10 QC Testing Solutions

QC Testing Solutions

Endotoxin Detection Assays

Instrumentation and Software

Accessory Products

10

Endotoxin Detection Assays

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Introduction

Endotoxin Detection: A Brief History

Ever since the pharmaceutical industry began manufacturing injectables, pyrogen detection tests have been an absolute necessity. Pyrogens are substances that can cause fever, shock, and even death if high levels are introduced into the body. Endotoxins are natural compounds found in the outer cell membrane of Gram-negative bacteria and are released upon cell lysis. Endotoxins are a type of pyrogen. Today, endotoxin detection tests are performed on raw materials, in-process materials, and for the final release of pharmaceutical and medical device products.

For most of the 20th century the rabbit pyrogen test was the standard method of testing for pyrogenicity. This test, which takes approximately four hours, is accomplished by injecting the drug being analyzed into a rabbit's ear. If the animal develops a fever it confirms the presence of pyrogens.

The LAL (Limulus Amebocyte Lysate) test was commercially introduced in the 1970s. LAL is derived from the blood cells, or amebocytes, of the Atlantic horseshoe crab (Limulus polyphemus). LAL was developed into a test for endotoxin after Frederick Bang and Jack Levin observed that the amebocytes of the horseshoe crab contain a clotting agent that forms in the presence of Gram-negative bacteria. They recognized that this clotting agent could be used as a definitive way to test pharmaceutical drugs for the presence of Gram-negative bacteria and their endotoxins. In a notice published in the Federal Register on November 4, 1977, the FDA described conditions for the use of LAL as an end-product test for endotoxin in human biological products and medical devices. The FDA widely recognizes that the LAL test is much faster, more economical, and more efficient than the rabbit pyrogen test. In addition, the LAL test is less labor intensive than the rabbit test, which makes it possible to perform many tests in a single day.

To obtain the lysate required for the LAL test, horseshoe crabs are taken from the ocean floor and a small amount of their blood is drawn. The animals are then returned returned to the sea unharmed. The crab's blood cells, or amebocytes, are then separated and lysed to obtain the cellular proteins.

As LAL became the preferred endotoxin detection test, different methods were developed, each method with its own unique benefits. For example, Gel Clot LAL (PYROGENT™) provides a simple positive / negative result and is mentioned in most pharmacopeial monographs as the official referee test. The kinetic turbidimetric LAL assay (PYROGENT™-5000) gives a quantitative result and offers an economical choice for water or large volume parenterals. The endpoint chromogenic LAL test (QCL-1000™) offers a quantitative result and exhibits less product interference than LAL methods utilizing the clotting protein. Our most sensitive LAL assay, the kinetic chromogenic LAL assay (Kinetic-QCL™), provides the benefit of less product interference for proteins, vaccines, LAL, and other biologicals while also being able to detect as low as 0.005 EU/mL.

Currently the FDA, the United States Pharmacopeia (USP), the European Pharmacopeia (EP), and the Japanese Pharmacopeia (JP) accept all of the above LAL methods, as do most individual country pharmacopeias.

More recently, Lonza scientists have developed a reliable and sustainable endotoxin detection test method that is not derived from horseshoe crab blood. The PyroGene™ Assay is based on the recombinantly expressed Factor C, which is the first component in the LAL clotting cascade activated by endotoxin. It is specific for endotoxin and offers a reliable alternative for endotoxin release testing. The PyroGene™ Assay promises to reduce the dependence on animal-based endotoxin assays. In 2009, the FDA approved 510(K) applications that included the PyroGene™ Assay as the final release test. The latest FDA Guidance for Industry document on "Pyrogen and Endotoxins Testing: Questions and Answers" from 2012 accepts the use of PyroGene™ as an alternative method. Please refer to page 370 for further information.

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Overview of LAL Testing Procedures

There are four basic types of assays, each of which is designed to perform a different aspect of LAL testing. Our WinKQCL™ Software supports all of these assay types and is the ideal tool to accompany your quantitative endotoxin assays. It offers a fully integrated and compliant solution for reporting and analyzing your endotoxin assay results.

Routine

A routine assay calculates the concentration of endotoxin in unknowns by comparison to the performance of a series of endotoxin standards. As part of a routine assay, the user has the option to include a Positive Product Control (PPC) as a monitor for product inhibition or enhancement. A PPC is a sample of product to which a known amount of endotoxin has been added. For quantitative assays, our WinKQCL™ Software automatically calculates the amount of endotoxin recovered in the PPC and compares it to the known amount of the endotoxin in the well to give the user a percentage of recovery.

Inhibition/Enhancement

The Limulus Amebocyte Lysate reaction is enzyme mediated and, as such, has an optimal pH range, specific salt concentrations, and divalent cation requirements. Occasionally, test samples may alter these optimal conditions to an extent that the lysate is rendered insensitive to endotoxin. Negative results with samples that inhibit the LAL test do not necessarily indicate the absence of endotoxin.

An inhibition/enhancement assay is designed to determine what level of product dilution or other treatment overcomes inhibition or enhancement. Each product dilution must be accompanied by a Positive Product Control (PPC). For quantitative assays, our WinKQCL™ Software calculates the amount of endotoxin recovered in the PPC for comparison to the known amount of endotoxin spike. In this manner it can be determined which product dilutions are non-interfering.

RSE/CSE

An RSE/CSE assay is designed to determine the potency of a Control Standard Endotoxin (CSE) in terms of the concentration units of the Reference Standard Endotoxin (RSE). The assay requires a single series of RSE dilutions and one or more sets of dilutions of the CSE. If you buy matched reagents, Lonza has already performed this test for you. Our CSE is matched against the USP RSE. Matched CSE is either part of the kit or is available separately.

Initial Qualification

An Initial Qualification assay is required as part of the validation of the LAL assay and is also to be performed with each new lot of reagents. It serves to confirm reagent performance and assure reproducibility. In addition, it shows analyst qualification. For this assay, a series of endotoxin standards is prepared and tested in at least triplicate. To confirm sensitivity/linearity, the test result must meet regulatory requirements as defined by the pharmacopeia. For gel clot assays, the determined end-point must fall between 2 λ and 0.5 λ of the labeled sensitivity. For the quantitative assays, the results are used to generate a standard curve which must have a correlation coefficient of $\geq |0.980|$. The Initial Qualification assay does not provide for the inclusion of any samples.

Overview of Endotoxin Detection Methods

Endotoxin Detection Methods

Qualitative
(Yes/No Answer)

Product: PYROGENT™ Gel Clot LAL Assay

- **Method** – Visual inspection of gel formation
- **Maximum sensitivity** – 0.03 EU/mL
- **Instrument required** – A dry heat block or water bath

Benefits
- Simple LAL test not requiring sophisticated instrumentation and software

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Overview of Endotoxin Detection Methods

Continued

Quantitative

(Results calculated from standard curve)

Product: Kinetic-QCL™ Kinetic Chromogenic LAL Assay

- **Method** – Kinetic measurement of color development
- **Maximum sensitivity** – 0.005 EU/mL
- **Instrument required** – Incubating absorbance reader

Benefits

- Our most sensitive LAL-based method
- Less sensitive to product inhibition
- Ideal for biological products such as vaccines and antibiotics

Product: QCL-1000™ Endpoint Chromogenic LAL Assay

- **Method** – Endpoint measurement of color development
- **Maximum sensitivity** – 0.1 EU/mL
- **Instrument required** – Spectrophotometer or absorbance reader, dry heat block

Benefits

- Results in 16 minutes

Product: PYROGENT™-5000 Kinetic Turbidimetric LAL Assay

- **Method** – Kinetic measurement of turbidity development
- **Maximum sensitivity** – 0.01 EU/mL
- **Instrument required** – Incubating absorbance reader

Benefits

- Cost-effective method for water and large volume parenterals

Product: PyroGene™ Recombinant Factor C Assay

- **Method** – Endpoint measurement of fluorescence
- **Maximum sensitivity** – 0.005 EU/mL
- **Instrument required** – Incubating fluorescence reader

Benefits

- Elimination of false positive glucan reactions
- Less lot-to-lot variability
- Animal-free source and security of supply
- FDA acknowledged alternative to LAL

Kinetic Chromogenic LAL Assay Overview

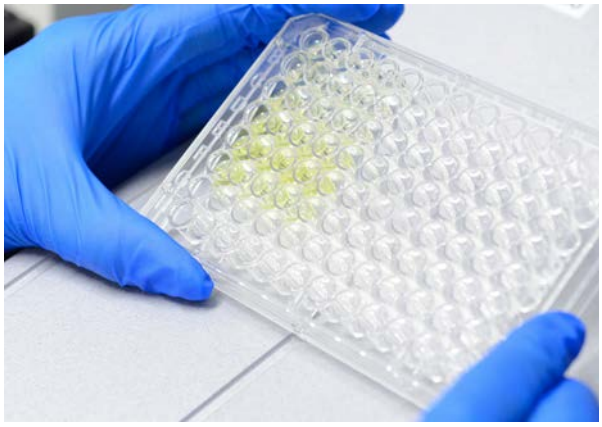
The Kinetic-QCL™ Kinetic Chromogenic Assay is a quantitative, kinetic assay for the detection of Gram-negative bacterial endotoxin. A sample is mixed with the reconstituted LAL reagent in a 96-well plate and placed in an incubating absorbance plate reader that measures absorbance at 405nm. The reaction is automatically monitored over time for the appearance of a yellow color.

