Crosswalk of Guidance and Standards for Assigning Beyond-Use Dates in Sterile Compounding

The following are accreditation and regulatory standards for assigning beyond-use dates (BUDs) in sterile compounding. For further definition of a BUD, and considerations involved in determining the appropriate BUD, refer to the ASHP Pharmacist Guide to Assigning a Beyond Use Date to a Compounded Sterile or Nonsterile Preparation.

This crosswalk is an ASHP member resource prepared by a workgroup of the Section of Inpatient Care Practitioner's Advisory Group on Compounding Practice. This resource is neither affiliated with nor endorsed by the below accreditation/regulatory organizations. The information contained in this guide is provided for informational purposes. It is not to be considered as medical, legal, or other professional advice.

Organization	Comment
Ampule	
Example(s): cosyntropin injection ampule, digoxin injection ampule Ampules are a subset of single-dose containers [6]. A container capable of being hermetically sealed, intended to hold sterile materials [7]. Ampules usually are made of glass and designed to be broken open to access or withdraw contents. As a result, use of a filter needle is required to transfer or withdraw contents. Once accessed, the ampule is an open system and must be used immediately.	
CDC	Expects compliance with nationally recognized standards, including USP <797>.
CMS	Expects compliance with nationally recognized standards (e.g., CDC, USP). "All compounding, packaging, and dispensing of drugs and biologicals must be under the supervision of a pharmacist and performed consistent with State and Federal laws. " When available, BUD should be based on information provided by manufacturers. If not available from manufacturer, must be based on policies and procedures as well as professional principles equivalent or more conservative than USP [3]
FDA	Out of scope for the FDA. Refers to USP <797> for 503A compounding. [4]
TJC[a]	The institution must label compounded sterile products to include beyond-use dates "in accordance with state and federal law and regulation and hospital policies." [5]

Organization	Comment
	Sterile medication compounding must occur within a proper environment "in accordance with state and federal law and regulation and hospital policies." [5] Single-dose ampules cannot be stored for any time period once opened [5]. (references CMS 482.25(b)(1))
USP	Use immediately regardless of air quality where the ampule is opened. Discard any remainder with no chance of re-use (must not be stored for any time period) [6].
Single-dose container	
Example(s): cefTAROline vial, pembrolizumab vial, tetanus-diphtheria vaccine prefilled syringe, nicardipine ready-to-use premix A container of sterile product for parenteral administration (e.g., injection or infusion) that is designed for use with a single patient as a single injection/infusion. A single-dose container usually does not contain a preservative [6].	
CDC	Expects compliance with nationally recognized standards, including USP <797>. Single-dose containers should not be used for more than one patient and not stored for future use on the same patient [1]. Splitting of single-dose container contents to multiple single-use containers (e.g., syringes, sterile vials, etc.) are considered repackaging and must comply with USP <797> and manufacturer recommendations [1]. It is not acceptable to pool leftover contents of single-dose vials for future doses [1].
CMS	Expects compliance with nationally recognized standards (e.g., CDC, USP). "All compounding, packaging, and dispensing of drugs and biologicals must be under the supervision of a pharmacist and performed consistent with State and Federal laws. " When available, BUD should be based on information provided by manufacturers. If not available from manufacturer, must be based on policies and procedures as well as professional principles equivalent or more conservative than USP [3].
FDA	Out of scope for the FDA. Refers to USP <797> for 503A compounding. [4]
TJC[a]	The institution must properly store compounded sterile preparations of nonhazardous and hazardous medications. Labels include beyond-use dates "in accordance with state and federal law and regulation and hospital policies." [5]

Organization	Comment
	Sterile medication compounding must occur within a proper environment "in accordance with state and federal law and regulation and hospital policies." If accessed in an ISO 5 air quality or better, and stored per labeling requirements, may be used up to 12 hours (or sooner if required by manufacturer labeling) from initial puncture or opening. [5] (references CMS 482.25(b)(1))
USP	The BUD assigned is dependent on the air quality where the single-dose container is opened [6]: • If accessed in ISO 5 air quality or better, it may be assigned a BUD of 12 hours if stored according to manufacturer labeling for storage requirements. Does not apply to ampules (see above). • If opened in worse than ISO 5 air quality, then it must be used immediately (i.e., use within 4 hours unless manufacturer labeling dictates a shorter interval). Discard any remainder. Note that repackaging is considered sterile compounding and therefore within jurisdiction of USP <797>. When used as a component in a sterile compound, care is required to minimize risk of contamination for the final product [6]. Single-dose containers must not be used for more than 1 patient [6]. Vial-bag connection systems, if assembled and activated outside of the sterile compounding area, must be used immediately. If docked or attached but not activated in pharmacy, this is a compounding action and <797> BUD requirements apply [8].
Multiple-dose container	
Example(s): insulin U-100 vial A container of sterile product for parenteral administration (e.g., injection or infusion) that is designed to contain more than one dose of the sterile product. A multiple-dose container is usually required to meet the antimicrobial effectiveness testing criteria [6].	
CDC	Expects compliance with nationally recognized standards, including USP <797>. Once multiple-dose container has been opened or accessed should be dated and discarded within 28 days unless otherwise specified by manufacturer labeling. Medication vials should always be discarded whenever sterility is compromised or cannot be confirmed. Additionally, CDC expects compliance with USP [1]. BUD should not exceed manufacturer's original expiration date [2].

