FINAL GMP REPORT: 21-00512-M1

AMOEBOCYTE LYSATE TEST FOR INHIBITION AND ENHANCEMENT TESTING OF ENDOTOXINS (KINETIC–QCL METHOD) – USP

Test Article

Polyether ether ketone (PEEK) Sensors- (Solvay KT-880 NT)Part# CSEN-8103-C-153I0SH1-001 Serial # 62912-0001 and 62912-0002 . Manufacturing date : Feb 3rd 2021

21 CFR Part 820
Good Manufacturing Practice

Final Report Date

5/3/2021

Study Director

Linda Haggerty, M.S.

Sponsor

Malema Sensors
1060 S. Rogers Circle
Boca Raton, FL 33487

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STUDY SUMMARY

Three (3) test articles of Polyether ether ketone (PEEK) Sensors- (Solvay KT-880 NT)Part# CSEN-8103-C-153I0SH1-001 Serial # 62912-0001 and 62912-0002 . Manufacturing date : Feb 3rd 2021, contained within flow cells, were analyzed for Inhibition and Enhancement using the chromogenic method - USP <85>, Bacterial Endotoxins Test. The flow cell fluid pathway was filled with 230.0 mL of Sterile Water for Injection (SWFI) heated to 37 ± 1 ºC; the SWFI remained in contact with the fluid pathway at room temperature for 60 ± 2 minutes. The pH of each extract was determined and was pH 6.57 for Test Article 1, pH 6.33 for Test Article 2, and 6.30 for Test Article 3. No pH adjustment was necessary. Each extract was assayed in duplicate at the neat concentration. Positive Product Controls (PPC) were prepared containing 0.09 mL of each test article extract and 0.01 mL of the 5 EU/mL endotoxin standard to give a final concentration of 0.5 EU/mL. A standard curve was prepared with *Escherichia coli* (*E. coli*) endotoxin concentrations ranging from 5.0 to 0.005 EU/mL. Water for Bacterial Endotoxins Test (BET) and SWFI served as the negative controls. The Positive Product Control (PPC) values were 117% for Test Article 1, 120% for Test Article 2, and 111% for Test Article 3. All PPC values were within the 50 - 200% range required by USP <85>, current revision. The absolute value of the correlation coefficient for the linear regression was calculated to be 0.995. Test article extracts from Polyether ether ketone PEEK)Sensors- (Solvay KT-880 NT)Part# CSEN-8103-C-153I0SH1-001 Serial # 62912-0001 and 62912-0002 . Manufacturing date : Feb 3rd 2021, did not inhibit or enhance the endotoxin reaction per USP <85> Bacterial Endotoxins Test, current revision. The study and its design employed methodology to minimize uncertainty of measurement and control of bias for data collection and analysis.

STUDY DIRECTOR AND QUALITY ASSURANCE SIGNATURES AND VERIFICATION DATES

SIGNATURES

Signature Information	
Protocol Number	p21-0203-00a
Study Director	Linda Haggerty, M.S.
Company	Toxikon Corporation

VERIFICATION DATES

The study initiation day is the date the protocol is signed by the Study Director.

Verification Dates	
Test Article Receipt	2/10/2021
Project Log	4/26/2021
Study Initiation	4/26/2021
Study Completion	5/3/2021

J. M. Nigrelli — 5/3/21

James Nigrelli, B.S.
Quality Assurance

Date

Linda Haggerty — 5-03-2021

Linda Haggerty, M.S.
Study Director

Date

1.0 PURPOSE

The purpose of this study was to determine if a test article extract inhibited or enhanced the Bacterial Endotoxins Test, Kinetic Chromogenic technique.

2.0 REFERENCES

The study was based upon the following references:

- United States Pharmacopeia 43, National Formulary 38, 2020 <85> Bacterial Endotoxins Test.
- United States Pharmacopeia 43, National Formulary 38, 2020. <161> Medical Devices – Bacterial Endotoxin and Pyrogen Tests.
- Limulus Amoebocyte Lysate (LAL), Kinetic-QCL™, Kit Instruction, Lonza.
- ISO/IEC 17025, 2017, General Requirements for the Compliance of Testing and Calibration Laboratories.

