TEXAS STATE BOARD OF PHARMACY

Regulatory Compliance Rule Submission Memorandum

To: Regulatory Compliance Division Director, Office of the Governor

From: Megan Holloway, General Counsel, Texas State Board of Pharmacy

Date: February 4, 2025

Subject: Sterile Compounding Proposed Rule

The Texas State Board of Pharmacy has proposed amendments 22 TAC §291.133, as published in the December 27, 2024, issue of the *Texas Register*. The proposed rule potentially affects market competition and is submitted to the Regulatory Compliance Division for review. The PDF version of the preamble and text of the proposed rule as published in the *Texas Register*, and the language of any amendments to the proposed rule that the Texas State Board of Pharmacy intends to adopt, are attached to this memorandum.

To facilitate the Regulatory Compliance Division's review of the proposed rule, the Texas State Board of Pharmacy provides answers to the following questions.

1. Briefly describe the proposed rule.

The amendments, if adopted, update the personnel, environment, compounding process, cleaning and disinfecting, beyond-use dating, cleansing and garbing, environmental testing, sterility testing, recall procedure, and recordkeeping requirements for pharmacies compounding sterile preparations.

2. What is the purpose of the proposed rule?

The purpose of the amendments is to ensure the safety and efficacy of compounded sterile preparations for patients, improve the health, safety, and welfare of patients by ensuring that Class A, Class B, Class C, and Class E pharmacies engaged in sterile compounding operate in a safe and sanitary environment, and provide clearer regulatory language that is appropriately informed by the recently updated guidance in the United States Pharmacopeia-National Formulary.

3. Describe any relevant factual background to the proposed rule and the impetus for the state agency to consider rulemaking.

Revisions to the standards found in the United States Pharmacopeia General Chapter <797> Pharmaceutical Compounding- Sterile Preparations were published November 1, 2022, and became effective on November 1, 2023. At the May 2, 2023, Board meeting, the Board voted to create a

Compounding Rules Advisory Group Sterile Subcommittee to review the revisions issued by USP and current Board rules regarding the compounding of sterile preparations and requested nominations for licensees to serve as members. The Subcommittee was convened in August 2023 and met on five different dates. The recommendations of the Subcommittee were presented at the February 6, 2024, and May 7, 2024, Board meetings. At the August 6, 2024, Board meeting the Board heard oral comments from Subcommittee members and voted to propose amendments to §291.133 which were then published in the September 20, 2024, edition of the *Texas Register*. At the November 5, 2024, Board meeting, the Board received written and oral comments from the public regarding the published proposed amendments. The Board voted to make changes to the previously proposed amendments and propose the updated amendments.

4. Describe the legal authority for the proposed rule.

a. Is the proposed rule specifically required or authorized by state statute? If so, list the statute(s).

Yes, the proposed rule is specifically authorized by state statute. The Board interprets §560.053 as authorizing the agency to adopt rules to establish and regulate additional pharmacy classifications to protect the public health, safety, and welfare.

b. Is the proposed rule within the scope of the state agency's general authority to regulate in a given occupation or industry? If so, describe how the proposed rule is within the scope, and reference the applicable state statute(s).

Yes, the proposed amendments are within the scope of the Board's general authority to regulate the practice of pharmacy. The amendments are authorized under §§551.002, 551.003, 554.001, and 554.051 of the Texas Pharmacy Act (Chapters 551 - 569, Texas Occupations Code). The Board interprets §551.002 as authorizing the agency to protect the public through the effective control and regulation of the practice of pharmacy. The Board interprets §551.003(9) as authorizing the agency to adopt rules concerning the compounding of prescriptions. The Board interprets §551.003(33) as authorizing the agency to adopt rules concerning the practice of pharmacy. The Board interprets §554.001(a) as authorizing the agency to adopt rules to administer and enforce the Act and rules adopted under the Act as well as enforce other laws relating to the practice of pharmacy. The Board interprets §554.051(a) as authorizing the agency to adopt rules for the proper administration and enforcement of the Act.

5. Describe the process that the state agency followed in developing the proposed rule, including any public hearings held, public comments invited, studies conducted, and data collected or analyzed.

At the May 2, 2023, Board meeting, the Board voted to create a Compounding Rules Advisory Group Sterile Subcommittee to review the revisions to the standards found in the United States Pharmacopeia General Chapter <797> Pharmaceutical Compounding- Sterile Preparations and current Board rules regarding the compounding of sterile preparations and requested nominations for licensees to serve as members. The Subcommittee was convened in August 2023 and met on five different dates. The recommendations of the Subcommittee were presented at the February 6, 2024, and May 7, 2024, Board meetings. At the August 6, 2024, Board meeting, the Board heard oral comments from Subcommittee members and voted to propose amendments to §291.133 which were then published in the September 20, 2024, edition of the *Texas Register*. At the November 5, 2024, Board meeting, the Board received written and oral comments from the public regarding the

published proposed amendments. The Board voted to make changes to the previously proposed amendments and propose the updated amendments.

6. Describe the harm that the proposed rule is intended to address and how the proposed rule will address the harm.

The proposed amendments aim to reduce the risk to patients of contamination, infection, or incorrect dosing. The amendments are intended to ensure patient safety by preventing harm from microbial contamination, excessive bacterial endotoxins, and other potential contaminants and minimizing the risk of adverse events. The proposed amendments reflect advances in science and pharmacy practice to ensure patients receive appropriate pharmacy care.

