

CHAPTER 20
PHARMACY COMPOUNDING PRACTICES

657—20.1(124,126,155A) Purpose and scope. The requirements of this chapter apply to compounding of drugs by Iowa-licensed pharmacists and pharmacies and are minimum good compounding practices for the preparation of drug products for dispensing or administration to humans or animals. Pharmacists and pharmacies engaged in the compounding of drugs shall reference the USP General Chapter entitled <1161> Pharmacy Compounding Practices and shall comply with all applicable provisions of Iowa and federal laws and regulations.

657—20.2(124,126,155A) Definitions.

“*Bulk drug substance*” means any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.

“*Component*” means any ingredient, other than a bulk drug substance, intended for use in the compounding of a drug product, including those that may not be identifiable in the final product.

“*Compounding*” means the preparation, mixing, assembling, packaging, or labeling of a drug or device:

1. For an identified individual patient as a result of a practitioner’s prescription drug order or initiative based on the prescriber/patient/pharmacist relationship in the course of professional practice, or
2. For the purpose of, or as an incident to, research, teaching, chemical analysis, and not for sale or dispensing.

Compounding also includes the preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns pursuant to subrule 20.3(3). Compounding does not include mixing or reconstituting according to a product’s labeling or to the manufacturer’s directions.

“*FDA*” means the United States Department of Health and Human Services, Food and Drug Administration.

“*Manufacturing*” means the production, preparation, propagation, conversion, or processing of a drug or device, either directly or indirectly, by extraction from substances of natural origin or independently by means of chemical or biological synthesis and includes any packaging or repackaging of the substances or labeling or relabeling of its container. Manufacturing also includes the preparation, promotion, and marketing of commercially available products from bulk compounds for resale by pharmacists, practitioners, or other persons.

657—20.3(124,126,155A) General requirements.

20.3(1) *Compounding commercially available product.* Based on the existence of a pharmacist/patient/prescriber relationship and the presentation of a valid prescription, pharmacists may compound, for an individual patient, drug products that are commercially available in the marketplace, if the compounded product is changed to produce for that patient a significant difference, as determined by the prescriber, between the compounded drug and the comparable commercially available drug product. “Significant difference” would include the removal of a dye for a medical reason such as an allergic reaction. When a compounded product is to be dispensed in place of a commercially available product, the prescriber and patient shall be informed that the product will be compounded.

20.3(2) *Substances and components.* In compounding prescriptions, pharmacists shall receive, store, and use components which meet the United States Pharmacopeia (USP) or National Formulary (NF) monograph standards, if such a monograph exists, and which comply with the USP chapter on pharmacy compounding. Pharmacists shall receive, store, and use bulk drug substances manufactured by an establishment which is registered with FDA under the federal Food, Drug, and Cosmetic Act and which sends a valid certificate of analysis for each drug product. Certificates of analysis shall be maintained pursuant to 657—20.12(124,126,155A). Bulk drug substances to be used in compounding prescriptions:

- a. When a monograph exists, shall comply with the applicable USP or NF monograph and the USP chapter on pharmacy compounding; or
- b. If not subject to a monograph, shall be ingredients of drugs that FDA has approved; or
- c. If not subject to a monograph and not ingredients of FDA-approved drugs, shall appear on the FDA list of approved bulk drug products not subject to a monograph.

20.3(3) *Prescriber/patient/pharmacist relationship.* A prescription for a compounded drug shall either be unsolicited or marked with a notation by the pharmacist, and approved by the physician, that the compounded drug is necessary. Pharmacists may compound drugs in very limited quantities prior to receiving a valid prescription based on a history of receiving valid prescriptions that have been generated solely within an established pharmacist/patient/prescriber relationship provided that they maintain the prescriptions on file for all such products compounded at the pharmacy as required by Iowa law and that such compounding is in compliance with the requirements of 657—20.11(126). The sale or other distribution of compounded products to other pharmacies or to prescribers without a prescriber/patient/pharmacist relationship is considered manufacturing. However, compounded products may be provided to a prescriber for the prescriber's use in treatment of the prescriber's patients.