3.0 COMPLIANCE

This study conformed to the current 21 CFR Part 820 Good Manufacturing Practice, as applicable to a testing laboratory. Toxikon is accredited to ISO/IEC 17025, 2017, General Requirements for the Competence of Testing and Calibration Laboratories. Toxikon's Quality System also encompasses the general principles and practices of GxP regulations, specifically GLPs.

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).

4.1 Test Article:

Name: Polyether ether ketone PEEK)Sensors- (Solvay KT-880 NT)Part# CSEN-8103-C-153I0SH1-001 Serial # 62912-0001 and 62912-0002 . Manufacturing date : Feb 3rd 2021

CAS/Code Number: Not Supplied by Sponsor (N/S)

Lot/Batch Number: N/S

Physical State: N/S

Color: N/S

Expiration Date: N/S

Density: N/S

Stability: N/S

Sterility: Sterile

Sterilization Conditions: N/S

Storage Condition: Room Temperature

Safety Precautions: N/S

Intended Use: N/S

4.2 Negative Control Articles (Toxikon Supplied):

4.2.1 Negative Control Article 1:

Name: USP Sterile Water for Injection (SWFI)

Toxikon QC Number: CSC-20-11-00126

4.2.2 Negative Control Article 2:

Name: Water for Bacterial Endotoxins Test (BET)

Toxikon QC Number: CSC-20-07-00098

4.3 Positive Control Articles (Toxikon Supplied):

4.3.1 Positive Control Article 1:

Name: *Escherichia coli* endotoxin

Toxikon QC Number: CSC-20-10-00034

4.3.2 Positive Control Article 2:

Name: Limulus Amoebocyte Lysate

Toxikon QC Number: CSC-20-10-00033

5.0 IDENTIFICATION OF TEST SYSTEM

The assay determined whether the test article inhibited or enhanced the Bacterial Endotoxins Test, Kinetic Chromogenic technique. The test system used Amoebocyte Lysate obtained from aqueous extracts of the circulating amebocytes of the horseshoe crab, *Limulus polyphemus*. Amoebocyte Lysate, prepared and characterized for use, is commercially available and reacts with a colorimetric substance to detect endotoxin.

6.0 JUSTIFICATION OF TEST SYSTEM AND ROUTE OF ADMINISTRATION

6.1 Justification of Test System:

The Inhibition and Enhancement assay is recommended by USP guidelines as a method to determine if a test article causes inhibition or enhancement of the Bacterial Endotoxins Test, Kinetic Chromogenic technique.

6.2 Route of Administration:

Each test article extract was spiked, *in vitro*, directly with a known amount of endotoxin.

7.0 EXPERIMENTAL DESIGN AND DOSAGE

7.1 Test Article Preparation:

7.1.1 Liquid Test Articles:

All test articles were collected in endotoxin–free containers and were stored per Sponsor-specified storage conditions until tested. If conditions were not specified, liquid samples were stored at room temperature. No preparation was required, unless specified by the Sponsor.

7.1.2 Preparation of Test Articles and Dosage:

The fluid pathway of the Test Article was filled with 230.0 mL of SWFI heated to 37 ± 1 ºC. The SWFI remained in contact with the fluid pathway at room temperature for 60 ± 2 minutes. The temperature was recorded at the beginning and end of the extraction period.

Note: Toxikon's standard procedure is to use SWFI as the extraction fluid unless specified by the Sponsor.

For unusually large or small devices, the surface area of the device, which comes in contact with the patient, was used as an adjustment factor in selecting the rinsing or extracting volume. The endotoxin limit was adjusted accordingly.

It is necessary for the sample to have a pH in the range of 6.0-8.0. The pH of each extract was prepared and was found to be pH 6.57 for Test Article 1, pH 6.33 for Test Article 2, and pH 6.30 for Test Article 3. No pH adjustment was necessary. The pH of sample aliquots was measured using a calibrated pH probe.

