Basis and Purpose: The purpose of the amendments to this rule are to: (1) implement SB 15-053 concerning pharmacists use of a protocol and standing order to dispense a non-controlled substance opioid antagonist for an opiate-related drug overdose event; and (2) implement HB 15-1039 concerning the donation of prescription medications by licensed health care facilities.

Authority for Promulgation of Rules: Sections 12-42.5-101, 12-42.5-105, 12-42.5-106(2) and (3), 12-42.5-120, 12-42.5-133 and 24-4-103, C.R.S.

3.00.00 DISPENSING.

3.00.10 Limitations. Except as provided in CRS 12-42.5-120(2), no order shall be dispensed or refilled after one year from the date of issue by the practitioner.

3.00.20 Medical Need. No licensee or registrant shall compound, dispense, deliver or distribute any drug to any person in such quantity or in any situation where the licensee or registrant knows or reasonably should know said drug has no recognized medical utility or application. Violation of this rule shall constitute prima facie proof of violation of CRS 12-42.5-123.

The pharmacist may not dispense a prescription drug or a controlled substance to a practitioner based on an order that does not list a specific patient. A prescription order for "office use" is not a valid order.

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 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. 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.

3.00.22 The dispensing of an opiate antagonist, as described in Rule 3.00.21, by a pharmacist shall not constitute unprofessional conduct pursuant to CRS 12-42.5-123 if he or she dispensed the opiate antagonist in good faith pursuant to an order or standing orders and protocols issued to or for the following:

a. A person who is at increased risk of experiencing or likely to experience an opiate-related drug overdose event, ~~which is defined as an acute condition, including but not limited to a decreased level of consciousness or respiratory depression resulting from the consumption or use of a controlled substance, or another substance with which a controlled substance was combined, and that a layperson would reasonably believe to be an opiate-related drug overdose event that requires medical attention~~; or

b. A family member, friend, or other person who is in a position to assist a person who is at increased risk of experiencing or likely to experience an opiate-related drug overdose event; ~~as defined in subsection a. of this Rule 3.00.22.~~ or

c. An employee or volunteer of a harm reduction organization; or

d. A first responder.

e. For the purpose of this Rule 3.00.20, the following definitions apply:

1) "First responder" means a peace officer, firefighter, or volunteer firefighter.

2) "Harm reduction organization" means an organization that provides services, including medical care, counseling, homeless services, or drug treatment, to individuals at risk of experiencing an opiate-related drug overdose event or to the friends and family members of an at-risk individual.

3) "Opiate-related drug overdose event" means an acute condition, including but not limited to, a decreased level of consciousness or respiratory depression resulting from the consumption or use of a controlled substance, or another substance with which a controlled substance was combined, and that a layperson would reasonably believe to be an opiate related drug overdose event that requires medical attention.

4) "Protocol" means a specific written plan, as maintained in a uniform and readily retrievable manner for the purpose of inspection at the prescription drug outlet for at least two (2) years from the date of the latest dispensing transaction related to protocol, for a course of medical treatment containing a written set of specific directions created by a physician, group of physicians, hospital medical committee, pharmacy and therapeutics committee, or other similar practitioners or groups of practitioners with expertise in the use of opiate antagonists.

5) "Standing order" means a prescription order, as maintained in a readily retrievable manner for the purpose of inspection at the prescription drug outlet for at least two (2) years from the date of the latest dispensing transaction related to order, written by a practitioner that is not specific to and does not identify a particular patient.

f. Each prescription drug outlet shall maintain, in a uniform and readily retrievable manner for at least two (2) years from the date of latest transaction related to a standing order, the following record detailing the dispensing of a non-controlled substance opioid antagonist pursuant to a standing order:

1) The full name of the patient, person who is in a position to assist a person who is at increased risk of experiencing or likely to experience an opiate-related drug overdose event, first responder, or harm reduction organization receiving the drug;

2) The full address of the first responder or harm reduction organization receiving the drug;

3) The name, strength and dosage form of the drug dispensed;

4) The quantity of drug dispensed; and

5) The date of dispensing.

3.00.25 First Dose Dispensing. A pharmacist at a prescription drug outlet may dispense up to a seventy two (72) hour supply of a non-controlled substance prescription drug to an LTCF resident pursuant to a duplicate copy of an LTCF chart order provided by another prescription drug outlet for the purpose of providing immediate patient care, on a one time per order basis, if the following conditions are met:

a. The receiving prescription drug outlet records on the prescription order the name and address of the originating prescription drug outlet and the date the order was received by the receiving prescription drug outlet;

b. The receiving prescription drug outlet maintains the order as a prescription order and complies with all requirements for prescription orders specified in Board Rules 2.01.10 through 2.01.40, 3.00.10 through 3.00.51, and 11.04.10; and

c. The originating prescription drug outlet records on the LTCF chart order the name and address of the receiving prescription drug outlet and the date the order was provided to the receiving prescription drug outlet.

3.00.30 Labeling. When a prescription drug is dispensed pursuant to an order, the name of the drug that appears on the container label shall correspond with the identity of the drug contained therein unless otherwise requested by the practitioner.

3.00.40 Expiration Dating. No drug or device shall be dispensed which will be outdated prior to utilization by the consumer, based on the practitioner's directions for use.

3.00.50 Initial Interpretation and Final Evaluation.

a. Initial interpretation means the review of an order accompanied by order entry. The pharmacist(s) conducting the initial interpretation shall be held accountable for the accuracy of the electronic order entry/manual transcription and for drug regimen review.

b. Final evaluation means the review of the final prescription to ensure that the ordered medication is properly prepared and placed in a suitable container with appropriate labeling. The pharmacist(s) conducting the final evaluation shall be held accountable for assuring that the identity of the drug that appears on the prescription label corresponds with identity of drug contained therein. When refills are dispensed, the pharmacist conducting the final evaluation shall be held accountable for the appropriate dispensing of refills including all drug utilization reviews as they pertain to refill dispensing.

c. Drug regimen review includes but is not limited to the evaluation of order(s) and patient records(s) for:

1) Known allergies;

2) Rational therapy and contraindications;

3) Reasonable dose, duration of use, and route of administration considering age, gender, and other patient factors;

4) Reasonable directions for use;

5) Potential or actual adverse drug reactions;

6) Drug-drug interactions;

7) Drug-food interactions;

8) Drug-disease contraindications;

9) Therapeutic duplication;

10) Proper utilization (including over- or under-utilization) and optimum therapeutic outcomes; and

11) Abuse/misuse.

d. A pharmacist shall conduct an initial interpretation of each new order and a pharmacist shall conduct the final evaluation of each order dispensed. When refills are dispensed, the pharmacist making the final evaluation shall be held accountable for the appropriate dispensing of refills. The pharmacist manager shall be held accountable for the maintenance of all appropriate records.

e. The pharmacist making the initial interpretation and final evaluation on prescription or LTCF chart orders shall be identified by either license number, initials, name, or secure electronic identifier on a uniformly maintained, readily retrievable document. The uniformly maintained, readily retrievable document shall bear the license number, initials, name, or secure electronic identifier of any additional pharmacists involved in the dispensing of the order. The pharmacist conducting the initial interpretation and final evaluation may be the same person.

f. In the case where the computer software utilized is not password protected, the initial interpretation and final evaluation shall be maintained in a handwritten format bearing the license number, initials, or name of the responsible pharmacist. In addition, the identification of any other pharmacists involved in the dispensing shall be maintained in the same handwritten format.

3.00.51 Records of Initial Interpretation and Final Evaluation.

a. Records detailing both the initial interpretation and final evaluation shall be retained at the prescription drug outlet for each prescription dispensed and for at least two years from the date of any transaction pertaining to the order. These records shall include at least the following:

1, The license number, initials, name, or secure electronic identifier of the pharmacist conducting the initial interpretation for each new order;

2. The license number, initials, name, or secure electronic identifier of the pharmacist conducting the final evaluation for each new and refill prescription; and

3. The specific date on which each initial interpretation and final evaluation occurred. In the event the initial interpretation and final evaluation for a new order are conducted on separate dates, both dates shall be recorded to state specifically when both occurred.

b. Each outlet shall maintain, in written format, a notice detailing how initial

interpretations and final evaluations are documented in the outlet. Such notice shall include and comply with the following:

1. The manner in which initial interpretations are recorded and maintained in the outlet for all new orders.

2. The manner in which final evaluations are recorded in the outlet for all new and refill prescriptions.

3. A statement that all pharmacy personnel involved in the dispensing of prescriptions have the ability to print, upon request, a record detailing the initial interpretation for each new prescription dispensed and final evaluation for each new and refill prescription dispensed.

4. Such written notice shall be signed and dated by the pharmacist manager. In the event the pharmacist manager changes, the incoming pharmacist manager shall review, sign and date the notice within 72 hours of assuming the duties of pharmacist manager. In the event there is a lapse between the time one pharmacist manager ceases the duty and another assumes the duty, the previous method of recording initial interpretations and final evaluations shall remain in effect.

5. If there are any changes to the outlet's method of documenting initial interpretations and final evaluations, a new written notice detailing the requirements of sections 1, 2, 3, and 4 above shall be executed. This notice shall detail the effective date of change.

6. The outlet shall post these notices on a wall directly next to the outlet's most current Board registration.

7. These notices shall be retained at the outlet for a period of three years from the date last utilized.

8. In the event such notices are not posted, the pharmacist manager shall be held accountable for the failure to post the required notice and any dispensing errors. In the event such notices are not posted during the period of time between one pharmacist manager leaving the position and another assuming the position, the outlet shall be held accountable for the failure to post the required notice and any dispensing errors.

3.00.55 Prescription Flavoring. A flavor additive may be incorporated into a non-sterile prescription under the following conditions:

a. The patient, patient's caregiver, or practitioner who authorized the original prescription shall authorize the flavoring of each new and, if applicable, refilled prescription;

b. The flavor additive shall in no way compromise the stability, safety, or efficacy of the dispensed drug.

c. No expired flavor additive shall be incorporated into a prescription. No flavor additive shall be incorporated which will expire prior to utilization by the patient, based on the practitioner's directions for use.

d. For flavoring additives that do not have expiration dates assigned by the manufacturer or supplier, a pharmacist shall clearly and legibly label the container with the date of receipt and assign a conservative expiration date, not to exceed three (3) years after receipt, to the flavoring additive. In no event shall the labeled date of receipt or assigned expiration date be later altered after originally labeling the container.

e. The following information shall be recorded and maintained in a suitable hard-copy or electronic dispensing record for a period of two years from the date of flavoring the corresponding new or refilled prescription. This record shall be made available, in printed form, for the Board or its representatives immediately upon the request of the Board or its representatives.

(1) Additive's flavor;

(2) Flavor additive's manufacturer

(3) Flavor additive's lot number (if available); and

(4) Flavor additive's expiration date.

f. The pharmacist responsible for conducting the final evaluation of a new or refilled prescription shall also be responsible for the flavoring of the prescription as specified in subsections a., b., and c. of this Rule 3.00.55.

g. The pharmacist manager shall be responsible for subsection d. of this Rule 3.00.55 and the maintenance of records as specified in subsection e. of this Rule 3.00.55.

3.00.60 When a substitution is made on a prescription order, a patient shall be given oral and written notice of this fact at the time such substitution initially occurs, except as provided in CRS 12-42.5-122. On subsequent refilling of a prescription order, such oral and written notices shall not be required unless, in the professional judgment of the pharmacist, the best interest of the patient will be served by giving such notices.

3.00.70 Responsibility for pharmacy technicians. A pharmacist shall be responsible for pharmacy technicians and shall at all times comply with CRS 12-42.5-116(5).

3.00.75 The placement of a prescription into another outer container and the labeling of the container with the patient's name or any other identifying information constitutes the "Practice of Pharmacy" as a function of preparation, packaging, labeling and delivery under CRS 12-42.5-102(31). Individuals who perform this function shall be included in the ratio of pharmacy technicians or interns a pharmacist is permitted to supervise pursuant to 12-42.5-119(1).

