

Baxa Corporation

**Interpreting USP <797> to Set Expiration
Times for Single Dose Vials Used with
Exacta-Mix™ Compounders**

Technical Paper

An overview of beyond-use dating requirements for SDVs under
the revised USP Chapter <797>.

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Overview

The 27th revision of the United States Pharmacopeia (USP 27) was introduced on January 1, 2002 and was immediately enforceable by the US Food and Drug Administration (FDA). Since then, the guidelines under USP Chapter <797> Pharmaceutical Compounding – Sterile Preparations have been adopted by some pharmacy regulatory and accrediting bodies such as US State Boards of Pharmacy and the Joint Commission (TJC) as the standard of practice for health-system pharmacies. The Sterile Compounding Committee (SCC) completed a significant review and updating of the Chapter, which were released in December 2007 and become official in June 2008.¹

Pharmacy professionals challenged many aspects of the original Chapter, and those challenges resulted in the thorough review conducted by the SCC. Among the issues that have been brought up is that of setting expiration dates for single use vials within an ISO 5 area. This paper addresses that issue in the context of automated compounding devices.

Expiration Dates and Beyond-Use Dates

Before the release of the original USP Chapter <797>, some pharmacists used the terms ‘expiration dates’ and ‘beyond-use dates’ (BUDs) interchangeably. In the context of the Chapter, these two terms have very different definitions. In a document reviewing the USP <797> revisions, Clyde Buchanan (MS, FASHP and frequent speaker for state and national conferences on United States Pharmacopeia (USP) Chapter 797) offered the following clarification on compounded sterile products (CSPs).

“An expiration date reflects the shelf-life of a commercially manufactured product when stored according to FDA-approved labeling, in its original container. The beyond-use date is the date or time after which a CSP must not be stored. The beyond-use date is determined from the date or time the preparation is compounded.”²

Automated Compounding Devices (ACDs)

Baxa Corporation offers a range of automated systems that streamline multi-ingredient solution compounding by improving productivity and reducing labor costs. The most basic of these devices is their Repeater™ Pump, which performs routine pharmacy filling and fluid transfer applications from a single source container to single or multiple final containers. Using similar technology, Baxa developed their basic automated compounding System, the Exacta-Mix 600™ Universal Pump, which has a six-ingredient compounding capacity. Finally, the state-of-the-art Exacta-Mix™ 2400 (EM2400), with 24-source ingredient mixing, is the industry leader for pharmacy efficiency and innovation in ACDs.

The EM2400 has a variety of potential compounding applications, which includes parenteral nutrition (PN). Many of the PN ingredients are solutions supplied by the manufacturer only in single dose vials (SDV), which do not include preservatives. As a result, some Baxa customers have inquired about the interpretation of USP <797> BUD requirements, and what vial ‘expiration,’ or beyond-use-dating, time should be assigned to these SDVs. While the EM2400 system has the broadest pharmacy applications and will be referred to in the following discussion, the answer to the question applies to all Baxa automated compounders.

Expiration of Source Containers Used with ACDs

Even the December 2007 revised USP Chapter <797> does not address the expiry of source containers in a 'closed-system' environment such as that used with the EM2400 compounding system.¹ Nor is the expiry of tubing used in such an environment mentioned. The 'single-dose and multiple dose containers' section within the brand new category of 'Immediate Use CSPs' contains the most relevant language about the expiry of SDVs for this discussion:

"Opened or needle-punctured single-dose containers, such as bags, bottles, syringes, and vials of sterile products and CSPs shall be used within 1 hour if opened in worse than ISO Class 5 (see Table 1) air quality (see Immediate-Use CSPs), and any remaining contents must be discarded. Single-dose vials exposed to ISO Class 5 (see Table 1) or cleaner air may be used up to 6 hours after initial needle puncture."¹

Baxa pharmacists have contact officials at USP in order to get a direct interpretation from the SCC about the intention of the Chapter in regards to the expiry of source containers in 'closed-system' such as an automated compounding device. The best information that could be learned was that the tubing in such systems expires in accordance with the manufacturer's labeling. No answer was received about the question as to whether the solution inside the tubing expires after six hours as well. In effect, Baxa was left with the understanding that according to USP <797>, the tubing used with the SDV source containers expires in accordance with the manufacturers' labeling.

