Basis and Purpose: The purpose of the amendments and additions to these rules are: (1) Rule 3.00.21 - to make the rule consistent with the telehealth provisions of HB 15-1029; (2) Rule 3.00.27 – to specify the conditions under which outlet to outlet reconstitution of a drug may be permitted; (3) Rule 19.01.10 – to clarify the training requirements for pharmacists and pharmacy interns to administer vaccines and immunizations; (4) Rule 21.00.20 - to clarify to whom an in-state prescription drug outlet may distribute compounded prescription drugs, to include naturopathic doctors, direct-entry midwives, and acupuncturists; (5) Rules 21.11.20 and 21.21.90 - to clarify compounded drug recall requirements; (6) Rule 21.20.16 – to describe the conditions under which allergen extracts may be compounded; (7) Rule 21.20.20 – to clarify the requirements for compounding sterile products with 12-hour or less beyond-use dating; and (8) Rule 21.20.60 - To clarify environmental and quality control requirements for Compounding Aseptic Isolators and Containment Isolators.

Authority for Promulgation of Rules: Sections 12-29.5-102, 12-29.5-102.5, 12-37-105.5, 12-37.3-105, 12-42.5-101, 12-42.5-105, 12-42.5-106(2) and (3), 12-42.5-118(6)(b), 12-42.5-120, 12-42.5-130(2), 12-42.5-133, and 24-4-103, C.R.S.

3.00.21 A pharmacist shall make every reasonable effort to ensure that any order, regardless of the means of transmission, has been issued for a legitimate medical purpose by an authorized practitioner. A pharmacist shall not dispense a prescription drug if the pharmacist knows or should ~~have~~ known ~~n~~ that the order for such drug was issued ~~on the basis of an internet-based questionnaire, an internet-based consultation, or a telephonic consultation, all~~ without a valid preexisting patient-practitioner relationship. Such relationship need not involve an in-person encounter between the patient and practitioner if otherwise permissible under Colorado law. A pharmacist may, in good faith, dispense an opiate antagonist pursuant to an order that was issued without a valid preexisting patient-practitioner relationship under the following conditions:

a. The opiate antagonist is not a controlled substance; and

b. The opiate antagonist is approved by the Federal Food and Drug Administration for the treatment of a drug overdose.

3.00.27 Outlet to Outlet Drug Reconstitution. A pharmacist at a prescription drug outlet may reconstitute a prescription originally dispensed in an unreconstituted form pursuant to a patient-specific order at another prescription drug outlet or nonresident prescription drug outlet provided the following conditions are met:

a. The prescription is delivered directly from the originating outlet to the receiving outlet;

b. The prescription is at no time in the physical possession of the patient until after the prescription has been reconstituted;

c. The prescription is reconstituted according to the corresponding manufacturer's directions;

d. The prescription is not a controlled substance;

e. The pharmacist at the receiving outlet does not alter, label or relabel the prescription in any way other than to reconstitute and properly store the prescription; and

f. The originating outlet is ultimately accountable to the Board for the accurate dispensing and reconstitution of the prescription.

19.01.10 Qualifications.

a. A pharmacist certified in immunization, or pharmacy intern under the supervision of a pharmacist certified in immunization, may administer vaccines and immunizations per authorization of a physician. A copy of the authorization shall be maintained at the prescription drug outlet. Routine childhood immunizations, as defined by the Colorado State Board of Health, shall comply with CDC guidelines.

b. Licensees shall be considered "trained" to administer vaccines and immunizations to a person only if:

(1) The pharmacist or pharmacy intern has completed a pharmacy-based immunization delivery course ~~accredited by the Accreditation Council for Pharmacy Education ("ACPE") for~~ of at least 20 hours of training, including ~~12 hours of~~ didactic ~~training~~ and ~~at least 8 hours of~~ live hands-on training that is either accredited by the Accreditation Council for Pharmacy Education or provided by an accredited school or college of pharmacy as part of obtaining a pharmacy degree. Proof of completion of this training shall be posted at the pharmacist's or pharmacy intern's main practice location(s).

(2) The pharmacist or pharmacy intern holds a current basic cardiopulmonary resuscitation (CPR) certification issued by the American Heart Association or the American Red Cross or a basic cardiac life support certification. Proof of certification shall be available at pharmacist's main practice location.

