the ISO Acute Systemic Injection Test **have been met** by the test article.

QUALITY ASSURANCE UNIT SUMMARY

The objective of the Quality Assurance Unit is to monitor the conduct and reporting of nonclinical laboratory studies. This study has been performed under Good Laboratory Practices regulations (FDA, 21 CFR, Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies) and in accordance to standard operating procedures and a standard protocol. The Quality Assurance Unit maintains copies of study protocols and standard operating procedures and has inspected this study on the dates listed below. Studies are inspected at time intervals to assure the quality and integrity of the study.

Phase Inspected	Date	Study Director	Management
Ending	12/26/13	12/27/13	12/28/13
Final Report	12/28/13	12/28/13	12/28/13

The findings of these inspections have been reported to management and the Study Director.

Quality Assurance Auditor: Sheri J Hardy Date: 1-2-14
Sheri J. Hardy

GOOD LABORATORY PRACTICES STATEMENT

The study referenced in this report was conducted in compliance with U.S. Food and Drug Administration Good Laboratory Practice (GLP) regulations set forth in 21 CFR part 58.

The studies not performed by or under the direction of WuXi AppTec, are exempt from this Good Laboratory Practice Statement and include characterization and stability of the test compound(s)/test article.

Study Director: Sean McGurran Date: 01/02/14
Sean McGurran

Professional Personnel Involved:

Teri Tanquist, BS	Vice President of Process Improvement and Operations
Christine Olson, BS	Study Operations Director
Roxanne Miller, AA, CVT	Director, In-Life Operations
Sean McGurran, BS	Study Director
Jean Mesarich, AA	Client Relations Manager

PURPOSE: The purpose of this test was to screen test article extracts or solutions for potential toxic effects as a result of a single-dose systemic injection in mice.

TEST FACILITY: WuXi AppTec
2540 Executive Drive
St. Paul, MN 55120

DATE TEST ARTICLE RECEIVED: 12/09/13
STUDY INITIATION DATE: 12/11/13
STUDY COMPLETION DATE: 01/02/14

TEST ARTICLE IDENTIFICATION

Test Article Name:	Part Description: SLR Size Electronics Cover with Zipper, Part Number: EC2800, Part Lot Number: 130911
Lot/Batch #:	130911
Sterilization Method:	Radiation
Physical State:	Insoluble Material
Expiration Date:	Not Applicable
Storage Conditions:	Room Temperature
Intended Use/Application:	To be used to cover a variety of surgical and non-surgical equipment in various clinical settings.
Physical Description:	According to the Sponsor, the test article consisted of LDPE Bag.

CHARACTERIZATION
The Sponsor was responsible for all test article characterization data as specified in the GLP regulations. The identity, strength, stability, purity, and chemical composition of the test article were solely the responsibility of the Sponsor. The Sponsor was responsible for supplying to the testing laboratory results of these determinations and any others that may have directly impacted the testing performed by the testing laboratory, prior to initiation of testing.

Furthermore, it was the responsibility of the Sponsor to ensure that the test article submitted for testing was representative of the final product that was subjected to materials characterization. Any special requirements for handling or storage were arranged in advance of receipt and the test article was received in good condition.

SAMPLE STORAGE
Upon receipt by the Sample Receiving Department, the test samples were placed in a designated, controlled access storage area ensuring proper temperature conditions. Test and control article storage areas are designed to preclude the possibility of mix-ups, contamination, deterioration or damage. The samples remained in the storage area until retrieved by the technician for sample preparation and/or testing.

SAFETY
Appropriate routine safety procedures were followed in handling the test article, unless more cautious procedures were specified by the Sponsor. All applicable WuXi AppTec safety policies and procedures were observed during the performance of the test.

EXPERIMENTAL DESIGN

Experimental Summary
Animals were treated by intravenous or intraperitoneal routes to screen solutions or test article extracts for potential toxic effects as a result of a single-dose systemic injection. The animal species, number, and route of test article administration were as recommended in ISO 10993-11.

For the safety evaluation of the test article, mice were injected systemically with extracts of the test article in standard solutions (normal saline and sesame oil). The animals were observed for signs of toxicity immediately after injection and at 4, 24, 48, and 72 hours post-injection. The requirements of the test are met if none of the animals treated with the test article extract have a significantly greater adverse reaction than the animals treated with the vehicle control.