7.2 Reagent and Material Preparation:

All reagents were prepared per manufacturer's recommendations.

7.2.1 Preparation of Endotoxin Standard:

The Control Standard Endotoxin (CSE) in the Kinetic–QCL Kit that was previously standardized by the manufacturer against the Reference Standard Endotoxin (RSE) was used. The Endotoxin Standard was reconstituted with the specified amount of Bacterial Endotoxin Water and vortexed for fifteen (15) minutes. The reconstituted endotoxin had a potency of 50 Endotoxin Units (EU)/mL. A previously reconstituted endotoxin standard was vortexed for fifteen (15) minutes and was stored (mouth wrapped with parafilm) at 4 ± 2 ºC for up to four (4) weeks. The endotoxin standard was only used with the reagents in a particular kit. All unused working standard was stored for not more than one (1) day.

7.2.2 Preparation of Kinetic-QCL LAL Reagent:

The reagent was prepared immediately prior to use. The Amoebocyte Lysate powder was collected into the bottom of the vial by tapping on a firm surface. The metal seal of the reagent was torn off and the gray stopper gently removed. The powder was reconstituted with the amount of Water for BET specified by the manufacturer. Reconstituted Kinetic–QCL LAL Reagent was stable for eight (8) hours at 2–8 ºC; otherwise it was stored at –10 ºC or below for up to two (2) weeks.

7.2.3 Preparation of Glassware and Utensils:

Any glass containers, test tubes, utensils, etc., used in this assay were depyrogenated. The depyrogenation was done by wrapping the utensils in foil and heating for at least thirty (30) minutes at 250 ºC.

7.3 Test Method:

To identify whether the test article extract inhibited or enhanced the assay, the Water for BET was spiked with four (4) different concentrations of endotoxin (5 EU/mL, 0.5 EU/mL, 0.05 EU/mL, and 0.005 EU/mL) in duplicate. The test article dilutions (unspiked) and the test article dilutions spiked with 0.5 EU/mL of endotoxin (PPCs) were both assayed in duplicate. Multiple dilutions of the test article can be assayed up to the maximum valid dilution. The actual volume of test article in the appropriate well of the microplate is **always** 0.1 mL.

The filled plate was placed in the microplate reader and the lid was closed. The plate was pre–incubated for ≥ 10 minutes at 37 ± 1 ºC.

7.3.1 Addition of Lysate:

0.1 mL of reconstituted Amoebocyte Lysate was added to each well of the microplate reader containing 0.1 mL of test article or control. Amoebocyte Lysate was added to the negative control first, and from the lowest to highest concentration in each test series.

The microplate was immediately placed in the reader to initiate the test.

The correlation coefficient, (r), should be greater than or equal to the absolute value of 0.980.

7.4 Preparation of the Negative Controls and Blank:

The Blank for the Standard curve is always Water for BET. A 100 µL aliquot each of Water for BET and SWFI were also assayed as negative controls, in duplicate.

8.0 EVALUATION CRITERIA

8.1 Evaluation of Data:

Results were printed out at the completion of the assay. Replicate samples were run in order to establish good technique and low coefficient of variation. The coefficient of variation, CV, equals the “sample” standard deviation of the reaction times divided by the mean and was expressed as a percent. The % CV of the reaction times for replicate of a sample should be less than 10%.

The absolute value of the coefficient of correlation of the calculated standard curve should be ≥ 0.980.

If the PPC value is outside the range of 50-200% of the known spike concentration, the results show either inhibition or enhancement of the assay.

A device that fails this test can be retested once by another Bacterial Endotoxins Test. For devices that cannot be tested by the Bacterial Endotoxins Test because of non-removable inhibition or enhancement, the Pyrogen Test (USP <151>) is applied.

8.2 Control of Bias Statement:

The study as designed employs methodology to minimize uncertainty of measurement and control of bias for data collection and analysis, which includes but is not limited to: concurrent control data, system suitability assessment, and method controls such as blanks and replicates.