(3) The vaccines are administered in accordance with CDC guidelines.

(4) The prescription drug outlet shall have a current version available, either in hard copy or electronically available, of the CDC reference "Epidemiology and Prevention of Vaccine-Preventable Diseases".

21.00.20 Casual Sales/Distribution of Compounded Products.

a. An in-state prescription drug outlet shall only distribute a compounded product to:

(1) ~~a p~~Practitioners licensed and located in Colorado and authorized by law to prescribe the drug~~,~~;

(2) Colorado licensed/registered acupuncturists, direct-entry midwives, or naturopathic doctors who are located in Colorado and authorized by law to obtain the drug;

(3) ~~to a h~~Hospital prescription drug outlets registered and located in Colorado~~,~~; or

(4) ~~to a h~~Hospital other outlets registered and located in Colorado.

Distribution of the compounded product pursuant to this rule shall be for the sole purpose of drug administration. In-state Prescription Drug Outlets shall not distribute compounded products outside of the state. In-state Prescription Drug Outlets shall dispense compounded products and ship them out of the state only pursuant to patient-specific prescription orders.

b. Pursuant to 21 U.S.C. secs. 331(a), 353(b) and 355(a), nonresident prescription drug outlets shall not distribute compounded products into Colorado. Nonresident prescription drug outlets registered in Colorado shall dispense compounded products and ship them into Colorado only pursuant to valid, patient-specific prescription orders. ~~In-state Prescription Drug Outlets shall not distribute compounded products outside of the state. In-state Prescription Drug Outlets shall dispense compounded products and ship them out of the state only pursuant to patient-specific prescription orders.~~

~~b~~c. Except as provided under CRS 12-42.5-118(15)(a), (b)(I) and (b)(II), the amount of compounded drug product a prescription drug outlet compounds and distributes shall be no more than ten (10) percent of the total number of drug dosage units the prescription drug outlet dispenses and distributes on an annual basis. An in-state compounding prescription drug outlet registered pursuant to CRS 12-42.5-117(9) may distribute compounded product pursuant to CRS 12-42.5-118(15)(a), (b)(I) and (II). All prescription drug outlets shall comply with all applicable federal laws and rules pertaining to the distribution of controlled substance preparations.

~~c~~d. The distributing prescription drug outlet or compounding prescription drug outlet must retain the following information on a current basis for each practitioner, hospital prescription drug outlet or hospital other outlet or, when allowable, each prescription drug outlet, to whom it distributes compounded products:

(1) Verification of practitioner's license, or hospital prescription drug outlet's or hospital other outlet's registration; and

(2) Verification of practitioner's or hospital prescription drug outlet's or hospital other outlet's current Drug Enforcement Administration registration, if controlled substances are distributed;

~~d~~e. Labeling of compounded products which are distributed shall comply with rule 21.11.10(c) or (d) or 21.21.70(c) or (d), whichever is applicable.

~~e~~f. Records of distribution shall comply with rule 11.07.10 or 11.07.20, whichever is applicable.

21.11.20 Patient Monitoring, Adverse Events Reporting, and Product Recall.

a. Outlets which compound shall provide patients and other recipients of compounded preparations with a way to address their questions and report any concerns that they may have with these preparations.

b. The outlet shall have written policies describing specific instructions for receiving, acknowledging; and for recording, or filing, and evaluating reports of adverse events and of the quality of preparation claimed to be associated with compounded preparations.

c. The pharmacist manager shall report to the Board in writing significant errors related to compounded preparations such as those that result in serious personal injury or death of a patient.

d. If a compounded preparation is believed to be defective in any way, or if the Board or Federal Food and Drug Administration makes a written request for a recall of a specific preparation, the outlet shall immediately recall any product dispensed or distributed. Any product remaining in the outlet shall be immediately quarantined and shall not be dispensed or distributed. Recall records shall include at least the following:

(1) Product name, strength, dosage form;

(2) Reason for recall;

(3) Amount of product made;

(4) Date made; and

(5) Amount of product dispensed or distributed.

e. The outlet shall conduct tests, as appropriate, on the recalled product to identify reason product was defective. Results of these tests shall be retained at the outlet.

f. Adverse event reports and product recall records shall be retained and available for inspection at the outlet for at least two years.