Wearing proper garb reduces the shedding of particles from personnel thereby decreasing the chance of introducing microorganisms into the sterile environment and contaminating the preparation. Proper aseptic technique minimizes the risk of contamination during preparation. Preparation of compounded sterile preparations by or supervision of compounding procedures by personnel who lack proper training and competency increase contamination risk and potential harm to patients. Ensuring personnel are trained and competent in garbing, hand hygiene, and aseptic technique helps to prevent contamination. Gloved fingertip and thumb testing evaluates competency in correctly performing hand hygiene and garbing by detecting by counting the number of colony-forming units of microorganisms present on a sample of the personnel's gloved fingertips and thumbs. Surface sampling evaluates facility cleaning and material handling procedures, work surface cleaning and disinfecting procedures, and personnel competency in practices such as cleaning and disinfecting by counting the number of colony-forming units of microorganisms present on a sample of the surface. Media-fill testing is used to evaluate the aseptic technique of personnel or processes and to ensure that the processes used are able to produce sterile preparation without microbial contamination by counting the number of colony-forming units of microorganisms present on a sample test media, a sample of the personnel's gloved fingertips and thumbs, and a sample of the surface.

Depyrogenation renders glassware, metals, or other thermostable containers and components pyrogen (endotoxin) free decreasing the chance of contaminating the preparation. Pyrogens are organic compounds that are soluble in water and not removed by filtration or steam sterilization. Pharmaceutical ovens utilize dry heat to depyrogenate. Endotoxin challenge testing validates a dry heat dyprogenation cycle by measuring a sample's endotoxin level before and after the process. Autoclaves sterilize by using steam under pressure to kill microorganisms and spores, decreasing the change of contaminating the preparation. Autoclaves sterilize but do not depyrogenate.

Air exchange requirements impact the cleanliness of the environment by minimizing the risk of airborne contamination during the preparation of sterile compounded preparations and protecting patients from potential infections caused by microbial particles in the air.

Sterility testing of compounded preparations detects microbial contamination, which can cause infections and serious complications for patients. Method suitability validation is performed on a specific formulation to determine the appropriate test method. Sterility method suitability testing is performed to determine whether any inhibitory or antimicrobial properties in a formulation will prevent the sterility test from detecting the presence of viable microorganisms. It shows that the sterility test method is valid for the specific formulation and reduces the possibility of a sterile result on a compounded preparation of that formulation that is not sterile. Method suitability testing is performed on each formulation, as opposed to each compounded preparation batch of a formulation. Endotoxin testing of compounded preparations detects the presence of bacterial endotoxins, which

can cause serious adverse effects such as fever, inflammation, and septic shock, even when a compounded preparation is otherwise sterile. Container closure integrity testing evaluates the integrity of the container closure system of a preparation to maintain a sterile barrier against contaminants. Miniscule defects in a container that are not visible to the eye but detectable by testing can compromise sterility and stability of compounded preparations, thereby risking patient safety. Antimicrobial effectiveness testing for multiple-dose compounded sterile preparations assures the preservatives added to inhibit the growth of microorganisms that may be introduced by repeatedly withdrawing individual doses are sufficient for patient safety.

Beyond-use dates identify the date and time by which a preparation must be used before the preparation is at risk for physical or chemical degradation, microbial contamination and proliferation, and impact on the integrity of the container closure system. Beyond-use dates prevent patient harm by ensuring the preparation remains stable, sterile, and free from contamination.

7. Do any less restrictive alternatives to the proposed rule exist for addressing the same harm? If so, include a comparison of the proposed rule to the alternatives and a justification for not pursuing a less restrictive alternative. If no less restrictive alternatives exist, explain why.

The Board established a Compounding Rules Advisory Group Sterile Subcommittee to review the recently issued revisions to United States Pharmacopeia General Chapter <797> Pharmaceutical Compounding- Sterile Preparations. The Sterile Subcommittee reviewed the new provisions of USP <797>, discussed whether any of the provisions should be added to §291.133 to ensure patient safety in Texas, and considered various methods of achieving this purpose. The Sterile Subcommittee discussed the changes to USP <797> during its meetings held on August 2, 2023, August 23, 2023, October 3, 2023, October 30, 2023, and January 23, 2024 meetings. The Sterile Committee considered different options and levels of personnel training, beyond-use dating, environmental requirements, compounding processes, environmental testing requirements, recall procedures, and recordkeeping requirements in determining recommendations for the least restrictive methods of ensuring the safety and efficacy of compounded sterile preparations. In reviewing the new provisions of USP <797>, the Sterile Subcommittee recommended limiting or not adopting several of the new provisions, including preparation per approved labeling, initial gowning competency, use of isolators, precision and accuracy of pressure differentials, compounding notification on label, packaging of compounded sterile preparations, and compounding allergenic extracts.