3.00.80 Return or Exchange of Drugs, Prescriptions, Medical Devices, and Medical Supplies for Dispensing or Donation.

3.00.81 Definitions.

For the purposes of this rule 3.00.00, the following definitions apply:

a. "Automated cassette" is a container that is filled with a drug. This container may count the drug and may package the drug into a container suitable for dispensing, and may affix a label to the container. These cassettes may be used to dispense drugs in a traditional dispensing system or may be used to package unit-dose medication, or drugs in a unit of issue packaging system. An automated cassette shall not be used for schedule II controlled substances.

b. "Correctional facility" means a facility under the supervision of the United States, the Department of Corrections, or a similar state agency or department in a state other than Colorado in which persons are or may be lawfully held in custody as a result of conviction of a crime; a jail or an adult detention center of a county, city, or city and county; and a private contract prison operated by a state, county, city or city and county.

c. "Customized patient medication package" means a package which contains two or more drugs.

d. "Licensed Facility" means any of the following facilities licensed by the Colorado Department of Public Health and Environment: community mental health center, acute treatment unit, hospital unit, inpatient hospice, nursing care facility, assisted living residence, or long-term care facility.

e. "Medical Device" means an instrument, apparatus, implement, machine, contrivance, implant, or similar or related article that is required to be labeled pursuant to 21 CFR Part 801.

f. "Medical Supply" means a consumable supply item that is disposable and not intended for reuse.

g. "Nonprofit Entity" means a Board registered prescription drug outlet or other outlet which have nonprofit status.

h. "Originating Prescription Drug Outlet" means the prescription drug outlet which initially dispensed the prescription for a resident of a facility.

i. "Package" means to prepare a drug in a container other than the original container. The packaging might include a unit dose dispensing system, single dose, automated cassette, or a container suitable for a traditional system. Unless otherwise specified, this includes preparing a drug in advance of the immediate need for dispensing (prior to the receipt of an order), or pursuant to an existing order.

j. "Single dose package" means a package which contains a quantity of a drug intended for administration as a single dose.

k. "Traditional dispensing system" means a drug package system in which individual doses are not packaged in unit dose packages or unit of issue packages.

l. "Unique identifier" means an implicit or explicit unique identifier from which the originating prescription number can be determined.

~~l~~m. "Unit dose dispensing system" means a drug distribution system which is in a prescription drug outlet or hospital other outlet and uses unit dose packages or unit of issue packages that enable distribution of packaged doses in a manner that preserves the identity of the drug until the time of administration.

~~m~~n. "Unit dose package" means a package which contains one pharmaceutical unit.

~~n~~o. "Unit of issue package" means a package which provides multiple units of doses but separated in a medication card or other specifically designed container.

3.00.82 General Provisions

a. No prescription drug outlet shall accept returned or donated prescriptions, medical devices, or medical supplies for dispensing, or donation except in the following situations:

(1) A prescription drug outlet that complies with rules 3.00.82 through 3.00.~~88~~89 may accept prescriptions, medical devices, and medical supplies for return, dispensing, and donation.

(2) A hospital prescription drug outlet may accept prescriptions and drugs for dispensing or reissue from all areas of the hospital, provided that the integrity of the product and package are maintained and the following requirements are met:

(a) An appropriate, uniformly maintained and readily retrievable record shall be maintained which indicates at least the total number of doses of the drug which were actually administered. This record may be combined with the record permitted by rule 2.01.20(c); or

(b) If the drug was distributed as floor stock in the facility, an appropriate, uniformly maintained and readily retrievable record of such return shall be made. This record shall state the following:

(I) The name of the drug;

(II) The strength of the drug;

(III) The dosage form of the drug if appropriate;

(IV) The quantity of the drug;

(V) The location within the facility to which the drug was originally distributed; and

(VI) The date of the return.

b. ~~Any~~ No prescription drug returned for redispensing or donation from a facility or donated by a prescription drug outlet shall ~~bear an expiration date that is at least six months after the date the prescription was returned~~ be redispensed if it expires prior to utilization by the consumer based on the prescribing practitioner's directions for use.

c. Rules 3.00.80 through 3.00.~~88~~89 do not apply to the Colorado Cancer Drug Repository.

3.00.83 Entities Eligible to Donate or Return Prescriptions ~~to Prescription Drug Outlets~~.

The following may donate or return drugs ~~to prescription drug outlets~~:

a. A correctional facility as defined in 3.00.81(b), ~~and~~ a licensed facility as defined in 3.00.81(d), or any other facility that is required to be licensed pursuant to section 25-3-101, C.R.S. may return prescriptions to ~~the~~ a prescription drug outlet ~~which originally dispensed them~~.

b. A correctional facility ~~and~~, a licensed facility, or any other facility that is required to be licensed pursuant to section 25-3-101, C.R.S. may donate prescriptions to a nonprofit entity as defined in 3.00.81(g) or to a practitioner authorized by law to dispense the prescription.

c. A prescription drug outlet may donate a returned or donated prescription to a nonprofit entity as defined in 3.00.81(g) or to a practitioner authorized by law to dispense the prescription.

3.00.84 Eligibility for Return or Donation.

a. For all prescriptions, medical devices, or medical supplies accepted for return or donation, the prescription drug outlet must ensure that the prescription, medical device, or medical supply was properly stored prior to return or donation. This includes storage at the facility shipment to and from the facility.

b. Drugs which have been dispensed to a resident of a correctional facility, ~~or~~ licensed facility, or any other facility that is required to be licensed pursuant to section 25-3-101, C.R.S. that are eligible for return or donation are as follows:

(1) Drugs which are liquid and the vial is still sealed and properly stored;

(2) Drugs that have been individually packaged and the packaging has not been damaged; and

(3) Drugs that are in the original, unopened, sealed, and tamper-evident unit dose package, unit of issue package, or unit dose dispensing system.

c. Drugs which have been dispensed to a resident of a correctional facility, ~~or~~ licensed facility, or any other facility that is required to be licensed pursuant to section 25-3-101, C.R.S. that are not eligible for Return or Donation are as follows:

(1) Any drug declared to be a controlled substance under any state or federal law or rule except as provided in 3.00.82 a(2);

(2) Any drug dispensed in a traditional dispensing system;

(3) Any drugs dispensed in a customized patient medication package;

(4) Any drug packaged in a single dose package, a unit dose dispensing system, a unit dose package, or a unit of issue package that is not labeled in accordance with 3.01.20 and 3.01.21;

(5) A compounded drug;

(6) Drugs that are adulterated or misbranded as determined by the pharmacist;

(7) Drugs that require refrigeration, freezing, or special storage;

(8) Drugs that require special registration with the manufacturer;

(9) Drugs that do not bear an expiration date at least six months or more from the date of return or donation;

(10) Dispensed drugs that are received from facilities or pharmacies located outside of Colorado; and

(11) Any drug that was not dispensed pursuant to an order.

3.00.85 Records of Receipt of Returned or Donated Prescriptions, Medical Devices, and Medical Supplies.

a. The prescription drug outlet shall retain records for at least two years detailing receipt of donated or returned prescriptions that contain at least the following information:

(1) Name and address of facility or donating prescription drug outlet;

(2) Name and address of originating prescription drug outlet;

(3) Prescription number or unique identifier assigned at originating prescription drug outlet;

(4) Name and address of each prescription drug outlet having possession of the drug, device, or supply after the originating prescription drug outlet and the dates the product was in each prescription drug outlet's possession.

(5) Date of return or donation;

(6) Name, strength, and NDC number of drug received;

(7) Name of medical device or medical supply received; if applicable;

(8) Quantity received;

(9) Date received;

(10) Drug, medical device, or medical supply expiration date;

(11) Receipt record must state, "Returned or Donated Prescription, Device, or "Supply."

b. Records detailing the receipt of returned or donated prescriptions, devices, and supplies, as required by rule 3.00.84(a)(1) through (11) may be maintained electronically if the following requirements are met:

(1) The prescription drug outlet must ensure a daily (i.e., every twenty-four hours) back up is performed for use in restoring required information in case of a system failure;

(2) Have and maintain a complete on-line receipt file that is printable on the inspector's request;

(3) Have a "lock-out" feature that prevents editing of receipt information;

(4) The Board or its inspectors must be able to inspect and review all of the prescription drug receipt transactions of the outlet for the preceding two years. Therefore, immediately upon the oral or written request of the Board or its inspectors, the outlet shall either:

(a) Print a report of all prescription drug receipt transactions for a period of time as the Board or its inspector(s) may specify. The system must be capable of retrieving and printing such a report within a limited time not to exceed two hours; or

(b) Provide a computer terminal and monitor for the sole use of the Board or its inspector(s) to inspect and review prescription drug receipt transactions, and if necessary, provide a person to assist the Board or its inspector(s) for a period of time not to exceed two hours in operating the system. If the outlet elects to comply with this subparagraph (2), the system must also be capable of printing the same reports described in subparagraph (1); or

(5) It is the responsibility of the pharmacist manager of the outlet to ensure that all outlet staff is aware of the requirements of subparagraphs (1) and (2). Any failure or refusal by the pharmacist manager and/or staff to comply with a request by the Board or its inspector(s) will be deemed to be a willful violation of these rules.

3.00.86 Storage of Returned or Donated Prescription, Medical Devices/Supplies, and ~~Medical Supplies~~ Establishment of Handling Fee.

a. Returned or donated prescriptions, medical devices, and medical supplies shall be stored in a separate area from other drug stocks belonging to the pharmacy. This area shall be conspicuously labeled with a sign indicating that such area contains only returned or donated prescriptions, medical devices, or medical supplies.

b. An entity that receives a donated medication, medical device or medical supply may charge the end user a handling fee, which shall not exceed three (3) dollars for each complete prescription, medical device or medical supply dispensed to the end user and shall not resell the donated medication, medical device or medical supply for profit.

3.00.87 Dispensing of Returned or Donated Prescriptions, Medical Devices, or Medical Supplies.

a. Special Conditions for Dispensing Returned or Donated Drugs:

(1) Drug products in manufacturer's unit dose or unit of issue packages may be redispensed as often as necessary, provided that the integrity of the product and package are maintained.

(2) Drug products which have been packaged into unit dose or unit of issue packages in the prescription drug outlet may be redispensed one time only, except as provided for in 3.00.82((a)(2), provided that the integrity of the product and the package are maintained.

(3) Drug products which have been packaged into unit of issue packages in the prescription drug outlet may be redispensed one time only and then only in the package in which originally dispensed, except as provided in (5) below. Partially-used unit of issue packages may not be emptied and the

drugs removed and packaged, nor may additional units of medication be added to partially-used unit of issue packages.

(4) Drug products which have been packaged into single dose packages in the prescription drug outlet may be redispensed one time only and then only in the package in which originally dispensed, except as provided in (5) below. Single dose packages may not be emptied and the drugs removed and packaged.

(5) Drug products which have been packaged into unit of issue packages or single dose packages may be removed from such packages and packaged for dispensing in a traditional dispensing system.

(6) Prescriptions dispensed using returned or donated prescriptions shall be labeled according to CRS 12-42.5-121. Additionally, the label shall state, "Donated or Returned Drug."

b. Records of Dispensing

All records of dispensing shall be compliant with rules 2.00.00, 3.00.00, and 11.00.00. These records of dispensing, including prescription orders, shall be maintained separately from dispensing records of drugs that were not donated or returned.

3.00.88 Donating Returned or Donated Prescriptions, Medical Devices, or Medical Supplies.

a. Prescription drug outlets may donate the returned or donated prescriptions, medical devices, or medical supplies. to any of the following:

(1) Nonprofit entity as defined in 3.00.81(g); or

(2) A practitioner authorized by law to ~~prescribe~~ dispense the drug.

b. Records of donation shall include the following:

(1) The name of the drug, medical device, or medical supply;

(2) The strength of the drug;

(3) The dosage form if appropriate;

(4) The quantity of the drug, medical device, or medical supply;

(5) The manufacturer name and/or NDC number of the drug if labeled only with its generic name;

(6) The date of donation;

(7) The name and address of the donating prescription drug outlet;

(8) The name and address and registration number of the nonprofit entity receiving the drug, medical device, or medical supply, or the name, address, and license number of the practitioner receiving the drug, medical device, or medical supply.

(9) The name and address of the originating prescription drug outlet;

(10) The prescription number or unique identifier assigned to the prescription at the originating prescription drug outlet.

(11) The date the medication expires; and

(12) The name and address of each prescription drug outlet, other than the originating prescription drug outlet, having possession of the prescription and the dates the prescription was in that prescription drug outlet's possession.

c. A copy of the donation record shall be maintained at the prescription drug outlet and a copy of the same record shall be furnished to the receiving individual or entity.

d. Records detailing the donation of prescriptions, medical devices, and medical supplies, as required by rule 3.00.88(b)(1) through (12) may be maintained electronically if the following requirements are met:

(1) The prescription drug outlet must ensure a daily (i.e., every twenty- four hours) back up is performed for use in restoring required information in case of a system failure;

(2) Have and maintain a complete on-line donation file that is printable on the inspector's request;

(3) Have a "lock-out" feature that prevents editing of donation information;

(4) The Board or its inspectors must be able to inspect and review all of the donation transactions of the outlet for the preceding two years. Therefore, immediately upon the oral or written request of the Board or its inspectors, the outlet shall either:

(a) Print a report of all donation transactions for a period of time as the Board or its inspector(s) may specify. The system must be capable of retrieving and printing such a report within a limited time not to exceed two hours; or

(b) Provide a computer terminal and monitor for the sole use of the Board or its inspector(s) to inspect and review donation transactions, and if necessary, provide a person to assist the Board or its inspector(s) for a period of time not to exceed two hours in operating the system. If the outlet elects to comply with this subparagraph (2), the system must also be capable of printing the same reports described in subparagraph (1).