21.20.16 Allergen Extracts as CSPs

a. Allergen extracts as CSPs are single dose and multiple dose intradermal or subcutaneous injections and are not subject to the environmental and storage requirements of for CSP Risk Levels provided they are compounded in accordance with the most recent USP <797> guidelines.

b. The compounding process involves simple transfer of commercial sterile allergen products and shall contain appropriate substances in effective concentrations to prevent the growth of microorganisms.

c. The label of each multiple dose container of allergen extracts as CSPs shall list the name of one specific patient and a BUD and storage temperature range based on manufacturers' recommendations or peer-review publications available at the outlet for inspection.

d. Single dose allergen extracts as CSPs shall not be stored for subsequent use.

21.20.20 Definitions of Sterile Compounded Products by Risk Level.

a. Immediate Use CSPS:

(1) Immediate use CSPS are intended only for emergency or immediate patient administration of a CSP, and are exempt from the requirements for low-risk CSPS if:

(a) The compounding process involves a transfer of not more than three (3) commercially manufactured sterile nonhazardous products from the manufacturers' original containers and not more than two (2) entries into any one (1) container;

(b) The compounding process takes less than one (1) hour;

(c) Aseptic technique is followed when compounding occurs outside of ~~class~~ class 5 air quality;

(d) Product administration begins no later than one (1) hour after product preparation; and

(e) The product is labeled with a one (1) hour BUD.

b. Low Risk CSPs;

(1) Low risk CSPs with greater than 12-hour BUD: Applies to compounding sterile products that exhibit characteristics (a) and (b) stated below. All low risk CSPs shall be compounded with aseptic manipulations entirely within ISO Class 5 or better air quality. The products shall be prepared with sterile equipment, sterile ingredients and solutions and sterile contact surfaces for the final product. Low risk includes the following:

(a) The compounding involves only transfer, measuring, and mixing manipulations using no more than three commercially manufactured sterile products and entries into one container package of sterile product to make the CSP; and

(b) Manipulations are limited to aseptically opening ampules, penetrating sterile stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile administration devices, package containers of other sterile products, and containers for storage and dispensing.

(2) Low risk CSPs with 12-hour or less BUD: Applies to low-risk, nonhazardous or radiopharmaceutical CSPs dispensed pursuant to a patient-specific order which are prepared and administered within 12 hours of the preparation or as stated in the corresponding manufacturer's package insert (whichever is less) and the following conditions are met:

(a) The PEC is a CAI; or

(b) The CACI cannot provide isolation from the room and maintain an ISO Class 5 environment during dynamic operating conditions; or

(c) The LAFW or a BSC cannot be located within an ISO Class 7 buffer area; and

(d) This shall not apply to chemotherapeutic preparations subject to USP/NF Chapter 800. Low risk CSPs with 12-hour or less BUD shall meet all of the characteristics of (e) through (h) below: ~~Applies to CSPs if the PEC is a CAI, CACI, LAFW, or BSC that cannot be located within an ISO Class 7 buffer area and that exhibit characteristics (a) through (e) as stated below:~~

~~(a) This subsection (a) shall only apply to low risk level non-hazardous preparations which are compounded pursuant to a patient-specific order. Administration must occur only within the same location where prepared, except in the case or radiopharmaceuticals, and shall begin within 12 hours of preparation or as recommended in the manufacturer's package insert, whichever is less. This subsection (a) shall not apply to chemotherapeutic preparations subject to USP/NF Chapter 800;~~

(~~b~~e) PECs (LAFWs, BSCs, CAIs, CACIs) shall be certified as required and shall maintain ISO Class 5 air quality;

(~~c~~f) PECs shall be in a segregated compounding area restricted to sterile compounding activities that minimize the risk of CSP contamination;

(~~d~~g) The segregated compounding area shall not be in a location that has unsealed windows or doors that connect to the outdoors or high traffic flow, or that is adjacent to construction sites, warehouses, or food preparation or any area that could cause contamination. The segregated area shall not be located next to a sink; and

(~~e~~h) The specifications in cleaning and disinfecting the sterile compounding area, personnel training and competency evaluation of garbing, aseptic work practices and cleaning/disinfection procedures, and viable and non-viable environmental sampling testing shall be followed.

