

## Endotoxin Testing

- 5.2.1.3 Endotoxin testing should be carried out in a solution that is at a neutral pH (6.0-8.0) and has a balance of divalent cations.
- 5.2.1.4 The sensitivity claimed of each batch of the LAL reagent should be verified.
- 5.2.1.5 The absence of interference should be established for each test item by performing Inhibition/Enhancement validation studies.
- 5.2.1.6 Endotoxin test methods should be validated and demonstrated to be appropriate for their intended use.
- 5.2.1.7 Appropriate preventative maintenance procedures for critical equipment and systems should be approved and in place.
- 5.2.1.8 Critical instruments and equipment should be calibrated and included in the routine calibration program.
- 5.2.1.9 Endotoxin elimination (depyrogenation) cycles for internal processes, supplies, equipment and materials should be validated.
- 5.2.1.10 Endotoxin test analysts or technicians should have appropriate training and documentation of that training should be on file and available for review.
- 5.2.1.11 Endotoxin test methods and/or procedures should be approved, current and available for use by the analysts or technicians.
- 5.2.1.12 Endotoxin limits and MVD or MVC should be established for each test item.
- 5.2.1.13 Inhibition/Enhancement testing should be performed on each raw material, packaging component, in-process material and drug product requiring a BET specification. Ideally three separate batches or individual shipments of the item should be used for this testing.
- 5.2.1.14 Product test assays shall be validated before being used to release final product.
- 5.2.1.15 Revalidation shall be performed as prescribed by Pharmacopoeia (e.g. at product reformulation, changes in concentration, change in drug substance or drug product).

### 5.2.2 **Methods & Procedures**

The following items or issues should be addressed in approved methods and/or procedures:

- 5.2.2.1 Validation and Revalidation of Endotoxin Test Methods.
- 5.2.2.2 Sample Collection, Transport and Storage.
- 5.2.2.3 Endotoxin Test Methods.