(5) It is the responsibility of the pharmacist manager of the outlet to ensure that all outlet staff are aware of the requirements of subparagraphs (1) and (2). Any failure or refusal by the pharmacist manager and/or staff to comply with a request by the Board or its inspector(s) will be deemed to be a willful violation of these rules.

3.00.89 Record Retention

a. All records of receipt and dispensing shall be maintained for a period of two years from the date of receipt, or from the last dispensing transaction date. Such records shall be maintained separately from all other records of the prescription drug outlet.

b. All records of donation shall be maintained for a period of three years from the date of donation. Such records shall be maintained separately from all other records of the prescription drug outlet.

Basis and Purpose: The purpose of the amendment to this rule is to clarify the requirements of pharmacy personnel identification to the public.

Authority for Promulgation of Rules: Sections 12-42.5-101, 12-42.5-105, 12-42.5-106(2) and (3) and 24-4-103, C.R.S.

4.06.00 Identification of Licensee. A pharmacist, pharmacy intern, pharmacy technician, pharmacy clerk, store manager, or assistant store manager shall at all times while on duty within a prescription drug outlet wear a badge which is visible to the patient and which shall state at least the title accurately reflecting a person's role in the outlet such as Pharmacist, Pharmacy Intern, Pharmacy Technician, Pharmacy Clerk, Store Manager, or Assistant Store Manager ~~and license number. Interns shall wear a badge labeled intern pharmacist~~.

Basis and Purpose: The purpose of the amendment to this rule is to expand the participation of drug therapy management with qualified pharmacists to include advanced practice registered nurses with prescriptive authority in conjunction with the Colorado State Board of Nursing.

Authority for Promulgation of Rules: Sections 12-38-111.6, 12-42.5-101, 12-42.5-105, 12-42.5-106(1)(e) and (2), and 24-4-103, C.R.S.

6.00.00 PHARMACEUTICAL CARE, DRUG THERAPY MANAGEMENT AND PRACTICE BY PROTOCOL.

6.00.10 Definitions.

a. "Pharmaceutical care" means the provision of drug therapy and other pharmaceutical patient care services by a pharmacist intended to achieve outcomes related to the cure or prevention of a disease, elimination or reduction of a patient's symptoms, or arresting or slowing of a disease process. In addition to the preparation, dispensing, and distribution of medications, "pharmaceutical care" may include assessment and evaluation of the patient's medication related needs and development and communication of a therapeutic plan with defined outcomes in consultation with the patient and the patient's other health care professionals to attain the desired outcome. This function includes efforts to prevent, detect, and resolve medication related problems for individual patients. "Pharmaceutical care" does not include prescriptive authority.

b. For the purpose of this Board Rule 6.00.00, a "prescriber" means a physician who is actively and unconditionally licensed by the Colorado Medical Board or an advanced practice registered nurse with prescriptive authority who is actively and unconditionally licensed by the Colorado State Board of Nursing.

~~b~~c. Drug therapy management means the review and evaluation of drug therapy regimens for patients undertaken by a pharmacist in order to provide drug therapy, monitor progress, and modify drug therapy. Drug therapy management may only be undertaken pursuant to an initial diagnosis made by a ~~physician~~ prescriber, a valid order for the therapy, and a written agreement, which delineates proper protocols, to be used and the type of interaction that must occur between the pharmacist and the ~~physician~~ prescriber. Therapeutic interchange programs in inpatient and group model integrated closed HMO settings that are approved by medical staff committees are not considered drug therapy management for purposes of these rules.

~~c~~d. Drug therapy management may include:

1. Collecting and reviewing patient drug histories;

2. Obtaining and checking vital signs;

3. Ordering and evaluating the results of laboratory tests directly, related to management of the drug therapy when performed in compliance with the protocol ordered by the ~~physician~~ prescriber;

4. Modifying drug therapy, when appropriate, in compliance with the protocol ordered by the ~~physician~~ prescriber; and

5. Implementing the drug therapy plan agreed upon between the ~~physician~~ prescriber and the pharmacist, using protocols and managing the therapy according to those protocols.

~~d~~e. Protocol means a specific written plan for a course of medical treatment containing a written set of specific directions created by the ~~physician~~ prescriber, groups of ~~physicians~~ prescribers, hospital medical committee, or pharmacy and therapeutics committee.

1. Protocols must describe the nature and scope of drug therapy management appropriate for certain conditions or diagnoses, and include specific directions for the drug to be used, the specified dosage regimen, dosage forms or route of administration which are authorized. Protocols must include clear criteria and specific directions pharmacists are to follow when implementing and monitoring drug therapy. If the protocol includes ordering and evaluating laboratory tests, the protocol must provide precise instruction as to what tests are to be ordered, the criteria for ordering the tests, how the tests are to be interpreted, and what action the pharmacist is to take dependent upon the test results. If the protocol includes modifying drug therapy, the protocol must provide precise instruction as to the criteria dictating a change, and exactly how the therapy is to be changed.

2. Protocols without specific directions regarding patient treatment or those that are nonspecific, vague, or rely on discretion without definition, are insufficient and may not be used in drug therapy management by the ~~physician~~ prescriber or the pharmacist.

3. Protocols must also include specific instructions for responding to acute allergic or other adverse reactions. The protocols shall be signed and dated by the authorizing ~~physician~~ prescriber or chairperson of the authorizing group or committee.

4. Evidence based protocols. Protocols used by ~~physicians~~ prescribers and pharmacists engaging in drug therapy management must demonstrate a plan of treatment that constitutes evidence-based medicine. This means that the plan of treatment must be guided by or based on current, objective, supportive scientific evidence as published in scientific literature rather than anecdotal observations. Through the use of such protocols, drug therapy management must provide care that meets the standard of care in ~~both~~ all applicable professions.

5. The protocols shall be signed and dated by the authorizing ~~physician~~ prescriber or chairperson of the authorizing group or committee.

~~e~~f. Agreement means a written agreement between a Colorado licensed pharmacist and a Colorado licensed ~~physician~~ prescriber, or a group of Colorado licensed pharmacists and a group of Colorado licensed ~~physicians~~ prescribers that sets forth the specific information required to assure the competent practice of pharmacy in an integrated health care fashion. Either party may withdraw from the agreement at any time.

6.00.20 Drug therapy management requirements for all practice settings.

a. Drug therapy management may only be conducted by a pharmacist upon the presentation of a valid order for a specific, individual patient from that patient's ~~physician~~ prescriber. The order must specify the protocol to be used, and the protocol must either accompany the order, or otherwise be provided to the pharmacist in advance of starting drug therapy management.

b. The pharmacist must ensure that the ~~physician~~ prescriber with whom the pharmacist is working is licensed in Colorado, in good standing, and the protocols used are within the scope of the ~~physician's~~ prescriber's current practice.

c. Prior to initiation of drug therapy management in any setting, the pharmacist or institution must inform the patient that he/she may refuse to participate in drug therapy management. Inpatient or group model integrated closed HMO settings may use the patient's signature on the institution's general consent to treat as the patient's indication to participate in drug therapy management.

d. At a minimum, the written agreement for carrying out drug therapy management between ~~physicians~~ prescribers and pharmacists shall be reviewed annually, and revised, if necessary.

e. Pharmacists may perform by protocol all aspects of drug therapy management referenced in 6.00.10 b and c, provided the protocol complies with 6.00.10 d, and the pharmacists performing these functions are qualified as set forth in section 6.00.30 and are working pursuant to a written agreement with an appropriately qualified ~~physician~~ prescriber.

f. Filing requirements.

1. Pharmacists engaging in drug therapy management must maintain a current copy of the written agreement between the ~~physician~~ prescriber and the pharmacist at the location where drug therapy management is occurring. Pharmacists conducting such therapy in inpatient settings or group model integrated closed HMO's shall maintain a current copy of the general authorization plan as required by 6.00.40 at the location where drug therapy management is occurring. Upon request by the Board or its inspectors such written agreements and general authorization plans shall be submitted to the Board.

2. Pharmacists practicing drug therapy management must also provide the Board documentation of their successful completion of all qualification requirements as set forth below in 6.00.30 upon request. Copies of pharmacy degrees are not required. Copies of completion of residency or other educational programs or certifications must be on file in the location of practice. Attestations from the supervising pharmacist or ~~physician~~ prescriber for clinical practice must be on file.

3. Pharmacists practicing drug therapy management must have a copy of the pertinent protocols at the location at which they are practicing. Upon request by Board inspectors, pharmacists must produce the scientific literature upon which their protocols are derived.

6.00.30 Pharmacist Qualifications.

Any pharmacist engaged in drug therapy management shall meet the following qualifications:

a. Have and maintain an unrestricted license in good standing to practice pharmacy in Colorado; and

b. Meet one of the following qualifications:

1. Proof of completion of a pharmacy residency accredited by the American Society of Health Systems Pharmacists or the American Pharmacists Association in the specialty being practiced; or

2. Proof of completion of one (1) year of practice experience in pharmacotherapy, and 40 hours of onsite supervised clinical practice and training in each area in which the pharmacist is choosing to practice; or

3. Completion of a certificate program accredited by the Accreditation Council for Pharmacy Education in each area of practice, and 40 hours of on-site supervised clinical practice and training in each area in which the pharmacist is choosing to practice; or

4. Completion of at least 40 hours of ACPE approved continuing education regarding clinical practice and 40 hours of onsite supervised clinical practice and training in the area in which the pharmacist is choosing to practice; or

5. Current Board specialty certification from the Board of Pharmaceutical Specialties, current certification from the National Institute for Standards in Pharmacist Credentialing, or current certification from the Commission for Certification in Geriatric Pharmacy. Such credentials must be in the area of pharmacy practice undertaken in the drug therapy management; or

6. In an inpatient or group model integrated closed HMO setting, all of the following criteria shall be met in order to practice drug therapy management:

   a. Forty (40) hours of onsite supervised clinical practice and training in the area(s) in which the pharmacist is choosing to practice;

   b. Protocols must be approved by the health-system's medical committee, or pharmacy and therapeutics committee; and

   c. Documented competency of each area of practice in which the pharmacist is choosing to practice shall be maintained on site.

c. Licensed Colorado pharmacists practicing drug therapy management prior to August 1, 2005, must attest and certify that they were provided clinical training, experience, and oversight practicing in the disease state(s) that they work in, and the physician with whom they are currently practicing must attest that they are practicing to the standard of care required for management of the specific disease. Such attestations must be on file at the site of practice. Documentation of their employment dates must be on file as proof of practice prior to August 2, 2005.

6.00.40 Drug Therapy Management in Inpatient and Group Model Integrated Closed HMO Settings.

a. Pharmacists engaging in drug therapy management in inpatient and group model integrated closed HMO settings must conduct activities pursuant to a valid order and must follow the protocols set forth by the hospital medical committee, or pharmacy and therapeutics committee. They must record all of the items required in subsection c. below for each patient, or the hospital may create a general authorization plan, identifying where such information will be located, and how it will be accessed throughout the facility by participating pharmacists and ~~physicians~~ prescribers. The general authorization plan serves as the pharmacist/~~physician~~prescriber agreement in these settings. The general authorization plan must identify which ~~physicians~~ prescribers and pharmacists are authorized and have agreed to participate in the facility to engage in drug therapy management. The hospital medical committee or pharmacy & therapeutics committee serves as the authorizing agent for the organization's medical staff,

identifying which ~~physician~~ prescriber groups are authorized to participate, and may restrict authorization for certain protocols to specific ~~physician~~ prescriber groups or specialties. A pharmacist engaging in drug therapy management must read, sign and date the plan and the pertinent protocols that he/she agrees to use in the cases undertaken.

b. The pharmacist manager shall ensure that the general authorization plans for drug therapy management are on file in the prescription drug outlet. Changes to the plan must be made as they occur, including the identification of persons participating. Protocols shall be onsite where the drug therapy management takes place and revised as medically necessary.

c. Prior to initiation of drug therapy management, the pharmacist must review the following information:

1. Patient's name, gender, date of birth, height, and weight;

2. Patient diagnosis or diagnoses (from physician);

3. Medication history;

4. Prior lab values;

5. Patient vital signs;

6. Patient known allergies;

7. Emergency contact number.

d. Records of all activity by the pharmacist shall be documented in the patient's chart prior to administration.

e. Pharmacists engaging in drug therapy management shall not delegate drug therapy management activities to any other staff.