In the presence of endotoxin the lysate will begin to cleave the chromogenic substrate, causing the solution to become yellow. The time required for the change is inversely proportional to the amount of endotoxin present. The concentration in unknown samples can be calculated from a standard curve. Due to the nature of this assay, the Kinetic-QCL™ Assay is less impacted by inhibitory products that may interfere with the clotting mechanism in turbidimetric and gel clot assays. This feature, along with the sensitivity range of 0.005 to 50 EU/mL, makes this assay optimal for biological products such as vaccines and antibiotics.

Using our extensive experience and practical expertise with endotoxin detection and its regulatory requirements, Lonza has developed an integrated system to support quantitative endotoxin detection. Each system component has been validated and can be verified. This all leads to reliable, reproducible, and accurate quantitative results.

Each quantitative system incorporates three elements:
- Kinetic-QCL™ Kinetic Chromogenic LAL Assay
- WinKQCL™ Endotoxin Detection and Analysis Software
- Incubating Absorbance Plate Reader

These elements integrate seamlessly to meet your testing requirements, providing meaningful results that allow you to be confident in your critical decisions.



Benefits
- Sensitivity range from 0.005 to 50 EU/mL

Applications
- Ideal for biological products such as vaccines and antibiotics

Requirements
- Incubating Absorbance Plate Reader
- WinKQCL™ Software
- LAL Reagent Water (for larger kits)
- Pyrogen-free Test Tubes
- LAL Reagent Grade Multi-well Plates

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Kinetic-QCL™ Kinetic Chromogenic LAL Assay

The Kinetic-QCL™ Kinetic Chromogenic Assay kit contains co-lyophilized lysate/substrate and matched control standard endotoxin (Cat. No. 50-650U also contains LAL Reagent Water).

Kinetic Chromogenic LAL and matched control standard endotoxin are packaged separately but should be ordered together. These bulk configurations are made to order and therefore require a lead time. **Bulk kit configurations are also available*.**

Please contact Customer Service for more information.

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/kqcl

2° C to 8°C

Benefits

- Sensitivity range from 0.005 to 50 EU/mL
- Less sensitive to product inhibition than assays requiring gel formation
- Available in 192-, 2040-, and 2400-test kit and bulk configurations

Ordering Information – Kinetic-QCL™ Kinetic Chromogenic LAL Assay

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
50-650U	50-650U	Kinetic-QCL™ Kinetic Chromogenic LAL Assay	8 × 24 tests/vial Lysate, 2 vials endotoxin, 3 × 30 mL vial LAL Reagent Water	192 tests	0.005 to 50
50-650NV	50-650NV	Kinetic-QCL™ Kinetic Chromogenic LAL Assay	85 × 24 tests/vial Lysate, 15 vials endotoxin	2,040 tests	0.005 to 50
50-650H	50-650H	Kinetic-QCL™ Kinetic Chromogenic LAL Assay	100 × 24 tests/vial Lysate, 10 vials endotoxin	2,400 tests	0.005 to 50
*K50-643L	*K50-643L	Kinetic-QCL™ Bulk Kinetic Chromogenic LAL Assay	25 × 24 tests/vial Lysate	600 tests	0.005 to 50
*K50-643U	*K50-643U	Kinetic-QCL™ Bulk Kinetic Chromogenic LAL Assay	100 × 24 tests/vial Lysate	2,400 tests	0.005 to 50

*LAL and CSE are packaged separately but must be ordered together. this requires E50-643L

Control Standard Endotoxin for Kinetic-QCL™ Bulk Kinetic Chromogenic LAL

The Control Standard Endotoxin, derived from *E. coli* 055:B5, is referenced against the USP Reference Standard Endotoxin.

Ordering Information – Control Standard Endotoxin for Kinetic-QCL™ Bulk Kinetic Chromogenic LAL

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
E50-643L	E50-643L	Control Standard Endotoxin for Kinetic-QCL™ Bulk Kinetic Chromogenic LAL, *E. coli* Strain 055:B5	50 EU/mL	25 vials

Control Standard Endotoxin, (E50-643L), for use with K50-643L/U

Related Products	Page
WinKQCL™ Endotoxin Detection and Analysis Software	384
ELx808™ Incubating Absorbance Plate Reader	381
LAL Reagent Grade Multi-well Plates	388
LAL Reagent Water (LRW)	390
Pyrogen-free Test Tubes	387
Pipette Tips and Reagent Reservoirs	389

QCL-1000™ Endpoint Chromogenic LAL Assay

The QCL-1000™ Endpoint Chromogenic LAL Assay is the most rapid of the LAL tests. This chromogenic LAL method is based on the formation of a yellow color and is measured photometrically at 405–410 nm. With the QCL-1000™ Assay, a multichannel pipette, a dry heat block and a 96-well plate, you can run a quantitative endotoxin assay in 16 minutes. This assay can also be run in tubes.

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/qcl1000

2°C to 8°C

Benefits

- Less sensitive to product inhibition than assays requiring gel formation
- Sensitivity from 0.1 to 1 EU/mL
- Quantitative results in 16 minutes
- Flexible format - use test tubes or 96-well plates
- Can be run with a simple spectrophotometer, no need for incubating absorbance plate reader

Ordering Information – QCL-1000™ Endpoint Chromogenic LAL Assay

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
50-647U	**50-647U**	QCL-1000™ Endpoint Chromogenic LAL Assay	5 × 24 tests/vial Lysate, 1 × 1 mL vial endotoxin, 2 × 6.5 mL vial chromogenic substrate, 2 × 30 mL vial LAL Reagent Water	120 tests	0.1 to 1
50-648U	**50-648U**	QCL-1000™ Endpoint Chromogenic LAL Assay	5 × 60 tests/vial Lysate, 2 × 1 mL vial endotoxin, 5 × 6.5 mL vial chromogenic substrate	300 tests	0.1 to 1

Ordering Information – Control Standard Endotoxin for QCL-1000™ Endpoint Chromogenic LAL

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
E50-640	**E50-640**	Control Standard Endotoxin for QCL-1000™ Endpoint Chromogenic LAL, *E. coli* Strain 0111:B4	Endotoxin, 15 to 40 EU/mL	1 vial	n/a

E50-640 requires matched LAL

Related Products	Page
LAL Reagent Water (LRW)	390
Pyrogen-free Test Tubes	387
LAL Reagent Grade Multi-well Plates	388
LAL Reagent Reservoirs	389
Eppendorf® 2–200 µL Biopur® Pipette tips	389
Eppendorf® 50–1000 µL Biopur® Pipette tips	389
Heat Block and Adaptor	390

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Kinetic Turbidimetric LAL Assay Overview

The PYROGENT™-5000 Assay is a quantitative, kinetic assay for the detection of Gram-negative bacterial endotoxin. A sample is mixed with the reconstituted LAL reagent in a 96-well plate and placed in an incubating absorbance plate reader that measures absorbance at 340 nm. The reaction is automatically monitored over time for the appearance of turbidity.

In the presence of endotoxin the lysate will begin to gel, causing the solution to become cloudy or turbid. The time required for this change is inversely proportional to the amount of endotoxin present. The concentration in unknown samples can be calculated from a standard curve.

The PYROGENT™-5000 Assay is perfect for laboratories needing to process a large number of samples. It is ideal for water samples, large volume parenterals, and the water rinse from medical devices.

Using our extensive experience and technical expertise with endotoxin detection and its regulatory requirements, Lonza has developed an integrated system to support quantitative endotoxin detection. Each system component has been validated and can be verified. This all leads to reliable, reproducible, and accurate quantitative results.

Each quantitative system incorporates three elements:
- PYROGENT™-5000 Kinetic Turbidimetric LAL Assay
- WinKQCL™ Endotoxin Detection and Analysis Software
- Incubating Absorbance Plate Reader

These elements integrate seamlessly to meet your testing requirements, providing meaningful results that allow you to be confident in your critical decisions.

Benefits
- Sensitivity range from 0.01 to 100 EU/mL
- Select from a wide range of kit sizes

Applications
- Cost-effective method for water and large volume parenterals

Requirements
- Incubating Absorbance Plate Reader
- WinKQCL™ Software
- LAL Reagent Water
- Pyrogen-free Test Tubes
- LAL Reagent Grade Multi-well Plates

PYROGENT™-5000 Kinetic Turbidimetric LAL Assay

The PYROGENT™-5000 kit contains turbidimetric lysate, reconstitution buffer for the lysate, and matched control standard endotoxin. Bulk kit configurations are available with the three assay components packaged separately. The kinetic turbidimetric LAL, reconstitution buffer, and matched Control Standard Endotoxin should be ordered together. These bulk configurations are made to order and therefore require a lead time. Please contact Customer Service for more information.

