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Endosafe®-PTS™ in Sterile Compounding Pharmacy

The Endosafe® - PTS™, is a rapid endotoxin (pyrogen) assay that provides quantitative test results in about 15 minutes. The PTS™ test system is very user-friendly and utilizes a handheld reader and disposable cartridges preloaded with all of the materials needed to run a test. The PTS™ requires only a small amount of product at a non-interfering dilution and requires no preparation of endotoxin standards.

The cartridges used with the reader are licensed by the FDA for in-process and final product release testing of parenterals such as Compounded Sterile Products (CSPs). The PTS™ is fully compatible with USP chapters <85> Bacterial Endotoxins Test and <797> Sterile Compounding and is the optimum solution for bacterial endotoxins testing of compounded drugs due to its simplicity and speed.

Test Technology

The PTS™ system utilizes a cartridge containing precise amounts of FDA-licensed LAL reagent, chromogenic substrate, and control standard endotoxin (CSE). Each cartridge contains duplicate channels for sample analysis and positive product control. The cartridges are manufactured according to rigid quality control procedures promoting test accuracy and product stability. A calibration code is provided for each batch of cartridges that relates to a specific standard curve. After the assay reaction occurs, color intensity is measured optically and compared against the internally-archived, batch-specific standard curve to provide quantitative endotoxin levels for the test sample. In keeping with USP guidelines, the PTS™ simultaneously performs testing in duplicate and averages the results. The results are corrected for dilution and reported in endotoxin concentration, EU/mL.

Analysis and Acceptance Criteria

At the conclusion of the test, the endotoxin measurement and the assay acceptance criteria are displayed on the screen. The instrument can be used to detect endotoxin levels as high as 10 EU/mL and as low as 0.01 EU/mL. Recovery of the positive controls within 50-200% means that the results are valid because there was no test intefrence.

Endosafe® - PTS™ Features

- Quantitative results in about 15 minutes
- Compatible with suitable dilutions of all common CSP drugs
- No technical training required; easy keypad operation
- Stores 100 test results for printing or downloading
- No need to prepare endotoxin standards
- Download data into standard reports for official documentation
- 1-year warranty provided; extended warranty available
- Technical assistance available

Assay Procedure

- Add 25 µL of sample (diluted CSP) to each of 4 channels in a cartridge
- Input sample data
- Press enter
- Pump moves samples through cartridge
- Optical cells are read kinetically at 395nm
- Results displayed on screen

Tips for Testing Sterile Compounded Drugs for Intraspinal Administration

The most potent route of administration for endotoxin is the cerebrospinal fluid. Compounded intraspinal drugs must be diluted to avoid conditions that inhibit or otherwise interfere with the assay. The assay is so sensitive that the dilution scheme recommended in this system does not exceed the intraspinal endotoxin limit of 14 EU/mL, an accepted index of safety.[1] A suitable sterile tube for dilutions is a 14 mL Polystyrene sterile tube no. 2057 by Becton Dickinson. The following guideline for dilution-prior-to-testing applies to opioids and antispasmodic drugs commonly used for intraspinal infusions.[1]

Intraspinal infusions ≤ 20 mg/mL: Make a 1:80 dilution by transferring 25 µL of CSP to 2 mL LRW (or SWI) in a sterile tube. The sensitivity (LOD, limit of detection) of an assay will be 4 EU/mL, when using a cartridge with a standard curve of 0.05 to 5 EU/mL.

Intraspinal infusions > 20 mg/mL: Make a 1:280 dilution by transferring 25 µL of CSP to 7 mL LRW (or SWI) in a sterile tube. The sensitivity (LOD, limit of detection) of an assay will be 14 EU/mL, when using a cartridge with a standard curve of 0.05 to 5 EU/mL.

Intraspinal mixtures: As directed above, make a 1:80 dilution for infusions that contain ≤20 mg/mL of total drug components and 1:280 dilution for > 20 mg/mL. The intraspinal endotoxin limit is always met when the test result is less than 14 EU/mL.

Tips for Testing Sterile Compounded Drugs for IV, IM or other Routes of Delivery

Intravenous or IM solutions ≤ 20 mg/mL: Make a 1:100 dilution by transferring 25 µL of CSP to 2.5 mL LRW (or SWI) in a sterile tube. The sensitivity (LOD, limit of detection) is 5 EU/mL.

Intravenous or IM solutions > 20 mg/mL: Make a 1:400 dilution by transferring 25 µL of CSP to 10 mL LRW (or SWI) in a sterile tube. The LOD is 20 EU/mL.

Suspensions: Make a 1:200 dilution by transferring 25 µL of CSP to 5 mL of LRW (or SWI) in a sterile tube.

The above recommended dilutions will fall within the endotoxin limits specified by the USP. The dilutions also allow for suitable recovery of the positive control for all frequently prepared CSPs. Should one encounter a drug entity of combination that fails to indicate validity by recovery within the specified range, contact Technical Services at 1.800.762.7016 for help in resolving interfering conditions.

[1]Cooper, JF and LA Thoma. Screening extemporaneously compounded intraspinal injections with the bacterial endotoxins test. Am J Health-Syst Pharm. 2002;59:2426-33.

For additional information on the Endosafe® - PTS™, please call 1.877.CRIVER.1 or visit our web site, www.criver.com.

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