Therefore it seems reasonable to conclude that SDV's opened in ISO Class 5 air, such as that typically found in pharmacy laminar flow hoods, will expire after 6 hours. The only alternative to this conclusion would be if a different expiration period is specifically stated by the solution manufacturer.

As far as the tubing is concerned, users must follow the manufacturers' recommendation for the expiration of opened tubing. The comments of the USP Subcommittee seem to indicate that any liquid in this tubing can be used up until the manufacturers' recommended expiration for the tubing, at which time the liquid would 'expire' as well. While this decision seems prudent, the final decision must be made by the responsible pharmacist in each individual health-system pharmacy.

Baxa Tube Set Recommendations

The manufacturer's recommendations for the EM2400 tube sets are quite clear. Baxa recommends that EM2400 tubing be changed after 24 hours of use, or 150 liters pumped³. Other Baxa compounders have tubeset change recommendations of 24 hours, or a maximum of 120 liters pumped.⁴

Individual pharmacies always can choose to change tubing components more frequently than the 24-hour maximum recommended by Baxa. A good example for this might be for solutions such as lipids and dextrose that are known fertile mediums for microbacterial growth. Highly concentrated electrolyte solutions are most likely less susceptible to growth, which supports longer inlet tubing set changes. Once again, the only absolute specified by Baxa is the total number of liters pumped and the 24-hour maximum.

On a practical level, sophisticated Baxa operating software makes such decisions quite easy to implement in the EM2400. Among the many user-definable choices for the

system are the ability to program in a warning for tubing expiration and individual ingredient expiration.^{3,4}

Summary

Setting expiration times for the single-dose vials used on Exacta-Mix Automated Compounders is not complicated, but USP Chapter <797> does not completely address every question that a pharmacy might have about the process. However, a couple of issues are clearly mandated.

1. USP <797> specifically states that single-dose vials must be discarded within 6 hours, even if opened in ISO Class 5 (hood) air. The only exception to this is if the vial manufacturer indicates a different expiration period.
2. Baxa, as the ACD tubeset manufacturer, recommends that compounder tube sets be discarded within 24 hours, or after a specific number of liters pumped, according to the individual compounder being used. Some pharmacies may choose to change their entire setup, or change out only specific inlet sets, sooner than this recommendation based on their more conservative interpretation of the relative risk of contamination.

This, then, leaves to the pharmacy what to do with any solution remaining in the tubing beyond the 6-hour maximum after a single-dose vial has been changed. USP <797> does not specifically detail what to do in this situation and thus leaves it up to the discretion of the individual pharmacist. Baxa also cannot take a specific position on this question. The functional reality is that it is likely most pharmacists will choose to leave the fluid in the tubing as long as the tubeset has not expired.

About Baxa Corporation

Baxa Corporation is a customer-focused medical device company that provides innovative, solution-based technologies for medication handling and delivery. Its systems and devices promote the safe and efficient preparation, handling, packaging, and administration of medications. Key products include the PadLock[®] Set Saver, Rapid-Fill[™] Automated Syringe Fillers, Exacta-Med[®] Oral Dispensers, MicroFuse[®] Syringe Infusers, Repeater[™] Pharmacy Pumps, and Exacta-Mix[™] and MicroMacro[™] Multi-Source Automated Compounders; used worldwide in hospitals and healthcare facilities. Privately held, Baxa Corporation has subsidiaries and sales offices in Canada and the United Kingdom; direct representation in Austria, Belgium, Finland, France, Germany, Luxembourg, The Netherlands and Switzerland; and distribution partners worldwide. Further information is available at www.baxa.com.

References

- ¹ USP General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. United States Pharmacopeia. 2007.
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- ³ Baxa Corporation. Exacta-Mix™ 2400 Technical Manual. B0801. Pages 23, 33, 52, 71. Copyright 2008.
- ⁴ Baxa Corporation. Exacta-Mix 600™ (EM600) Technical Manual. J0701. Pages 14, 25, 54. Copyright 2007.