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Implementation of a Ph. Eur. compliant recombinant method for testing of bacterial endotoxins in sterile pharmaceuticals

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What was done?

The hospital pharmacy implemented a modern system for testing for bacterial endotoxins as a part of the quality control of raw materials (i.e. water for injection (WFI)) and sterile pharmaceuticals manufactured at the pharmacy, replacing the old gel-clot test.

Why was it done?

- Endotoxin testing by the gel-clot method is a limit test, and relies on the operator's subjective evaluation of the results. The procedure itself contains several steps and dilutions, and it is time and resource consuming.
- The availability of the amoebocyte lysate reagent can also vary since it's harvested from the endangered horseshoe crab.
- The recombinant factor C method (rFC) is a fluorimetric method based on the gene sequence of the horseshoe crab, providing quantitative results with no interpretation by an operator.
- The rFC method consists of less handling and is less susceptible to human error.

How was it done?

01

MVD and endotoxin limit
Maximum valid dilution (MVD) and endotoxin limit was established for the raw materials and sterile preparations.

02

Establishing optimal dilution
Different dilutions within the established MVD were tested to find the optimal

03

Testing of different batches
Products were then tested with three different batches to ensure valid results regardless of any batch-to-batch variation.

04

Validation of products
Validation started with the most frequently manufactured preparations, and subsequently continued throughout the year.

05

Finalisation of validation
To expedite the full validation of some preparations, expired batches were used simultaneously with at least one recently produced batch due to infrequent production.

What has been achieved?

- 25 sterile pharmaceuticals and raw materials were successfully validated for endotoxin testing by rFC during 2021 and 2022.
- The gel-clot method is no longer in use at the hospital pharmacy, reducing the negative impact on the horseshoe crab population.
- The rFC method streamlined the testing for endotoxins, reducing the time spent on performing the analysis by 50% due to less handling and increased capacity.
- Results are quantitative and objective, not relying on observations by the operator, thereby improving the quality.

What next?

The rFC method increases both quality and capacity of testing, opening up for expanded testing in the pharmacy, and including samples from other departments or hospitals.

Keywords:
- Preparation and compounding> **Sterile production**
- QC/QA> **Microbiological testing**
- QC/QA> **Quality control**

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