

tion (see Chapter (1191), *Observing Products for Evidence of Instability*). However, excessive chemical degradation and other drug concentration loss due to reactions may be invisible more often than visible.

General Guidelines for Assigning Beyond-Use Dates

In the absence of stability information that is applicable to a specific drug and preparation, the following table presents maximum BUDs recommended for (1) nonsterile compounded drug preparations that are packaged in tight, light-resistant containers and stored at controlled room temperature, unless otherwise indicated; and for (2) sterile preparations for which a program of sterility testing is in place (see the *General Notices and Requirements, Preservation, Packaging, Storage, and Labeling*). Drugs or chemicals known to be labile to decomposition will require shorter BUDs.

BUD by Type of Formulation ^a
For Nonaqueous Formulations —The BUD is not later than the time remaining until the earliest expiration date of any API or 6 months, whichever is earlier.
For Water-Containing Oral Formulations —The BUD is not later than 14 days when stored at controlled cold temperatures.
For Water-Containing Topical/Dermal and Mucosal Liquid and Semisolid Formulations —The BUD is not later than 30 days.

^a These maximum BUDs are recommended for nonsterile compounded drug preparations in the absence of stability information that is applicable to a specific drug or preparation. The BUD shall not be later than the expiration date on the container of any component.

Susceptible preparations should contain suitable antimicrobial agents to protect against bacteria, yeast, and mold contamination inadvertently introduced during or after the compounding process. When antimicrobial preservatives are contraindicated in such compounded preparations, storage of the preparation at controlled cold temperature is necessary; to ensure proper storage and handling of such compounded preparations by the patient or caregiver, appropriate patient instruction and consultation is essential. Antimicrobial preservatives should not be used as a substitute for good compounding practices.

For information on assigning BUDs when repackaging drug products for dispensing or administration, see the *General Notices and Requirements, Preservation, Packaging, Storage, and Labeling, Labeling, Expiration Date and Beyond-Use Date, and Packaging and Repackaging—Single-Unit Containers* (1136).

Assurance of sterility in a compounded sterile preparation is mandatory. Compounding and packaging of sterile drugs (including ophthalmic preparations) requires strict adherence to guidelines presented in Chapter (797) and in the manufacturers' labeling instructions.

PACKAGING AND DRUG PREPARATION CONTAINERS

The compounder shall ensure that the containers and container closures used in packaging compounded preparations meet USP requirements (see (659) *Packaging and Storage Requirements; Containers—Glass* (660); *Containers—Plas-*

tics (661); *Containers—Performance Testing* (671); Chapter (1136)); and when available, compounding monographs. Compounders are not expected to perform the tests described in these chapters but should be knowledgeable about the standards described in them. Container suppliers shall supply, upon request, verification of USP container compliance. Containers and container closures intended for the compounding of sterile preparations must be handled as described in Chapter (797).

The containers and closures shall be made of suitable clean material in order not to alter the quality, strength, or purity of the compounded drug preparation. The container used depends on the physical and chemical properties of the compounded preparation. Container–drug interaction should be considered for substances that have sorptive or leaching properties.

The containers and closures shall be stored off the floor, handled and stored to prevent contamination, and rotated so that the oldest stock is used first. The containers and container closures shall be stored in such a way as to permit inspection and cleaning of the storage area.

COMPOUNDING DOCUMENTATION

Documentation, written or electronic, enables a compounder, whenever necessary, to systematically trace, evaluate, and replicate the steps included throughout the preparation process of a compounded preparation. All compounders who dispense prescriptions must comply with the record-keeping requirements of their state boards of pharmacy. When the compounder compounds a preparation according to the manufacturer's labeling instructions, then further documentation is not required. All other compounded preparations require further documentation as described in this section.

These records should be retained for the same period of time that is required for any prescription under state law. The record may be a copy of the prescription in written or machine-readable form and should include a Master Formulation Record and a Compounding Record.

