The need for rapid methods in the compounding pharmaceutical industry

Balancing patient care, quality products, and safe shelf lives for unique formulations.

USP chapter <797> "Pharmaceutical Compounding – Sterile Preparations" has been effective for a year and the massive overhaul of the parameters used to assign beyond-use dates (BUDs) is no longer a surprise. In most cases, compounded products will have shorter shelf lives. This heavily impacts batch planning and availability to patients, yet there are some ways to extend the BUDs that are outlined in the new revision. Most notably, performing a sterility test on each lot can often double the BUD window. However, waiting for a sterility test takes at least two weeks, which significantly cuts into that window.

Another seemingly minor change can also help alleviate this issue. First, let's look at the previous version of the chapter: in that version, there was a single line buried in the sterility test section that briefly mentioned alternative methods. "A method not described in the USP may be used if verification results demonstrate that the alternative is at least as effective and reliable as the USP Membrane Filtration method or the USP Direct Inoculation of the Culture Medium method where the Membrane Filtration method is not feasible." That previous reference offered no direction for demonstrating method effectiveness. Without direction as to what will be accepted by relevant regulatory bodies, the reference was nearly useless. It is difficult to invest in a project without a clear road map for approval.

Rapid acceptance of alternative methods

The simple change in the USP <797> revision is the addition of three cross-references to another USP chapter, <1223> "Validation of Alternative Microbiological Methods". One reference is in the new introduction section, which signals alternative methods are front of mind for the standard setters. The other two references are in the Sterility Test section, highlighting the test with a pressing need for faster results. USP <1223> is the roadmap that hopeful rapid method users were looking for. Using a rapid sterility test boosts the BUD timeline while minimising the impact of the traditional incubation period.

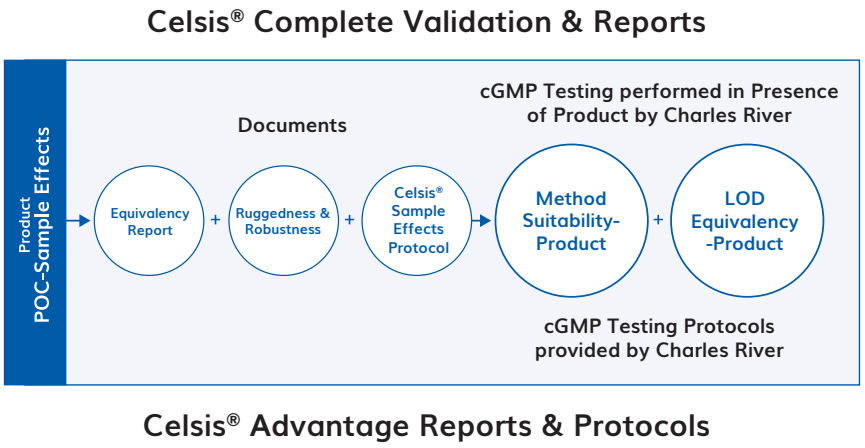
Prominent service laboratories and large 503b compounding networks have successfully validated rapid sterility methods like Celsis®. Charles River offers customised packages for Celsis users, enabling system validation and IT regulatory approval. Even though the update to <1223> is relatively new, rapid methods in good regulatory standing are available today.

Shelf-life considerations

The compounding industry is critical to meeting unique patient needs. The shift in regulatory standards around BUDs undoubtedly makes it more difficult to meet those needs. However, regulators who act on behalf of patients want these products to be safe as well.

Large pharmaceutical manufacturers are required to have stability studies to define a stable shelf life for their product. Compounded products, which typically contain a unique formula alteration, don't have that requirement. Hence, justifying an extended shelf life without that data is difficult.

For USP <797> writers, unless proven otherwise, it is safer to assume a mixture of these active pharmaceutical ingredients (APIs) and excipients will lose effectiveness prior to any of the individual material expiration dates. There's room for pushback because the dates seem arbitrary, which is why they allow for extensions of BUDs with appropriate stability data. It is a difficult position to be in when standardising such a broad market. With that in mind, the challenge with BUDs exists for a good reason – patient safety. Rapid methods minimise the impact of this challenge.



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