20.3(4) *Advertising and resale of compounded drug products.* Pharmacists shall not offer compounded drug products to other licensed persons or commercial entities for subsequent resale except in the course of professional practice for a practitioner to administer to an individual patient. Compounding pharmacies or pharmacists may advertise or otherwise promote the fact that they provide prescription compounding services; however, they shall not make a claim, assertion, or inference of professional superiority in the compounding of drug products which cannot be substantiated, nor shall they advertise the compounding of any specific drug, class of drug, or type of drug. All advertisements shall meet the requirements contained in 657—8.6(155A,126).

20.3(5) *Compounding prohibited.* Pharmacists shall not compound:

- a. A drug that has been identified by FDA as withdrawn or removed from the market because the drug was found to be unsafe or not effective.
- b. Regularly or in inordinate amounts drugs which are essentially copies of a commercially available drug product except as provided in subrule 20.3(1).
- c. Drugs which have been identified by FDA or the board as products which may not be compounded.

657—20.4(126,155A) Organization and personnel.

20.4(1) *Pharmacist responsible.* As in the dispensing of all prescriptions, the pharmacist has the responsibility and authority to inspect and approve or reject all components, bulk drug substances, drug product containers, closures, in-process materials, and labeling, and has the authority to prepare and review all compounding records to ensure that no errors have occurred in the compounding process. The pharmacist is also responsible for the proper maintenance, cleanliness, and use of all equipment used in prescription compounding practice.

20.4(2) *Pharmacist competence.* All pharmacists who engage in compounding of drugs shall be proficient in compounding commensurate with the level of their compounding activity. Pharmacists shall maintain that proficiency through current awareness and documented training. Every pharmacist who engages in drug compounding shall be aware of, familiar with, and comply with all details of these good compounding practices and all applicable state and federal laws and regulations.

20.4(3) *Pharmacy technicians.* While pharmacy technicians may assist in the compounding of drug products, the supervising pharmacist remains responsible for all work performed by the pharmacy technician.

20.4(4) *Protective apparel.* Personnel engaged in the compounding of drug products shall wear clean clothing appropriate to the operation being performed. Protective apparel shall be worn as necessary to protect personnel from chemical exposure and drug products from contamination.

20.4(5) *Health of personnel.* Only personnel authorized by the responsible pharmacist shall be in the immediate vicinity of the drug compounding operation. Any person shown at any time, either by medical examination or pharmacist determination, to have an apparent illness or open lesions that may adversely affect the safety or quality of a drug product being compounded shall be excluded from direct contact with components, bulk drug substances, drug product containers, closures, in-process materials, and drug products until the condition is corrected or determined by competent medical personnel not to jeopardize the safety or quality of the products being compounded. All personnel who normally assist the pharmacist in compounding procedures shall be instructed to report to the pharmacist any health conditions that may have an adverse effect on drug products.

657—20.5(126,155A) *Drug compounding facilities.* Pharmacies engaging in compounding shall have a specifically designated and adequate area or space for the orderly placement of equipment and materials to be used to compound medications. The drug compounding area for sterile products shall be separate and distinct from the area used for the compounding or dispensing of nonsterile drug products. Any area used for the compounding of drugs shall be maintained in a good state of repair.

20.5(1) *Component and bulk drug substances storage.* Bulk drugs and other materials used in the compounding of drug products shall be stored in adequately labeled containers in a clean, dry area or, if required, under proper refrigeration.

20.5(2) *Facility requirements.* Adequate lighting and ventilation shall be provided in all drug compounding areas. Adequate washing facilities, easily accessible to compounding areas of the pharmacy, shall be provided. These facilities shall include, but not be limited to, hot and cold water, soap or detergent, and air dryers or single-source towels.

20.5(3) *Facility maintenance.* All areas used for the compounding of drug products shall be maintained in a clean and sanitary condition and shall be free of infestation by insects, rodents, and other vermin. Trash shall be held and disposed of in a timely and sanitary manner. Sewage, trash, and other refuse in and from the pharmacy and immediate drug compounding areas shall be disposed of in a safe and sanitary manner.

