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# Endotoxin Indicator for Depyrogenation

## DEFINITION

An Endotoxin Indicator is an article (challenge vial of endotoxin or a carrier spiked with endotoxin) designed for use in depyrogenation studies. The endotoxin (a purified lipopolysaccharide) is validated for use in or on an Endotoxin Indicator. The carrier is made from a material appropriate for the intended depyrogenation processes to which it will be subjected. The endotoxin on a carrier is added at a concentration sufficient to allow recovery of a minimum of 1000 USP Endotoxin Units/carrier. The Endotoxin Indicator would allow for accurate indication of at least a 3-log reduction in USP Endotoxin Units during depyrogenation process challenges.

## IDENTIFICATION

• **Characteristics**

The endotoxin (lipopolysaccharide) has equivalent characteristics to those of the USP Endotoxin RS.

## PERFORMANCE TESTS

• **Carrier:** The carrier should be the same as or chemically similar to the surface or material used for measuring depyrogenation, e.g., glass or stainless steel. If not similar, then the carrier and endotoxin combination must be at least as resistant to the depyrogenation process as the surface or material being measured. The carrier must be depyrogenated, or the inherent endotoxin level of the carrier should be determined before the addition of the endotoxin to the carrier.

• **Endoxin Recovery Tests**

**Analysis:** Proceed as directed for the relevant technique under *Bacterial Endotoxins Test* ⟨85⟩.

**Acceptance criteria:** The determined endotoxin concentration is within a factor of 2 of the labeled endotoxin concentration.

## SPECIFIC TESTS

• **Purity**

**Absence of assay enhancing substances**

**Analysis:** Proceed as directed in the test for interfering factors in *Bacterial Endotoxins Test* ⟨85⟩.

**Acceptance criteria:** The Endotoxin Indicator should contain no substances (e.g., glucans) that can result in enhancement of endotoxin spike recovery.

**Absence of depyrogenation enhancing/inhibiting substances:** No substance (e.g., lactose, albumin, polyethylene glycol) should be present as filler for the endotoxin, as this can result in enhanced or inhibited depyrogenation effects.

## ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Store in the original package under conditions recommended on the label, and protect from light, toxic substances, excessive heat, and moisture. The packaging and container materials do not adversely affect the performance of the article, when used as directed on the labeling.

• **Expiration date:** The expiration date is determined on the basis of stability studies from the date of manufacture, which is the date on which the first determination of Endotoxin Units was made.

• **Labeling:** The label states that the article is or may be used as an Endotoxin Indicator. It indicates the concentration in USP Endotoxin Units/indicator and the recommended storage conditions. The labeling states the source of the endotoxin (e.g. species and strain number) and includes instructions for preparation and safe disposal of the indicator. If the carrier is labeled, the label must be either easily removable or heat resistant, with no substances that could interfere with the assay. For Endotoxin Indicator vials, the label must include instructions for removal of the stopper from vials before use. If the stopper is heat resistant and designed to be left in the vial, the maximum processing temperature is stated.

• **Disposal:** For destruction or discard, follow instructions recommended by the manufacturer, or depyrogenate at 250° for NLT 120 min.

• **USP Reference Standards**

USP Endotoxin RS

**Auxiliary Information** - Please check for your question in the FAQs before contacting USP.

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| ENDOTOXIN INDICATOR FOR DEPYROGENATION | Leslie Furr<br>Associate Scientific Liaison | GCM2022 General Chapters - Microbiology 2022 |

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