USP Provides Guidance on the Use of Recombinant Reagents for Bacterial Endotoxin Test

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For some time, USP has recognized the need for guidance on the use of alternative methods/reagents for endotoxins testing as permitted under General Notices (GN) 6.30 *Alternative and Harmonized Methods and Procedures*. More specifically, we acknowledge the need for guidance to drive the adoption of recombinant reagents as alternatives to naturally sourced reagents from horseshoe crabs (LAL or TAL). This approach advances USP's commitment to transition methods from using animal-derived materials to synthetic and recombinant materials.

In a recent publication in the *Pharmacopeial Forum* [45(5)], the USP Microbiology Expert Committee (EC) proposed the inclusion of recombinant factors for endotoxin testing in chapter <85> *Bacterial Endotoxins* (currently, the official procedure is based on the naturally-derived reagent, LAL). Based on public comments received, the EC decided to cancel this proposal and start the development of a separate chapter that expands on the use, validation, and comparability of endotoxin tests based on recombinantly derived reagents. Nevertheless, companies retain the option to use an alternative to the compendial method if they prove that their method is validated and provides comparable results to the compendial procedure (see GN 6.30).

The purpose of the new general chapter in development is to provide guidance in the adoption of alternative testing to allow flexibility in compendial approaches to support the pharmaceutical industry,

- The new proposed chapter contains recommendations for the qualification of recombinant reagents as alternatives to naturally sourced reagents from horseshoe crabs, Limulus polyphemus or Tachypleus tridentatus hemolymph (LAL or TAL) for the purposes of quantitating endotoxins activity in injectable drugs, biologics and medical devices where applicable.
- The new proposed chapter's approach to qualification is based on General Notices 6.30, *Alternative and Harmonized Methods and Procedures*, and General Chapter <1225> *Validation of Compendial Procedures*.
- In addition to validation, users are expected to demonstrate that comparable results are obtained with the alternative method. For endotoxins testing, it will be required to demonstrate the comparability of endotoxins detection and quantitation between LAL and the proposed recombinant reagent, by comparing test results using product that contains known levels of endotoxins.
- The new proposed chapter also provides suggestions for the evaluation of a recombinant reagent supplier.

The new proposed chapter is expected to be available for public comment in Pharmacopeial Forum 46(5) [Sep.-Oct. 2020]. For information regarding the content of proposed chapter <1085.1> please click here.

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*This Notice was updated on July 30, 2020 to specify the expected *Pharmacopeial Forum* publication.