Guidelines for the Establishment of Appropriate Beyond Use Dating of Sterile Compounded Admixtures

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ABSTRACT

To support compounding of products that are sterile and chemically stable, beyond use dating of admixtures must include a thorough evaluation of appropriate resources. In most instances, resources provide documentation of a specific compounded admixture, at a specific concentration and storage parameters, that does not coincide with current operations or patient-specific requirements. To meet the operational demands of a pharmacy, institutions employ a referenced guideline approach to guide decision making for safe sterile admixing. Often these guidelines are established and maintained at individual practicing locations with varying levels of detail and accuracy. In an effort to improve sterile compounding across a multihospital system, we developed and implemented beyond use dating guidelines to improve consistency and patient safety while meeting regulatory concerns.

Key Words—beyond use dating, BUD, stability, sterile compounding, USP <797>

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Beyond use date (BUD) is the date after which a compounded preparation shall not be used, and it is set based on the date on which the preparation was compounded. To support compounding of products that are both sterile and chemically stable, beyond use dating of sterile compounded admixtures must include a thorough evaluation of appropriate resources. In most instances, resources provide documentation of a specific compounded admixture, at a specific concentration and storage parameters, that does not coincide with current operations or patient-specific requirements. Prior to admixing, literature should be evaluated to determine the chemical stability of each medication at a referenced concentration range, within a specified diluent, and stored at appropriate temperature within an appropriate container. The chemical stability must also be cross-referenced with current US Pharmacopeial Convention standards to ensure that sterility is maintained throughout the storage period.

It is important to note that BUDs and expiration dates are not the same. USP <797> standards describe expiration dates as the chemical and physical

stability of manufactured sterile products determined by rigorous analytical and performance testing indicated in the package insert or published references. Beyond use dating applies the same expiration dating principles, but adds the consideration of sterility. USP <797> presents maximum BUDs for 3 contamination categories (low, medium, and high) for compounded sterile preparations. Each category differs in the potential for microbial contamination during the compounding of the admixture.

To meet the operational demands of a pharmacy, institutions employ a referenced guideline approach to guide decision making for safe sterile admixing. By following this guideline, compounding personnel ensure consistent compounding practices. The guideline also serves as quick reference of stability information for appropriate assignment of beyond use dating. These guidelines are established and maintained at individual practicing locations with varying levels of detail and accuracy. Most often, the guidelines are generic; stability is granted for a particular medication in a particular diluent, without

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appropriate references for specific concentrations. In an effort to improve sterile compounding across a multihospital system, we developed the following beyond use dating guidelines (eAppendix) to improve consistency and patient safety while meeting regulatory concerns. These guidelines may serve as an operational reference for compounding personnel to guide the application of appropriate beyond use dating in compounding single patient preparations.

METHODS

All medications compounded in each facility in our health care system were selected for inclusion in the guidelines. We developed several assumptions before researching the available literature on chemical stability. USP <797> beyond use dating would be utilized based on associated compounding risk level. The beyond use dating referenced within USP <797> for low-, medium-, and high-risk level compounding would be used to limit the referenced chemical stability depending on the storage conditions detailed within the literature assessed.

The assigned beyond use dating would only be applicable if the compounding of a specific admixture occurred within a certified ISO Class 5 environment located within a facility design that, according to USP <797>, allowed for full utilization of beyond use dating without any restrictions. This assumption applied to the reconstituted vial and the compounding of the admixture.

The beyond use dating would only be applicable under the assumption that the admixture was compounded for a single patient and not for anticipated batch compounding. The associated beyond use dating for batch compounding would be adjusted for compounding risk level and assigned through an automated system for capturing batch-specific information.

These guidelines were not intended for proprietary bag systems, as manufacturer-specific guidance would be sought for those systems. In addition, nonreferenced manufacturer medication information may differ in stability data.

Unless otherwise indicated through limited chemical stability, the indicated beyond use dating would allow for administration of the admixture until the date and/or time referenced. If limited chemical stability was a factor, this was indicated for applicable admixtures within the guideline by an associated expiration date.

For each medication listed, information was provided that was vital to safe, accurate, and consistent compounding throughout the organization. Separate columns were developed within the guidelines for medication vial specifics and secondary admixture specifics. Information to drive consistency or compounding safety was indicated within the “other information” section.

The chart template was completed for each medication, starting with the most recent manufacturer package insert information for which vial reconstitution and stability were indicated. The diluent information, if applicable, was then entered from the same package insert, along with any concentration specifics indicated by the manufacturer. At times, all the information, including stability information, could be found in the package insert, therefore this information was entered and beyond use dating adjusted as necessary per USP <797> standards. Published reference standards were consulted for information that was not found within the package insert.

The primary goal of the beyond use dating guideline was to provide a comprehensive information source for safe and consistent admixing. A secondary goal was to research opportunities to extend beyond use dating, within USP <797> standards, outside of available manufacturer package insert information. Published references were used to find extended chemical stability at reference ranges, which were indicated within the chart. An upper and lower concentration reference range was needed to establish a range of stability concentrations at the indicated BUD. Necessary temperature, diluent, and container information was also found to ensure that admixing was in accordance with the study referenced. After the guideline was developed, it was reviewed for accuracy by the second author (N.L.).

DISCLAIMER

The beyond use dating guideline is to serve as a guide, not a resource, for appropriate use of beyond use dating of sterile products. Some of information is specific to operations at specific facilities and therefore must not be used without a thorough confirmation of its appropriateness at other facilities.

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