9.0 RESULTS

The results are indicated in Table 1. Table 1 shows the % PPC recovery for each of the test article extracts at the neat concentration. PPC recoveries of 117%, 120%, and 111% were recovered at the neat concentration for Test Articles 1, 2 and 3, respectively. The % CV was

< 10% for each Test Article. The absolute value of correlation coefficient for the linear regression was calculated to be 0.995.

10.0 CONCLUSION

The test articles, Polyether ether ketone PEEK)Sensors- (Solvay KT-880 NT)Part# CSEN-8103-C-153I0SH1-001 Serial # 62912-0001 and 62912-0002 . Manufacturing date : Feb 3rd 2021, at the neat concentration, did not inhibit or enhance the LAL endotoxin test, chromogenic method - USP <85>, Bacterial Endotoxins Test, current revision. The study and its design employed methodology to minimize uncertainty of measurement and control of bias for data collection and analysis.

11.0 RECORDS

- Original raw data will be archived by Toxikon Corporation.
- A copy of the final report and any report amendments will be archived by Toxikon Corporation.
- The original final report and a copy of any protocol amendments or deviations will be forwarded to the Sponsor.
- The test articles, used and unused, will be returned to the Sponsor.
- Test article retention upon study completion is the responsibility of the Sponsor.

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 UNFORESEEN CIRCUMSTANCES

Any unforeseen circumstances were documented in the raw data. However, no unforeseen circumstances that affected the integrity of the study were noted.

14.0 PROTOCOL AMENDMENTS/DEVIATIONS

There were no protocol amendments or deviations. No changes to the protocol were required.

TABLE 1:
Inhibition and Enhancement Validation Results

Test Article #	pH	Dilution	%CV	% PPC Recovery	Valid PPC (Yes/No)
1	6.57	Neat	1.68	117	Yes
2	6.33	Neat	2.63	120	Yes
3	6.30	Neat	1.01	111	Yes

CV = Coefficient of Variation; PPC = Positive product Control

APPENDIX I:
Software Systems

Software	Use	21 CFR Part 11 Status	Publisher/Vendor	Location
Adobe Acrobat 8, 9, and 10 Professional	Document preparation	Not Applicable	Adobe Systems, Inc.	San José, CA
Matrix Gemini 5.3.19	Laboratory Information Management System	Compliant	Autoscribe Limited	Reading, UK
MS Office 2010 Small Business Suite and MS Office 2013 Professional Suite and higher	Business software (suite includes Word, Excel, PowerPoint, Outlook, Publisher, Office tools)	Not Applicable	Microsoft Corporation	Redmond, WA
Rees Scientific Centron Presidio 3.0	Automated Environmental Monitoring	Compliant	Rees Scientific	Trenton, NJ
TMS Web 7	Document management for SOPs and training records management software system	Compliant	Quality Systems Integrators	Eagle, PA
Toxikon Protocol Manager 1.0	Protocol requisition application	Not Applicable	Toxikon Corporation	Bedford, MA
Win KQCL Version 3.1	Micro plate reader	Compliance-Ready	Lonza	Walkersville, MD

TOXIKON TEST PROTOCOL
FDA GMP REGULATIONS
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AMOEBOCYTE LYSATE TEST FOR INHIBITION AND ENHANCEMENT TESTING OF ENDOTOXINS (KINETIC–QCL METHOD) – USP

TOXIKON PROTOCOL NUMBER: p21-0203-00a

21 CFR Part 820 Compliance
Good Manufacturing Practice

MANAGEMENT OF THE STUDY

Performing Laboratory	Sponsor
Toxikon Corporation	Malema Sensors
15 Wiggins Avenue	1060 S Rogers Circle
Bedford, MA 01730	Boca Raton, FL 33487

PROTOCOL SIGNATURES

Kalash Thamb
PRINT NAME

Kthamb
Sponsor's Representative Approval
Malema Sensors
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Boca Raton, FL 33487

02/5/21
Date

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02/08/2021
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Study Director Signature
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15 Wiggins Avenue
Bedford, MA 01730

4-26-21
Date

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Appendix:

1.0 PURPOSE

The purpose of this study is to determine if a test article extract or liquid sample inhibits or enhances the Bacterial Endotoxins Test, Kinetic Chromogenic technique.