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/turb

2°C to 8°C

Benefits

- Sensitivity range from 0.01 to 100 EU/mL
- Available in 100-, 200-, 2250-, and 4500-test kit and bulk configurations

Ordering Information – PYROGENT™-5000 Kinetic Turbidimetric LAL Assay

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
N383	N383	PYROGENT™-5000 Kinetic Turbidimetric LAL Assay	2 × 50 tests/vial Lysate, 2 vials reconstitution buffer, 1 vial endotoxin	100 tests	0.01 to 100
N384	N384	PYROGENT™-5000 Kinetic Turbidimetric LAL Assay	2 × 100 tests/vial Lysate, 2 vials reconstitution buffer, 1 vial endotoxin	200 tests	0.01 to 100
N588	N588	PYROGENT™-5000 Kinetic Turbidimetric LAL Assay	45 × 50 tests/vial Lysate, 45 vials reconstitution buffer, 10 vials endotoxin	2,250 tests	0.01 to 100
N688	N688	PYROGENT™-5000 Kinetic Turbidimetric LAL Assay	45 × 100 tests/vial Lysate, 45 vials reconstitution buffer, 10 vials endotoxin	4,500 tests	0.01 to 100
T50-300L	T50-300L	PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL Assay	25 × 50 tests/vial Lysate	1,250 tests	0.01 to 100
T50-300U	T50-300U	PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL Assay	100 × 50 tests/vial Lysate	5,000 tests	0.01 to 100
T50-600L	T50-600L	PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL Assay	25 × 100 tests/vial Lysate	2,500 tests	0.01 to 100
T50-600U	T50-600U	PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL Assay	100 × 100 tests/vial Lysate	10,000 tests	0.01 to 100

Bulk Assay require matched endotoxin

Reconstitution Buffer for PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL

The reconstitution buffer is provided for rehydration of the PYROGENT™-5000 LAL Reagent.

Ordering Information – PYROGENT™-5000 Bulk Kinetic Turbidimetric Reconstitution Buffer

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
B50-300L	B50-300L	PYROGENT™-5000 Bulk Kinetic Turbidimetric Reconstitution Buffer	Reconstitution buffer for T50-300L	25 vials
B50-300U	B50-300U	PYROGENT™-5000 Bulk Kinetic Turbidimetric Reconstitution Buffer	Reconstitution buffer for T50-300U	100 vials
B50-600L	B50-600L	PYROGENT™-5000 Bulk Kinetic Turbidimetric Reconstitution Buffer	Reconstitution buffer for T50-600L	25 vials
B50-600U	B50-600U	PYROGENT™-5000 Bulk Kinetic Turbidimetric Reconstitution Buffer	Reconstitution buffer for T50-600U	100 vials

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Control Standard Endotoxin for PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL

The Control Standard Endotoxin, derived from *E. coli* 055:B5, is referenced against the USP Reference Standard Endotoxin.

Ordering Information – Control Standard Endotoxin for PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity
7460L	7460L	Control Standard Endotoxin for PYROGENT™-5000 Bulk Kinetic Turbidimetric LAL, *E. coli* Strain 055:B5	100 EU/mL	25 vials	n/a

Matched LAL required

Related Products	Page
WinKQCL™ Endotoxin Detection and Analysis Software	384
ELx808™ Incubating Absorbance Plate Reader	381
LAL Reagent Grade Multi-well Plates	388
LAL Reagent Water (LRW)	390
Pyrogen-free Test Tubes	387
Pipette Tips and Reagent Reservoirs	389

PyroGene™ Recombinant Factor C Assay

The PyroGene™ Recombinant Factor C Assay is an animal-free alternative to LAL that has been accepted by the FDA as an alternative method.* It is based on a recombinantly produced form of Factor C (rFC), the first component in the horseshoe crab clotting cascade. It is activated by endotoxin binding. The active moiety created then acts to cleave a synthetic substrate, which results in the release of a fluorophore. The reaction is run in a 96-well microplate and measured at time zero and again after a one-hour incubation in a fluorescence microplate reader using excitation/emission wavelengths of 380/440 nm.

A global, multi-center study demonstrated that the recovery of endotoxin from water and other tested products using the PyroGene™ Recombinant Factor C Assay was comparable to that of LAL-based methods. The results of the assay validation were published in the Pharmacopeial Forum Vol. 36(1) (Jan. – Feb. 2010).

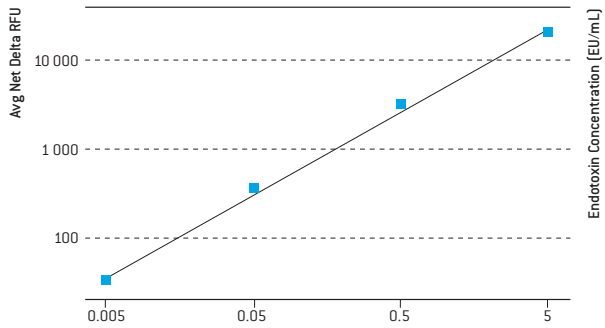
In June 2012, the FDA issued the document "Guidance for Industry - Pyrogen and Endotoxins Testing: Questions and Answers" which allows for the use of a recombinant Factor C based assay as an alternative to Limulus Amebocyte Lysate (LAL)-based assays. In July 2016, rFC became officially recognized by the European Pharmacopoeia (Ph. Eur.) as an alternative endotoxin detection methodology to the LAL and Rabbit Pyrogen Tests in the new draft of Chapter 5.1.10.

USP 28–NF 33 General Notices allows alternative methods if they provide advantages regarding accuracy, sensitivity, precision, selectivity, or adaptability to automation. However, to use these alternative methods for final release testing, one may need to validate the test method on their products as described in the general chapter "Validation of Compendial Procedures" <1225> and it must be shown to give equivalent or better results.

Each quantitative system incorporates three elements:
- PyroGene™ Recombinant Factor C Assay
- WinKQCL™ Endotoxin Detection and Analysis Software
- Fluorescence Plate Reader

These elements integrate seamlessly to meet your testing requirements, providing meaningful results that allow you to be confident in your critical decisions.

Applications
- Water testing
- In-process testing
- Final release testing
- Testing plant-based material



Standard curve illustrating assay range from 0.005 to 5 EU/mL

Benefits
- Sensitivity range from 0.005 to 5 EU/mL
- Higher endotoxin specificity
- Elimination of false positive glucan reactions
- Less lot-to-lot variability
- Animal-free
- Security of supply
- FDA acknowledged alternative to LAL

Requirements
- Incubating fluorescence reader
- WinKQCL™ Software
- Pyrogen-free test tubes
- LAL reagent grade multi-well plates
- LAL Reagent Water (for larger kits)

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/pyrogene

2°C to 8°C

* According to the FDA "Guidance for Industry - Pyrogen and Endotoxins Testing: Questions and Answers" document from June 2012, alternative assays should be validated as described in the USP General Chapter <1225>, "Validation of Compendial Procedures".

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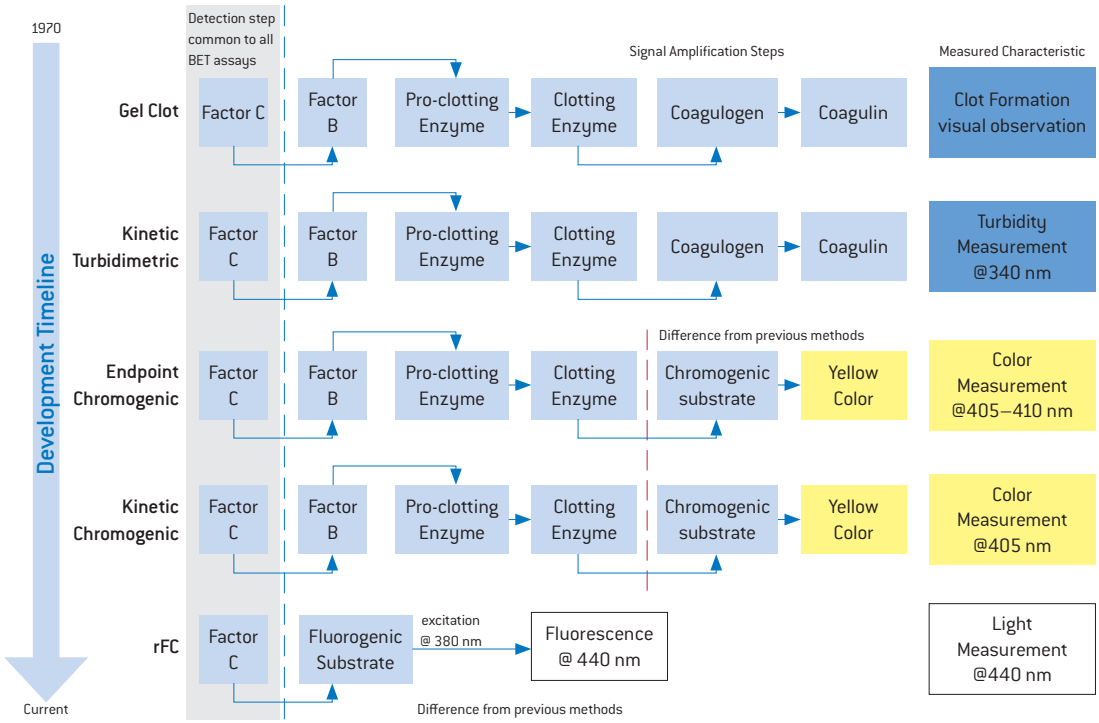
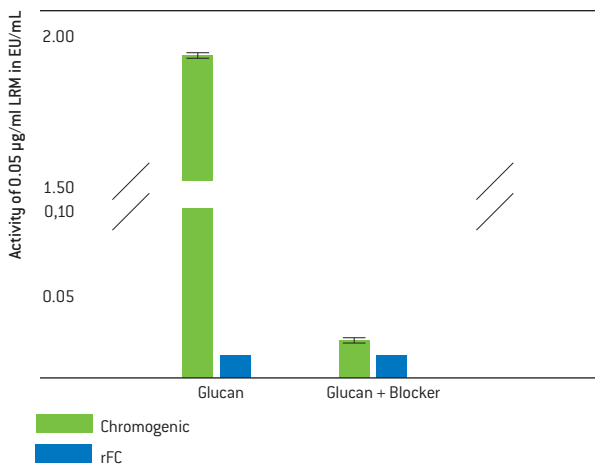
PyroGene™ Recombinant Factor C Assay