6.00.50 Drug Therapy Management in other settings.

a. Every pharmacist or group of pharmacists engaged in drug therapy management in an outpatient setting must have a valid order from the patient's ~~physician~~ prescriber for each specific patient for such therapy, and must operate according to a written agreement and protocol referenced in section 6.00.10.

b. Written agreements shall contain the following information:

1. Participating ~~P~~pharmacist name(s);

2. ~~Physician's~~ Participating prescriber name(s);

3. Diagnoses relevant to the drug therapy to be managed and other patient conditions relevant to maintenance of the patient's health during drug therapy management;

4. Protocols to be employed;

5. Functions and activities the pharmacist will perform, and restrictions or limitations on the pharmacist's management;

6. Method, content and frequency of reports to the ~~physician~~ prescriber;

7. Manner in which pharmacist's drug therapy management will be monitored by the ~~physician~~ prescriber, including method and frequency;

8. A specified time, not to exceed 24 hours, within which the pharmacist must notify the ~~physician~~ prescriber of any modifications of drug therapy;

9. A provision that allows the ~~physician~~ prescriber to override any action taken by the pharmacist when the ~~physician~~ prescriber deems it to be necessary;

10. An effective date of the agreement, and signatures of both parties.

11. A provision addressing how drug therapy management will be handled when the patient has more than one ~~physician~~ prescriber involved in evaluating or treating the medical condition which is the subject of the agreement. All ~~physicians~~ prescribers who are actively involved in the management of the relevant conditions shall be parties to the agreement.

c. Prior to implementation of drug therapy management, pharmacists shall secure the following information:

1. Patient's name, gender, date of birth, height, and weight;

2. Patient diagnosis or diagnoses (from ~~physician~~ prescriber);

3. Medication history;

4. Prior lab values;

5. Patient vital signs;

6. Patient known allergies;

7. Emergency contact number.

d. Pharmacists engaging in drug therapy management shall not delegate drug therapy management responsibilities to any other staff.

6.00.60 Recordkeeping.

a. Pharmacists must document all actions taken in drug therapy management, including but not limited to any data required by the protocol. Records of each patient visit must be transmitted to the ~~physician~~ prescriber in the manner specified in the agreement. Records must indicate when and how the record was transmitted to the ~~physician~~ prescriber.

b. Pharmacists must keep patient records that include:

1. Patient's name, gender, date of birth, height, and weight;

2. Patient diagnosis or diagnoses (from physician);

3. Medication history;

4. Prior lab values;

5. Patient vital signs;

6. Patient known allergies;

7. Date and time the service was rendered;

8. Type of service rendered;

9. Results of interviews with the patient and any diagnostic tests or other pertinent information about the patient's disease;

10. When and how the record was transmitted to the ~~physician~~ prescriber; and

11. Emergency contact number.

6.00.70 Retention of Records.

a. All records of drug therapy management shall be retained for a minimum of seven years from the last date of drug therapy management, or seven years from the patient's 18th birthday, whichever is later. Such records shall be available for inspection by the patient, the ~~physician~~ prescriber, the Board, or any other authorized local, state, or federal law enforcement or regulatory agency.

b. Records may be maintained in an alternative data retention system, such as a data processing system or direct imaging system provided that:

1. The records maintained in the alternative system contain all of the information required on the manual record;

2. The data processing system is capable of producing a hard copy of the record upon the request of the Board, its representative, or of other authorized local, state, or federal law enforcement or regulatory agencies;

3. A back-up is conducted of the data processing system every 24 hours; and

4. The records are immediately available for the previous two years.

6.00.90 Confidentiality.

a. The pharmacist shall provide adequate security to prevent indiscriminate or unauthorized access to confidential records. If confidential health information is transmitted through a data communication device, the confidential health information may not be accessed or maintained by the operator of the data communication device unless specifically authorized to do so by the patient.

b. Patient information is confidential and may be released only as authorized by state and federal law. All protected health information obtained and maintained, including that obtained from the physician or other providers, must be strictly controlled in accordance with the requirements of ~~HIPAA~~ Health Insurance Portability and Accountability Act of 1996 and any rules promulgated pursuant to the act and other federal and state laws and rules. Specifically, pharmacists can only release patient information to:

1. The patient or the patient's agent;

2. A practitioner or another pharmacist if, in the pharmacist's professional judgment, the release is necessary to protect the patient's health and well-being;

3. **The Board or to a person or another state or federal agency authorized by law to receive the confidential record;**

4. **A person employed by a state agency that licenses a practitioner, if the person is performing the person's official duties; and/or**

5. **An insurance carrier or other third party payer authorized by the patient to receive the information.**

6.01.10 Participation Not Mandatory.

a. **No person or entity, as a condition of employment, participation on an insurance provider panel, or otherwise, shall require any ~~physician~~ prescriber to participate in or authorize drug therapy management.**

6.01.20 Board Review.

a. **Board staff will review compliance with this rule and report to the Board regarding complaints and other relevant data associated with the rule every three years.**

Basis and Purpose: The purpose of the amendment to this rule is to clarify the requirements of the electronic maintenance of immunization records.

Authority for Promulgation of Rules: Sections 12-42.5-101, 12-42.5-105, 12-42.5-106(2) and (3) and 24-4-103, C.R.S.

19.00.00 ADMINISTRATION.

19.01.00 Vaccines and Immunizations.

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 at least 12 hours of didactic training and at least 8 hours of live hands-on training. 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".

19.01.20 A trained pharmacist may delegate the administration of vaccines and immunizations only to a trained pharmacy intern.

19.01.30 Policies and Procedures

a. Prior to administering vaccines or immunizations, pharmacists and pharmacy interns must be trained in a pharmacy-based immunization delivery course accredited as detailed in rule 19.01.10(b).

b. The prescription drug outlet must maintain and follow written policies and procedures for handling and disposal of used and contaminated equipment

and supplies. The prescription drug outlet must obtain a physician protocol for addressing allergic reactions to immunizations.

c. The prescription drug outlet must give the appropriate "Vaccine Information Statement" (VIS) to the patient or legal representative with each dose of vaccine covered by these forms. The pharmacist must ensure that the patient or legal representative has received and signed the informed consent form and has had their questions answered prior to the administration of the vaccine.

d. The prescription drug outlet must report adverse events as required by the Vaccine Adverse Events Reporting System (VAERS) and to the primary care provider as identified by the patient.

19.01.40 Recordkeeping.

a. The following information must be maintained by the prescription drug outlet for three years for each dose of vaccine or immunization administered:

(1) The name, address, and date of birth of the patient;

(2) Patient responses to screening questions for indications/contraindications to the immunization or vaccine being administered;

(3) The date of the administration and site of injection of the immunization or vaccine;

(4) The name, dose, manufacturer, lot number, and expiration date of the vaccine or immunization;

(5) The name and address of the patient's primary health care provider as identified by the patient;

(6) The name or identifiable initials of the administering pharmacist. If the administration is by a pharmacy intern, the initials of both the intern and supervising pharmacist;

(7) The signed informed consent document for each administration;

(8) Which vaccine information statement (VIS)was provided;

(9) The date the VIS was provided; and

(10) The name and address of the facility at which the vaccine or immunization was administered, if administered off-site.

b. The above records shall be maintained separately from other records of the prescription drug outlet.

c. All records required to be maintained pursuant to this Rule 19.00.00 may be maintained electronically so long as such records are maintained in a uniform and readily retrievable manner, are printable upon request of the

Board or its inspectors, and can be reviewed at a viewable rate that may customarily be reviewed when otherwise in hard-copy form.

19.01.50 Off-Site Administration of Immunizations and Vaccines

a. A prescription drug outlet may allow a licensed pharmacist to remove immunizations and vaccines from the prescription drug outlet, provided the following requirements are met:

(1) The prescription drug outlet maintains records which detail the removal of the immunizations and vaccines with at least the following information:

(a) Name, strength, dosage form, and NDC number of the immunization or vaccine removed;

(b) Quantity removed;

(c) Date removed;

(d) Name and license number of pharmacist removing the immunization or vaccine.

(2) The immunizations and vaccines are properly stored at compendial temperatures during transport and storage at the off-site location.

(3) The vaccines and immunizations shall be secured during transport and storage at the off-site location so as to allow only licensed pharmacists and interns affiliated with the prescription drug outlet to have access to them.

(4) The remaining vaccines and immunizations shall be returned to the prescription drug outlet the day they were removed.

(5) The prescription drug outlet shall maintain records detailing the vaccines and immunizations returned with at least the following information:

(a) Name, strength, dosage form, and NDC number of the immunizations or vaccines returned;

(b) Quantity returned;

(c) Date returned; and

(d) Name and license number of pharmacist returning the immunization or vaccine.

b. All required records shall be maintained in a manner that is uniformly maintained, readily retrievable, and available for inspection for a period of three years from the date of removal off immunizations or vaccines for off-site administration.

Basis and Purpose: The purpose of the amendments to this rule are to clarify the requirements for: (1) compounding radiopharmaceuticals; and (2) the electronic maintenance of records required to be kept under Board Rule 21.00.00.

Authority for Promulgation of Rules: Sections 12-42.5-101, 12-42.5-105, 12-42.5-106(2) and (3), and 24-4-103, C.R.S.

21.00.00 COMPOUNDING.

The purpose of this rule is to codify the compounding of preparations to assure that they are of acceptable strength, quality and purity.

If the pharmacist compounds a preparation according to the manufacturer's labeling instructions, then further documentation is not required. All other compounded preparations require further documentation as set forth in this rule.

Compounding of investigational products may be exempt from sections of rule 21.00.00 when compounding is restricted to utilizing ingredients that are regulated by the Federal Food and Drug Administration through an Investigational Review Board (IRB) and when the IRB- approved protocol requires deviation from this rule.

21.00.10 Limitations and Record-Keeping.

a. No non-controlled substance preparation shall be compounded in advance in such quantity as may exceed a 90-day supply or is necessary to accurately compound the preparation. A 90-day supply shall be determined by the average number of dosage units dispensed or distributed of said preparation during the previous 6 month period. All prescription drug outlets shall comply with all applicable federal laws and rules pertaining to the compounding and dispensing of controlled substance preparations, including any federal laws or rules pertaining to compounding controlled substance preparations in anticipation of immediate need.

b. No expired components may be used in compounding. No component may be used which will expire prior to the beyond-use date of the final compounded product. No expired final compounded product shall be dispensed or distributed.

c. All records required to be maintained pursuant to this Rule 21.00.00 may be maintained electronically so long as such records are maintained in a uniform and readily retrievable manner, are printable upon request of the Board or its inspectors, and can be reviewed at a viewable rate that may customarily be reviewed when otherwise in hard-copy form.

21.00.20 Casual Sales/Distribution of Compounded Products.

a. An in-state prescription drug outlet shall only distribute a compounded product to a practitioner licensed and located in Colorado and authorized by law to prescribe the drug, to a hospital prescription drug outlet registered and located in Colorado, or to a hospital other outlet registered and located in Colorado. Distribution of the compounded product pursuant to this rule shall be for the sole purpose of drug administration. 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. 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 ~~or compounding 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 ~~or compounding 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. 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. 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. Records of distribution shall comply with rule 11.07.10 or 11.07.20, whichever is applicable.

21.00.30 Definitions. When used in this Rule 21.00.00, the following words and terms shall have the following meanings, unless the context clearly indicates otherwise.

a. Active Pharmaceutical Ingredient (API): Chemicals, substances or other components of preparations intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases in human or other animals or for use as dietary supplements.

b. Batch (Lot): Multiple units of the same compounded preparation in a single discrete process, by the same individuals, carried out during one limited time period.

c. Beyond-Use Date (BUD): A date after which a compounded preparation should not be stored, used or transferred and is determined from the date the preparation is compounded.

d. Component (ingredient): Any substance which is contained in a compounded preparation.

e. Compounding:

(1) The preparation, mixing, or assembling, of one or more active ingredients with one or more other substances, or the assembling of a finished device:

(a) Formulated for use on or for the patient as the result of a practitioner's prescription drug order, chart order, or initiative, based on the relationship between the practitioner, patient, and pharmacist in the course of professional practice; or

(b) For the purpose of, or as an incident to, research, teaching, or chemical analysis and not for sale or dispensing; or

(c) In anticipation of prescription orders based on routine, regularly-observed prescribing patterns.