At the May 7, 2024, Board meeting, four Subcommittee members made oral public comments concerning the Subcommittee's recommendations. The Board reviewed the recommendations and provided direction to Board staff on items for which the Subcommittee could not come to consensus. The Board voted to publish the proposed amendments for public comment during its August 6, 2024, Board meeting. The amendments were published in the September 20, 2024, issue of the *Texas Register*. The Board received eight written public comments concerning the amendments. Additionally, the Board received six oral public comments at the November 5, 2024, Board meeting. After reviewing and considering the comments, the Board proposed amendments to the previously proposed amendments. Many of the proposed amendments are less restrictive than USP <797>. The Board finds that alternative regulatory methods would not be consistent with the health, safety, and welfare of patients.

8. Indicate how the proposed rule affects market competition (See Section 57.105(d), Texas Occupations Code).

The proposed amendments could potentially result in higher prices or reduced competition for a product or service provided by or to a license holder in the state.

9. Describe the specific impact that the proposed rule will have on market competition and how that effect is consistent with state policy as established by the Legislature in state statute.

The proposed amendments could result in an economic impact to a pharmacy that engages in the compounding of sterile preparations if the pharmacy does not currently comply with these standards, which could potentially result in higher prices or reduced competition. The economic impact of the proposed amendments on a particular pharmacy would be dependent on that pharmacy's current environment and the policies and procedures the pharmacy previously had in place for compounding sterile preparations. The additional costs of training personnel who do not compound nor supervise compounding personnel on a pharmacy's SOPs (*see* (c)(4)(A)) are estimated to be $0 to $1,200 per employee. The additional costs of the updated media-fill testing procedures depend on the compounding risk-level in which a pharmacy is currently engaged (*see* (c)(4)(E)-(K)). For a pharmacy that is currently engaged in only low-risk and medium-risk compounding, the additional costs are estimated to be $9.95 to $300 annually per employee who engages in sterile compounding. For a pharmacy that is currently engaged in high-risk compounding, no additional costs are anticipated. The additional costs of the updated gloved fingertip sampling depend on the compounding risk-level in which a pharmacy is currently engaged (*see* (c)(4)(L)). For a pharmacy that is currently engaged in only low-risk and medium-risk compounding, the additional costs are estimated to be $90 to $250 annually per employee who engages in sterile compounding. For a pharmacy that is currently engaged in high-risk compounding, no additional costs are anticipated. The additional costs of the updated garbing competency testing depend on the compounding risk-level in which a pharmacy is currently engaged (*see* (c)(4)(L)). For a pharmacy that is currently engaged in only low-risk and medium-risk compounding, the additional costs are estimated to be $0 to $220 annually per employee who engages in sterile compounding. For a pharmacy that is currently engaged in high-risk compounding, no additional costs are anticipated. The additional costs of the updated surface sampling requirements (*see* (c)(4)(M)) are estimated to be $85 to $300 per sample taken. The additional costs of the updated sterilization and depyrogenation requirements (*see* (d)(3)), for a pharmacy that does not already possess a pharmaceutical oven or autoclave, are one-time costs of $1,000 to $6,000 for an autoclave, $1,000 to $4,000 for a pharmaceutical oven, and $500 for temperature logs and monitors, annual costs of $300 for calibration and $210 for endotoxin testing, and $40 to $50 per usage for washing and wrapping supplies. Preliminary testing is estimated to cost $510 to $1,800 per formulation for method suitability testing for those formulations requiring such testing, $150 to $345 per formulation for sterility testing for those formulations requiring such testing (*see* (d)(1)(B), (d)(8)(J), (d)(17)(C)) $500 per formulation for endotoxin validation method for those formulations requiring such testing (*see* (d)(16)(B)(i)), $110 to $210 per formulation for endotoxin testing for those formulations requiring such testing, $250 to $1,200 per formulation for container closure integrity testing for those formulations requiring such testing (*see* (d)(5)(H)), $1,275 per formulation for antimicrobial effectiveness testing for those formulations requiring such testing (*see* (d)(5)(F)-(G)), and $1,000 per formulation for a method suitability test for antimicrobial effectiveness testing for those formulations requiring such testing. The additional costs of the updated air exchange requirements (*see* (d)(8)(A), (d)(16)(C)(v)-(vi)) are estimated to be a one-time cost of $0 to $5,000 based on the extent of the modifications, if any, needed for a pharmacy's cleanroom. The additional costs of expanded disinfecting with sterile 70% isopropyl alcohol in place of non-sterile 70% isopropyl alcohol (*see* (d)(8)(H)) are estimated to be a net increase of $4.69 per 32-ounce bottle. The additional costs of sterile low-lint garments and coverings (*see* (d)(15)(C)(iv)) are estimated to $0 to $45 per set. The additional costs of expanded sterility and bacterial endotoxin testing are estimated to be $300 to $500 per batch for those batches requiring such testing (*see* (d)(16)(B)(i)). The estimated

cost of the new beyond-use date requirements is dependent on the pharmacy's current practices (*see* (d)(8)(J)). A shortened beyond-use date may require the compound to be made more frequently or discarded more often. Additional testing costs may be incurred to prove that a specific compounded preparation can exceed a new beyond-use date standard.

Section 551.002 of the Texas Occupations Code provides that the Texas Pharmacy Act shall be liberally construed to regulate in the public interest the practice of pharmacy in this state. The proposed amendments promote, preserve, and protect the public health, safety, and welfare through effectively controlling and regulating the compounding of sterile preparations, which is a part of the practice of pharmacy.

