Comment Submission Template for:
General Chapter <797> *Pharmaceutical Compounding—Sterile Preparations*

Revision proposed in *Pharmacopeial Forum* 41(6) Nov/Dec 2015

Send completed template to CompoundingSL@usp.org by January 31, 2016

Commenter's Name:	**Position:**	**Full Contact Details:**
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General Comments:

The American Society of Retina Specialists (ASRS) is the largest retinal organization in the world, representing nearly 2800 board certified ophthalmologists who have completed fellowship training in the medical and surgical treatment of retinal diseases.

The ASRS supports the desire of USP to develop a more evidence-based approach to the development of compounding guidelines and shares its overall goal of decreasing the risk of mass casualties and patient harm.

The ASRS, however, is concerned that the new proposed BUDs in Table 8 are overly restrictive and do not allow for pharmacies to do the appropriate testing to extend the BUDs beyond 42 refrigerated and 45 days frozen. When the time necessary to complete the sterility testing is subtracted, the BUDs are even more restrictive. This one-size-fits-all approach establishes the same BUDs for non-equivalent preparations. Eye drops and ointments are treated the same as betadine and preservative free steroids, despite widely varied risk for different treatments that are prepared by a compounding pharmacy. The ASRS supports the options provided in the previous version of <797> that allowed extending BUDs based on the scientific literature or through product-specific experimental studies. The ASRS concurs with the UPS's statement in the current version of <797> that basing BUDS on product-specific experimental studies is more accurate than basing them on theoretical models. Given this limitation and the USP's ongoing stated commitment to establishing scientifically based guidelines, the ASRS proposes that USP retains its original language and adds a provision that requires product-specific experimental studies for certain preparations. This approach would allow low risk preparations, such as eye drops and ointments, to have BUDs based on the literature and to make the standard for allowing the extension of BUDs for higher risk preparations, such as injectable sterile products, higher and only based on additional scientific studies.

As an example, the proposed guidelines for BUD would limit the maximum BUD for bevacizumab (Avastin) to 42 days refrigerated. This would create a major change in current practice as the standard BUD for prepared syringes of bevacizumab is 6 months. This standard is based on in vivo studies (Bakri/Snyder, Paul, Chen, Ornek references) that demonstrated stability and safety of the drug to 6 months, and on retrospective series (Fong, Hsu), clinical trials (CATT, DRCR), and medical claims data (Vanderbeek) that confirm safety and efficacy over such a time period. Hsu and colleagues reviewed 503,890 injections of anti-VEGF therapy in a multicenter retrospective study from 5 different geographic locations across the US and found that the infection rate after injection of repackaged bevacizumab was low and no different from the infection rate after injections of single-use alternative therapies. Similarly, Vanderbeek and colleagues reviewed 530,382 intravitreal injections between 2005 and 2012 from the medical claims data of a national medical carrier and also found excellent safety for repackaged bevacizumab as compared to non-compounded alternatives. In two major prospective multi-center clinical trials evaluating the safety and efficacy of bevacizumab vs. other therapies, a university-based compounding pharmacy successfully extended the BUD for repackaged bevacizumab out to 2 years, based

on sterility and stability testing, under the guidance and approval of the FDA. We strongly recommend that USP <797> guidelines continue as is to allow for scientific evidence and product-specific testing to be used in the determination of maximum BUD.

Please see attached reference list.

Specific Comments:

Section(s)	**Line Number(s)**	**Existing text:** (Provide the proposed text.)	**Suggested change:** (Provide the revised suggestion to replace the existing text.)	**Comment**	**Rationale / Scientific Evidence**
Table 8	1504		**Reinstate deleted section on** "Determining Beyond-Use Dates" to allow method of extending BUDs listed in Table 8	**See above statement in general comments**	**See above statement**

(Add additional lines to the table as necessary.)