



BACTERIAL ENDOTOXIN TESTING (BET)

ALSO CALLED: LIMULUS AMEBOCYTE LYSATE (LAL) TESTING

Pyrogens are fever-producing materials that most often originate from gram-negative bacterial cell walls, but can also originate as leachates from some chemicals and materials. Pyrogens from bacterial cell walls (the most commonly encountered type of pyrogen) are referred to as bacterial endotoxin and are readily detected by Limulus Amebocyte Lysate (LAL) testing systems.

LAL gel clot testing is a semi-quantitative method for testing of most medical devices/products. This method has been replaced in most cases by the more sensitive kinetic methods. The kinetic chromogenic LAL method provides direct quantification of the detected endotoxin level and is especially useful for very low-level detection, determining the endotoxin reduction of various production processes, monitoring the quality of water systems, and providing endotoxin levels for lot release of products. The kinetic turbidimetric method is similar to the chromogenic method and is used where there may be color interferences (e.g., blood-containing product). WuXi AppTec follows the FDA, USP and AAMI guidelines when performing LAL tests.

Each time a new device/product is produced, or a significant change in material formulation is made on an existing device/product, a validation must be performed on samples from three production lots. The purpose of this is to ensure that the materials used in the construction of the device do not impart an inhibiting or enhancing effect on the LAL test system. Other changes, such as a change in the testing laboratory, may only require a single lot validation.

Sample requirements for both the validation testing and routine testing are typically determined by the size of the production lots from which the samples are selected.

NOTE: Chemical pyrogens, also called materials-mediated pyrogens, can only be detected using the USP Rabbit Pyrogen Test or Materials Mediated Test. [See Page B-18.]

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KINETIC CHROMOGENIC LAL TESTS

TURNAROUND TIME 2 - 3 days

130501

**Kinetic Chromogenic
LAL Limit Test –
Finished Product Testing**

Quantitative determination of endotoxin level for finished devices or other materials.

SAMPLE REQUIREMENTS [FDA Guidelines]

For lots of less than 30 units – 2 sample devices

For lots of 30-100 units – 3 sample devices

For lots of 101 units or greater – 3% of lot, up to maximum of 10

[It is recommended that samples be sterile.]

130601

**Kinetic Chromogenic
LAL Test Validation**

Validation of the inhibition or enhancement properties of the materials on the test system.

SAMPLE REQUIREMENTS [FDA and AAMI Guidelines]

Samples from three (3) production lots should be tested for inhibition and enhancement before this test is considered validated for use with the test product.

NOTE: Validation testing can be performed at the same time and on the same samples as the lot release (finished product) testing.

130701

**Kinetic Chromogenic
LAL Liquid Test**

Endotoxin testing of water system samples or other non-biological liquids.

SAMPLE REQUIREMENTS

5 mL in sealed endotoxin-free polystyrene or glass container.

TURNAROUND TIME 2 - 3 days

Quantitative determination of endotoxin level for finished devices or other materials.

SAMPLE REQUIREMENTS [FDA Guidelines]

For lots of less than 30 units – 2 sample devices
For lots of 30-100 units – 3 sample devices
For lots of greater than 100 units – 3% of lot, up to maximum of 10
[It is recommended that samples be sterile.]

130800

**Kinetic Turbidimetric
LAL Limit Test –
Finished Product Testing**

Validation of the inhibition or enhancement properties of the materials on the test system.

SAMPLE REQUIREMENTS [FDA and AAMI Guidelines]

Samples from three (3) production lots should be tested for inhibition and enhancement before this test is considered validated for use with the test product.

NOTE: Validation testing can be performed at the same time and on the same samples as the lot release (finished product) testing.

130802

**Kinetic Turbidimetric
LAL Test Validation**

Endotoxin testing of water system samples or other liquids.

SAMPLE REQUIREMENTS

5 mL in sealed endotoxin-free polystyrene or glass container.

130801

**Kinetic Turbidimetric
LAL Liquid Test**

GEL CLOT LAL TESTS

TURNAROUND TIME 5 - 7 days

131100

Gel Clot LAL Limit Test – Finished Product Testing

Semi-quantitative determination of pass/fail endotoxin limit for finished devices or other materials.

SAMPLE REQUIREMENTS [FDA Guidelines]

For lots of less than 30 units – 2 sample devices

For lots of 30-100 units – 3 sample devices

For lots of greater than 100 units – 3% of lot, up to maximum of 10

[It is recommended that samples be sterile.]

130200

Gel Clot LAL Test Validation

Sample extractant is "spiked" with endotoxin and run in a quadruplicate dilution series parallel with the standard endotoxin curve. Results are evaluated for an enhancing or inhibiting effect.

SAMPLE REQUIREMENTS [FDA and AAMI Guidelines]

Samples from three (3) production lots should be evaluated for inhibition and enhancement before this test is considered validated for use with the test product.

130400

Gel Clot LAL Liquid Test

Endotoxin testing of water system samples or other liquids.

SAMPLE REQUIREMENTS

15 mL in sealed endotoxin-free polystyrene or glass container.

130300

Gel Clot LAL Dilution Assay

Determination of a semi-quantitative endotoxin value per product weight or volume.

SAMPLE REQUIREMENTS

Positive LAL sample