10. Does the proposed rule relate to a question that is the subject of an opinion request pending before the Office of the Attorney General? Does the proposed rule relate to an opinion previously issued by the Office of the Attorney General?

The Board is not aware of a related opinion request or opinion.

11. Does the proposed rule relate to a matter on which there is pending litigation or a final court order?

The Board is not aware of any related pending litigation or final court order.

12. Is there anything else that the state agency would like the Regulatory Compliance Division to know about the proposed rule?

At the November 5, 2024, Board meeting, the Board requested that commenters presenting higher economic impact estimates provide documentation of the higher costs utilized in their calculations. To date, the Board has not received any documentation reflecting higher costs than those utilized by staff in the economic impact analysis in the preamble of the proposed amendments.

The agency certifies that legal counsel has reviewed the proposal and found it to be within the state agency's legal authority to adopt.

Filed with the Office of the Secretary of State on December 13, 2024.

TRD-202406012
Doug Jennings
General Counsel
Texas Department of Licensing and Regulation
Earliest possible date of adoption: January 26, 2025
For further information, please call: (512) 475-4879

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TITLE 22. EXAMINING BOARDS

PART 15. TEXAS STATE BOARD OF PHARMACY

CHAPTER 291. PHARMACIES

SUBCHAPTER G. SERVICES PROVIDED BY PHARMACIES

22 TAC §291.133

The Texas State Board of Pharmacy proposes amendments to §291.133, concerning Pharmacies Compounding Sterile Preparations. The amendments, if adopted, update the personnel, environment, compounding process, cleaning and disinfecting, beyond-use dating, cleansing and garbing, environmental testing, sterility testing, recall procedure, and recordkeeping requirements for pharmacies compounding sterile preparations.

Daniel Carroll, Pharm.D., Executive Director/Secretary, has determined that, for the first five-year period the rules are in effect, there will be no fiscal implications for state or local government as a result of enforcing or administering the rule. Dr. Carroll has determined that, for each year of the first five-year period the rule will be in effect, the public benefit anticipated as a result of enforcing the amendments will be to ensure the safety and efficacy of compounded sterile preparations for patients, improve the health, safety, and welfare of patients by ensuring that Class A, Class B, Class C, and Class E pharmacies engaged in sterile compounding operate in a safe and sanitary environment, and provide clearer regulatory language that is appropriately informed by the recently updated guidance in the United States Pharmacopeia-National Formulary. For each year of the first five-year period the rule will be in effect, the probable economic cost to persons required to comply with the amendments is estimated to be $0-$1,970 per employee, $0-$300 in fixed costs, and $0-$1,109.69 per batch in variable costs based on number of batches and formulations. Additionally, dependent on a pharmacy's current operations and equipment, a pharmacy would potentially incur one-time expenses of $0-$5,000 for cleanroom modifications, $0-$6,000 for an autoclave, $0-$4,000 for a pharmaceutical oven, $0-$500 for temperature logs and monitors, and $0-6,330 per formulation for preliminary testing.

Economic Impact Statement

The Texas State Board of Pharmacy (Board) anticipates a possible adverse economic impact on some small or micro-businesses (pharmacies) or rural communities as a result of the proposed amendments to §291.133. The Board is unable to estimate the number of small or micro-businesses subject to the proposed amendments. As of November 21, 2024, there are 877 Class A, Class B, Class C, and Class E pharmacies that perform sterile compounding, as indicated by the pharmacies on Board licensing forms. The Board estimates that 77 rural communities in Texas have a Class A, Class B, Class C, or Class E pharmacy that performs sterile compounding.

The economic impact of the proposed amendments on a particular pharmacy would be dependent on that pharmacy's current environment and the policies and procedures the pharmacy previously had in place for compounding sterile preparations. The additional costs of training personnel who do not compound nor supervise compounding personnel on a pharmacy's SOPs are estimated to be $0 to $1,200 per employee. The additional costs of the updated media-fill testing procedures depend on the compounding risk-level in which a pharmacy is currently engaged. For a pharmacy that is currently engaged in only low-risk and medium-risk compounding, the additional costs are estimated to be $9.95 to $300 annually per employee who engages in sterile compounding. For a pharmacy that is currently engaged in high-risk compounding, no additional costs are anticipated. The additional costs of the updated gloved fingertip sampling depend on the compounding risk-level in which a pharmacy is currently engaged. For a pharmacy that is currently engaged in only low-risk and medium-risk compounding, the additional costs are estimated to be $90 to $250 annually per employee who engages in sterile compounding. For a pharmacy that is currently engaged in high-risk compounding, no additional costs are anticipated. The additional costs of the updated garbing competency testing depend on the compounding risk-level in which a pharmacy is currently engaged. For a pharmacy that is currently engaged in only low-risk and medium-risk compounding, the additional costs are estimated to be $0 to $220 annually per employee who engages in sterile compounding. For a pharmacy that is currently engaged in high-risk compounding, no additional costs are anticipated. The additional costs of the updated surface sampling requirements are estimated to be $85 to $300 per sample taken. The additional costs of the updated sterilization and depyrogenation requirements, for a pharmacy that does not already possess a pharmaceutical oven or autoclave, are one-time costs of $1,000 to $6,000 for an autoclave, $1,000 to $4,000 for a pharmaceutical oven, and $500 for temperature logs and monitors, annual costs of $300 for calibration and $210 for endotoxin testing, and $40 to $50 per usage for washing and wrapping supplies. Preliminary testing is estimated to cost $510 to $1,800 per formulation for method suitability testing, $150 to $345 per formulation for sterility testing, $500 per formulation for endotoxin validation method, $110 to $210 per formulation for endotoxin testing, $250 to $1,200 per formulation for container closure integrity testing, $1,275 per formulation for antimicrobial effectiveness testing, and $1,000 per formulation for a method suitability test for antimicrobial effectiveness testing. The additional costs of the updated air exchange requirements are estimated to be a one-time cost of $0 to $5,000 based on the extent of the modifications, if any, needed for a pharmacy's cleanroom. The additional costs of expanded disinfecting with sterile 70% isopropyl alcohol in place of non-sterile 70% isopropyl alcohol are estimated to be a net increase of $4.69 per 32-ounce bottle. The additional costs of sterile low-lint garments and coverings are estimated to $0 to $45 per set. The additional costs of expanded sterility and bacterial endotoxin testing are estimated to be $300 to $500 per batch. The estimated cost of the new beyond-use date requirements is dependent on the pharmacy's