Justification for Selection of the Test System
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 as recommended in ISO 10993-11.

Institutional Animal Care and Use Committee (IACUC)
The protocol and any amendments or procedures involving the care or use of animals on this study were reviewed and approved by the WuXi AppTec IACUC prior to the initiation of such procedures.

IACUC Protocol / Effective Date: 98-03F / June, 2013

PROTOCOL AMENDMENTS/DEVIATIONS
There were no amendments or deviations that occurred during the course of this study.

IDENTIFICATION OF TEST SYSTEM

Species/Strain: All animals used in this study were albino Swiss mice (*Mus musculus*), CFW, naïve.

Source: Animals were obtained from Charles River Laboratories, a previously approved vendor of commercial laboratory animals.

Sex: All of the animals used were female, nulliparous and non-pregnant.

Weight Range: All animal weights (21.5 – 26.7 grams) were within ± 20% of the mean body weight at the start of the study.

Age: All animals were approximately 5 weeks old at the start of the study.

Number: The study used 10 mice/ extract vehicle (5 test, 5 control).

Animal Identification: The animals were identified per WuXi AppTec SOP: ILS-0112.

Animal Numbers:	**Mouse #**
0.9% Normal Saline Test Group:	1 - 5
0.9% Normal Saline Control Group:	21 - 25
Sesame Oil Test Group:	11 - 15
Sesame Oil Control Group:	31 - 35

HUSBANDRY

Receipt: Animals were received on 12/11/13 according to WuXi AppTec SOP: ILS-0092. Each animal was examined for signs of disease and injury. The animals were acclimated for a minimum of 5 days under the same conditions as the actual test.

Housing: Animals were housed in groups of five in polycarbonate cages with contact bedding. Housing density complied with AAALAC International recommendations and NIH guidelines. The test and control animals were housed separately.

Environment: The environmental conditions in the animal rooms were maintained according to WuXi AppTec SOP: ILS-0018. The temperature and photo-period were set to meet the AAALAC International recommendations for these species. The laboratory and animal rooms were maintained as limited-access facilities.

Diet: Animals were supplied with a certified commercial rodent diet. No known contaminants present in the feed were expected to interfere with the test results.

Water: Animals were supplied with potable water obtained from the St. Paul municipal water supply. No known contaminants present in the water were expected to interfere with the results.

TEST MATERIAL PREPARATION

The test article was cut for extraction, placed into test tubes and prepared at a ratio of 120 cm^2 to 20 mL of extraction vehicle.

Table 1: Test Article Record

Extract Vehicle	Test Article Area (cm^2)	Vehicle Amount (mL)	Number of Test Articles Used per Extract
0.9% Normal Saline (NS)	3909.00	651.5	1
Sesame Oil (SO)	3909.00	651.5	1

Test Article Extraction: The extraction mixtures and corresponding control blanks were incubated for 72 ± 2 hours at 50 ± 2 °C. At the start of the extraction, the solutions appeared clear and free of particulates. The extracts were agitated during the course of the extraction period. At the end of the extraction period, the vessels were shaken well and the liquid aseptically decanted into a sterile vessel. The test article was observed after all extractions to be intact with no macroscopically observable degradation. The extracts were clear, free from particulates, and normal in color. After decanting, the extracts were not filtered prior to use. The extracts were maintained at room temperature and used within 24 hours of preparation. See Tables 1-3.

Table 2: Extraction Record

Vehicle	Extraction Temperature (In)	Date/Time of Extraction Start	Extraction Temperature (Out)	Date/Time of Extraction End
NS	50.4 °C	12/20/13 8:00 am	50.4 °C	12/23/13 6:30 am
SO	50.4 °C	12/20/13 8:00 am	50.4 °C	12/23/13 6:30 am

Table 3: Vehicle Record

Vehicle Identification	Lot #	Supplied By	Expiration
NS	J3P440	Braun	05/2016
SO	2CJ0092	Spectrum	05/14/14

SELECTION OF ANIMALS

Animals were randomly placed in cages upon receipt and were placed on study as available. Animals considered unsuitable due to poor health or outlying body weight were excluded from the study.