c. Medium Risk CSPs: Sterile products exhibit characteristics (1), (2), or (3) stated below. When CSPs are compounded aseptically under low risk conditions, and one or more of the following conditions exists, such CSPs are at a medium risk level of contamination:

(1) Multiple individual or small doses of sterile products are combined or pooled to prepare a CSP that will be administered either to multiple patients or to one patient on multiple occasions; or

(2) The compounding process includes complex aseptic manipulations other than the single volume transfer; or

(3) The compounding process requires unusually long duration, such as that required to complete dissolution or homogeneous mixing.

d. High Risk CSPs: CSPs compounded under any of the following conditions are either contaminated or at high risk to become contaminated with infectious microorganisms:

(1) Products compounded from non-sterile ingredients or compounded with non-sterile components, containers or equipment before terminal sterilization; or

(2) Sterile contents of commercially manufactured products, CSPs that lack effective antimicrobial preservatives, and sterile surfaces of devices and containers for the preparation, transfer, sterilization, and packaging of CSPs are exposed to air quality worse than ISO Class 5 for more than 1 hour; or

(3) Before sterilization, non-sterile procedures such as weighing and mixing are conducted in air quality worse than ISO Class 7, compounding personnel are improperly garbed and gloved; or water–containing preparations are stored for more than 6 hours; or

(4) It is assumed, and not verified by examination of labeling and documentation from suppliers or by direct determination, that the chemical purity and content strength of ingredients meet their original or compendial specifications in unopened or in opened packages of bulk ingredients.

21.20.60 Environmental Quality and Controls.

a. All CSPs shall be compounded in air quality of a Class 100 (ISO Class 5) environment or better.

b. For the compounding of non-radiopharmaceuticals, all primary engineering controls shall be placed in a buffer area that is of air quality Class 10,000 (ISO Class 7) or better. If the PEC is a CAI or a CACI that provides isolation from the room and maintains ISO Class 5 conditions during dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of CSPs, then it is not required to be placed in an ISO Class 7 buffer area. For the compounding of radiopharmaceuticals, all primary engineering controls shall be placed in a buffer area that is of air quality Class 100,000 (ISO Class 8) or better.

c. The surfaces of the ceiling, walls, floor, fixtures, shelving, counters, and cabinets in the buffer area or clean room shall be smooth, impervious, free from cracks and crevices and non-shedding. Junctures of ceilings to walls shall be coved or caulked. There shall be no sink or floor drains in the buffer area or clean room.

d. An anteroom shall be physically isolated from the buffer area or clean room. In this area, supplies are uncartoned and disinfected. Hand sanitizing and gowning occurs in this area. A demarcation line or barrier identifies the separation of the buffer area from the anteroom area. The air quality of the anteroom shall be Class 100,000 (ISO Class 8) or better.

e. Presterilization procedures for high-risk level CSPs, such as weighing and mixing, shall be completed in no worse than an ISO Class 8 environment.

21.21.90 Patient Monitoring, Adverse Events Reporting, and Product Recall.

a. Outlets which compound CSPs shall provide patients and other recipients of CSPs with a way to address their questions and report any concerns that they may have with CSPs and their administration devices.

b. The outlet shall have written policies describing specific instructions for receiving, acknowledging, and dating receipts; and for recording, or filing, and evaluating reports of adverse events and of the quality of preparation claimed to be associated with CSPs.

c. The pharmacist manager shall report to the Board in writing significant errors related to compounded CSPs such as those that result in serious personal injury or death of a patient.

d. If a CSP is believed to be defective in any way, or if the Board or Federal Food and Drug Administration makes a written request for a recall of a specific preparation, the outlet shall immediately recall any product dispensed or distributed. Any product remaining in the outlet shall be immediately quarantined and shall not be dispensed or distributed. Recall records shall include at least the following:

(1) Product name, strength, dosage form;

(2) Reason for recall;

(3) Amount of product made;

(4) Date made; and

(5) Amount of product dispensed or distributed.

e. The outlet shall conduct tests, as appropriate, on the recalled product to identify the reason the product was defective. Results of these tests shall be maintained at the outlet for at least two years.

f. Adverse event reports and product recall records shall be retained and be available for inspection at the outlet for at least two years.