Continued

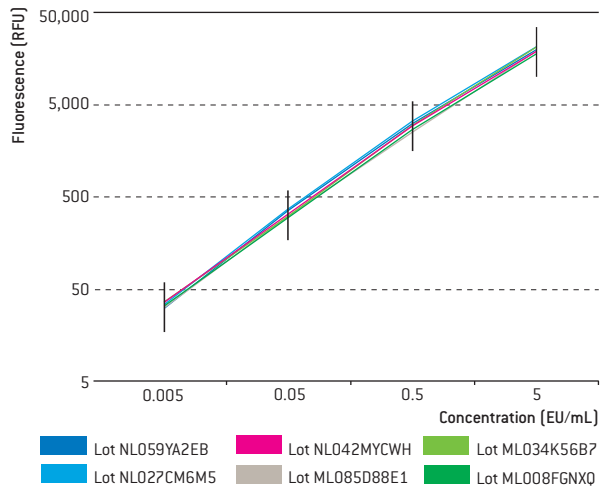
Comparison of Amplification Methods in Bacterial Endotoxin Detection Assays



rFC is the same binding protein operating in the LAL assay. The activated recombinant Factor C enzyme cleaves a substrate directly instead of activating another enzyme in a series (the LAL cascade). The substrate has a fluorescent tag, which gives a wide dynamic range with better resolution.



Comparison of reactivity towards glucans between kinetic chromogenic LAL and rFC. The false positive signal from the LAL assay is reduced in the presence of a glucan blocker. rFC does not detect any glucan activity; it is endotoxin-specific.



Endotoxin standard curves using 6 different lots of rFC. The log net fluorescence is proportional to the log endotoxin concentration and is linear in the 0.005 - 5 EU/mL range. Lot-to-lot standard curves exhibit excellent reproducibility.

PyroGene™ Validation Timeline

A possible validation scheme is outlined below. One validation can be accomplished in as little as 5 days, assuming that the product has been previously validated with a quantitative LAL method. The validation scheme is identical to that which would be needed for any LAL-based method with just the addition of one extra step– "Validation of alternative method". Lonza offers a full validation protocol that can be followed for your convenience. For further information, please contact Scientific Support or your local sales representative.

Preparation	Initial Qualification	Inhibition/ Enhancement Testing	Validation of Alternative Method	Product Validation
– IOP/Q – Sensitivity assay for rFC – Initial qualification of current and rFC method and analyst	– Not necessary if previously qualified reagent lots are used	– Only for rFC – Time depending on extent of testing required to find a suitable dilution/pre-treatment	– Tests with both current and rFC method – Good planning can save time	– 3 production lots
2 days	0.5 days	>0.5 days (minimum)	>1.5 days (minimum)	0.5 days

Ordering Information –PyroGene™ Recombinant Factor C Endpoint Fluorescent Assay

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
50-658U	**50-658U**	PyroGene™ Recombinant Factor C Endpoint Fluorescent Assay	2 × 96 tests/vial rFC enzyme solution, 2 × 6 mL vial fluorogenic substrate, 2 × 5 mL vial rFC assay buffer, 2 vials endotoxin, 2 × 30 mL vial LAL Reagent Water	192 tests	0.005 to 5
50-658NV	**50-658NV**	PyroGene™ Recombinant Factor C Endpoint Fluorescent Assay	30 × 96 tests/vial rFC enzyme solution, 30 × 6 mL/vial fluorogenic substrate, 30 × 5 mL/vial rFC assay buffer, 10 vials endotoxin	2,880 tests	0.005 to 5

Related Products	Page
Pyrogen-free Test Tubes	387
LAL Reagent Grade Multi-well Plates	388
LAL Reagent Reservoirs	389
Eppendorf® 2–200 µL Biopur® Pipette tips	389
Eppendorf® 50–1000 µL Biopur® Pipette tips	389
PyroWave™ XM Fluorescence Plate Reader	382

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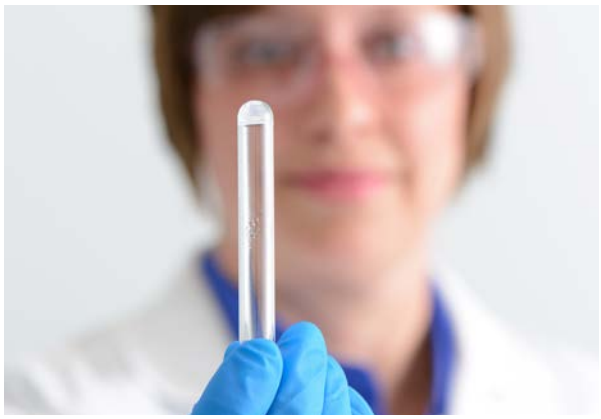
PYROGENT™ Gel Clot LAL Assay Overview

The PYROGENT™ Gel Clot LAL Assay is a qualitative LAL test for Gram-negative bacterial endotoxin. The gel clot assay is performed in tubes that are placed in a water bath or dry heat block at 37°C. After a one-hour incubation period, the tubes are inverted 180°. A firm clot that stays in the bottom of the tube indicates a positive reaction. If liquid flows down the side of the tube, the result is negative for endotoxin.

Like other enzymatic reactions, the LAL assay is pH dependent. The PYROGENT™ lysate formulation contains a buffer to help with these adjustments. As a result, many products will not require pH adjustments prior to testing.

PYROGENT™ Gel Clot LAL kits are available in two formats:

	Lysate	Matched Endotoxin
PYROGENT™ Gel Clot LAL	■	
PYROGENT™ Plus Gel Clot LAL	■	■



Benefits

- Easy-to-read qualitative results
- Simple LAL test not requiring sophisticated instrumentation and software
- Select from a wide range of kit sizes and sensitivities

Applications

- Water testing
- In-process testing
- Final release testing
- Testing plant-based material
- Testing acidic/basic material

Requirements

- A water bath or dry heat block
- LAL Reagent Water (LRW)
- Pyrogen-free test tubes

PYROGENT™ Gel Clot LAL Assay

PYROGENT™ Gel Clot LAL Assay standard kit sizes include 250 tests and 80 tests. Both the 250- and 80-test kits require depyrogenated 10 × 75 mm glass reaction tubes to run the assay.

These kits do not include a matched control standard endotoxin. However, the standard can be purchased separately (Control Standard Endotoxin, page 377).

Benefits

- Sensitivities of 0.03, 0.06, 0.125, and 0.25 EU/mL available
- Easy-to-read qualitative results
- Also available as bulk kits

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/gelclot

2°C to 8°C

Ordering Information – PYROGENT™ Gel Clot LAL Assay (without endotoxin)

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
N183-06	N183-06	PYROGENT™ Gel Clot LAL Assay (without endotoxin)	5 × 16 tests/vial Lysate	80 tests	0.06
N183-125	N183-125	PYROGENT™ Gel Clot LAL Assay (without endotoxin)	5 × 16 tests/vial Lysate	80 tests	0.125
N194-03	N194-03	PYROGENT™ Gel Clot LAL Assay (without endotoxin)	5 × 50 tests/vial Lysate	250 tests	0.03
N194-06	N194-06	PYROGENT™ Gel Clot LAL Assay (without endotoxin)	5 × 50 tests/vial Lysate	250 tests	0.06
N194-125	N194-125	PYROGENT™ Gel Clot LAL Assay (without endotoxin)	5 × 50 tests/vial Lysate	250 tests	0.125
N184-25	N184-25	PYROGENT™ Gel Clot LAL Assay (without endotoxin)	5 × 50 tests/vial Lysate	250 tests	0.25

Control Standard Exdotoxin (CSE), must be purchased separately

Related Products	Page
Control Standard Endotoxin for Gel Clot LAL	377
Bulk kits	376
LAL Reagent Water (LRW)	390
Pyrogen-free Test Tubes	387
Eppendorf® 2–200 µL Biopur® Pipette tips	389
Eppendorf® 50–1000 µL Biopur® Pipette tips	389

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PYROGENT™ Plus Gel Clot LAL Assay

The PYROGENT™ Plus Gel Clot LAL Assay combines PYROGENT™ LAL with a matched control standard endotoxin together in one kit box. Standard kit sizes include 4,000 tests, 200 tests, or 64 tests. These kits require depyrogenated 10 × 75 mm glass reaction tubes to run the assay.