TEST ARTICLE ADMINISTRATION
Groups of five animals were injected with either the test article extract or the corresponding control vehicle as indicated in the table below:

Extract or Control	Route	Dose/Kg	Injection Rate
NS	Intravenous	50 mL	~0.1 mL/sec
SO	Intraperitoneal	50 mL	Not Applicable

OBSERVATIONS

Body Weights: Body weight recordings, to the nearest 0.1 g, were made on the day of dosing and at 24 ± 2, 48 ± 2 and 72 ± 2 hours post-injection. See Data Table 5 for individual weight results.

Clinical Signs: Observations for mortality and signs of pharmacological and/or toxicological effects were made immediately post-injection and at 4 ± 0.75, 24 ± 2, 48 ± 2, and 72 ± 2 hours post-injection.

TERMINATION
Following the final observations the animals were euthanized by CO_2 asphyxiation.

EVALUATION CRITERIA
According to ISO guidelines, the test is considered negative if none of the animals injected with the test article extract show a significantly greater biological reaction than the animals treated with the control vehicle extract. Death in two or more mice or other toxic signs such as convulsions, prostration, or body weight loss greater than 10% in three or more mice are interpreted as significant biological reactions.

ASSAY VALIDITY
Final evaluation of the validity of the assay and test article results was based upon the following criteria and scientific judgment:

A control failure is defined as death in two or more control animals showing signs of toxicity such as convulsions or prostration or weight loss of more than 10% of body weight in three or more mice.

METHOD FOR CONTROL OF BIAS: Not applicable.

DATA ANALYSIS: Not applicable.

STATISTICAL METHODS: Descriptive statistics are presented in Data Table 5.

RECORD RETENTION: An exact copy of the original final report and all raw data pertinent to this study will be stored by WuXi AppTec. It was the responsibility of the Sponsor to retain a sample of the test article.

COMPLIANCE

Animal Welfare

WuXi AppTec maintains the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International accreditation. All applicable portions of the study also conformed to the following regulations and guidelines regarding animal care and welfare:

- NIH guidelines as reported in the "Guide for the Care and Use of Laboratory Animals," National Research Council of the National Academies, eighth edition, 2011;
- (OPRR), "Public Health Service Policy on Humane Care and Use of Laboratory Animals," Health Research Extension Act of 1985 (Public Law 99-158), Revised 1986;
- USDA, Department of Agriculture, Animal and Plant Health Inspection Service, 9 CFR, Parts 1, 2, and 3, *Animal Welfare*, Final Rule 1989; and
- WuXi AppTec Policy on Humane Care.

International Standards

The study was also in compliance with the following international standards:

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

ISO 10993-12:2012 Biological Evaluation of Medical Devices, Part 12: Sample Preparation and Reference Materials

TEST ARTICLE DISPOSITION: Unused test samples remain in the storage area until all testing is completed. Once completed, the remaining samples were discarded or returned as requested by the Sponsor.

RESULTS

None of the animals on study were observed with abnormal clinical signs indicative of toxicity during the 72 hour test period. All were alive at the end of the 72 hour test duration and body weight loss was within acceptable parameters over the course of the study. See Table 4.

Table 4: Mortality, Clinical Signs and Weight Loss Incidence

Extract	Fatalities		Toxicity Clinical Signs		Animals with >10% Body Weight Loss	
	Test	Control	Test	Control	Test	Control
NS	0/5	0/5	0/5	0/5	0/5	0/5
SO	0/5	0/5	0/5	0/5	0/5	0/5

ANALYSIS AND CONCLUSION

The vehicle control treated animals had no signs of toxicity at any of the observation periods and no animals lost weight in excess of 10%, indicating a valid test. None of the test article extract treated animals were observed with clinical signs consistent with toxicity at any of the observation periods. Body weight changes were within acceptable parameters over the course of the study. These findings indicate that the requirements of the ISO Acute Systemic Injection Test **have been met** by the test article.

