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Summary

The Endosafe®-PTS™ was not available when the 1987 and 1991 FDA Guidelines and Interim Guidance documents were written. This technical sheet provides insight on how they help users understand how our FDA-licensed LAL cartridge technology is compliant with existing harmonized guidelines.

MICROBIAL SOLUTIONS

Endosafe® nexgen-PTS™ and Regulatory Requirements: FDA Guidelines

The Endosafe® nexgen-PTS™ technology was not available when the 1987 and 1991 FDA Guidelines Interim Guidance documents were written. These guidelines stated that archived standard curve requirements apply to LAL test systems that a) require daily preparations of PPC, which is a significant source of variability in the LAL laboratory, and b) require reconstituted multi-test LAL reagent. Activity of the reagents can change over time, even when refrigerated. Because of these LAL testing variables, spike recovery requirements were ± 25%.

nexgen-PTS™ System and FDA Guidelines

The nexgen-PTS™ represents a single-use LAL test system. The variability associated with daily preparation of endotoxin standards and PPC has been eliminated. Likewise, the variability associated with activity change in the reconstituted LAL reagent has been eradicated. The package insert for the single-use nexgen-PTS™ cartridge allows a 50-200% recovery, which is consistent with all compendial photometric techniques.

FDA-Licensed Endosafe® nexgen-PTS™ Cartridges

In July 2006, PTS™ cartridges received approval as a supplement to Endosafe's BLA 1197. The approval is for the single-use cartridges, which contain all the reagents for a photometric LAL technique. Spectrophotometers (PTS™, nexgen-PTS™, nexgen-MCS™ Readers), like microplate or tube readers currently used in traditional photometric techniques, are not part of this approval.

nexgen-PTS™ QC Release Process

The nexgen-PTS™ QC release includes precision and accuracy testing, which is neither required nor performed on traditional LAL reagents. The nexgen-PTS™ archived standard curve is challenged during QC batch release testing, using 3 concentrations (high, middle, and low range) with 15 cartridges for each concentration.

Benefits of Endosafe® nexgen-PTS™ Versus Traditional Methods

FDA Process Analytical Technologies (PAT)

Endosafe® nexgen-PTS™

The Endosafe® nexgen-PTS™ can be used in conventional quality control settings or as a point of use test to support the drug development process

Traditional Methods

- Samples are collected and sent to the lab
- Assays are done at periodic intervals when sufficient samples have been collected
- Assays are rarely done one sample at a time – each assay requires control curve (gel-clot) or standard curve (kinetics)
- Lysate vials reconstituted based on multiple sample assays
- Results of in-process samples; therefore, are available to production staff several hours later
- Real-time results hardly adaptable with traditional methods, therefore they conflict with PAT

Required Accessories

Endosafe® nexgen-PTS™

- Disposable, single-use cartridge
- LAL reagent water and depyrogenated dilution tubes
- Pipettors for delivery of accurate sample volumes

Traditional Methods

- LAL vials
- Control standard endotoxin (CSE)
- LAL reagent water
- Depyrogenated dilution tubes
- Pipettors for delivery of accurate spike and sample volumes
- Depyrogenated reaction tubes (10 x 75 mm) or microplate
- Water bath, heat block, or micro-plate reader and computer with software

Sample Testing

Endosafe® nexgen-PTS™

- FDA-approved cartridges pre-loaded with all required reagents
- Standard details stored in archived curve; a certificate of analysis is provided
- Prepare sample dilution if required
- Anyone can run the assay even if they are not highly trained
- Rapid results can be delivered in 15 minutes or less depending on the cartridge sensitivity selected

Traditional Methods

While the traditional methods have some advantages, they have many limitations:

- User must prepare standard curve dilutions
- User may have to prepare sample dilution(s) if required
- Lysate requires reconstitution
- The length of assay is greater than 1 hour; this does not support real-time analysis
- Highly trained technicians are required to run the assay
- As central lab assay, it lacks portability

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