These kits do include a matched control standard endotoxin. For your convenience, the Certificate of Analysis documenting the FDA and USP required RSE/CSE correlation is available online:

www.lonza.com/coa

www.lonza.com/gelclot

Benefits

- Sensitivities of 0.03, 0.06, 0.125 and 0.25 EU/mL available
- No need to purchase CSE separately
- Also available as bulk kits

2°C to 8°C

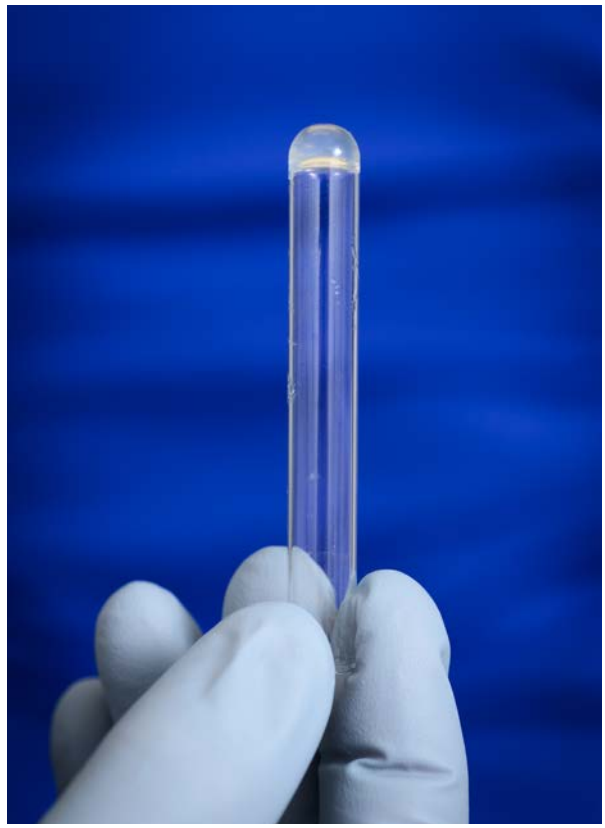
Ordering Information – PYROGENT™ Plus Gel Clot LAL Assay (with endotoxin)

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
N283-06	N283-06	PYROGENT™ Plus Gel Clot LAL Assay (with endotoxin)	4 × 16 tests/vial Lysate, 1 vial endotoxin	64 tests	0.06
N283-125	N283-125	PYROGENT™ Plus Gel Clot LAL Assay (with endotoxin)	4 × 16 tests/vial Lysate, 1 vial endotoxin	64 tests	0.125
N294-03	N294-03	PYROGENT™ Plus Gel Clot LAL Assay (with endotoxin)	4 × 50 tests/vial Lysate, 1 vial endotoxin	200 tests	0.03
N294-06	N294-06	PYROGENT™ Plus Gel Clot LAL Assay (with endotoxin)	4 × 50 tests/vial Lysate, 1 vial endotoxin	200 tests	0.06
N294-125	N294-125	PYROGENT™ Plus Gel Clot LAL Assay (with endotoxin)	4 × 50 tests/vial Lysate, 1 vial endotoxin	200 tests	0.125
N284-25	N284-25	PYROGENT™ Plus Gel Clot LAL Assay (with endotoxin)	4 × 50 tests/vial Lysate, 1 vial endotoxin	200 tests	0.25
N494-03	N494-03	PYROGENT™ Plus Bulk Gel Clot LAL Assay (with endotoxin)	80 × 50 tests/vial Lysate, 20 vials endotoxin	4,000 tests	0.03
N494-06	N494-06	PYROGENT™ Plus Bulk Gel Clot LAL Assay (with endotoxin)	80 × 50 tests/vial Lysate, 20 vials endotoxin	4,000 tests	0.06
N494-125	N494-125	PYROGENT™ Plus Bulk Gel Clot LAL Assay (with endotoxin)	80 × 50 tests/vial Lysate, 20 vials endotoxin	4,000 tests	0.125
N288-25	N288-25	PYROGENT™ Plus Bulk Gel Clot LAL Assay (with endotoxin)	80 × 50 tests/vial Lysate, 20 vials endotoxin	4,000 tests	0.25

Related Products	Page
Bulk kits	376
LAL Reagent Water (LRW)	390
Pyrogen-free Test Tubes	387
Eppendorf® 2–200 µL Biopur® Pipette tips	389
Eppendorf® 50–1000 µL Biopur® Pipette tips	389

PYROGENT™ Bulk Gel Clot LAL Assay

Bulk kit configurations of PYROGENT™ Gel Clot LAL are available for laboratories using large volumes of reagents. These configurations are made to order and production lead times are required. Please inquire with your sales representative for more information.



Benefits

- Bulk configurations for large volume use
- Bulk kits with and without endotoxin standard available
- Sensitivities of 0.03, 0.06, 0.125, and 0.25 EU/mL available

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/gelclot

2°C to 8°C

Ordering Information – PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
E194L-03	E194L-03	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	25 × 50 tests/vial Lysate	1,250 tests	0.03
E194L-06	E194L-06	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	25 × 50 tests/vial Lysate	1,250 tests	0.06
E194L-125	E194L-125	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	25 × 50 tests/vial Lysate	1,250 tests	0.125
E209L-25	E209L-25	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	25 × 50 tests/vial Lysate	1,250 tests	0.25
F245U-06	F245U-06	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	100 × 16 tests/vial Lysate	1,600 tests	0.06
F245U-125	F245U-125	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	100 × 16 tests/vial Lysate	1,600 tests	0.125
E194U-03	E194U-03	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	100 × 50 tests/vial Lysate	5,000 tests	0.03
E194U-06	E194U-06	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	100 × 50 tests/vial Lysate	5,000 tests	0.06
E194U-125	E194U-125	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	100 × 50 tests/vial Lysate	5,000 tests	0.125
E209U-25	E209U-25	PYROGENT™ Bulk Gel Clot LAL Assay (without endotoxin)	100 × 50 tests/vial Lysate	5,000 tests	0.25

Bulk kits require separate bulk CSE kit. Bulk kits do not include endotoxin.

Related Products	Page
LAL Reagent Water (LRW)	390
Pyrogen-free Test Tubes	387
Eppendorf® 2–200 µL Biopur® Pipette tips	389
Eppendorf® 50–1000 µL Biopur® Pipette tips	389
Control Standard Endotoxin for PYROGENT™ Gel Clot LAL	377

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Control Standard Endotoxin for PYROGENT™ Gel Clot LAL

Lonza's Control Standard Endotoxin is referenced against the USP Reference Standard Endotoxin.

Certificates of Analysis showing potency are available online:
www.lonza.com/coa

2°C to 8°C

Ordering Information – Control Standard Endotoxin for PYROGENT™ Gel Clot LAL

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size	Sensitivity (EU/mL)
N186	N186	Control Standard Endotoxin for PYROGENT™ Gel Clot LAL Assays	Endotoxin, *E. coli* 055:B5	5 vials	n/a
7360L	7360L	Bulk Control Standard Endotoxin for PYROGENT™ Gel Clot LAL Assays	Endotoxin, *E. coli* 055:B5	25 vials	n/a

Bulk CSE Required with bulk LAL

Related Products	Page
Gel Clot LAL Assays	374
LAL Reagent Water (LRW)	390
Pyrogen-free Test Tubes	387
Eppendorf® 2–200 µL Biopur® Pipette tips	389
Eppendorf® 50–1000 µL Biopur® Pipette tips	389

QC Insider™ Toolbox

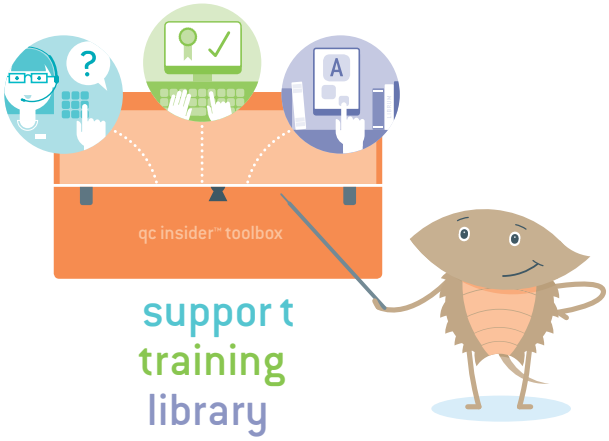
Endotoxin Expertise At Your Fingertips™

The QC Insider™ Toolbox has been designed for endotoxin testing novices as well as experts to provide endotoxin testing expertise at any level. The online portal contains a comprehensive offering of beginner and advanced support tools, a wide range of training resources, and a library of information that can be accessed at any time and from anywhere with internet access. The QC Insider™ Toolbox is organized into three categories so that users can easily navigate directly to the support tool they need.

The QC Insider™ Support offers one-on-one guidance, detailed information about software support, recertification and testing services, reader installation and maintenance, and workflow optimization.

The QC Insider™ Training contains self-directed training resources that will help users increase their endotoxin testing expertise, including a series of how-to videos that demonstrate different assay procedures.

The QC Insider™ Library consists of technical resources such as package inserts, quick guides, and technical tips that will help lead to success with endotoxin testing.