Table 5: Animal Weights (g) and Standard Deviation Calculations

Group	Animal #	Initial	24 Hrs	48 Hrs	72 Hrs	BW Change
Test NS	1	23.8	24.6	24.7	25.4	1.6
	2	23.9	25.2	24.2	24.8	0.9
	3	21.5	22.5	22.2	22.3	0.8
	4	26.3	26.8	26.8	28.0	1.7
	5	26.7	27.4	26.4	27.0	0.3
Average Body Weight		**24.4**	**25.3**	**24.9**	**25.5**	**1.1**
Standard Deviation		**2.1**	**1.9**	**1.8**	**2.2**	**0.6**
Control NS	21	22.8	23.4	23.5	23.9	1.1
	22	26.7	27.0	27.0	27.4	0.7
	23	21.9	22.2	22.6	23.2	1.3
	24	23.7	24.7	24.9	25.5	1.8
	25	24.3	25.4	24.4	25.3	1.0
Average Body Weight		**23.9**	**24.5**	**24.5**	**25.1**	**1.2**
Standard Deviation		**1.8**	**1.8**	**1.7**	**1.6**	**0.4**
Test SO	11	23.4	23.4	23.9	24.1	0.7
	12	24.0	24.0	24.5	25.9	1.9
	13	23.9	25.4	25.4	26.0	2.1
	14	24.1	23.1	23.5	24.8	0.7
	15	22.4	22.1	23.0	24.0	1.6
Average Body Weight		**23.6**	**23.6**	**24.1**	**25.0**	**1.4**
Standard Deviation		**0.7**	**1.2**	**0.9**	**1.0**	**0.7**
Control SO	31	24.4	22.5	22.6	25.0	0.6
	32	23.0	21.3	22.4	23.4	0.4
	33	26.5	25.3	25.9	27.5	1.0
	34	23.1	22.3	22.9	23.9	0.8
	35	23.2	22.7	23.6	24.9	1.7
Average Body Weight		**24.0**	**22.8**	**23.5**	**24.9**	**0.9**
Standard Deviation		**1.5**	**1.5**	**1.4**	**1.6**	**0.5**

REFERENCES

U.S. Pharmacopeia, Section 88, current revision.

WuXi AppTec Reference Library Contents, Form ALS-4650-1

WuXi AppTec SOP: ALS-0260, Sample Extraction Procedures

WuXi AppTec SOP: ILS-0018, Environmental Conditions in the Animal Facility

WuXi AppTec SOP: ILS-0092, Placing Animal Orders and Receiving Shipments of Animals

WuXi AppTec SOP: ILS-0112, Animal Identification

WuXi AppTec SOP: ILS-0115, ISO/USP/Japanese Acute Systemic Injection Test

WuXi AppTec SOP: ILS-0233, Proper Handling of Sick, Injured, and/or Moribund Animals

Test Facility:
1265 Kennestone Circle
Marietta, GA 30066

药明康德 WuXi AppTec

Report Number
949433
Page 1 of 1

Whitney Medical Solutions
6153C West Mulford Street
Niles, IL 60714

Attn: Saagar Patel

December 11, 2013
P.O. #: SP131029A

CHEMISTRY TEST REPORT

Sample Information: Part Description: SLR Size Electronics Cover with Zipper, Part Number: EC2800, Part Lot Number: 130911, Gamma Sterilization Date: 11-19-13

Date Received: December 06, 2013
Date in Test: December 09, 2013
Date Completed: December 11, 2013

Test Information: Test Code: 400280
Procedure #: CH226WMS.201

USP PHYSICOCHEMICAL EXTRACTION PARAMETERS				
Surface Area	**Extraction Time**	**Extraction Media**	**Volume Used (mL)**	**Extraction Temp.**
3909 cm^2	24 Hours	Purified Water	652	70 °C

RESULTS

Parameter	Current USP Specifications	Results	
Non-Volatile Residue	≤ 15 mg	PASS	< 0.1 mg
Residue On Ignition	≤ 5 mg	Not Required Non-Volatile Residue	< 5 mg
Heavy Metals	≤ 1 ppm (as Pb)	PASS	< 1 ppm
Buffering Capacity	≤ 10 mL 0.01 N Titrant	PASS	0.01 mL

12-11-13
Technical Reviewer **Date**

Testing conducted in accordance with current Good Manufacturing Practices.

January 21, 2014

Saagar Patel
Whitney Medical Solutions
6153C West Mulford St
Niles, IL 60714

Re: Memorandum of Understanding for a Biocompatibility Risk Assessment in support of not having to do Sensitization Testing for an “eShield” Cover used to Prevent Surgical and Non-Surgical Equipment from contaminating various Clinical/Surgical Procedures.