657—20.6(126,155A) *Sterile products and radiopharmaceuticals.*

20.6(1) *Sterile products.* If sterile products are being compounded, the requirements contained in 657—8.30(126,155A) shall be met.

20.6(2) *Radiopharmaceuticals.* If radiopharmaceuticals are being compounded, the requirements of 657—Chapter 16 shall be met.

657—20.7(126,155A) *Special precaution products.* If drug products with special precautions for contamination are involved in a compounding operation, appropriate measures, including either the dedication of equipment for such operations or the meticulous cleaning of contaminated equipment prior to its return to inventory, shall be utilized in order to prevent cross-contamination.

657—20.8(126,155A) Equipment. Equipment used in the compounding of drug products shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance. Equipment used in the compounding of drug products shall be of suitable composition so that surfaces that contact components, in-process materials, or drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond that desired.

20.8(1) *Equipment maintenance.* Equipment and utensils used for compounding shall be cleaned and sanitized prior to use to prevent contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond that desired. In the case of equipment, utensils, and containers or closures used in the compounding of sterile drug products, cleaning, sterilization, and maintenance procedures as set forth in 657—8.30(126,155A) shall be followed.

20.8(2) *Equipment storage.* Equipment and utensils used for compounding drugs shall be stored in a manner to protect them from contamination. Immediately prior to the initiation of compounding operations, they shall be inspected by the pharmacist and determined to be suitable for use.

20.8(3) *Use of automated equipment.* Automatic, mechanical, or electronic equipment, or other types of equipment or related systems that will perform a function satisfactorily, may be used in the compounding of drug products. If such equipment is used, it shall be routinely inspected, checked, or calibrated if necessary to ensure proper performance.

657—20.9(126,155A) Control of bulk drug substances, components and drug product containers and closures. Drug product containers and closures shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the compounded drug beyond the desired result. Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the compounded drug product. Drug product containers and closures shall be clean and, where indicated by the intended use of the drug, sterilized and processed to remove pyrogenic properties to ensure that they are suitable for their intended use.

20.9(1) *Storage.* Components, bulk drug substances, drug product containers, closures, and bagged or boxed parts of drug product containers and closures used in the compounding of drug products shall be handled and stored in a manner to prevent contamination and to permit inspection and unhindered cleaning of the work area, including floors. Components, bulk drug substances, drug product containers, and closures for use in the compounding of drug products shall be rotated so that the oldest stock is used first.

20.9(2) *Sterile product containers and closures.* Drug product containers and closures intended for the compounding of sterile products shall be handled, sterilized, and stored in keeping with the requirements of 657—8.30(126,155A). Methods of cleaning, sterilizing, and processing to remove pyrogenic properties shall be written and followed for drug product containers and closures used in the preparation of sterile pharmaceuticals, if these processes are performed by the pharmacist or under the pharmacist's supervision, following the requirements of 657—8.30(126,155A).

657—20.10(124,126,155A) Drug compounding controls. Accountability for quality control is the responsibility of the compounding pharmacist.

20.10(1) *Procedures required.* There shall be written procedures for the compounding of drug products to ensure that the finished products have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include a listing of the bulk drug products and components, their amounts in weight or volume, the order of drug product and component addition, and a description of the compounding process. All equipment and utensils and the container/closure system, relevant to the sterility and stability of the intended use of the drug product, shall be listed. These written procedures shall be followed in the execution of the drug compounding procedure.

20.10(2) Accuracy. Components and bulk drug substances for drug product compounding shall be accurately weighed, measured, or subdivided as appropriate. These operations should be checked and rechecked by the compounding pharmacist at each stage of the process to ensure that each weight or measure is correct as stated in the written compounding procedures. If a component or bulk drug substance is removed from the original container to another, such as a powder taken from the original container, weighed, placed in a container, and stored in another container, the new container shall be identified with the component or bulk drug substance name and weight or measure.