Become a QC Insider™ Expert today and ensure the support you need is always within reach.

www.lonza.com/qcinsider

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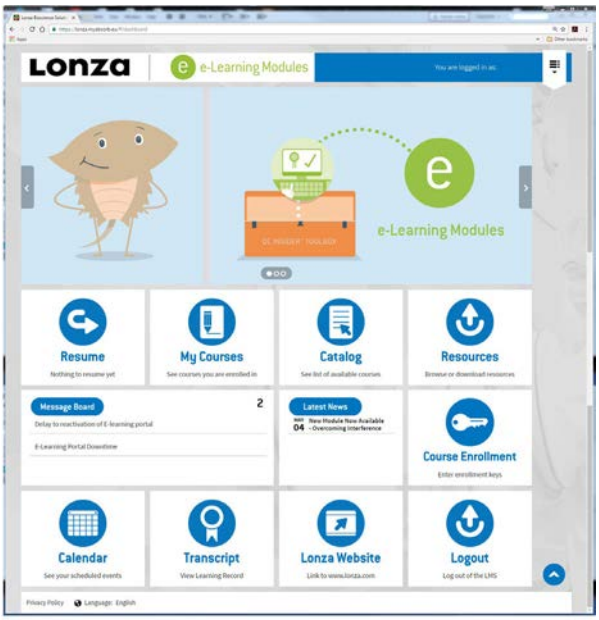
QC Insider™ e-Learning Modules

The e-Learning Modules are a series of interactive, online training courses designed to deliver technical knowledge you and your team need without interrupting your daily workflow. These training programs can be purchased and taken at your convenience, when your schedule permits.

Each course concludes with a Knowledge Test, which is a series of questions covering the content delivered during the module. Upon successful completion of the test, a Certificate of Completion is issued, which then becomes part of the learner's training records.



www.lonza.com/elearning

Benefits

- Learning at your own pace as your schedule permits
- No travel costs
- Creating customized training packages targeted to your training needs
- An integrated test and certification

Who should participate?

- QC professionals
- QA specialists
- Researchers
- Production/Manufacturing personnel

Ordering Information – QC Insider™ e-Learning Modules

Cat. No. NA	Cat. No. EU	Product Name	Product Description
LAL-EL-1	LAL-EL-1	An Introduction to Endotoxin Testing	This module introduces the learner to the basics of endotoxin, the effects endotoxin can cause to the body, regulatory compliance and calculating acceptable endotoxin limits.
LAL-EL-2	LAL-EL-2	Understanding the Bacterial Endotoxins Test	This introductory module introduces assay mechanisms, the basic assay requirements, the need for endotoxin controls and how Limulus Amebocyte Lysate (LAL) is made.
LAL-EL-3	LAL-EL-3	Working with the Gel Clot Assay	This module describes how to work with the gel clot assay including calculation of the Maximum Valid Dilution (MVD), product validation and the Initial Qualification (IQ) assay.
LAL-EL-4	LAL-EL-4	Working with Photometric Assays	This module covers the basic principles of working with photometric methods including an assay demonstration video and sections dealing with calculating the MVD, product characterization, product validation and routine testing.
LAL-EL-5	LAL-EL-5	Overcoming Interference	This module covers causes of interference by stage and type, inhibition vs. enhancement and proposes some solutions for the different categories of interfering products.

Instrumentation and Software

North America – Customer Service: +1 800 638 8174 (toll free); order.us@lonza.com; Scientific Support: +1 800 521 0390 (toll free) scientific.support@lonza.com

ELx808™ Incubating Absorbance Plate Reader

For Kinetic-QCL™ and PYROGENT™-5000 Kinetic LAL Assays

The ELx808™ Incubating Absorbance Plate Reader has been validated as part of our quantitative endotoxin detection systems. This 96-well microplate reader features 4 insulated incubating zones, providing the best well-to-well temperature uniformity available on the market. Utilizing interference filters instead of monochromators, the reader is optimized for the LAL-based endotoxin tests and comes pre-configured with the following interference filters: 340nm, 405nm, 450nm, 490nm, and 630nm. The ELx808™ Reader seamlessly interfaces with Lonza's WinKQCL™ Endotoxin Detection and Analysis Software.

For the kinetic and endpoint LAL assays, the ELx808™ Reader is highly reliable and easy to use. It features fully-automated kinetic reads of the 96-well plate via the WinKQCL™ Software. This reader can also be used as a standard spectrophotometer and results can be read from the QCL-1000™ Endpoint Chromogenic LAL Assay and ELISA Assays.

On-site service and preventive maintenance contracts are available to help ensure that your instrument is working properly.

Benefits

- Excellent temperature uniformity
- Precise and accurate
- Cost effective filter-based reader
- Special reader configuration optimized for LAL testing
- Vendor QC release testing specific for endotoxin detection
- Three year warranty

ELx808™ Absorbance Reader Specifications	
Wavelength Range	340 to 900 nm
Filters Supplied	340, 405, 450, 490 and 630 nm
Absorbance Range	0.000 to 4.000 OD @ 400 to 900 nm 0.000 to 3.000 OD @ 340 to 400 nm
Temperature Control	4°C above ambient to 50°C
Read Method	Kinetic or endpoint under WinKQCL™ Control
Light Source	Tungsten halogen bulb
Dimensions	16-inches deep × 15.5-inches wide × 8.75-inches high (40.6 cm × 39.4 cm × 22.2 cm)
Weight	35 lb (15.9 kg)

Ordering Information – ELx808™ Reader

Cat. No. NA	Cat. No. EU	Product Name	Product Description
25-315S	25-315S	ELx808™ Reader	Incubating Absorbance Reader
25-342	25-342	Stepped Neutral Density Plate*	For optical density validation across eight channels, recertification service
7260522	7260522	BioTek™ Absorbance Test Plate	For alignment, repeatability, and accuracy validation
05105	LAL3400508	Replacement Bulb for ELx808™ Reader	
196171	75053	Computer Connection Cable for ELx808™ Reader	9 pin female to 25 pin female RS232 cable
196004		UPS-APC 1500VA	Uninterruptible power supply with LCD, 120 V output (US edition)
	BE00196004	UPS-APC 1500VA	Uninterruptible power supply with LCD, 230 V output (European edition)
196005	196005	4-Port Serial PCI Card	Standard/low profile PCI card
25-361	25-361	USB to Serial Port Converter	10 cm cable with LED communication indicator lights

*Recertification service is available (see Recertification Services. page 406)

PyroWave™ XM Fluorescence Reader

For the Pyrogene™ Recombinant Factor C Assay

The PyroWave™ XM Fluorescence Reader is a part of the quantitative endotoxin detection system that supports the Pyrogene™ Recombinant Factor C Assay. This reader replaces the Lonza FLx800™ LBS reader, bringing a new generation in fluorescence technology to users of the PyroGene™ Assay. Optimized specifically for Lonza's PyroGene™ Assay, this reader brings new and improved technology to the laboratory. The PyroWave™ XM Reader offers numerous enhancements in incubation, optics, automation compatibility, and overall reader maintenance and robustness. Controlled by Lonza's WinKQCL™ Endotoxin Detection and Analysis Software, version 5.3 and higher, Lonza delivers a high performance and easy-to-use system for users interested in an alternative to the horseshoe crab-based endotoxin detection test methods.

On-site service and preventive maintenance contracts are available to help ensure that your instrument is working properly.

Benefits

- Improved PyroGene™ Assay performance
- Reduced reader maintenance
- Automation compatible
- High performance optics
- 4-Zone™ Incubation at 37°C
- Three year warranty

PyroWave™ XM Fluorescence Reader Specifications	
Read capabilities	Fluorescence, luminescence**, TRF**, FP**
Read position	Top read
Light source	Xenon flash lamp
Detection	High performance photo multi-plier tube
Fluorescence sensitivity	Fluorescein @ 1 pM/well in a 96-well plate
Wavelength range	200 to 850 nm**
Filters	One easy-to-swap filter cube with the following filter configuration:

Assay Type	Excitation Filter (nm)	Emission Filter (nm)	Dichroic Mirror (nm)
PyroGene™	380/20	440/30	400
Fluorescein	485/20	528/20	510

**Additional filter cubes and filters must be purchased from reader manufacturer for additional wavelengths and read capabilities

Temperature control	±0.2 °C at 37 °C
Power	100 – 240 Volts AC 50/60 Hz
Dimensions	39.1 cm W x 47.2 cm D x 32.8 cm H (15.4" W x 18.6" D x 12.9" H)
Weight	22.5 kg (50 lbs)

Ordering Information – PyroWave™ XM Reader

Cat. No. NA	Cat. No. EU	Product Name	Product Description
25-345S	25-345S	PyroWave™ XM Fluorescence Reader	Incubating fluorescence reader
196004		UPS-APC 1500VA	Uninterruptible power supply with LCD, 120 V output (US edition)
	BE00196004	UPS-APC 1500VA	Uninterruptible power supply with LCD, 230 V output (European edition)
196005	196005	4-Port Serial PCI Card	Standard/low profile PCI card
204511	7160013	Fluorescent Liquid Test Kit	Sodium fluorescein test kit for FLx800™ Reader validation

Related Products	Page
WinKQCL™ Endotoxin Detection and Analysis Software	384
Pyrogene™ Recombinant Factor C Assay	370

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PyroTec™ Liquid Handling System

The PyroTec™ Liquid Handling System is a robotic workstation to help automate endotoxin detection testing. The system includes a user-defined platform size to accommodate tips, reagent troughs and 96-well plates. The robotic arm picks up tips and dispenses samples and reagents into 96-well plates. Heating units can incubate plates prior to delivery into plate readers.

WinKQCL™ Software is fully integrated with the Tecan® Freedom EVOware® Software, allowing assay templates to be executed using robotic scripts for the PyroTec™ Liquid Handling System.

The PyroTec™ System can be tailored to your testing needs. Contact your local Lonza sales representative or scientific support for additional information.

On-site service and preventive maintenance contracts are available to help ensure that your instrument is working properly.

Benefits

- Flexible platform to automate filling of assay plates
- Help high throughput labs manage their large daily sample requirements

Ordering Information – PyroTec™ Liquid Handling System

Cat. No. NA	Cat. No. EU	Product Name	Product Description
25-601	25-601	PyroTec™ 200 Liquid Handling System	Robotic workstation for filling nine 96-well plates at one time
25-602	25-602	PyroTec™ 150 Liquid Handling System	Robotic workstation for filling three 96-well plates at one time
25-603	25-603	PyroTec™ 150 Positive ID System	Robotic barcode scanner

Related Products	Page
WinKQCL™ Endotoxin Detection and Analysis Software	384
Kinetic-QCL™ Kinetic Chromogenic LAL Assay	365
PYROGENT™-5000 Kinetic Turbidimetric LAL Assay	368
Pyrogene™ Recombinant Factor C Assay	370

WinKQCL™ Endotoxin Detection and Analysis Software

Quantitative methods such as the Kinetic-QCL™ Assay generate significant amounts of raw data that require careful analysis before reporting can take place. The WinKQCL™ Software offers a fully integrated solution for your quantitative endotoxin detection testing, data management, and reporting needs.

WinKQCL™ 5 Software meets 21 CFR Part 11 technical requirements for electronic records, signatures, audit trails, and database archiving. Reader validation tests can be run from the WinKQCL™ Software and are stored in the same database. The built-in database backup and maintenance scheduler makes it easy to maintain the system.

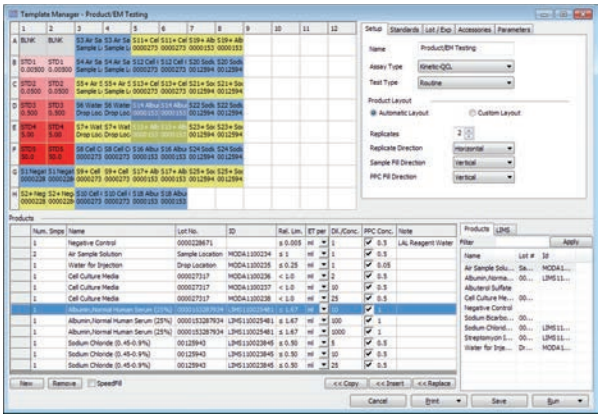
Benefits

- Kinetic SmartStop™ monitoring feature to address split pair and other reaction conditions, without sacrificing time waiting for a fixed number of reads
- Enterprise level IT features including wide area network support, ability to work across time zones, application virtualization, Active Directory® integration, and data segregation by lab
- Bi-directional interface with 3rd party database systems
- Customizable endotoxin test reports
- Multi-language user interface: English, French, German, Italian, Japanese, Spanish, Portuguese, Simplified Chinese and Traditional Chinese

Applications

- For use with the PyroWave™ XM, ELx808™ , and FLx800™ Readers. Extended reader integration now includes Molecular Devices® SpectraMax®, Gemini™ and VersaMax™ Readers; and the BioTek® Eon™ and Synergy™ 2 Readers. The software is also interfaced with the Tecan® Sunrise™ Reader
- Tecan® EVOware® interface integration for PyroTec™ Liquid Handling System
- Supports all quantitative endotoxin detection assays from Lonza including QCL-1000™ Endpoint Chromogenic LAL, Kinetic-QCL™ Kinetic Chromogenic LAL, PYROGENT™-5000 Kinetic Turbidimetric LAL and Pyrogene™ Recombinant Factor C Assays
- Installation as a simple standalone system or as an interface with multiple robots and readers in multiple labs around the world, all storing data in a single database

The user-friendly and flexible Template Manager allows you to customize plate layout with a click of a mouse using the SpeedFill™ and drag 'n drop features. The enhanced trending tools provide meaningful results on demand, helping you easily detect drift and enabling you to make proactive decisions.



The endotoxin detection instruments and software from Lonza are available fully supported with Installation, Operational and Performance Qualification (IOPQ) manuals and a WinKQCL™ 5 Software Validation Package. In addition, a trained specialist from Lonza can perform the IOPQ of the complete system to help you with your system validation process. Please inquire with your local sales representative for further details.

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WinKQCL™ Endotoxin Detection and Analysis Software

Continued

Ordering Information – WinKQCL™ Endotoxin Detection and Analysis Software

Cat. No. NA	Cat. No. EU	Product Name	Product Description
25-501	25-501	WinKQCL™ 5 Software Package	Installation DVD, workgroup license, reader license
25-502	25-502	WinKQCL™ 5 Workgroup License	Additional workgroup license
25-503	25-503	WinKQCL™ 5 Reader License	Additional reader license
25-504	25-504	WinKQCL™ 5 Qualification Manual	DVD containing IOPQ files for software and readers
25-505	25-505	WinKQCL™ 5 Validation Package	DVD containing software validation information
25-339S	25-339S	System Qualification Service	IQ/OQ/PQ validation on site, labor only
25-501SUP	25-501SUP	Annual WinKQCL™ Support for Cat. No. 25-501	Advanced IT/software support for WinKQCL
25-502SUP	25-502SUP	Annual WinKQCL™ Support for Cat. No. 25-502	Advanced IT/software support for data management
25-503SUP	25-503SUP	Annual WinKQCL™ Support for Cat. No. 25-503	Advanced IT/software support for instrument control

Ordering Information – WinKQCL™ Software Delivered Immediately by Email

Cat. No. NA	Cat. No. EU	Product Name	Product Description
25-501E	25-501E	E-Delivered WinKQCL™ 5 Software Package	Installation files, workgroup license, reader license
25-502E	25-502E	E-Delivered WinKQCL™ 5 Workgroup License	Additional workgroup license
25-503E	25-503E	E-Delivered WinKQCL™ 5 Reader License	Additional reader license
25-504E	25-504E	E-Delivered WinKQCL™ 5 Qualification Manual	IOPQ files for software and readers
25-505E	25-505E	E-Delivered WinKQCL™ 5 Validation Package	File containing software validation information

Accessory Products

Accessory Products

North America – Customer Service: +1 800 638 8174 (toll free); order.us@lonza.com; Scientific Support: +1 800 521 0390 (toll free) scientific.support@lonza.com

Introduction

In addition to the endotoxin detection kits, instruments, and software, Lonza offers many of the accessory items necessary to run endotoxin detection assays. Many of the items have been tested with the Kinetic-QCL™ Kinetic Chromogenic LAL Assay to help ensure their compatibility with our endotoxin detection methods. We also offer products such as the Endotoxin Challenge Vials™ to help with your oven depyrogenation validations.

Test Tubes

All test tubes are made from USP Type I flint borosilicate glass.

Both products N201 and N205 are recommended for use as reaction tubes in gel clot assays. N201 are provided with polypropylene screw caps. Product number N207 is recommended for dilution of endotoxin standards and test samples for all endotoxin detection assays.

Benefits

– Certified to contain less than 0.005 EU/mL endotoxin

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/accessories

Ordering Information – Test Tubes

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
N207	N207	Pyrogen-free Test Tubes	Without caps, 13 × 100 mm	30/foil pack
N201	N201	Pyrogen-free Test Tubes	With caps, 10 × 75 mm	50/box
N205	N205	Pyrogen-free Test Tubes	Without caps, 10 × 75 mm	50/foil pack

Sample Containers

Sample containers are intended for transporting product samples for endotoxin analysis or sample storage. Proper container and storage conditions need to be validated for each individual sample.

Products 80-507L and 80-507U contain 10 mL glass vials with screw caps. Products BE2098 and BE2099 are plastic sample containers that offer greater capacity at a reduced cost.

Benefits

– Certified to contain less than 0.005 EU/mL endotoxin

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/accessories

Ordering Information – Sample Containers

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
80-507L	80-507L	Sample Containers	Depyrogenated, 10 mL glass bottle with screw cap	25/box
80-507U	80-507U	Sample Containers	Depyrogenated, 10 mL glass bottle with screw cap	100/box
	BE2098	Polypropylene Sample Containers	Endotoxin tested, 50 mL tubes	50/pack
	BE2099	Polystyrene Sample Containers	Endotoxin tested, 15 mL tubes	50/pack

Plates

96-well plates can be used with the QCL-1000™ Endpoint Chromogenic LAL Assay, Kinetic-QCL™ Kinetic Chromogenic LAL Assay, PYROGENT™-5000 Kinetic Turbidimetric LAL Assay and Pyrogene™ Recombinant Factor C Assay. Each case contains individually wrapped plates.

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www.lonza.com/accessories

Benefits

– Certified to contain less than 0.0005 EU/well endotoxin
– Certified for compatibility with the endotoxin detection assays
– Certified to be free from inhibition

Ordering Information – Plates

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
25-340	BE25-340	LAL Reagent Grade Multi-well Plates	96-well plates, endotoxin-tested (<0.0005 EU/well)	50/case

North America – Customer Service: +1 800 638 8174 (toll free); order.us@lonza.com; Scientific Support: +1 800 521 0390 (toll free) scientific.support@lonza.com

Pipette Tips

Pyrogen-free pipette tips are to be used when testing with any of our endotoxin detection systems. Eppendorf® Biopur® pipette tips are certified to contain <0.001 EU/mL endotoxin. The new design of the tips allows compatibility with different pipettors. Catalog Number 25-416 is for use with multi-channel pipettes. Products BE25-413 and BE25-414 are certified to contain <0.005 EU/mL endotoxin. They can be used with pipettes from different manufacturers. Eppendorf® Combitips® are for use with a multi-step pipette.