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CMS	Expects compliance with nationally recognized standards (e.g., CDC, USP). “All compounding, packaging, and dispensing of drugs and biologicals must be under the supervision of a pharmacist and performed consistent with State and Federal laws. ” When available, BUD should be based on information provided by manufacturers. If not available from manufacturer, must be based on policies and procedures as well as professional principles equivalent or more conservative than USP [3].
FDA	Out of scope for the FDA. Refers to USP <797> for 503A compounding. [4]
TJC[a]	The institution must properly store compounded sterile preparations of nonhazardous and hazardous medications. Labels include beyond-use dates “in accordance with state and federal law and regulation and hospital policies.” [5] Sterile medication compounding must occur within a proper environment “in accordance with state and federal law and regulation and hospital policies.” [5] Opened multiple-dose containers of injectable medications are stored according to manufacturer labeling requirements and must be used within 28 days unless otherwise specified by manufacturer [5]. (references CMS 482.25(b)(1))
USP	A multiple-dose container is intended to provide more than one dose of the sterile product and typically contains preservatives. Regardless of what air quality the multiple-dose container is opened in, it may be assigned a BUD of 28 days unless otherwise specified by manufacturer labeling [6]. A multiple-dose CSP contains more than one dose of sterile preparation, may be accessed multiple times, and usually contains a preservative. Multiple-dose CSPs must meet criteria for antimicrobial effectiveness testing (USP <51>). Use from initial entry cannot exceed 28 days or the assigned BUD, whichever is shorter. Multi-dose CSP must be prepared as a Category 2 or 3 CSP [6].
Pharmacy Bulk Package	
Example(s): vancomycin for infusion 10g bulk package A conventionally manufactured sterile product for parenteral use that contains many single doses intended for use in a pharmacy admixture program. A pharmacy bulk package may either be used to prepare admixtures for infusion or, through a sterile transfer device, for filling sterile containers. Also refer to USP <659>: Injection Packaging Systems, Pharmacy bulk package [6]. Manufacturer labeling may specify a maximum number of times the vial septum may be accessed.	

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USP	A pharmacy bulk package is a single-dose container that contains multiple doses and must only be opened in ISO Class 5 air or better air quality. It is restricted to use in pharmacy admixture programs and labeled with "Pharmacy Bulk Package – Not for direct infusion" per manufacturer labeling. The manufacturer labeling should be used as a guide for assigning a BUD [6]. Often in practice, pharmacy bulk packages will have in-use times specified that are less than the usual 4 hours allowed for immediate use. A pharmacy bulk package must only be punctured or opened in ISO class 5 air or better [8].
Allergenic Extracts	
USP	USP <797> has a specific section regarding compounding allergenic extracts in detail. These are individualized preparations mixed and diluted to prepare prescription sets for administration to patients. A prescription set is a vial or set of vials of premixed licensed allergenic extracts for subcutaneous immunotherapy that have been diluted with an appropriate diluent for an individual patient [6]. Preparation of allergenic extract prescription sets is not subject to all of the requirements in USP <797>. The standards for compounding allergenic extracts, apply when:

Organization	Comment
	1) The compounding process involves transfer via sterile needles and syringes of conventionally manufactured sterile allergen products and appropriate conventionally manufactured sterile added substances; and 2) Manipulations are limited to penetrating stoppers on vials with sterile needles and syringes and transferring sterile liquids in sterile syringes to sterile vials [6]. The BUD for the prescription set must be no later than the earliest expiration date of any allergenic extract or any diluent that is part of the prescription set, and the BUD must not exceed 1 year from the date the prescription set is mixed or diluted [6].

BUD = beyond-use date; **CDC** = Centers for Disease Control and Prevention; **CMS** = Centers for Medicare and Medicaid Services; **CSP** = Compounded Sterile Product; **FDA** = Food and Drug Administration; **ISO** = International Organization for Standardization; **TJC** = The Joint Commission; **USP** = United States Pharmacopeia.

[a] TJC is represented as the example of an accreditation organization for U.S. healthcare organizations and programs because it is the most commonly used.[The Joint Commission Hospital Accreditation Fact Sheet (https://www.jointcommission.org/resources/news-and-multimedia/fact-sheets/facts-about-hospital-accreditation)] However, other CMS-approved hospital accreditation organizations exist: Center for Improvement in Healthcare Quality (CIHQ), Det Norske Veritas Healthcare (DNV), and the Healthcare Facilities Accreditation Program (HFAP).

Last Updated October 2024

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