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Endotoxin Testing

Endotoxin testing (LAL test) ensures that sterile pharmaceutical products are safe for human use.

Endotoxins are bacterial structural components that are released when such a cell is lysed. These components are toxic if administered to humans and/or animals, causing a pyrogenic response (rise in body temperature). For this reason it is important that drugs and medical devices which are either injected or implanted must be tested for their endotoxin content.

There are several methods available for conducting the endotoxin test, which includes the *in vivo* pyrogen test and the *in vitro* limulous amoebocyte lysate test (LAL test), the most common approach to endotoxin testing. This can be accomplished by various options including gel clot, kinetic chromogenic and kinetic turbidimetric assays.

This methodology is also used for the evaluation of medical devices such as single-use disposable equipment and implants. This is done by extracting the test product with pyrogen - free water (PFW) and testing for the presence of endotoxin in the extracts.

Why Choose Eurofins BioPharma Product Testing?

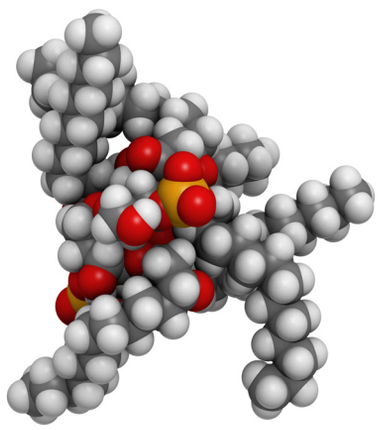
Eurofins BioPharma Product Testing is able to perform all methods, the kinetic chromogenic and turbidimetric assays as well as the gel clot assay.

All tests can be carried out quickly, and results can be available within one week of sample receipt.

Endotoxin Testing completes our microbiology testing portfolio for raw materials, including the bacterial count determination as well as the preservative challenge.

Kinetic Chromogenic and Kinetic Turbidimetric Method

The chromogenic method involves an enzymatic reaction between the endotoxin and lysate which results in the production of a yellow colour in the presence of endotoxin. The intensity of the colour production is directly linked to the quantity of endotoxin present in the sample. With the kinetic variation of



the assay, the time of onset of the colour reaction is measured. Therefore, with the use of endotoxin standards we are able to calculate the value of endotoxin present in or on the product. Some products are of a colour that would interfere with this form of testing, and so the turbidimetric method can be used to avoid any such interference. In this case a different lysate is used and the reaction with endotoxin results in the solution becoming turbid, thus allowing quantitation of endotoxin content without relying on the colour present. Both methods are equally effective in obtaining the endotoxin content in a product, but often, one is more suitable than the other. Both methods use objective measurements to determine endotoxin content and are quantitative in nature.

Gel Clot Assay

The gel clot assay was the original LAL method. It is a qualitative or semi-quantitative test that is used to screen for the presence of endotoxins. A clot formation is interpreted as a positive result for the presence of endotoxin and if no clot forms, this is interpreted as the sample being endotoxin free. The results are from the subjective interpretation of the clot formation.

Method Reference

1. Bacterial Endotoxins Test:
   The US Pharmacopeia. USP <85>. Current.
2. Test for Bacterial Endotoxins:
   British Pharmacopoeia (BP) Appendix XIV C. Current.
3. Bacterial Endotoxins:
   European Pharmacopeia.EP 2.6.14. Current.