Chapter 22

Batch Compounding

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Introduction

Batch compounding involves the compounding of multiple sterile and/or nonsterile components, in a single discrete process, by the same individuals during one limited time period. It is medium risk only if sterile ingredients and equipment come in contact with the preparation. Batch compounding becomes high risk if any nonsterile ingredients or equipment are used during the compounding process.

The term *batch compounding* has often been associated with compounding of units for multiple patients, but a batch also may be compounded for one patient. For example, hospital pharmacists may compound a batch of identical cardioplegic solutions for multiple patients, while home care practitioners may compound a batch of parenteral nutrition solutions for a single patient's use over several days. Careful documentation of raw materials, preparative processes, product evaluations, final preparation tests and checks is necessary to maintain quality control of batch compounding.

USP Chapter <1075> Good Compounding Practices lists 11 points to account for in control of compounding. Note: USP Chapter <1075> was deleted from the *USP–NF* in May 2011 and is no longer an official chapter. Salient points were merged into USP Chapter <795> Pharmaceutical Compounding—Nonsterile Preparations, which is currently official[1]:

1. The compounder should ensure that there are written procedures for the compounding of drug products to ensure that the finished products have the identity, strength, quality, and purity that they purport to have.
2. The compounder shall establish procedures that include a description of the components, their amounts, the order of component additives, and the compounding process; the required equipment and utensils; and the drug product container and closure system.
3. The written procedures described above shall be followed in execution of the compounding process.

Note: The author acknowledges E. Clyde Buchanan who authored this chapter in the previous edition.

4. The compounder shall accurately weigh, measure, and subdivide as appropriate.
5. The compounder shall check and recheck each procedure at each stage of the process to ensure that each weight or measure is correct as stated in the written compounding procedures.
6. If a component is transferred from the original container to another container (e.g., a powder is taken from the original container, weighed, placed in a container, and stored in the other container), the new container shall be identified with the component name, weight or measure, the lot or control number, the expiration or beyond-use date, and the transfer date.
7. The compounder should have established written procedures that will describe the tests or examinations to be conducted on the preparation compounded (e.g., the degree of weight variation among capsules) to ensure uniformity and integrity of compounded drug preparations.
8. Appropriate control procedures should be established to monitor the output and to evaluate the performance of these compounding processes that may be responsible for causing variability in the final compounded preparations. Factors that may cause variability include capsule weight variations; adequacy of mixing to ensure uniformity and homogeneity; and clarity, completeness, or pH of solutions.
9. Appropriate written procedures should be designed to prevent microbiological contamination of compounded drug preparations purporting to be sterile, and those procedures shall be followed. Such procedures shall include validation of sterilization processes.
10. The compounder should establish appropriate beyond-use dates determined either from available *USP–NF* [*United States Pharmacopeia–National Formulary*] monographs, appropriate testing, or from peer-reviewed journals.
11. The compounder should adopt appropriate storage requirements.

Master Formula Sheets

Master formula sheets and batch control records serve as the foundation of procedures used to establish and maintain quality control for batch compounded sterile preparations (CSPs).

A standardized record of compounding or master formula sheet should be developed for routinely compounded batch preparations (**Figure 22-1**). A master formula sheet will satisfy all of the USP Chapter <795> best quality control practices. To keep batches identical, all compounding activities should be reproduced uniformly by following this master formula sheet or card.

The master formula sheet for a batch of sterile preparations should include the following:

- Name of the CSP
- Beyond-use date of the finished CSP
- Name of ingredients (and chemical grades, if pertinent; see Chapter 4)
- Quantity of ingredients (weight or volume)
- Spaces for the manufacturer's name or national drug code (NDC) number, lot numbers, and expiration dates of ingredients
- Signature space for the compounder doing the weighing or measuring
- Signature space for the pharmacist or compounding supervisor doing in-process checking
- Complete step-by-step directions for compounding
- Packaging instructions
- Labeling instructions (see Chapter 15)
- Control number and beyond-use date of the batch based on the risk level of the preparation (see Chapter 14)
- Theoretical and actual yield (e.g., numbers of units)
- Storage instructions (see Chapter 14)
- Types of assays to be done and the method of collection of samples (e.g., sterility, pyrogen, pH, etc.; see Chapter 18)
- Quarantine period, if any
- Signature space for the pharmacist or compounding supervisor's approval for release of the preparation

The master formula sheet can be copied or printed out and used as the batch control record if it has a location for a batch label; spaces for