Master Formulation Record

This record shall include:

- official or assigned name, strength, and dosage form of the preparation
- calculations needed to determine and verify quantities of components and doses of active pharmaceutical ingredients
- description of all ingredients and their quantities
- compatibility and stability information, including references when available
- equipment needed to prepare the preparation, when appropriate
- mixing instructions that should include:
 1. order of mixing
 2. mixing temperatures or other environmental controls
 3. duration of mixing
 4. other factors pertinent to the replication of the preparation as compounded

- sample labeling information, which shall contain, in addition to legally required information:
 1. generic name and quantity or concentration of each active ingredient
 2. assigned BUD
 3. storage conditions
 4. prescription or control number, whichever is applicable
- container used in dispensing
- packaging and storage requirements
- description of final preparation
- quality control procedures and expected results

Compounding Record

The Compounding Record shall contain:

- official or assigned name, strength, and dosage of the preparation
- Master Formulation Record reference for the preparation
- names and quantities of all components
- sources, lot numbers, and expiration dates of components
- total quantity compounded
- name of the person who prepared the preparation, name of the person who performed the quality control procedures, and name of the compounder who approved the preparation
- date of preparation
- assigned control or prescription number
- assigned BUD
- duplicate label as described in the Master Formulation Record
- description of final preparation
- results of quality control procedures (e.g., weight range of filled capsules, pH of aqueous liquids)
- documentation of any quality control issues and any adverse reactions or preparation problems reported by the patient or caregiver

Standard Operating Procedures

All significant procedures performed in the compounding area should be covered by written standard operating procedures (SOPs). Procedures should be developed for the facility, equipment, personnel, preparation, packaging, and storage of compounded preparations to ensure accountability, accuracy, quality, safety, and uniformity in compounding. Implementing SOPs establishes procedural consistency and also provides a reference for orientation and training of personnel.

Material Safety Data Sheets File

MSDSs shall be readily accessible to all employees working with drug substances or bulk chemicals located on the compounding facility premises. Employees should be instructed on how to retrieve and interpret needed information.

QUALITY CONTROL

The safety, quality, and performance of compounded preparations depend on correct ingredients and calculations, accurate and precise measurements, appropriate formulation conditions and procedures, and prudent pharmaceutical judgment. As a final check, the compounder shall review each procedure in the compounding process. To ensure accuracy and completeness, the compounder shall observe the finished preparation to ensure that it appears as expected and shall investigate any discrepancies and take appropriate corrective action before the prescription is dispensed to the patient.

Compounding Controls

1. The Master Formulation Record, the Compounding Record, and associated written procedures shall be followed in execution of the compounding process. Any deviation in procedures shall be documented.
2. The compounder shall check and recheck each procedure at each stage of the process. If possible, a trained second person should verify each critical step in the compounding process.
3. The compounder shall have established written procedures that describe the tests or examinations conducted on the compounded preparation (e.g., the degree of weight variation among capsules) to ensure their uniformity and integrity.
4. Appropriate control procedures shall be established to monitor the output and to verify the performance of compounding processes and equipment that may be responsible for causing variability in the final compounded preparations.
5. For further guidance on recommended quality control procedures, see Chapter (1163).

PATIENT COUNSELING

At the time of dispensing the prescription, the patient or the patient's agent shall be counseled about proper use, storage, handling, and disposal of the compounded preparation. The patient or the patient's agent shall also be instructed to report any adverse event and to observe and report to the compounder any changes in the physical characteristics of the compounded preparation (see Chapter (1191), *Responsibility of the Pharmacist*). The compounder shall investigate and document any reported problem with a compounded preparation and shall take corrective action.

TRAINING

All personnel involved in the compounding, evaluation, packaging, and dispensing of compounded preparations shall be properly trained for the type of compounding conducted. It is the responsibility of the compounder to ensure that a training program has been implemented and that it is ongoing. Compounding personnel should be evaluated at least annually. Steps in the training procedure include the following: