Chapter 18

Finished Preparation Release Checks and Tests

Angela W. Yaniv

Introduction

Compounding processes must be designed to prevent errors. Checking processes must be designed to detect any errors that occurred during compounding. Although these concepts seem self-evident, there is a long history of compounding misadventures that have led to patient harm. Chapter 1 discusses this in more detail, and there are several articles outlining compounding errors in the United States.[1,2]

ASHP published a technical assistance bulletin on the topic in 1993 with subsequent revisions in 2000 and 2014.[3-5] In January 2004, the U.S. Pharmacopeial Convention (USP) published USP Chapter <797> Pharmaceutical Compounding—Sterile Preparations, the first national and enforceable requirements for sterile compounding. USP Chapter <797> has been revised since in 2008 with another significant revision currently in draft form as of this writing.[6] The goal of USP Chapter <797> is to prevent harm to patients receiving compounded sterile preparations (CSPs) that could result from microbial contamination, bacterial endotoxins, variability in intended strength of correct ingredients, incorrect ingredients, ingredients of inappropriate quality, or unintended physical or chemical contaminants.[7]

Despite enforceable requirements in place as of 2004, catastrophic compounding errors involving variability from intended strength of ingredients and microbial contamination have occurred.[8-14] Such errors could have been avoided if robust preparation release checks and tests had been in place.

Medication Order Writing and Transcription

Paper medication orders must be transcribed in some fashion to create a compounding label. Preparation of preprinted order forms may help reduce errors in prescribing the appropriate dose or base solution for a CSP. Preprinted orders may also reduce the need for extraneous

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calculations. Because errors can occur in transcription, it is necessary to compare the compounding label with the original order. In manual transcription systems, it is helpful to implement double-checks of order-entry and preparation labels especially for medications and populations at high risk for harm such as chemotherapy orders, neonatal/pediatric patients, and high-alert medications.

When orders are electronically generated and verified, the compounding label represents the electronic order. Electronic medication ordering can be used to standardize concentrations, doses, and base solutions. Properly constructed medication files and electronic order sets can reduce or eliminate the need for extraneous dosing calculations and can ensure that sterile products are ordered in compatible fluids at the appropriate concentrations. Pharmacists with a thorough knowledge of drug dosing and preparation should be involved in constructing drug files and order sets. For batch production of sterile preparations, the batch "recipe" must be defined in writing with all compounding processes detailed so that each batch is made in the same way each time.

Good Documentation Practices

Review of compounding documentation is a critical final release check. Good documentation ensures that all steps in the compounding process actually occurred and is the proof that written policies and procedures were followed. Before final release of the CSP, the pharmacist must verify documentation to ensure the following:

- Proper components were used (vials, ampuls, and final solution container).
- Proper compounding methods were used and were verified (e.g., reconstitution, solution transfer quantities).
- Proper quantities of components were used when compared to desired versus actual yield. For a patient-specific product, the amount of drug needed matches the amount used (i.e., two 500-mg vials were used to prepare one 1,000-mg dose). For a batch, the amount of drug used yields the expected number of doses (i.e., 10 1-g antibiotic syringes were expected and 10 syringes were prepared using one 10-g source vial of antibiotic with no residual solution in the source container).
- Correct labels were used. The label accurately reflects the ingredients used in compounding and is applied to the product without obstructing information needed in administration, such as syringe graduations. For a patient-specific preparation, the label includes the appropriate patient information and identifiers. For batched products, the label includes an internal lot number to identify that batch. Also for batched products, the number of labels printed corresponds with the number of items in the batch. Instances of insufficient or extra labels are investigated as this indicates a potential error in the compounding or labeling of the batch (Chapters 15, 16, and 22).

Good documentation provides enough information to determine how a product or batch was made without relying on the recollection of the compounder or checking pharmacist. It allows retrospective review of a compounding process and provides traceability in the event of an unexpected or untoward outcome. It must be complete, correct, and legible. Elements of good documentation include the following:

- Identification of the compounder
- Identification of the pharmacist responsible for final check and release
- Identification of pharmacist(s) responsible for any interim checks
- Ingredients used in compounding, including lots, expirations, and amounts
- Equipment used in compounding
- Steps followed in the compounding process
- Date the compounding occurred

Component Standards

The selection of appropriate ingredients to use in CSPs is critical to the quality of resulting CSPs. Commercially available sterile components should be sourced only from FDA-registered manufacturers that are required to perform release testing to ensure that the product meets *USP–NF* monograph requirements for purity and strength. Nonsterile active pharmaceutical ingredients (APIs) and