Benefits
- Endotoxin tested
- Broad offering for various pipette types

For your convenience, Certificates of Analysis are available online:
www.lonza.com/coa

www.lonza.com/accessories

Ordering Information – Pipette Tips

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
25-415	BE25-415	Eppendorf® 2–200 µL Biopur™ Pipette Tips	< 0.001 EU/mL	5 trays/pkg; 96 tips/tray
25-416	BE25-416	Eppendorf® 2–300 µL Biopur™ Pipette Tips	< 0.001 EU/mL, for multi-channel pipettors	5 trays/pkg; 96 tips/tray
25-417	BE25-417	Eppendorf® 50–1000 µL Biopur™ Pipette Tips	< 0.001 EU/mL	5 trays/pkg; 96 tips/tray
	89634	Eppendorf® Combitips®, 0.5 mL	Single packed	100
	BE4910000026	Eppendorf Pipette 2-20 µL		1 each
	BE3114000158	Eppendorf Pipette Multichannel 30-300 µL		1 each
	BE3111000149	Eppendorf Pipette Research 10-100 µL		1 each
	BE3111000165	Eppendorf Pipette Research 100-1000 µL		1 each
	89650	Eppendorf® Combitips®, 2.5 mL	Single packed	100
	89669	Eppendorf® Combitips®, 5 mL	Single packed	100
	89677	Eppendorf® Combitips®, 10 mL	Single packed	100
	BE10035	Eppendorf® Pipette Tips, 2–200 µL	Endotoxin tested, single packed	100/box
	BE10051	Eppendorf® Pipette Tips, 50–1000 µL	Endotoxin tested, single packed	100/box
	BE25-413	LAL Reagent Grade Pipette Tips, 2–200 µL	<0.005 EU/mL	10 × 96 tips
	BE25-414	LAL Reagent Grade Pipette Tips, 50–1250 µL	<0.005 EU/mL	10 × 96 tips
	BE7521	Pipette BD Falcon™, 1 mL	Endotoxin tested, single packed	100
	BE7507	Pipette BD Falcon™, 2 mL	Endotoxin tested, single packed	100
	BE7543	Pipette BD Falcon™, 5 mL	Endotoxin tested, single packed	200
	BE7551	Pipette BD Falcon™, 10 mL	Endotoxin tested, single packed	200

Reservoirs

The LAL Reagent Reservoirs are for use with multi-channel pipettes when adding reagents to a 96-well plate. The reservoirs are provided in a zip closure bag enabling you to conveniently store unused reservoirs for later use.

For your convenience, Certificates of Analysis are available online:
www.lonza.com/coa

www.lonza.com/accessories

Benefits
- Certified to contain less than 0.005 EU/mL endotoxin

Ordering Information – LAL Reagent Reservoirs

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
190035	190035	LAL Reagent Reservoirs	<0.005 EU/mL	10/pack

Dry Heat Block, Inserts and Vortex Mixer

The dry heat block is used for incubation of LAL gel clot assays. The aluminum block with lid adaptor for a dry heat block allows a 96-well plate to be incubated at 37°C for use with the QCL-1000™ Endpoint Chromogenic LAL Assay.

www.lonza.com/accessories

Ordering Information – Dry Heat Block, Inserts and Vortex Mixer

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
25-038A	25-038A	Aluminum Block with Lid	Heat block insert for 96-well plate	Each
BEF3503	BEF3503	Aluminum Insert Block for Techne Dry Heat Block		For 20 tubes
FDB03DD	FDB03DD	Techne Dry Heat Block	Digital, from 25°C to 100°C, requires 3 × BEF3503	For 60 tubes
	BENP5051	Vortex Genie® 2		

LAL Reagent Water

LAL Reagent Water is recommended for reconstituting LAL reagents, as well as for the dilution of control standard endotoxin and test samples for endotoxin testing. LAL Reagent Water is equivalent to Water for Bacterial Endotoxins Test (BET). In addition to USP-required WFI tests, Lonza tests LAL Reagent Water for compatibility with our endotoxin detection assays.

Benefits

- Certified to contain less than 0.005 EU/mL endotoxin
- Available in a variety of sizes
- Certified for Positive Product Control Recovery within 75 to 150%

2°C to 8°C (W50-640)

15°C to 30°C (W50-100, W50-500, W50-1000)

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/accessories

Ordering Information – LAL Reagent Water

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
W50-640	W50-640	LAL Reagent Water	<0.005 EU/mL, 30 mL	1 bottle
W50-100	W50-100	LAL Reagent Water	<0.005 EU/mL, 100 mL	1 bottle
W50-500	W50-500	LAL Reagent Water	<0.005 EU/mL, 500 mL	1 bottle
W50-1000	W50-1000	LAL Reagent Water	<0.005 EU/mL, 1000 mL	1 bottle

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β-G-Blocker

β-D-glucans can produce false positive results in LAL assays. Some examples of glucan sources include yeast and cellulosic materials such as hemodialysis filters. β-G-Blocker may be used with any of our LAL assays.

For your convenience, Certificates of Analysis are available online:
www.lonza.com/coa

www.lonza.com/accessories

Benefits
- Certified to contain less than 0.005 EU/mL endotoxin
- Functionality tested to demonstrate a reduction of enhancement caused by β-D-glucans

2°C to 8°C

Ordering Information – β-G-Blocker

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
N190	N190	β-G-Blocker	Glucan blocker, 5 mL/vial	5 vials

PYROSPERSE™ Dispersing Agent

PYROSPERSE™ Dispersing Agent, helps eliminate endotoxin binding or masking in some samples – solving problems of inhibitory behavior. Examples of samples that may show endotoxin binding behavior include plasma protein fractions, electrolyte solutions, and lipid emulsions. PYROSPERSE™ Dispersing Agent may be used with any of our LAL kits.

For your convenience, Certificates of Analysis are available online:
www.lonza.com/coa

www.lonza.com/accessories

Benefits
- Endotoxin and functionality tested

2°C to 30°C (unopened)

Ordering Information –PYROSPERSE™ Dispersing Agent

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
N188	N188	PYROSPERSE™ Dispersing Agent	5 mL/vial	5 vials

$MgCl_2$

$MgCl_2$ can be used as the sample diluent when attempting to overcome inhibitory chelation effects. Examples of samples that chelate divalent cations include heparin and EDTA. $MgCl_2$ may be used to prepare samples for any endotoxin detection assay.
For your convenience, Certificates of Analysis are available online:
www.lonza.com/coa

www.lonza.com/accessories

Benefits
- Certified to contain less than 0.005 EU/mL endotoxin

2°C to 30°C (unopened)

Ordering Information – $MgCl_2$ 10 mM Solution

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
S50-641	S50-641	$MgCl_2$ 10 mM Solution	30 mL/vial	1 vial

Tris Buffer

Tris Buffer can be used in place of water as the sample diluent for highly acidic or basic samples (for endotoxin testing, sample test dilutions should be between pH 6–8 after lysate addition). Tris Buffer may be used to prepare samples for any of our endotoxin detection assays.

For your convenience, Certificates of Analysis are available online:
www.lonza.com/coa

www.lonza.com/accessories

Benefits
- Certified to contain less than 0.005 EU/mL endotoxin
- Certified pH range from 7.0 to 7.4 @ 25°C
- Certified to ensure good buffering performance

2°C to 8°C

Ordering Information – Tris Buffer 50 mM

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
S50-642	S50-642	Tris Buffer 50 mM	30 mL/vial	1 vial

North America – Customer Service: +1 800 638 8174 (toll free); order.us@lonza.com; Scientific Support: +1 800 521 0390 (toll free) scientific.support@lonza.com

Endotoxin and Endotoxin Challenge Vials™

Endotoxin (*E. coli*) Challenge Vials™ are for use in oven validation studies. Each vial contains >1,000 EU/vial. The vials may be tested using any of our endotoxin detection kits. Product 193783 contains high potency endotoxin and is intended for use in endotoxin removal system challenges, i.e. depyrogenation ovens, and other spiking studies. Each vial contains >1,250,000 EU/vial. E700 is the USP Reference Standard Endotoxin. Each vial contains 10,000 EU/vial.

For your convenience, Certificates of Analysis are available online:

www.lonza.com/coa

www.lonza.com/accessories

Benefits

– Products 192568 and 193783 are devoid of fillers

192568 and 193783 are stored at 2°C to 8°C

E700 storage conditions are -20°C

Ordering Information – Endotoxin and Endotoxin Challenge Vials™

Cat. No. NA	Cat. No. EU	Product Name	Product Description	Size
193783	193783	Endotoxin, *E. coli* 055:B5	> 1.25 million EU/vial	5 vials
192568	192568	Endotoxin Challenge Vials™	>1,000 EU/vial	25 vials
E700	E700	USP Reference Standard Endotoxin	10,000 EU/vial	1 vial