2.0 REFERENCES

The study will be based upon the following references:

- United States Pharmacopeia 43, National Formulary 38, 2020. <85> Bacterial Endotoxins Test.
- United States Pharmacopeia 43, National Formulary 38, 2020. <161> Medical Devices – Bacterial Endotoxin and Pyrogen Tests.
- Limulus Amoebocyte Lysate (LAL), Kinetic–QCL™, Kit Instruction, Lonza.
- ISO/IEC 17025, 2017, General Requirements for the Compliance of Testing and Calibration Laboratories.

3.0 COMPLIANCE

This study conforms to the current 21 CFR Part 820 Good Manufacturing Practice, as applicable to a testing laboratory. Toxikon is accredited to ISO/IEC 17025, 2017, General Requirements for the Competence of Testing and Calibration Laboratories. Toxikon's Quality System also encompasses the general principles and practices of GxP regulations, specifically GLPs.

4.0 IDENTIFICATION OF TEST AND CONTROL ARTICLES

The Sponsor will supply the following information on a Test Requisition Form or other correspondence, wherever applicable (excluding confidential or trade secret information).

4.1 Test Article:

Name: To Be Determined (TBD)

CAS/Code Number: TBD

Lot/Batch Number: TBD

Physical State: TBD

Color: TBD

Expiration Date: TBD

Density: TBD

Stability: TBD

Sterility: TBD

Sterilization Conditions: TBD

Storage Condition: TBD

Safety Precautions: TBD

Intended Use: TBD

4.2 Negative Control Article(s) (Toxikon Supplied, unless specified by the Sponsor):

4.2.1 Negative Control Article 1:

Name: USP Sterile Water for Injection (SWFI)

Toxikon QC Number: To Be Determined (TBD)

4.2.2 Negative Control Article 2:

Name: Water for Bacterial Endotoxins Test (BET)

Toxikon QC Number: To Be Determined (TBD)

4.3 Positive Control Article(s) (Toxikon Supplied, unless specified by the Sponsor):

Name: *Escherichia coli* endotoxin

Toxikon QC Number: To Be Determined (TBD)

5.0 IDENTIFICATION OF TEST SYSTEM

The assay determines whether the test article inhibits or enhances the Bacterial Endotoxins Test, Kinetic Chromogenic technique. The test system will use Amoebocyte Lysate obtained from aqueous extracts of the circulating amebocytes of the horseshoe crab, *Limulus polyphemus*. Amoebocyte Lysate, prepared and characterized for use, is commercially available and reacts with a colorimetric substance to detect endotoxin.

6.0 JUSTIFICATION OF TEST SYSTEM AND ROUTE OF ADMINISTRATION

6.1 Justification of Test System:

The Inhibition and Enhancement assay is recommended by USP guidelines as a method to determine if a test article causes inhibition or enhancement of the Bacterial Endotoxins Test, Kinetic Chromogenic technique.

6.2 Route of Administration:

The liquid test article or the test article extract will be spiked *in vitro* directly with a known amount of endotoxin.

7.0 EXPERIMENTAL DESIGN AND DOSAGE

7.1 Test Article Preparation:

7.1.1 Liquid Test Articles:

All test articles will be collected in endotoxin–free containers and will be stored per Sponsor-specified storage conditions until tested. If conditions are not specified, liquid samples will be stored at room temperature. No preparation will be required, unless specified by the Sponsor.