(2) Compounding does not include the preparation of copies of commercially available drug products. Compounded preparations that produce, for the patient, a significant difference between the compounded drug and the comparable commercially available drug product as determined, by the prescriber, as necessary for the medical best interest of the patient are not copies of commercially available products. "Significant differences" may include, but are not limited to, the removal of a dye for medical reasons (such as allergic reaction), changes in strength, and changes in dosage form or delivery mechanism. Price differences are not a "significant" difference to justify compounding.

f. Preparation or Product: A compounded drug dosage form, a compounded dietary supplement, or a finished device.

g. Quality Assurance (QA): Set of activities used to ensure that the processes used in the preparation of non-sterile or sterile drug products lead to products that meet predetermined standards of quality.

h. Quality Control (QC): Set of testing activities used to determine that the ingredients, components and final non-sterile or sterile drug products prepared meet pre-determined requirements with respect to strength, identity, quality, and purity.

i. Repackaging: The subdivision or transfer of a product from one container or device to a different container or device. Repackaging does not constitute compounding, whether or not the product being repackaged was previously compounded.

j. SOPS: Standard operating procedures.

k. Stability: Extent to which a preparation retains, within specified limits, and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of compounding.

l. USP/NF: The current edition of the United States Pharmacopeia/National Formulary.

m. Validation: Documented evidence providing a high degree of assurance that specific processes will consistently produce a product meeting predetermined specifications and quality attributes.

n. Vehicle: A component for internal or external use that is used as a carrier or diluent in which liquids, semisolids, or solids are dissolved or suspended. Examples include, but are not limited to, water, syrups, elixirs, oleaginous liquids, solid and semisolid carriers, and proprietary products.

21.10.00 Compounding of Non-Sterile Products.

21.10.10 Policy and Procedure Manual.

a. A manual, outlining policies and procedures encompassing all aspects of non-sterile compounding shall be available for inspection at the pharmacy. The manual shall be complied with and shall be reviewed on an annual basis. Such review shall be signed and dated by the pharmacist manager. In the event the pharmacist manager changes, the new manager shall review, sign, and date the manual within 30 days of becoming pharmacist manager. The pharmacist manager shall ensure compliance with the manual.

b. The policy and procedure manual shall address at least the following:

(1) Responsibility of compounding personnel;

(2) Verification of compounding accuracy;

(3) Personnel training and evaluation in compounding skills;

(4) Environmental quality and control;

(5) Labeling and recordkeeping;

(6) Finished preparation release check;

(7) Quality control procedures, as appropriate;

(8) Storage and beyond-use dating;

(9) Adverse event reporting and recalls; and

(10) Quality assurance program.

21.10.20 Personnel Education, Training and Evaluation.

a. All pharmacy personnel preparing non-sterile compounded products must receive suitable training.

b. Documentation of training of personnel shall be retained at the pharmacy and be available for inspection.

21.10.30 Environmental Quality and Controls.

a. The area used for compounding shall have adequate space for the orderly placement of equipment and materials to prevent mix-ups between ingredients, containers, labels, in-process materials, and finished preparations.

b. The compounding area shall be designed, arranged, used, and maintained to prevent adventitious cross-contamination.

c. Non-sterile compounding areas shall be separate and distinct from any sterile compounding area.

d. The entire compounding area is to be well-lighted. Heating, ventilation, and air conditioning systems are to be controlled to avoid decomposition of chemicals.

e. Storage areas shall provide an environment suitably controlled to ensure quality and stability of bulk chemicals and finished preparations.

f. All components, non-freestanding equipment, and containers shall be stored off of the floor and in a manner to prevent contamination and permit inspection and cleaning of the compounding / dispensing area.

g. Compounding areas shall be maintained in a clean and sanitary condition. Adequate washing facilities are to be provided, including hot and cold running water, soap or detergent, and air driers or single-service towels. The plumbing system shall be free of defects that could contribute to contamination of any compounded preparation.

h. Purified water shall be used for compounding nonsterile preparations when formulations indicate the inclusion of water. Purified water shall also be used for rinsing equipment and utensils used in compounding.

i. Sewage, trash, and other refuse in the compounding area are to be disposed of in a safe, sanitary, and timely manner.

j. Special precautions shall be taken to clean equipment and compounding areas meticulously after compounding preparations that contain allergenic ingredients.

21.10.40 Equipment.

a. Equipment shall be of appropriate design and capacity, and be operated within designed operational limits.

b. Equipment shall be of suitable composition so that surfaces that contact components, in-process material, 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 the desired result.

c. Appropriate cleaning processes shall be in place to insure cleanliness of equipment.

d. Written procedures outlining required equipment, calibration, appropriate maintenance, monitoring for proper function, controlled procedures for use of the equipment and specified time frames for these activities shall be established and followed. Results of equipment calibration and appropriate maintenance reports shall be kept on file at the outlet for at least two years from the report date. These results shall be available for inspection.

21.10.60 Components.

a. Compounding personnel shall ascertain that ingredients for compounded products are in compliance with rule 21.00.10(b) and are of the correct identity and appropriate quality using the following information: vendors' labels, labeling, certificates of analysis, direct chemical analysis, and knowledge of compounding facility storage conditions. No expired components may be used in compounding. No component may be used which will expire prior to the beyond-use date of the preparation.

b. Ingredients used in a compounded preparation shall either originate from FDA-approved sources, ~~if~~ when available, or be USP/NF grade substances, when such sources are not available and identified on the FDA drug shortage list.

c. If neither USP/NF grade substances nor FDA-approved substances are available, or when food, cosmetics, or other substances are, or must be used, the substance shall be of a chemical grade in one of the following categories:

(1) Chemically Pure (CP);

(2) Analytical Reagent (AR); or

(3) American Chemical Society (ACS); or

(4) Food Chemical Codex.

d. For all ingredients, unless FDA-approved, the pharmacist shall establish purity and stability by obtaining a certificate of analysis from the supplier. The certificate of analysis, when applicable, shall be maintained at the prescription drug outlet for at least two years from the date of preparation.

e. For components that do not have expiration dates assigned by the manufacturer or supplier, a pharmacist shall clearly and legibly label the container with the date of receipt and assign a conservative expiration date, not to exceed three (3) years after receipt, to the component based on the nature of the component and its degradation mechanism, the container in which it is packaged, and the storage conditions. A pharmacist shall clearly and legibly label the container with the assigned expiration date. In no event shall the labeled date of receipt or assigned expiration date be later altered after originally labeling the container.

f. A manufactured drug product may be a source of active ingredient. Only manufactured drugs from containers labeled with a lot number and an expiration date are acceptable as a potential source of active ingredients. When compounding with manufactured drug products, the compounder must consider all ingredients present in the drug product relative to the intended use of a compounded preparation.

g. Drug preparations that have been withdrawn or removed from the market for safety reasons shall not be compounded. Such preparations may be compounded exclusively for veterinary use provided no documentation exists which indicates that the preparation is unsafe for such use.

h. Any ingredient regulated by the FDA through an Investigational Review Board (IRB) is exempt from rule 21.10.60 provided the research requirements for the receipt of the ingredient is followed and meets the requirements of CRS 12-42.5-128(2).

21.10.65 Packaging and Drug Preparation Containers

a. Pharmacy personnel shall ensure that the containers and container closures used in the packaging of compounded preparations meet all applicable USP requirements and, when available, compounding monographs.

b. The containers and closures shall be made of suitable clean material in order not to alter the quality, strength, or purity of the compounded preparation in any way.

c. The containers and closures shall be stored off of the floor, handled and stored to prevent contamination, and rotated so that the oldest stock is used first. The containers and closures shall be stored in such a way as to permit inspection and cleaning of the compounding / dispensing area.

21.10.70 Finished Preparation Release Checks.

a. Physical Inspection

(1) Written procedures for physical inspection of compounded preparations shall be followed. Immediately after compounding, and prior to dispensing or distribution, each product shall be inspected for evidence of particulates or other foreign matter, container-closure integrity, and any other apparent visual defect. Defective product shall be segregated from other product and shall not be dispensed or distributed.

b. Compounding Accuracy Checks

(1) Written procedures for double-checking compounding accuracy shall be followed for every compounded product during preparation and immediately prior to release. Outlets which compound shall have at least the following written procedures for verifying the correct identity and quality of compounded products prior to dispensing or distribution:

(a) Verification of label for accuracy; and

(b) Correct identities, purities, and amounts of ingredients have been used by comparing the original written order to the written compounding record for the compounded product.

21.10.80 Storage and Beyond-Use Dating.

a. Completed compounded preparations that are not immediately dispensed or distributed shall be stored according to the guidelines in the formulation record.

b. In the absence of stability information that is applicable to the lowest and highest dose or concentration of a specific preparation compounded at the outlet, the following maximum beyond-use dates are to be used for non-sterile compounded preparations that are packaged in tight, light-resistant containers and stored at controlled room temperature unless otherwise indicated.

(1) For non-aqueous liquids and solid formulations

(a) Where the manufactured drug product is the source of the active ingredient, the beyond-use date shall not exceed 25% of the time remaining until the product's expiration date or 6 months, whichever is earlier;

(b) Where a USP/NF substance is the source of active ingredient, the beyond-use date shall not be greater than 6 months;

(2) For water-containing oral formulations prepared from ingredients in solid form, regardless of whether an ingredient contains water or water by itself is an ingredient, the beyond-use date shall not be greater than 14 days when stored at cold temperatures;

(3) For intranasal formulations, the beyond-use date shall not be greater than 30 days;

(4) For all other formulations, including topical, dermal, mucosal, liquids and semi-solid formulations, the beyond-use date shall not be greater than the intended duration of therapy or 90 days;

(5) The beyond-use date limits may be exceeded when there is supporting valid scientific stability information that is directly applicable to the specific preparation. This information shall be retained on-site at the outlet and be available for inspection.

21.10.90 Formulation Record.

a. For each compounded preparation, a uniform, readily retrievable formulation record shall be maintained and available for inspection for two years from the date last utilized, documenting:

(1) The official or assigned name, strength, dosage form, and route of administration of the compounded preparation;

(2) Calculations needed to determine and verify quantities or concentrations of components and doses of APIs;

(3) All ingredients and their quantities;

(4) Compatibility and stability information, including references when available;

(5) The equipment used to compound the preparation;

(6) Mixing instructions that shall include:

(a) order of mixing;

(b) mixing temperatures or other environmental controls:

(c) duration of mixing; and

(d) other factors pertinent to the replication of the preparation as compounded;

(7) Sample labeling information which shall include, in addition to other required information;

(a) generic name and quantity or concentration of each API;

(b) assigned BUD;

(c) storage conditions; and

(d) assigned prescription or control number, whichever is applicable;

(8) The assigned BUD;

(9) The containers used in dispensing;

(10) Packaging and storage requirements;

(11) Physical description of final product; and

(12) Procedures for quality control, if applicable.

21.11.00 Compounding Record.

a. For each compounded product prepared, a record shall be maintained and available for inspection for two years on the original order, or on a separate, uniform, and readily retrievable record documenting the following:

(1) The official or assigned name and strength of the compounded preparation;

(2) Formulation record reference for the preparation;

(3) Names and corresponding quantities of all components used in the preparation;

(4) Sources, lot numbers, and expiration dates of each component;

(5) Total number of dosage units compounded;

(6) Name of the person who compounded the preparation;

(7) Name of the pharmacist who approved the preparation;

(8) Batch (lot) number assigned, if multiple units compounded;

(9) Date prepared;

(10) Assigned BUD;

(11) Assigned prescription number(s) or control number(s), whichever is applicable;

(12) Storage conditions;

(13) Physical description of the final product;

(14) Results of quality control procedures, if applicable; and

(15) Documentation of any quality control issues and any adverse reactions or preparation problems reported by the patient or caregiver.

21.11.10 Labeling of Non-Sterile Compounded Preparations.

a. Labeling of non-sterile compounded products dispensed pursuant to a prescription order or LTCF chart order shall include at least the following:

(1) All requirements of CRS 12-42.5-121;

(2) Batch (lot) number, if appropriate;

(3) Assigned BUD;

(4) Storage directions when appropriate; and

(5) A clear statement that this product was compounded by the pharmacy, except for radiopharmaceuticals prepared from FDA-approved, commercially available kits and/or drug products.

b. Labeling of non-sterile compounded products dispensed pursuant to a hospital chart order shall include at least the following:

(1) All requirements of CRS 12-42.5-121;

(2) Batch (lot) number, if appropriate;

(3) Assigned BUD; and

(4) Storage directions, when appropriate.

c. Labeling of non-sterile compounded products distributed to practitioners, other prescription drug outlets, or other outlets allowed by law or made in anticipation of orders shall include at least the following:

(1) Name and address of the outlet;

(2) Name and strength of the drug(s) / active ingredient(s) in the final product;

(3) Total quantity in package;

(4) Assigned BUD;

(5) Batch (lot) number;

(6) Specific route of administration;

(7) Storage directions, when appropriate;

(8) "Rx only"; and

(9) "This product was compounded by the pharmacy", except for radiopharmaceuticals prepared from FDA-approved, commercially available kits and/or drug products.

d. Labeling of non-sterile compounded products distributed within hospitals as floor stock shall include at least the following:

(1) Name of the outlet;

(2) Name and strength of the drug(s);

(3) Total quantity in package;

(4) Quantity of active ingredient in each dosage unit;

(5) Assigned BUD;

(6) Batch (lot) number;

(7) Specific route of administration; and

(8) Storage directions, if appropriate.