20.10(3) Product testing and examination. To ensure the reasonable uniformity and integrity of compounded drug products, written procedures shall be established and followed that describe the tests or examinations to be conducted on the product being compounded, as in the compounding of capsules. Such control procedures shall be established to monitor the output and to validate the performance of those compounding processes that may be responsible for causing variability in the final drug product. Such control procedures shall include, but are not limited to, the following as appropriate:

- a. Capsule weight variation.
- b. Adequacy of mixing to ensure uniformity and homogeneity.
- c. Clarity, completeness, or pH of solutions.

20.10(4) Sterilization. Appropriate written procedures designed to prevent microbiological contamination of compounded drug products purporting to be sterile shall be established and followed. Such procedures shall include validation of any sterilization process.

20.10(5) Labeling with expiration date. Where applicable, the compounded product shall be labeled with an expiration date based upon professional judgment, appropriate testing, or published data.

20.10(6) Labeling and control of excess products. In the case where a quantity of a compounded drug product in excess of that to be initially dispensed in accordance with the general provisions described above is prepared, the excess product shall be labeled or documentation referenced with the complete list of bulk drug substances and components, the preparation date, and the assigned expiration date based upon professional judgment, appropriate testing, or published data. Excess product shall be stored and accounted for under conditions dictated by its composition and stability characteristics to ensure its strength, quality, and purity.

At the completion of the drug finishing operation, the product shall be examined for correct labeling in compliance with the label information requirements contained in rule 20.11(126).

657—20.11(126) Bulk compounding.

20.11(1) Control record. Pursuant to the provisions of subrule 20.3(3), pharmacies may compound drugs in bulk quantities for subsequent prescription labeling and dispensing. Such drugs shall be compounded by or under the direct supervision of a pharmacist. For each drug product compounded in bulk quantities, a master formula record shall be prepared containing the following information:

- a. Name of the product.
- b. Specimen or copy of label.
- c. List of ingredients and quantities.
- d. Description of container used.
- e. Compounding instructions, procedures and specifications.

20.11(2) Production record. For each batch of drug product compounded, a production record shall be prepared and kept containing the following information:

- a. A copy of the information on the master formula record.
- b. Records of each step in the compounding process including:
 - (1) Dates.
 - (2) Identification of ingredients (including lot numbers).

- (3) Quantities of ingredients used.
- (4) Initials of person preparing each process.
- (5) Initials of pharmacist supervising each process.
 - c. A batch number.
 - d. Total yield.

20.11(3) Label information. For each batch of drug product compounded, labels shall be prepared and affixed to each container containing the following information:

- a. Identifying name or formula.
- b. Dosage form.
- c. Strength.
- d. Quantity per container.
- e. Internal control number or date.
- f. Expiration date (if any).
- g. Auxiliary labels, as needed.

657—20.12(124,126,155A) Records and reports. Records shall conform with the control and production record requirements contained in rule 20.11(126).

20.12(1) Record retention. Any procedures or other records required to be maintained in compliance with these good compounding practices shall be retained for at least two years from the date of such procedure or record.

20.12(2) Record availability. All records required to be retained under these good compounding practices shall be readily available for authorized inspection during the retention period at the establishment where the activities described in such records occurred. These records shall be subject to photocopying or other means of reproduction as part of such inspection.

20.12(3) Records form. Records required under these good compounding practices may be retained either as the original records or as other accurate reproductions of the original records.

These rules are intended to implement Iowa Code sections 124.302, 124.303, 124.306, 124.308, 124.501, 126.9, 126.10, 126.18, 155A.2, 155A.28, 155A.33, and 155A.35.

[Filed 10/6/95, Notice 8/16/95—published 10/25/95, effective 11/29/95]

[Filed 12/10/96, Notice 8/28/96—published 1/1/97, effective 2/5/97]

[Filed 2/27/97, Notice 1/1/97—published 3/26/97, effective 4/30/97]

[Filed 4/22/99, Notice 3/10/99—published 5/19/99, effective 6/23/99]