CHAPTER 20
PHARMACY COMPOUNDING PRACTICES

657—20.1(124,126,155A) Purpose and scope. The requirements of this chapter apply to the compounding of drugs by Iowa-licensed pharmacists and pharmacies and are minimum good compounding practices for the preparation of drug products for dispensing or administering to humans or animals. Pharmacists and pharmacies engaged in the compounding of drugs shall comply with all applicable provisions of state and federal laws, rules, and regulations.

657—20.2(124,126,155A) Definitions. For the purposes of this chapter, the following definitions apply:

"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. 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 ingredients that may not be identifiable in the final product.

"Compounding" means preparing, mixing, assembling, packaging, and labeling a drug or device 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 for the purpose of, or incident to, research, teaching, or chemical analysis, and not for sale or dispensing. All compounding, regardless of the type of product, is to be done pursuant to a prescription. Compounding also includes the preparation of drugs or devices in which all bulk drug substances and components are nonprescription or 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 a drug according to the product's labeling or to the manufacturer's directions.

"FDA" means the Food and Drug Administration of the U.S. Department of Health and Human Services.

"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 the drug's or device's container. Manufacturing also includes the promotion, marketing, or preparation from bulk drug substances of commercially available products 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 authorized by the prescriber, between the compounded drug and the comparable commercially available drug product, or if use of the compounded product is in the best interest of the patient. "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.* Pharmacists shall receive, store, and use bulk drug substances manufactured by an establishment that is registered with the FDA under the Federal Food, Drug, and Cosmetic Act and that, if requested, will provide a valid certificate of analysis for each drug product. Certificates of analysis shall be maintained pursuant to rule 20.12(124,126,155A). Bulk drug substances to be used in compounding drugs:

a. When a monograph exists, shall comply with the applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph and the USP chapter on pharmacy compounding; or

b. If not subject to a monograph, shall be ingredients of drugs that the 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 substances not subject to a monograph; or

d. If not subject to a monograph, peer-reviewed medical literature shall support the use and, in the professional judgment of the pharmacist, demonstrate the safety and effectiveness of the substance.

20.3(3) *Prescriber/patient/pharmacist relationship.* A prescription for a compounded drug shall be authorized by the prescriber for a specific patient. Prescriptions for all products compounded at the pharmacy shall be maintained on file at the pharmacy as required by Iowa law. Pharmacists may compound drugs prior to receiving a valid prescription based on a history of receiving valid prescriptions generated solely within an established pharmacist/patient/prescriber relationship. Compounding based on a prescription history is bulk compounding and shall comply with the requirements of rule 20.11(126).

20.3(4) *Advertising and resale of compounded drug products.* The sale of compounded drug products to other pharmacies or to prescribers, except as provided in this subrule, is considered manufacturing. 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. A pharmacy may sell to a hospital pharmacy a compounded drug product prepared pursuant to a prescriber's authorization for administration to a specific patient. The label affixed to the compounded drug product shall identify the pharmacy that compounded the product as the dispensing pharmacy. The original prescription drug order shall be maintained by the dispensing pharmacy. These rules shall not prohibit the hospital pharmacy from billing the patient or the patient's fiscal agent for a compounded product prepared for the patient and purchased by the hospital pharmacy pursuant to this subrule. Compounding pharmacies or pharmacists may advertise or otherwise promote the fact that they provide prescription drug compounding services. Compounding pharmacies or pharmacists shall not make a claim, assertion, or inference of professional superiority in the compounding of drug products that cannot be substantiated. All advertisements shall meet the requirements contained in 657—8.12(126,147). Nothing in these rules shall prohibit the centralized filling or processing of a prescription drug order for a compounded drug product by a central fill or processing pharmacy on behalf of an originating pharmacy as provided in 657—Chapter 18.

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

a. A drug that has been identified by the FDA as withdrawn or removed from the market because the drug was found to be unsafe or ineffective.

b. Regularly or in inordinate amounts drugs that are essentially copies of a commercially available drug product except as provided in subrule 20.3(1).

c. Drugs that have been identified by the 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 prescription drugs, 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. The pharmacist is also responsible for the preparation and review of all records relating to compounding to ensure that no errors have occurred in the compounding process and for the proper maintenance, cleanliness, and use of all equipment used in prescription compounding practice.

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

20.4(3) *Pharmacy technicians.* Pharmacy technicians may assist in the compounding of drug products, but 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 protective apparel as necessary to protect the individuals from chemical exposure and to protect drug products from contamination.

657—20.5(126,155A) Drug compounding facilities. Pharmacies engaged in compounding shall have a specifically designated and adequate area for the orderly placement of equipment and materials to be used to compound drugs. Sterile and nonsterile products shall not be compounded at the same time within the same area.

