Pharma&Biotech

Lonza

Medical Devices – Quick Guide

This is a step-by-step guide detailing how to test medical devices for endotoxin.

Step 1

Select at random not more than 10 devices for testing. The number of devices tested is dependent on several factors including lot size, level of control, statistical considerations and past performance.

Note: Suitability testing for each product or product family is required. Medical devices coming from cellulose-based components may contain glucans. If glucan interference is observed, the use of a glucan-blocking reagent, such as β-G-Blocker, may be needed.

Step 2

Ensure that the sample is in its final configuration and packaging, including all component parts that make up the final medical device.

Step 3

Soak or immerse the device(s) or flush the fluid pathway with LAL Reagent Water (LRW) that has been heated to 37 ±1° C, keeping the LRW in contact with the surface(s) not less than 1 hour. This can be done in a depyrogenated glass or stainless steel container. Materials may be rendered endotoxin-free by heating at 250°C for 30 minutes using a validated process. Adjust the volume for rinsing or extraction according to the size and configuration of the device.

Step 4

Calculate the Endotoxin Release Limit (ERL).

The endotoxin release limit for the extraction solution can be calculated using the following equation:

$$\frac{K \times N}{V}$$ where:

K = allowable endotoxin per device
20.0 EU/device
2.15 EU/device (for cerebrospinal contact)
N = number of devices tested
V = total volume of extraction solution

Example:
10 devices extracted in 1,000 mL of LRW

$$ERL = \frac{20\ EU/device \times 10\ devices}{1{,}000\ mL} = 0.2\ EU/mL$$

Step 5

Test the extract.

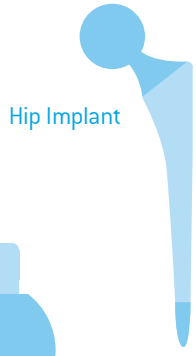
The extract should be tested with a positive product control, both in duplicate. In the event that there is interference evident, it is possible to dilute the extract further up to the Maximum Valid Dilution (MVD). The MVD can be calculated using the following equation:

$$\frac{ERL}{\lambda}$$ where:

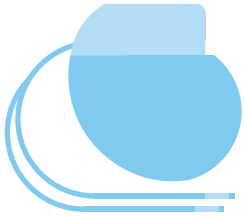
ERL = calculated in step 4
λ = the value of the lowest standard used in a quantitative assay or the labeled sensitivity of the gel clot lysate used

Example:
Extraction solution from example in step 4 tested with the kinetic chromogenic assay where the lowest standard is 0.005 EU/mL

$$MVD = \frac{0.2\ EU/mL}{0.005\ EU/mL} = 1{:}40$$


Hip Implant


Surgical Plate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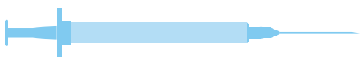
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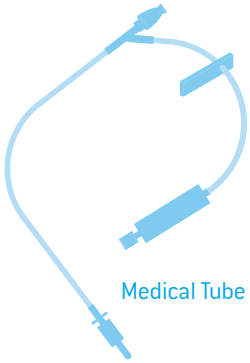
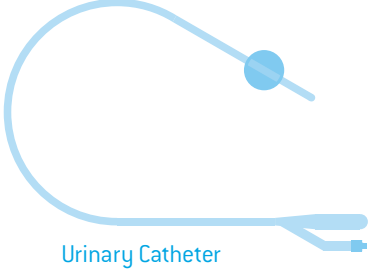

Medical Tube


Stent


Knee Replacement


Urinary Catheter


Orthopedic Implant Screws

www.lonza.com/pharmabiotech
www.lonza.com/lal

For more technical guidance register to our QC Insider™ Toolbox
www.lonza.com/qcinsider

Materials, Equipment & Documents Needed

Reagents
- Endotoxin detection kit (a variety of kits is available. Please contact your local sales representative for additional information.)
- LAL Reagent Water (LRW) (# W50-640, W50-100, W50-500, W50-1000)

Accessories
- Glass dilution tubes (# N207)
- Glass reaction tubes (# N201, N205), for use with the PYROGENT™ Gel Clot Assays
- Individually wrapped serological pipettes (optional)
- Tips
- 96-well plates (# 25-340), if using a plate-based method
- Reagent reservoirs (# 00190035), if using a plate-based method
- β-G-Blocker (# N190), optional

Use pyrogen-free accessories that have been qualified for endotoxin testing.

Equipment and Software
- Pipettors
- Timer
- Vortex mixer
- Test tube rack
- For use with the PYROGENT™ Gel Clot Assay: heating block or non-circulating hot water bath
- For use with the QCL-1000™ Endpoint Chromogenic Assay: heating block with adapter (# 25-038A) and spectro- or filterphotometer with 405-410 nm filter or microplate reader
- For use with the Kinetic-QCL™ or PYROGENT™-5000 Kinetic LAL Assays: incubating absorbance microplate reader
- For use with the PyroGene™ rFC Assay: incubating fluorescence microplate reader

Supporting Documents
- Certificate of Analysis (CoA)
- Endotoxin Detection Kit Package Insert
- Endotoxin Detection Assay Procedure Quick Guide
- Endotoxin Assay Selection Guide
- United States Pharmacopeial Convention. General Chapter <161> Medical Devices – Bacterial Endotoxin and Pyrogen Tests
- United States Pharmacopeial Convention. General Chapter <85> Bacterial Endotoxins Test
- European Pharmacopoeia (EP). European Directorate for the Quality of Medicines. Chapter 2.6.14 Bacterial Endotoxins

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