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, 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.

21.20.00 Compounding of Sterile Products (CSPs).

21.20.10 Definitions. In addition to the definitions set forth above in rule 21.00.30, when used in these rules 21.20.00 et seq., 21.21.00 et seq. and 21.22.00 et seq., the following words and terms shall have the following meanings, unless the context clearly indicates otherwise.

a. Anteroom: An ISO Class 8 (Class 100,000) or better area where personnel perform hand hygiene and garbing procedures, staging of components, order entry, labeling, and other activities which generate particulates. It is a transition area that provides assurance that air flows from clean to dirty areas.

b. Aseptic Processing: A mode of processing pharmaceutical and medical products that involves the separate sterilization of the product and of the packaging and the transfer of the product into the container and its closure under at least ISO Class 5 conditions.

c. Biological Safety Cabinet (BSC): A ventilated containment unit for personnel, product, and environmental protections having an open front with inward airflow for personnel protection, downward HEPA filtered laminar airflow for product protections, and HEPA filtered exhausted air for environmental protections.

d. Buffer Area: An ISO Class 7 (Class 10,000), or an ISO Class 8 for the preparation of radiopharmaceuticals, area where the primary engineering control is physically located. Activities conducted in this area include the preparation and staging of components and supplies when compounding sterile products. This area may also be referred to as a buffer or core room, buffer or cleanroom areas, buffer room area, buffer or clean area.

e. Class 100 Environment (ISO Class 5): An atmospheric environment which contains less than one hundred (100) particles 0.5 microns in diameter per cubic foot of air, according to federal standards.

f. Class 10,000 Environment (ISO Class 7): An atmospheric environment which contains less than ten thousand (10,000) particles 0.5 microns in diameter per cubic foot of air, according to federal standards.

g. Class 100,000 Environment (ISO Class 8): An atmospheric environment which contains less than one hundred thousand (100,000) particles 0.5 microns in diameter per cubic foot of air according to federal standards.

h. Clean Room: A room in which the concentration of airborne particles is controlled to meet a specified airborne particulate cleanliness class. Microorganisms in the environment are monitored so that a microbial level for air, surface, and personnel is not exceeded for a specified cleanliness class.

i. Compounding Aseptic Containment Isolator (CACI): A compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer process and to provide an aseptic environment for compounding sterile preparations. Air exchange

with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where volatile drugs are prepared, the exhaust air from the isolator should be appropriately removed by properly designed building ventilation.

j. Compounding Aseptic Isolator (CAI): A closed system made up of solid walls, an air-handling system, and transfer and interaction devices. The walls are constructed so as to provide surfaces that are cleanable with covering between wall junctures. The air-handling system provides HEPA filtration of inlet air. Transfer of materials is accomplished through air locks, glove rings, or ports. Transfers are designed to minimize the entry of contamination. Manipulations can take place through either glove ports or half suits. A barrier isolator is designed for compounding sterile products. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer process. Air exchange into the isolator from the surrounding environment should not occur unless it has first passed through a HEPA filter.

k. Compounded Sterile Products (CSPs): A sterile drug or nutrient compounded in a registered prescription drug outlet or other outlet. Such products may include, but are not limited to, implants, injectables, parenteral nutrition solutions, irrigation solutions, inhalation solutions, intravenous solutions and ophthalmic preparations.

l. Critical Area: An ISO Class 5 environment.

m. Critical Sites: Include sterile ingredients of CSPs and locations on devices and components used to prepare, package, and transfer CSPs that provide opportunity for contamination.

n. Cytotoxic Drugs: A pharmaceutical product that has the capability of direct toxic action on living tissue that can result in severe leucopenia and thrombocytopenia, depression of the immune system and the alteration of a host's inflammatory response system.

o. Disinfectant: An agent that frees from infections. It is usually a chemical agent but sometimes a physical one. It destroys disease-causing pathogens or other harmful microorganisms but may or may not kill bacterial spores. It refers to substances applied to inanimate objects.

p. High-Efficiency Particulate Air (HEPA) filter: A filter composed of pleats of filter medium separated by rigid sheets of corrugated paper or aluminum foil that direct the flow of air forced through the filter in a uniform parallel flow. HEPA filters remove 99.97% of all particles three-tenths (0.3) microns or larger. When HEPA filters are used as a component of a horizontal or vertical-laminar-airflow workbench, an environment can be created consistent with standards for a class 100 clean room.

q. Media-Fill Test: A test which is used to qualify aseptic technique of compounding personnel or processes and to ensure that the processes used are able to produce sterile product without microbial contamination. A microbiological growth medium such as soybean-casein digest medium (SCDM) is substituted for the actual drug product to simulate admixture compounding.

r. Multiple-Dose Container: A multiple-unit container for articles or preparations intended for parenteral administration only. These containers usually contain antimicrobial preservatives. The beyond-use date (BUD) for an opened or entered multi-dose container with antimicrobial preservatives is 28 days, unless otherwise specified by the manufacturer.

s. **Parenteral:** A sterile preparation of drugs for injection through one or more layers of skin.

t. **Pharmacy Bulk Package:** A container of a sterile preparation for parenteral use that contains multiple single doses. The contents of the package are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for infusion or, through a sterile transfer device, for the filling of empty sterile syringes. The closure shall by penetrated only one time after constitution with a suitable sterile transfer device or dispensing set, which allows measured dispensing of the contents. The pharmacy bulk package is to be used only in a suitable work area such as a laminar flow hood or an equivalent clean air compounding area. Such container shall be labeled with the following:

(1) The name, strength and quantity of drug or base solution;

(2) The statement "Pharmacy Bulk Package—Not For Direct Infusion;"

(3) Information on the proper technique to assure safe use of the product; and

(4) A statement limiting the time frame in which the container may be used once it has been entered, provided it is held under the labeled storage conditions.

u. **Primary Engineering Control (PEC):** A device or room that provides an ISO Class 5 environment for the exposure of critical sites when compounding CSPs. Such devices include, but are not limited to, laminar airflow workbenches (LAFWs), biological safety cabinets (BSCs) and compounding aseptic isolators (CAIs), and compounding aseptic containment isolators (CACIs).

v. **Process Validation or Simulation:** Microbiological simulation of an aseptic process with growth medium processed in a manner similar to the processing of the product and with the same container or closure system.

w. **Segregated Compounding Area:** A part of the designated compounding / dispensing area that is a specifically designated space, either a demarcated area or room, and that is restricted to preparing low-risk level CSPs with a 12-hour or less BUD. Such area shall contain a device that provides unidirectional airflow of ISO Class 5 air quality for preparation of CSPs and shall be void of activities and materials that are extraneous to sterile compounding.

x. **Single-Dose Container:** A single-unit container for articles or preparations intended for parenteral administration only. It is intended for single use and is labeled as such. Examples include, but are not limited to, prefilled syringes, cartridges, fusion-sealed containers, and closure-sealed containers when so labeled.

y. **Sterile Pharmaceutical:** A dosage form free from living microorganisms.

z. **Sterilization:** A validated process used to render a product free of viable organisms.

aa. **Sterilizing Grade Filter Membranes:** Filter membranes that are documented to retain 100% of a culture of 10_7 microorganisms of a strain of Brevundimonas (Pseudomonas) diminuta per square centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar). Such filter membranes are nominally at 0.22 or 0.2 micrometer porosity, depending on the manufacturer's practice.

bb. **Sterilization by Filtration:** Passage of a fluid or solution through a sterilizing grade filter to produce a sterile effluent.

cc. Terminal Sterilization: The application of a lethal process (e.g. steam under pressure or autoclaving) to sealed containers for the purpose of achieving a predetermined sterile assurance level of usually less than 10^{-6}, or a probability of less than one in one million of a non-sterile unit.

dd. Temperatures:

1. Frozen means temperatures between twenty five degrees below zero and ten degrees below zero Celsius (-25 and -10 degrees C.) or thirteen degrees below zero and fourteen degrees Fahrenheit (-13 and 14 degrees F.).

2. Refrigerated means temperatures between two and eight degrees Celsius (2 and 8 degrees C.) or thirty-six and forty-six degrees Fahrenheit (36 and 46 degrees F.).

3. Room temperatures mean room temperatures between fifteen and thirty degrees Celsius (15 and 30 degrees C.) or fifty-nine and eighty-six degrees Fahrenheit (59 and 86 degrees F.).

ee. Unidirectional Flow: An airflow moving in a single direction, in a robust and uniform manner, and at sufficient speed to reproducibly sweep particles away from the critical processing or testing area.

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 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 ~~and radiopharmaceuticals~~ 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 ~~anti-neoplastic~~ chemotherapeutic preparations subject to USP/NF Chapter 800;

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

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

(d) 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) 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.**

21.20.23 Single-Dose and Multiple-Dose Containers.

a. **Opened or needle-punctured single-dose containers shall be used within 1 hour if opened in worse than ISO Class 5 air quality. Single-dose containers exposed to ISO Class 5 air quality or cleaner air may be used up to 6 hours after initial puncture.**

b. **If multiple-dose containers include antimicrobial preservatives, the BUD shall not exceed 28 days from the initial date of entering or opening, unless otherwise specified by the manufacturer.**

21.20.25 Radiopharmaceuticals as CSPs.

a. **Production of radiopharmaceuticals for positron emission tomography (PET) shall comply with the most current Chapter 823 of the USP/NF <Radiopharmaceuticals for Positron Emission>.**

b. ~~All other r~~Radiopharmaceuticals shall be compounded in conformity ~~to~~ with rules 21.20.25(b)(1) through (~~5~~4) below, rule 12.00.00, and all other applicable sections of rule 21.00.00.

(1) Radiopharmaceuticals compounded from FDA-approved, commercially sterile components in closed sterile containers and with a volume of 100 ml or less for a single-dose injection or not more than 30 ml taken from a multiple-dose container shall be designated as, and conform to, the standards for low risk CSPs.

(2) Radiopharmaceuticals shall be compounded using appropriately shielded vials and syringes in a properly functioning and certified ISO Class 5 PEC located in an ISO Class 8 or cleaner air environment to permit compliance with special handling, shielding, and negative air flow requirements.

(3) Radiopharmaceutical vials designated for multiple use, compounded with technetium-99m, exposed to an ISO Class 5 environment, and punctured by needles with no direct contact contamination may be used up to the time indicated by the manufacturer's recommendations.

(4) Technetium-99m/molybdenum-99 generator systems shall be stored and operated under conditions recommended by the manufacturer and applicable state and federal rules. Such generator systems shall be operated in an ISO Class 8 or cleaner air environment to permit special handling, shielding, and air flow requirements. To limit acute and chronic radiation exposure of inspecting personnel to a level that is as low as reasonably achievable (ALARA), direct visual inspection of radiopharmaceutical CSPs containing high concentrations of doses of radioactivity shall be conducted in accordance with ALARA.

~~(5) Radiopharmaceuticals prepared as low risk CSPs with 12-hour or less BUD shall be prepared in a segregated compounding area. A line of demarcation defining the segregated compounding area shall be established. Materials and garbing exposed in a patient care and treatment area shall not cross a line of demarcation into the segregated compounding area.~~

21.20.30 Policy and Procedure Manual.

a. A manual, outlining policies and procedures encompassing all aspects of compounding low, medium or high risk products, shall be available for inspection at the pharmacy. This manual shall be complied with and shall be reviewed on an annual basis. Such review shall be signed and dated by the pharmacist manager. In the event the pharmacist manager changes, the new manager shall review, sign, and date the manual within 30 days of becoming pharmacist manager. The pharmacist manager shall ensure compliance with the manual.

b. The policy and procedure manual shall address at least the following:

(1) Responsibility of compounding personnel;

(2) Verification of compounding accuracy and sterilization;

(3) Personnel training and evaluation in aseptic manipulation skills;

(4) Environmental quality and control;

(5) Aseptic processing;

(6) Labeling and recordkeeping;

(7) Finished preparation release check;

(8) Storage and beyond-use dating;

(9) Maintaining product quality and control during transportation and delivery after the CSP leaves the pharmacy;

(10) Patient or caregiver training;

(11) Adverse event reporting and recalls;

(12) Quality assurance program;

(13) Quality control procedures, as appropriate; and

(14) Verification of work area cleaning effectiveness.