current practices. A shortened beyond-use date may require the compound to be made more frequently or discarded more often. Additional testing costs may be incurred to prove that a specific compounded preparation can exceed a new beyond-use date standard.

The Board established a Compounding Rules Advisory Group, comprised of a Sterile Subcommittee and a Non-Sterile Subcommittee, to review the recently issued revisions to United States Pharmacopeia General Chapter <795> Pharmaceutical Compounding- Nonsterile Preparations and United States Pharmacopeia General Chapter <797> Pharmaceutical Compounding- Sterile Preparations, and the proposed amendments are based on the recommendations of the Sterile Subcommittee. The Subcommittee's recommendations were initially presented at the May 7, 2024, Board meeting and four Subcommittee members made oral public comments concerning the recommendations. The Board reviewed the recommendations and provided direction to Board staff on items for which the Subcommittee could not come to consensus. The Board voted to published the proposed amendments for public comment during its August 6, 2024, Board meeting. The amendments were published in the September 20, 2024, issue of the *Texas Register* (49 TexReg 7588). The Board received eight written public comments concerning the amendments. Additionally, the Board received six oral public comments at the November 5, 2024, Board meeting. After reviewing and considering the comments, the Board proposed amendments to the previously proposed amendments. Alternative methods of achieving the purpose of the proposed amendments were considered by the Sterile Subcommittee and the Board and the proposed amendments reflect recommendations for the least restrictive methods of ensuring the safety and efficacy of compounded sterile preparations.

Regulatory Flexibility Analysis

The Texas State Board of Pharmacy (Board) anticipates a possible adverse economic impact on some small or micro-businesses (pharmacies) or rural communities as a result of the proposed amendments to §291.133. The Board established a Compounding Rules Advisory Group, comprised of a Sterile Subcommittee and a Non-Sterile Subcommittee, to review the recently issued revisions to United States Pharmacopeia General Chapter <795> Pharmaceutical Compounding- Nonsterile Preparations and United States Pharmacopeia General Chapter <797> Pharmaceutical Compounding- Sterile Preparations, and the proposed amendments are based on the recommendations of the Sterile Subcommittee. The Sterile Subcommittee reviewed the new provisions of USP <797>, discussed whether any of the provisions should be added to §291.133 to ensure patient safety in Texas, and considered various methods of achieving this purpose.

The Sterile Subcommittee discussed the changes to USP <797> during its meetings held on August 2, August 23, 2023, October 3, 2023, October 30, 2023, and January 23, 2024 meetings. The Sterile Committee considered different options and levels of personnel training, beyond-use dating, environmental requirements, compounding processes, environmental testing requirements, recall procedures, and recordkeeping requirements in determining recommendations for the least restrictive methods of ensuring the safety and efficacy of compounded sterile preparations. In reviewing the new provisions of USP <797>, the Sterile Subcommittee recommended limiting or not adopting several of the new provisions, including preparation per approved labelling, initial gowning competency, use of isolators, precision and accuracy of pressure differentials, compounding notification on label, packaging of compounded sterile preparations, and compounding allergenic extracts.

The Sterile Subcommittee's recommendations were initially presented at the May 7, 2024, Board meeting and four Subcommittee members made oral public comments concerning the recommendations. The Board reviewed the recommendations and provided direction to Board staff on items for which the Subcommittee could not come to consensus. The Board voted to published the proposed amendments for public comment during its August 6, 2024, Board meeting. The amendments were published in the September 20, 2024, issue of the *Texas Register* (49 TexReg 7588). The Board received eight written public comments concerning the amendments. Additionally, the Board received six oral public comments at the November 5, 2024, Board meeting. After reviewing and considering the comments, the Board proposed amendments to the previously proposed amendments. The Board finds that alternative regulatory methods would not be consistent with the health, safety, and environmental and economic welfare of the state.