20.5(1) *Component and bulk drug substance storage.* Bulk drug substances 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, a sink with hot and cold running 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 in a good state of repair and shall be free of infestation by insects, rodents, and other vermin. Sewage, trash, and other refuse in and from the pharmacy and immediate drug compounding areas shall be maintained and disposed of in a timely, 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 of 657—Chapter 13, in addition to the requirements of this chapter, shall be met.

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

657—20.7 Reserved.

657—20.8(126,155A) Equipment. Equipment used in the compounding of drug products shall be of appropriate design and 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 come into contact with 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—Chapter 13 shall be followed.

20.8(2) *Specialized equipment.* If drug products with special precautions to prevent 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.

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 and calibrated if necessary to ensure proper performance.

20.8(4) *Equipment storage.* Equipment and utensils used for compounding drugs shall be stored in a manner to protect them from contamination.

657—20.9(126,155A) Control of bulk drug substances, components, 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 the containers and closures 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 use in the compounding of sterile products shall be handled, sterilized, and stored in compliance with the requirements of 657—Chapter 13. Procedures shall be written, implemented, and followed for cleaning, sterilizing, and processing drug product containers and closures to remove pyrogenic properties.

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.* Procedures for the compounding of drug products shall be written, implemented, and followed to ensure the safety, identity, strength, quality, and purity of the finished product. Such procedures shall include a listing of the bulk drug substances and components, their amounts in weight or volume, the order of bulk drug substance and component addition, and a description of the compounding processes. All equipment, utensils, and the container closure system relevant to the sterility and stability of the intended use of the compounded drug product shall be listed as necessary.

20.10(2) *Accuracy.* Components and bulk drug substances used in the compounding of drug products shall be accurately weighed, measured, or subdivided as appropriate. These operations shall be verified 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 and stored in another container, the new container shall be identified with the name and lot number of the component or bulk drug substance.

20.10(3) *Record.* A production record shall be prepared and kept for each drug product compounded for an individual patient. The record shall include the following information:

a. Production date;

b. List of ingredients and quantity of each ingredient used;

c. Initials of each person involved in each of the compounding steps;

d. Initials of each pharmacist verifying each of the compounding steps;

e. Internal control or prescription number and, if the prescription is filled using a product compounded in bulk pursuant to rule 20.11(126), the internal control number assigned to the batch and recorded in the batch production record.

20.10(4) *Product testing and examination.* To ensure the reasonable uniformity and integrity of compounded drug products, written procedures shall be established, implemented, and followed that describe the tests or examinations to be conducted on the product being compounded to monitor the output and to validate the performance of compounding processes that may be responsible for causing variability in the final drug product. 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(5) *Sterilization.* Appropriate written procedures designed to prevent microbiological contamination of compounded drug products purported to be sterile, including validation of any sterilization process, shall be established and followed.

20.10(6) *Label information required.* The label affixed to or on the dispensing container of any compounded drug product dispensed by a pharmacy pursuant to a prescription drug order, excluding a sterile product compounded pursuant to 657—Chapter 13, shall bear the following:

a. Serial number (a unique identification number of the prescription);

b. The name, telephone number, and address of the pharmacy;

c. The name of the patient or, if such drug is prescribed and compounded for an animal, the species of the animal and the name of its owner;

d. The name of the prescribing practitioner;

e. The date the compounded drug product is dispensed;

f. The directions or instructions for use, including precautions to be observed;

g. The name and quantity or percentage of each bulk drug substance (active ingredient) contained in the compounded drug product. The use of auxiliary labels to accommodate this information is acceptable;

h. The initials or other unique identification of the dispensing pharmacist.

20.10(7) *Labeling—expiration date.* When applicable, the compounded product shall be labeled with an expiration date based on published data. When such data is unavailable, expiration dating shall be based on professional judgment or appropriate testing.

20.10(8) *Labeling and control of excess products.* When a quantity of a compounded drug product is prepared in excess of that to be initially dispensed, the excess product shall be labeled, stored, and accounted for pursuant to rule 20.11(126).

657—20.11(126) Bulk compounding.

20.11(1) *Master formula record.* Pursuant to the provisions of subrule 20.3(3), pharmacies may compound drugs in bulk quantities for subsequent prescription labeling and dispensing. For each drug product compounded in bulk quantity, a master formula record containing the following information shall be prepared:

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 containing the following information shall be prepared and maintained:

a. The information from the master formula record;

b. Records of each step in the compounding process including:

(1) Preparation date;

(2) Identification of ingredients (including lot numbers);

(3) Quantities of ingredients used;

(4) Initials of person completing each step;

(5) Initials of pharmacist verifying each step;

c. Expiration/beyond-use date;

d. Internal control number;

e. Total yield.

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

a. Drug product name or formula;

b. Dosage form;

c. Strength;

d. Quantity per container;

e. Internal control number;

f. Expiration/beyond-use date.

657—20.12(124,126,155A) Records. All records required by this chapter shall be retained as the original records and shall be readily available at the pharmacy for inspection and photocopying by agents of the board or other authorized authorities for at least two years following the date of the record.

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.

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