7.1.2 Preparation of Devices (Test Articles) and Dosage:

Devices will be stored at room temperature unless other storage conditions are specified by the Sponsor. Rinse or immerse the devices with an appropriate volume of extracting fluid that has

been maintained at 37 ± 1 °C or as specified by the Sponsor. The test articles will be extracted for 60 ± 2 minutes at room temperature or as specified by the Sponsor. The temperature will be recorded at the beginning and end of the extraction period. For devices labeled "non–pyrogenic fluid pathway" the fluid pathway will be filled or flushed with an appropriate volume of extracting fluid that will be heated to 37 ± 1 °C. For devices being flushed, the extraction fluid will be held in the fluid pathway for 60 ± 2 minutes at room temperature or as specified by the Sponsor. The effluents will be pooled, if applicable.

Note: Toxikon's standard procedure is to use SWFI as the extraction fluid unless specified by the Sponsor.

For unusually large or small devices, the surface area of the device, which comes in contact with the patient, may be used as an adjustment factor in selecting the rinsing or extracting volume. The endotoxin limit will be adjusted accordingly.

It is necessary for the sample to have a pH in the range of 6.0-8.0. If the pH is not in this range, the pH will be adjusted using an endotoxin-free buffer. The pH of aliquots of each sample will be measured using a calibrated pH probe. Endotoxin-free buffer will be added in small amounts until the pH of each aliquot reaches 6.0-8.0, and the ratio of buffer to sample aliquot will be used to determine the amount of buffer to be added to the original sample.

7.2 Reagent and Material Preparation:

All reagents will be prepared per manufacturer's recommendations.

7.2.1 Preparation of Endotoxin Standard:

The Control Standard Endotoxin (CSE) in the Kinetic–QCL Kit that has been previously standardized by the manufacturer against the Reference Standard Endotoxin (RSE) will be used. The endotoxin standard will be reconstituted with the specified amount of Water for BET, and vortexed for 15 minutes.

The reconstituted endotoxin will have a potency of 50 Endotoxin Units (EU)/mL. The reconstituted endotoxin standard will be stored (mouth wrapped with parafilm) at 4 ± 2 °C for up to four weeks. The endotoxin standard will be only used with the reagents in a particular kit. If using previously reconstituted endotoxin, the endotoxin shall be vigorously vortexed for not less than 15 minutes before diluting. All unused working standard will not be stored for more than one (1) day.

7.2.2 Preparation of Kinetic-QCL LAL Reagent:

The reagent shall not be prepared until immediately prior to use. The Amoebocyte Lysate powder will be collected into the bottom of the vial by tapping on a firm surface. The metal seal of the reagent will be torn off and the gray stopper gently removed. The powder will be reconstituted with the amount of Water for BET specified by the manufacturer. Reconstituted Kinetic–QCL LAL Reagent is stable for 8 hours at 2 – 8 °C; otherwise it can be stored at –10 °C or below for up to two weeks. The reconstituted reagent will only be frozen and thawed once.

7.2.3 Preparation of Glassware and Utensils:

Any glass containers, test tubes, utensils, etc., used in this assay will be depyrogenated. The depyrogenation will be done by wrapping the utensils in foil and heating for at least 30 minutes at 250 °C.

7.3 Test Method:

To identify whether the test article inhibits or enhances the assay, the Water for BET will be spiked with four different concentrations of endotoxin (5 EU/mL, 0.5 EU/mL, 0.05 EU/mL, and 0.005 EU/mL) in duplicate. The test article (unspiked) will be assayed in duplicate and the test article spiked with 0.5 EU/mL of endotoxin (Positive Product Control or PPC) will be assayed in duplicate. To make the PPC, 10 µL of the 5 EU/mL standard will be added to 90 µL of the test article extract for a final concentration of 0.5 EU/mL. Multiple dilutions of the test article can be assayed up to the maximum valid dilution. The actual volume of test article in the appropriate well of the microplate is always 0.1 mL.

The filled plate will be placed in the microplate reader and the lid closed. The plate will be pre–incubated for ≥ 10 minutes at 37 ± 1 °C.

7.3.1 Addition of Lysate:

0.1 mL of reconstituted Amoebocyte Lysate will be added to each well of the microplate reader containing 0.1 mL of test article or control. Amoebocyte Lysate will be added to the negative controls first, and from the lowest to highest concentration in each test series.

The microplate will be immediately placed in the reader to initiate the test.