21.20.40 Personnel Education and Training.

a. Low risk: All pharmacy personnel preparing sterile products must receive suitable didactic and experiential training.

b. Medium risk: In addition to low risk requirements, personnel training includes assessment of competency in all medium risk procedures.

c. High risk: In addition to low and medium risk requirements, operators have specific education, training and experience to prepare high risk products. The pharmacist knows principles of good compounding practice for risk level products, including:

(1) Aseptic processing;

(2) Quality assurance of environmental, component, and end-product testing;

(3) Sterilization; and

(4) Selection and use of containers, equipment, and closures.

21.20.50 Personnel Evaluation in Aseptic Manipulation Skills.

a. Personnel who prepare CSPs shall be provided appropriate training before they begin preparing CSPs.

b. Compounding personnel shall perform didactic review and pass written and media-fill testing of aseptic manipulative skills initially; at least annually thereafter for low and medium risk products; and every six months, thereafter, for high risk products.

c. Personnel who fail written tests, or whose media-fill test vials result in gross microbial colonization, must be immediately reinstructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies.

d. Results of these tests shall be retained and be available for inspection at the outlet for at least two years.

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. 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.

21.20.70 Environmental Monitoring.

a. Class 100 or better clean rooms and/or primary engineering controls shall be certified by qualified operators at least every six months and whenever the device or room is relocated or major service to the facility is performed. Certification records shall be maintained and be available for inspection at the outlet for at least two years from the certification date.

b. Certification that each ISO classified area is within established guidelines shall be performed no less than every six months and whenever the primary engineering control is relocated or the physical structure of the buffer area or anteroom has been altered. The testing shall be performed by qualified operators using state-of-the-art electronic equipment with the following results:

(1) Not more than 3,520 particles 0.5 micrometer size and larger per cubic meter of air for any primary engineering control (ISO Class 5).

(2) Not more than 352,000 particles of 0.5 micrometer size and larger per cubic meter of air (ISO Class 7) for any buffer room; and

(3) Not more than 3,520,000 particles of 0.5 micrometer size and larger per cubic meter of air (ISO Class 8) for any anteroom/area.

c. Certification records shall be maintained and be available for inspection at the outlet for at least two years from the certification date.

d. Tests shall be done for airborne microorganisms. Electronic air samplers are the preferred method. The instructions in the manufacturer's user manual for verification and use of the electronic air sample that actively collects volumes of air for evaluation must be followed. The sampling is performed at locations judged by compounding personnel to be the most prone to contamination. These tests shall be done at least every six months. The outlet shall have written policies to reevaluate cleaning procedures, operational procedures, and air filtration

efficiency if the number of colony forming units increases over the normal baseline level. Records of these tests shall be maintained and be available for inspection at the outlet for at least two years from the testing date.

e. Glove fingertip sampling shall be conducted at least annually for all compounding personnel if compounding low and medium risk CSPs and semi-annually if compounding high risk CSPs. When a finger plate result for personnel monitoring after proper incubation exceeds the action limit, a review of hand hygiene and garbing procedures as well as glove and surface disinfection procedures and work practices shall occur.

f. A pressure gauge ~~or velocity meter~~ shall be installed to monitor the pressure differential ~~or airflow~~ between the ISO Class 7 cleanroom and the ISO Class 8 anteroom and the anteroom and the general pharmacy area. The results shall be reviewed and documented on a daily basis. The pressure between the ~~ISO Class 7~~ cleanroom and general pharmacy area shall not be less than 5 ~~p~~Pa (0.02-inch water column, w.c.). The pressure differential between the cleanroom and the anteroom shall be greater than the pressure differential between the anteroom and the general pharmacy area, except for the preparation of radiopharmaceuticals where there is no pressure differential.

21.20.80 Cleaning and Disinfecting the Workspaces.

a. The cleaning and sanitizing of the workspaces shall be done pursuant to written procedures and shall be the responsibility of trained operators, using appropriate disinfecting agents.

b. The direct and contiguous compounding area (DCCA), including ISO Class 5 areas, shall be cleaned and disinfected prior to the beginning of each shift. All items shall be removed from the DCCA and all surfaces shall be cleaned of loose material and residue from spills prior to cleaning.

c. Work surfaces in the ISO Class 7 buffer areas and ISO Class 8 anteroom/areas are cleaned and disinfected at least daily.

d. Dust and debris shall be removed as necessary from the storage areas for compounding ingredients and supplies.

e. Storage shelving shall be disinfected at least monthly. All items shall be removed from the shelving prior to cleaning.

f. The walls and ceilings in the buffer and anteroom areas shall be cleaned and disinfected at least monthly.

g. Floors in the buffer and anteroom areas shall be mopped daily when no aseptic operations are in progress.

h. All cleaning tools, such as wipers, sponges, and mops shall be non-shedding and dedicated to use in the buffer or clean area. Floor mops may be used in both the buffer or clean area and anteroom area, but only in that order. Most wipers shall be discarded after one use. If cleaning tools are reused, their cleanliness shall be maintained by thorough rinsing and disinfection after use and by storing in a clean environment between uses. Trash shall be collected in suitable plastic bags and removed with minimal agitation.

21.20.90 Personnel Cleansing and Garbing.

a. Prior to entering the controlled (buffer) area, operators shall remove personal outer garments (such as lab jackets), makeup, and jewelry.

b. After donning dedicated appropriate garbing that includes shoes or shoe covers, head and facial hair coverings, and face masks, hands and arms shall be thoroughly scrubbed up to the elbow. After drying hands and arms, operators shall properly don non-shedding gowns that fit snugly around the wrists and enclosed at the neck.

c. Once inside the clean area, hands shall be cleansed with an antiseptic hand cleanser. Sterile, powder-free gloves shall then be donned, except for the preparation of radiopharmaceuticals where the prescription drug outlet can demonstrate statistically significant equivalence or superior sterility by using another method.

d. During protracted compounding activities, personnel shall intermittently resanitize their gloves.

e. For low and medium risk compounding: If personnel leave the buffer area, they shall don new hair covers, masks, shoe covers, and gloves prior to reentry. Gowns may be reused during the same compounding session if hung in the anteroom.

f. For high risk: If personnel leave the buffer area, they must don new hair covers, masks, shoe covers, gowns and gloves prior to reentry.

21.21.10 Components.

a. Compounding personnel shall ascertain that ingredients for CSPs are in compliance with rule 21.00.10(b) and are of the correct identity and appropriate quality using the following information: vendors' labels, labeling, certificates of analysis, direct chemical analysis, and knowledge of compounding facility storage conditions. No expired components may be used in compounding. No component may be used which will expire prior to the beyond-use date of the finished CSP.

b. Ingredients used in a compounded preparation shall either originate from FDA-approved sources, ~~if~~ when available, or be USP/NF grade substances when such sources are not available and identified on the FDA drug shortage list.

c. If neither USP/NF grade substances nor FDA-approved substances are available, or when food, cosmetics, or other substances are, or must be used, the substance shall be of a chemical grade in one of the following categories:

(1) Chemically Pure (CP);

(2) Analytical Reagent (AR); or

(3) American Chemical Society (ACS); or

(4) Food Chemical Codex.

d. For all ingredients, unless FDA-approved, the pharmacist shall establish purity and stability by obtaining a certificate of analysis from the supplier. The certificate of analysis, when applicable, shall be maintained at the prescription drug outlet for at least two years from the date of preparation.

e. A manufactured drug product may be a source of active ingredient. Only manufactured drugs from containers labeled with a lot number and an expiration date are acceptable as a potential source of active ingredients. When compounding with manufactured drug products, the compounder must consider all ingredients present in the drug product relative to the intended use of a compounded preparation.

f. Drug preparations that have been withdrawn or removed from the market for safety reasons shall not be compounded. Such preparations may be compounded exclusively for veterinary use provided no documentation exists which indicates that the preparation is unsafe for such use.

g. Sterile ingredients and components:

(1) A written procedure for physical inspection of ingredients and components prior to compounding shall be followed.

h. Non-sterile ingredients and components:

(1) If any non-sterile components or ingredients, including containers, devices, and ingredients, are utilized to make the CSP, the product shall be compounded at high risk.

(2) If non-USP or non-NF active ingredients, added substances, or excipients are utilized, a certificate of analysis from the supplier of the ingredient shall be maintained at the prescription drug outlet for at least two from the date of preparation.

(3) When non-sterile ingredients and components are received at the outlet, their container shall be marked, in indelible pencil or ink, with the date of receipt. In the absence of a supplier's expiration date on the product, the expiration date of the ingredient shall be one-year from the date of receipt, unless either appropriate inspection or testing indicates that the ingredient has retained its purity and quality for use in CSPs.

(4) Prior to compounding with non-sterile ingredients and components, the ingredients shall be visually inspected for evidence of deterioration, other types of unacceptable quality and wrong identification.

i. Any ingredient regulated by the FDA through an Investigational Review Board (IRB) is exempt from rule 21.21.10 provided the research requirements for the receipt of the ingredient is followed and meets the requirements of CRS 12-42.5-128(2).

21.21.20 Equipment.

a. Written procedures outlining required equipment, calibration, appropriate maintenance, monitoring for proper function, controlled procedures for use of the equipment and specified time frames for these activities shall be established and followed. Results of equipment calibration and appropriate maintenance reports shall be kept on file at the outlet for at least two years from the report date and shall be available for inspection.

b. Accuracy assessments of automated compounding devices (ACD) shall be conducted daily for each day used. At routine intervals, the pharmacist manager, or his or her designee, shall review these assessments to avoid potentially clinically significant cumulative errors over time. These assessments shall be

documented and be maintained and available for inspection at the outlet for at least two years.

21.21.30 Finished Preparation Release Checks and Tests.

a. Physical Inspection

(1) Finished CSPs shall be individually inspected after compounding pursuant to written procedures. Immediately after compounding, and prior to dispensing or distribution, each product shall be inspected for evidence of particulates or other foreign matter, container-closure integrity, precipitation, cloudiness, and any other apparent visual defect. Defective product shall be segregated from other product and shall not be dispensed or distributed.

b. Compounding Accuracy Checks.

(1) Written procedures for double-checking compounding accuracy shall be followed for every CSP during preparation and immediately prior to release. Outlets which compound CSPs shall have at least the following written procedures for verifying the correct identity and quality of CSPs prior to dispensing or distribution:

(a) Verification of label for accuracy;

(b) Correct identities, purities, and amounts of ingredients have been used; and

(c) Correct fill volumes in CSPs and correct quantities of filled units of the CSPs were obtained.

c. Sterility Testing.

(1) Sterility testing shall be done on the following high risk CSPs:

(a) Batches larger than 25 identical individual single-dose packages (ampules, bags, syringes, vials, etc);

(b) Multiple dose vials for administration to multiple patients;

(c) Product is exposed longer than 12 hours at refrigerator temperatures prior to sterilization; or

(d) Product is exposed longer than 6 hours to temperatures warmer than refrigerator temperature prior to sterilization.

(2) The sterility test shall be compliant with the most current USP/NF Chapter 71 <Sterility Tests>. A method not described in the USP/NF may be used if verification results demonstrate that the alternative is at least as effective and reliable as the USP/NF methods.

(3) When a high risk CSP is dispensed or distributed before receiving the results of the sterility test, there shall be a written procedure requiring daily observation of the incubating test specimens and requiring an immediate recall if there is any evidence of microbial growth. In addition, the patient and the practitioner of the patient to whom a potentially contaminated CSP was administered shall be notified of the potential risk. Positive sterility results shall prompt a rapid and systematic investigation of aseptic

technique, environmental and other sterility assurance controls to identify sources of contamination and correct problems in the methods or processes.

d. Bacterial Endotoxin (Pyrogen) Testing.

(1) Endotoxin testing shall be done on the following high risk CSPs that are to be administered parenterally:

(a) Batches larger than 25 identical individual single-dose packages (ampules, bags, syringes, vials, etc.);

(b) Multiple dose vials for administration to multiple patients;

(c) Product is exposed longer than 12 hours at refrigerator temperatures prior to sterilization; or

(d) Product is exposed longer than 6 hours to temperatures warmer than refrigerator temperature prior to sterilization.

(2) The endotoxin test shall be compliant with the most current USP/NF Chapter 85 <Bacterial Endotoxins Test>. In the absence of a bacterial endotoxins limit in the official monograph or other CSP formula source, the CSP must not exceed the amount of USP/NF Endotoxin Units (EU per hour per kg of body weight) specified for the route of administration.