For each year of the first five years the proposed amendments will be in effect, Dr. Carroll has determined the following:

(1) The proposed amendments do not create or eliminate a government program;

(2) Implementation of the proposed amendments does not require the creation of new employee positions or the elimination of existing employee positions;

(3) Implementation of the proposed amendments does not require an increase or decrease in the future legislative appropriations to the agency;

(4) The proposed amendments do not require an increase or decrease in fees paid to the agency;

(5) The proposed amendments do not create a new regulation;

(6) The proposed amendments both limit and expand an existing regulation by adding and amending operational standards for Class A, Class B, Class C, and Class E, pharmacies engaged in sterile compounding;

(7) The proposed amendments do not increase or decrease the number of individuals subject to the rule's applicability; and

(8) The proposed amendments would have a de minimis impact on this state's economy.

Written comments on the amendments may be submitted to Eamon D. Briggs, Deputy General Counsel, Texas State Board of Pharmacy, 1801 Congress Avenue, Suite 13.100, Austin, Texas, 78701-1319, FAX (512) 305-8061. Comments must be received by 5:00 p.m., January 25, 2025.

The amendments are proposed under §§551.002 and 554.051 of the Texas Pharmacy Act (Chapters 551 - 569, Texas Occupations Code). The Board interprets §551.002 as authorizing the agency to protect the public through the effective control and regulation of the practice of pharmacy. The Board interprets §554.051(a) as authorizing the agency to adopt rules for the proper administration and enforcement of the Act.

The statutes affected by these amendments: Texas Pharmacy Act, Chapters 551 - 569, Texas Occupations Code.

§291.133. Pharmacies Compounding Sterile Preparations.

(a) Purpose. Pharmacies compounding sterile preparations, prepackaging pharmaceutical products, and distributing those products shall comply with all requirements for their specific license classification and this section. The purpose of this section is to provide standards for the:

(1) compounding of sterile preparations pursuant to a prescription or medication order for a patient from a practitioner in Class A-S, Class B, Class C-S, and Class E-S pharmacies;

(2) compounding, dispensing, and delivery of a reasonable quantity of a compounded sterile preparation in Class A-S, Class B, Class C-S, and Class E-S pharmacies to a practitioner's office for office use by the practitioner;

(3) compounding and distribution of compounded sterile preparations by a Class A-S pharmacy for a Class C-S pharmacy; and

(4) compounding of sterile preparations by a Class C-S pharmacy and the distribution of the compounded preparations to other Class C or Class C-S pharmacies under common ownership.

(b) Definitions. In addition to the definitions for specific license classifications, the following words and terms, when used in this section, shall have the following meanings, unless the context clearly indicates otherwise.

(1) ACPE--Accreditation Council for Pharmacy Education.

(2) Airborne particulate cleanliness class--The level of cleanliness specified by the maximum allowable number of particles per cubic meter of air as specified in the International Organization of Standardization (ISO) Classification Air Cleanliness (ISO 14644-1). For example:

(A) ISO Class 5 (formerly Class 100) is an atmospheric environment that contains less than 3,520 particles 0.5 microns and larger in diameter per cubic meter of air (formerly stated as 100 particles 0.5 microns in diameter per cubic foot of air);

(B) ISO Class 7 (formerly Class 10,000) is an atmospheric environment that contains less than 352,000 particles 0.5 microns and larger in diameter per cubic meter of air (formerly stated as 10,000 particles 0.5 microns in diameter per cubic foot of air); and

(C) ISO Class 8 (formerly Class 100,000) is an atmospheric environment that contains less than 3,520,000 particles 0.5 microns and larger in diameter per cubic meter of air (formerly stated as 100,000 particles 0.5 microns in diameter per cubic foot of air).

(3) Ancillary supplies--Supplies necessary for the preparation and administration of compounded sterile preparations.

(4) Anteroom [~~Ante-area~~]--An ISO Class 8 or cleaner room with fixed walls and doors where personnel hand hygiene, garbing procedures, and other activities that generate high particulate levels may be performed. The anteroom is the transition room between the unclassified area of the pharmacy and the buffer room. [~~An ISO Class 8 or better area where personnel may perform hand hygiene and garbing procedures, staging of components, order entry, labeling, and other high-particulate generating activities. It is also a transition area that:~~]

[~~(A) provides assurance that pressure relationships are constantly maintained so that air flows from clean to dirty areas; and~~]

[~~(B) reduces the need for the heating, ventilating and air conditioning (HVAC) control system to respond to large disturbances.~~]

(5) Aseptic processing [~~Processing~~]--A mode of processing pharmaceutical and medical preparations that involves the separate sterilization of the preparation and of the package (containers-closures or packaging material for medical devices) and the transfer of the preparation into the container and its closure under at least ISO Class 5 conditions.

(6) Automated compounding device--An automated device that compounds, measures, and/or packages a specified quantity of individual components in a predetermined sequence for a designated sterile preparation.

(7) Batch--A specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced during a single preparation cycle.

(8) Batch preparation compounding--Compounding of multiple sterile preparation units, in a single discrete process, by the same individual(s), carried out during one limited time period. Batch preparation/compounding does not include the preparation of multiple sterile preparation units pursuant to patient specific medication orders.