The correlation coefficient, (r), shall be greater than or equal to the absolute value of 0.980.

7.4 Preparation of the Negative Control and Blank:

The Blank for the Standard curve should always be Water for BET. In the case of a device that is rinsed, immersed, or flushed, a 100 µL aliquot of the vehicle used in the extraction process is assayed as the negative control in duplicate.

8.0 EVALUATION CRITERIA

8.1 Evaluation of Data:

Results will be printed out at the completion of the assay. Replicate samples should be run in order to establish good technique and low coefficient of variation. The coefficient of variation, CV, equals the “sample” standard deviation of the reaction times divided by the mean and is usually expressed as a percent. The % CV of the reaction times for replicate of a sample should be less than 10%.

The absolute value of the coefficient of correlation of the calculated standard curve should be ≥ 0.980.

If the PPC value is outside the range of 50–200% of the known spike concentration, the results show either inhibition or enhancement of the assay.

A device that fails this test can be retested once by another Bacterial Endotoxins Test. For devices that cannot be tested by the Bacterial Endotoxins Test because of non-removable inhibition or enhancement, the Pyrogen Test (USP <151>) is applied.

8.2 Control of Bias Statement:

The study as designed employs methodology to minimize uncertainty of measurement and to control bias for data collection and analysis, which includes but is not limited to: control data

(retrospective, concurrent, or prospective), system suitability assessment, randomization, method controls such as blanks and replicates, or others as required by the specific study or guideline. Methods employed will be specified in the final report.

9.0 RECORDS

- Original raw data will be archived by Toxikon Corporation.
- A copy of the final report and any report amendments will be archived by Toxikon Corporation.
- The original final report and a copy of any the protocol and protocol amendments or deviations will be forwarded to the Sponsor.
- All used and unused test article will be handled as specified on the Test Requisition Form. If not indicated on the Test Requisition Form, all remaining test article will be disposed.
- Test article retention upon study completion is the responsibility of the Sponsor.

10.0 CONFIDENTIALITY AGREEMENT

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

11.0 UNFORESEEN CIRCUMSTANCES

All unforeseen circumstances will be documented in the raw data. Any unforeseen circumstances that affect the integrity of the study will be discussed in the final report.

12.0 PROTOCOL AMENDMENTS/DEVIATIONS

All changes to the approved protocol and the reason for the changes will be documented in writing, signed by the Study Director, dated, and maintained with the protocol. A Protocol Amendment (PA) or a Protocol Deviation (PD) will be generated as closely as possible to the time of the change. The document will be created and signed by the Study Director and sent to the Sponsor. Sponsor's signature will be required for amendments (PA) to indicate approval of the amendment. Acknowledgement of notification of deviations is preferred and may be with a signature or other form of documentation.

APPENDIX I:
Software Systems

The following are the proposed software systems to be used during the conduct of this study. The actual systems used, as well as 21 CFR Part 11 compliance if applicable, will be documented in the final report.

Software	Use	Publisher/ Vendor	Location
Adobe Acrobat 8, 9, and 10 Professional	Document preparation	Adobe Systems, Inc.	San José, CA
Matrix Gemini 5.3.19	Laboratory Information Management System	Autoscribe Limited	Reading, UK
MS Office 2010 Small Business Suite and MS Office 2013 Professional Suite and higher	Business software (suite includes Word, Excel, PowerPoint, Outlook, Publisher, Office tools)	Microsoft Corporation	Redmond, WA
Rees Scientific Centron Presidio 3.0	Automated Environmental Monitoring	Rees Scientific	Trenton, NJ
Report Automation 1.0	Custom software (add-in) for final report generation, review, approval, distribution to sponsors, and storage	Court Square Group	Springfield, MA
TMS Web 7	Document management for SOPs and training records management software system	Quality Systems Integrators	Eagle, PA
Toxikon Protocol Manager 1.0	Protocol requisition application	Toxikon Corporation	Bedford, MA
Win KQCL Version 3.1	Micro plate reader	Lonza	Walkersville, MD