21.21.40 Storage and Beyond-Use Dating.

a. The temperature of drug storage areas of CSPs shall be monitored and recorded daily, either manually or electronically. Temperature records shall be maintained and be available for inspection for at least two years.

b. Finished CSPs that are not immediately dispensed or administered shall be refrigerated or frozen unless their chemical and physical stability are known to be adversely affected by cold or freezing temperatures.

c. In the absence of sterility testing for each compounded batch compliant with the most current USP/NF Chapter 71 <Sterility Tests>, the beyond-use date (before administration) shall not exceed the following:

(1) Low risk CSPs with greater than 12-hour BUD:

Room temperature:	No more than 48 hours
Refrigerated temperature:	No more than 14 days
Frozen:	No more than 45 days

(2) Low risk CSPs with 12-hour or less BUD:

Room temperature:	No more than 12 hours
Refrigerated temperature:	No more than 12 hours
Frozen:	Not applicable

(3) **Medium risk CSPs:**

Room temperature:	**No more than 30 hours**
Refrigerated temperature:	**No more than 9 days**
Frozen:	**No more than 45 days**

(4) **High risk CSPs:**

Room temperature:	**No more than 24 hours**
Refrigerated temperature:	**No more than 3 days**
Frozen:	**No more than 45 days**

d. **For high risk products, there must be a reliable method for establishing all expiration dates, including sterility. There must be a reliable method for establishing all beyond-use dating. Products maintaining beyond-use dating of greater than thirty (30) days shall have lab testing of product stability and potency.**

e. **Each outlet shall adhere to manufacturers' instructions for handling and storing of Add-Vantage®, Mini Bag Plus®, Add A Vial®, Add-Ease® products, and any similar products.**

21.21.50 Formulation Record.

a. **For each CSP, a uniform, readily retrievable formulation record shall be maintained and available for inspection for two years from the date last utilized, documenting:**

(1) **The name, strength, dosage form, and route of administration of the compounded preparation;**

(2) **All ingredients and their quantities;**

(3) **The equipment used to compound the preparation, when appropriate, and mixing instructions;**

(4) **The beyond use date;**

(5) **The containers used in dispensing;**

(6) **Storage requirements; and**

(7) **Procedures for quality control, if applicable.**

21.21.60 Compounding Record.

a. **For each CSP prepared, a record shall be maintained and available for inspection for two years on the original order, or on a separate, uniform, readily retrievable record documenting the following:**

(1) **Name and strength of the compounded preparation;**

(2) **Formulation record reference for the preparation;**

(3) **Sources and lot number of each ingredient;**

(4) Manufacturer's expiration date of each ingredient, when applicable;

(5) Total number of dosage units compounded;

(6) Name of the person who compounded the preparation;

(7) Name of the pharmacist who approved the preparation;

(8) Batch (lot) number assigned, if multiple units compounded;

(9) Date of preparation;

(10) Beyond use date;

(11) Prescription number(s), if appropriate;

(12) Results of quality control procedures; and

(13) If a high risk product, the record shall also include comparisons of actual with anticipated yields, sterilization methods, and quarantine specifications.

21.21.70 Labeling of CSPs.

a. Labeling of CSPs dispensed pursuant to a prescription order or LTCF chart order shall include at least the following:

(1) All requirements of CRS12-42.5-121;

(2) Batch (lot) number, if appropriate;

(3) Beyond-use date;

(4) If for parenteral administration, the following shall be included:

(a) Name of base solution; and

(b) name and amounts of drugs added.

(5) Storage directions; and

(6) A clear statement that this product was compounded by the pharmacy, except for radiopharmaceuticals prepared from FDA-approved, commercially available kits and/or drug products.

b. Labeling of CSPs dispensed pursuant to a hospital chart order shall include at least the following:

(1) All requirements of CRS 12-42.5-121;

(2) Batch (lot) number, if appropriate;

(3) Beyond-use date;

(4) If for parenteral administration, the following shall be included;

(a) Name of base solution; and

(b) Name and amounts of drugs added; and

(5) Storage directions.

c. Labeling of CSPs distributed to practitioners, other prescription drug outlets, or other outlets allowed by law shall include at least the following:

(1) Name of the outlet;

(2) Name and strength of the drug(s);

(3) Total quantity in package;

(4) Quantity of active ingredient in each dosage unit;

(5) Beyond-use date;

(6) Batch (lot) number;

(7) Specific route of administration;

(8) Storage directions;

(9) "Rx only"; and

(10) "A clear statement that ~~T~~this product was compounded by the pharmacy, except for radiopharmaceuticals prepared from FDA-approved, commercially available kits and/or drug products."

d. Labeling of CSPs distributed within hospitals as floor stock shall include at least the following:

(1) Name of the outlet;

(2) Name and strength of the drug(s);

(3) Total quantity in package;

(4) Quantity of active ingredient in each dosage unit;

(5) Beyond-use date;

(6) Batch (lot) number;

(7) Specific route of administration; and

(8) Storage directions.

21.21.80 Maintaining Product Quality and Control After the CSP Leaves the Outlet or Hospital Location.

a. The outlet shall have written policies and procedures that are adhered to which shall ensure the CSP is packaged properly for transit, stored properly during transit, and stored properly at site of administration. Such policies and procedures shall also discuss patient or caregiver training.

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, 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.

21.22.00 Quality Assurance Program.

a. Outlets that make CSPs shall have a formal written quality assurance (QA) program which shall provide a mechanism for monitoring, evaluating, correcting, and improving the activities and processes regarding the compounding of sterile products.

b. At a minimum, the written QA program shall include the following:

(1) Consideration of all aspects of the preparation, dispensing, and distribution of products, including environmental testing, work area cleaning effectiveness, validation results, etc;

(2) Describe specific monitoring and evaluation activities;

(3) Specification of how results are to be reported and evaluated;

(4) Identification of appropriate follow-up mechanisms when action limits or thresholds are exceeded; and

(5) Delineation of the individuals responsible for each aspect of the QA program.

21.22.10 Cytotoxic Drug Preparation.

a. Cytotoxic drugs shall be compounded in a vertical flow, Class II biological safety cabinet (BSC) or CACI. Such BSC or CACI shall be placed in an ISO Class 7 area that is physically separated from other preparation areas and is negative pressure to adjacent positive pressure anteroom. If used for other products, the cabinet must be thoroughly cleaned;

b. Appropriate personnel protective equipment (PPE) shall be worn when compounding in a BSC or CACI and when using closed-system vial transfer devices (CSTDs). PPE should include gowns, face masks, eye protection, hair covers, shoe covers or dedicated shoes, double gloving with sterile chemo-type gloves, and compliance with manufacturers' recommendations when using a CACI;

c. Appropriate safety and containment techniques for compounding cytotoxic drugs shall be used in conjunction with the aseptic techniques required for preparing sterile products;

d. Appropriate disposal containers for used needles, syringes, and if applicable, cytotoxic waste from the preparation of chemotherapy agents and infectious waste from patients' homes. Disposal of cytotoxic waste shall comply with all applicable local, state and federal requirements;

e. Written procedures for handling major and minor spills and generated waste of cytotoxic agents must be developed and must be included in the policy and procedure manual; and

f. Prepared doses of cytotoxic drugs must be labeled with proper precautions inside and outside, and shipped in a manner to minimize the risk of accidental rupture of the primary container.

21.22.20 Exemption for Sterile Compounding of Products in Closed or Sealed System.

a. Pharmacists and pharmacies or other outlets where sterile compounding is provided may be exempt from this rule when compounding is restricted to utilizing compounds or products that are contained only in a closed or sealed system and can be transferred or compounded within this self-contained system or topical products that require further transfer or combination in order to achieve a finished product without further modification of the product.

Basis and Purpose: The purpose of the amendments to this rule are to: (1) require the first name of an animal to be submitted to the Prescription Drug Monitoring Program ("PDMP") when dispensing a controlled substance to a pet; and (2) codify the release of information from the PDMP in compliance with the Health Insurance Portability and Accountability Act of 1996 and any rules promulgated pursuant to the act.

Authority for Promulgation of Rules: Sections 12-42.5-101, 12-42.5-105, 12-42.5-106 (2) and (3), and 12-42.5-401 through 12-42.5-409.

23.00.40 Data Submission Format.

Prescription drug outlets shall submit to the PDMP the following data requirements:

a. Identifier (Transmission type identifier), if applicable;

b Bin (Bank Identification Number);

c Version Number (a number to identify the format of the transaction sent or received);

d. Transaction Code;

e. NABP or Drug Enforcement Administration number assigned to pharmacy;

f. Customer ID (number to identify the patient receiving the RX);

g. Zip Code (3 digit US Postal Code identifying the State Code), if applicable;

h. Customer's Birth Date;

i. Sex Code;

j. Date Filled;

k. Prescription Number;

l. New/Refill Number;

m. Metric Quantity;

n. Days Supply;

o. Compound Code;

p. NDC Number of the drug dispensed;

q. Prescriber's Drug Enforcement Administration registration;

r. Drug Enforcement Administration suffix, if applicable;

s. Date RX Written;

t. Number of Refills Authorized;

u. RX Origin Code;

v. Customer Location;

w. Diagnosis Code, if available;

x. Alternate Prescriber #, if applicable;

y. Patient Last Name (if an animal, the owner's last name);

z. Patient First Name (if an animal, the animal's first name);

aa. Patient Street Address;

bb. Patient's state of residence;

cc. Patient's zip code;

dd. Triplicate Serial Number, if appropriate; and

ee. Filler Field to be populated with Payment Type as designated by PDMP vendor.

23.00.70 PDMP Access

The PDMP shall be available for query only to the following persons or groups of persons:

a. Board staff responsible for administering the PDMP;

b. Any licensed practitioner, or up to three (3) trained individuals designated by the practitioner by way of registered PDMP sub-accounts of the prescriber to act on the prescriber's behalf in accordance with 12-42.5-403(1.5)(b), (c) and (d), C.R.S., with the statutory authority to prescribe controlled substances to the extent the query relates to a current patient of the practitioner to whom the practitioner is prescribing or considering prescribing a controlled substance;

c. Licensed pharmacists, or up to three (3) trained individuals designated by the pharmacist by way of registered PDMP sub-accounts of the pharmacist to act on the pharmacist's behalf in accordance with 12-42.5-403(1.5)(b), (c) and (d), C.R.S., or a pharmacist licensed in another state, with statutory authority to dispense controlled substances to the extent the information requested relates specifically to a current patient to whom the pharmacist is dispensing or considering dispensing a controlled substance or to whom the pharmacist is providing clinical patient care services;

d. Practitioners engaged in a legitimate program to monitor a patient's controlled substance abuse;

e. Law enforcement officials so long as the information released is specific to an individual patient, prescriber, or prescription drug outlet and part of a bona fide investigation and the request for information is accompanied by an official court order or subpoena. Such official court orders or subpoenas shall be submitted with the Board-provided form;

f. The individual who is the recipient of a controlled substance prescription so long as the information released is specific to such individual. The procedure for individuals to obtain such information is as follows:

1. The individual shall submit a written, signed request to the Board on the Board-provided form;

2. **The individual shall provide valid photographic identification prior to obtaining the PDMP information;**

3. **An individual submitting a request on behalf of another individual who is the recipient of a controlled substance prescription may only obtain PDMP information if the following documents are provided:**

   A. The original document establishing medical durable power of attorney of the individual submitting the request as power of attorney for the individual who is the recipient of the controlled substance prescription, and

   B. Valid photographic identification of the individual submitting the request.

g. State regulatory boards within the Colorado Division of Professions and Occupations and the Director of the Colorado Division or Professions and Occupations so long as the information released is specific to an individual prescriber and is part of a bona fide investigation and the request for information is accompanied by an official court order or subpoena. Such official court orders or subpoenas shall be submitted with the Board-provided form; and

h. A resident physician with an active physician training license issued by the Colorado medical board pursuant to section 12-36-122 and under the supervision of a licensed physician to the extent the query relates to a current patient of the resident physician to whom the resident physician is prescribing or considering prescribing a controlled substance.

i. The Department of Public Health and Environment for purposes of population-level analysis, but any use of the program data by the department is subject to the federal "Health Insurance Portability and Accountability Act of 1996 (HIPAA) and ~~implementing federal regulations~~ any rules promulgated pursuant to HIPAA, including the requirement to remove any identifying data unless exempted from the requirement.

j. A person authorized to access the PDMP may knowingly release PDMP information specific to an individual or to the individual's treating providers in accordance with HIPAA, Pub.L. 104-191, as amended, and any rules promulgated pursuant to HIPAA without violating Part 4 of Title 12, Article 42.5.