(9) Beyond-use date--The date, or hour and the date, after which a compounded sterile preparation shall not be used, stored, or transported. The date is determined from the date and time the preparation is compounded. [~~The date or time after which the compounded sterile preparation shall not be stored or transported or begin to be administered to a patient. The beyond-use date is determined from the date or time the preparation is compounded.~~]

(10) Biological safety cabinet [~~Safety Cabinet~~], Class II--A ventilated cabinet for personnel, product or preparation, and environmental protection having an open front with inward airflow for personnel protection, downward HEPA filtered laminar airflow for product protection, and HEPA filtered exhausted air for environmental protection.

(11) Buffer room [~~Area~~]--An ISO Class 7 or cleaner or, if a Class B pharmacy, an ISO Class 8 or cleaner, room with fixed walls and doors where primary engineering controls that generate and maintain an ISO Class 5 environment are physically located. The buffer room may only be accessed through the anteroom or another buffer room. [~~An ISO Class 7 or, if a Class B pharmacy, ISO Class 8 or better, area where the primary engineering control area is physically located. Activities that occur in this area include the preparation and staging of components and supplies used when compounding sterile preparations.~~]

(12) 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 gear are not exceeded for a specified cleanliness class.

(13) Cleaning agent--An agent, usually containing a surfactant, used for the removal of substances (e.g., dirt, debris, microbes, residual drugs or chemicals) from surfaces.

(14) Cleanroom suite--A classified area that consists of both an anteroom and buffer room.

(15) [~~(13)~~] Component--Any ingredient used in the compounding of a preparation, including any active ingredient, added substance, or conventionally manufactured product [~~intended for use in the compounding of a drug preparation, including those that may not appear in such preparation~~].

(16) [~~(14)~~] Compounding--The preparation, mixing, assembling, packaging, or labeling of a drug or device:

(A) as the result of a practitioner's prescription drug or medication order based on the practitioner-patient-pharmacist relationship in the course of professional practice;

(B) for administration to a patient by a practitioner as the result of a practitioner's initiative based on the practitioner-patient-pharmacist relationship in the course of professional practice;

(C) in anticipation of prescription drug or medication orders based on routine, regularly observed prescribing patterns; or

(D) for or as an incident to research, teaching, or chemical analysis and not for sale or dispensing, except as allowed under §562.154 or Chapter 563 of the Occupations Code.

(17) [~~(15)~~] Compounding aseptic isolator [~~Aseptic Isolator~~]--A form of barrier isolator specifically designed for compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer processes. Air exchange into the isolator from the surrounding environment shall not occur unless it has first passed through a microbial retentive filter (HEPA minimum).

(18) [~~(16)~~] Compounding aseptic containment isolator [~~Aseptic Containment Isolator~~]--A compounding aseptic isolator designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes 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 hazardous drugs are prepared, the exhaust air from the isolator should be appropriately removed by properly designed building ventilation.

(19) [~~(17)~~] Compounding personnel [~~Personnel~~]--A pharmacist, pharmacy technician, or pharmacy technician trainee who performs the actual compounding; a pharmacist who supervises pharmacy technicians or pharmacy technician trainees compounding sterile preparations, and a pharmacist who performs an intermediate or final verification of a compounded sterile preparation.

(20) [~~(18)~~] Critical area [~~Area~~]--An ISO Class 5 environment.

(21) [~~(19)~~] Critical sites [~~Sites~~]--A location that includes any component or fluid pathway surfaces (e.g., vial septa, injection ports, beakers) or openings (e.g., opened ampules, needle hubs) exposed and at risk of direct contact with air (e.g., ambient room or HEPA filtered), moisture (e.g., oral and mucosal secretions), or touch contamination. Risk of microbial particulate contamination of the critical site increases with the size of the openings and exposure time.

(22) Designated person(s)--One or more individuals assigned to be responsible and accountable for the performance and operation of the pharmacy and personnel as related to the preparation of compounded sterile preparations.

(23) [~~(20)~~] Device--An instrument, apparatus, implement, machine, contrivance, implant, in-vitro reagent, or other similar or related article, including any component part or accessory, that is required under federal or state law to be ordered or prescribed by a practitioner.

(24) [~~(21)~~] Direct compounding area [~~Compounding Area~~]--A critical area within the ISO Class 5 primary engineering control where critical sites are exposed to unidirectional HEPA-filtered air, also known as first air.

(25) [~~(22)~~] Disinfectant--An agent that frees from infection, usually a chemical agent but sometimes a physical one, and that destroys disease-causing pathogens or other harmful microorganisms but may not kill bacterial and fungal spores. It refers to substances applied to inanimate objects.

(26) [~~(23)~~] First air [~~Air~~]--The air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.

(27) [~~(24)~~] Hazardous drugs [~~Drugs~~]--Drugs that, studies in animals or humans indicate exposure to the drugs, have a potential for causing cancer, development or reproductive toxicity, or harm to organs. For the purposes of this chapter, radiopharmaceuticals are not considered hazardous drugs.

(28) [~~(25)~~] Hot water--The temperature of water from the pharmacy's sink maintained at a minimum of 105 degrees F (41 degrees C).

(29) [~~(26)~~] HVAC--Heating, ventilation, and air conditioning.

(30) [~~(27)~~] Immediate use--A sterile preparation that is not prepared according to USP 797 standards (i.e., outside the pharmacy and most likely not by pharmacy personnel) which shall be stored for no longer than four hours following the start of preparing [~~one hour after completion of~~] the preparation.

(31) [~~(28)~~] IPA--Isopropyl alcohol (2-propanol).