The “eShield” Cover consists of low density polyethylene film (along with 2 different tapes) and a zipper and non zipper portion. The Cover is manufactured to protect hand held equipment from contaminating scrubbed surgical personnel during procedures throughout the clinical/surgical setting. The Cover is designed so that the outside of the “eShield” remains sterile while the inside contains non-sterile equipment. The “eShield” was designed to allow scrubbed personnel to use handheld equipment, such as a camera, without compromising the sterile field.

There are 3 sizes of the “eShield” Cover. The smallest is 9”x14” and the largest is 14’x21”. There are zipper and non-zipper versions of each size. The way the “eShield” works is that after the non-sterile person puts the electronic device into the Cover, the sterile person tears off the top cuff. In the zipper version, the tearing occurs between the zipper and an adhesive tape. In the non-zipper version, this tearing occurs between 2 pieces of adhesive tape. The adhesive tapes are the same in each version. For both versions, after the top cuff is torn off the, it is folded over and sealed with another adhesive tape to prevent contact with the scrubbed surgical personnel. The “eShield” is printed with the ink printing on the inside of the Cover and under the folded portion. When used per the instructions for use, the scrubbed person will not contact the non-sterile inside of the “eShield”, the printing or the adhesive tape.

All sizes weigh less than 2 ounces. The “eShield” is not intended to have direct patient contact. The gloves of the scrubbed surgical personnel will have limited contact with the outside sterile surface of the Cover and then the gloves may have brief intermittent contact with the patient.

The Low Density Polyethylene Pellets, product code LD136.MN, are available from the selling affiliate Exxon Mobil Chemical Company, 13501 Katy Freeway, Houston, TX 77079. The pellets meet REACH Article 31 Standards for being nontoxic. The Pellets were sold to the polyethylene film supplier, Quality Extrusions, Inc. 1904 Willow St, Mankato, MN 56002-3068. The MSDS for the Polyethylene Film states that the Low Density Polyethylene Homopolymer film, Product Code 19978 is nontoxic. No processing aides or additives are used in the film manufacture. The Polyethylene Film is converted into the “eShield” Cover by Diamond Flexible Packaging and based upon their Quality System Procedures [Document No. F-SP-10-02(2)] indicates compliance with FDA regulations and was free of contamination. The final Tyvec-Mylar packaging for the “eShield” was made by PeelMaster Packaging. Whitney Medical Solutions package the “eShield” Covers which are then sterilized by a validated Gamma Radiation Sterilization Process.

The “eShield” Cover is intended to be substantially equivalent to Equipment Drapes manufactured by Microtek Medical, Inc: 510k: K050322 (2005) which the FDA found substantially equivalent to Medline Band Bags & Equipment Drapes, K032065 (2003). This information supports a long history of safe use and a minimum risk of adverse biocompatibility including Sensitization. The FDA finding of substantial equivalence of this device to a legally marketed predicate device resulted in a classification for the

devices that permitted them to proceed to the market without biocompatibility testing including Sensitization testing.

A USP661-Physicochemical Extractables Test for Plastic Containers was performed on radiation sterilized "eShield" SLR Size Electronics Cover with Zipper, Part No. EC2800 and Lot No. 130911, WuxiApptec Report No. 949433, Dec 11, 2013. The Non-volatile Residue, Residue on Ignition, Heavy Metals and Buffering Capacity test results were well within the current USP Specifications. This test has a long history of being used to qualify polymeric containers for drug use and meeting the Test Limits which support a minimum risk of adverse biocompatibility including Sensitization.

To strengthen the "eShield" biocompatibility data base, WuxiApptec was requested to perform, Cytotoxicity, Irritation and Systemic Toxicity tests using polar and nonpolar extractants. All biocompatibility testing was performed on the largest "eShield" zipper version which was considered the worst-case Cover. All these tests passed.

Based upon the above information and recognizing that (1) the "eShield" Cover is not intended to have direct contact with the patient and (2) that there is a minimum risk of transfer of "eShield" chemical residues and extractables, the intermittent surgical glove contact with the patient during a clinical/surgical procedure would not be expected to cause an adverse biocompatibility response including Sensitization.

Sincerely yours,

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