(32) [~~(29)~~] Labeling--All labels and other written, printed, or graphic matter on an immediate container of an article or preparation or on, or in, any package or wrapper in which it is enclosed, except any outer shipping container. The term "label" designates that part of the labeling on the immediate container.

(33) Master formulation record--A detailed record of procedures that describes how the compounded sterile preparation is to be prepared.

(34) [~~(30)~~] Media-fill test [~~Media-Fill Test~~]--A test used to qualify aseptic technique of compounding personnel or processes and to ensure that the processes used are able to produce sterile preparation without microbial contamination. During this test, a microbiological growth medium such as Soybean-Casein Digest Medium is substituted for the actual drug preparation to simulate admixture compounding. The issues to consider in the development of a media-fill test are the following: media-fill procedures, media selection, fill volume, incubation, time and temperature, inspection of filled units, documentation, interpretation of results, and possible corrective actions required.

(35) [~~(31)~~] Multiple-dose container [~~Multiple-Dose Container~~]--A multiple-unit container for articles or preparations intended for parenteral [~~potential~~] administration only and usually contains antimicrobial preservatives. The beyond-use date for an opened or entered (e.g., needle-punctured) multiple-dose container with antimicrobial preservatives is 28 days, unless otherwise specified by the manufacturer.

(36) [~~(32)~~] Negative pressure room [~~Pressure Room~~]--A room that is at a lower pressure compared to adjacent spaces and, therefore, the net flow of air is into the room.

(37) [~~(33)~~] Office use--The administration of a compounded drug to a patient by a practitioner in the practitioner's office or by the practitioner in a health care facility or treatment setting, including a hospital, ambulatory surgical center, or pharmacy in accordance with Chapter 562 of the Act, or for administration or provision by a veterinarian in accordance with §563.054 of the Act.

(38) [~~(34)~~] Pharmacy bulk package [~~Bulk Package~~]--A container of a sterile preparation for potential use that contains many single doses. The contents 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 be 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).

(39) [~~(35)~~] Prepackaging--The act of repackaging and relabeling quantities of drug products from a manufacturer's original container into unit dose packaging or a multiple-dose [~~multiple dose~~] container for distribution within a pharmacy [~~facility~~] licensed as a Class C pharmacy or to other pharmacies under common ownership for distribution within those pharmacies [~~facilities~~]. The term as defined does not prohibit the prepackaging of drug products for use within other pharmacy classes.

(40) [~~(36)~~] Preparation or compounded sterile preparation [~~Compounded Sterile Preparation~~]--A sterile admixture compounded in a licensed pharmacy or other healthcare-related facility pursuant to the order of a licensed prescriber. The components of the preparation may or may not be sterile products.

(41) [~~(37)~~] Primary engineering control [~~Engineering Control~~]--A device or room that provides an ISO Class 5 environment for the exposure of critical sites when compounding sterile preparations. Such devices include, but may not be limited to, laminar airflow workbenches, biological safety cabinets, compounding aseptic isolators, and compounding aseptic containment isolators.

(42) [~~(38)~~] Product--A commercially manufactured sterile drug or nutrient that has been evaluated for safety and efficacy by the U.S. Food and Drug Administration (FDA). Products are accompanied by full prescribing information, which is commonly known as the FDA-approved manufacturer's labeling or product package insert.

(43) [~~(39)~~] Positive control [~~Control~~]--A quality assurance sample prepared to test positive for microbial growth.

(44) [~~(40)~~] Quality assurance--The set of activities used to ensure that the process used in the preparation of sterile drug preparations lead to preparations that meet predetermined standards of quality.

(45) [~~(41)~~] Quality control--The set of testing activities used to determine that the ingredients, components (e.g., containers), and final compounded sterile preparations prepared meet predetermined requirements with respect to identity, purity, non-pyrogenicity, and sterility.

(46) [~~(42)~~] Reasonable quantity--An amount of a compounded drug that:

(A) does not exceed the amount a practitioner anticipates may be used in the practitioner's office or facility before the beyond-use [~~beyond use~~] date of the drug;

(B) is reasonable considering the intended use of the compounded drug and the nature of the practitioner's practice; and

(C) for any practitioner and all practitioners as a whole, is not greater than an amount the pharmacy is capable of compounding in compliance with pharmaceutical standards for identity, strength, quality, and purity of the compounded drug that are consistent with United States Pharmacopoeia guidelines and accreditation practices.

(47) Restricted-access barrier system--An enclosure that provides HEPA-filtered ISO Class 5 unidirectional air that allows for the ingress and/or egress of materials through defined openings that have been designed and validated to preclude the transfer of contamination, and that generally are not to be opened during operations.

(48) [~~(43)~~] Segregated compounding area [~~Compounding Area~~]--A designated space, area, or room that is not required to be classified and is defined with a visible perimeter. The segregated compounding area shall contain a PEC and is suitable for preparation of Category 1 compounded sterile preparations only. [~~A designated space, either a demarcated area or room, that is restricted to preparing low-risk level compounded sterile preparations with 12-hour or less beyond-use date. Such area shall contain a device that provides unidirectional airflow of ISO Class 5 air quality for preparation of compounded sterile preparations and shall be void of activities and materials that are extraneous to sterile compounding.~~]

(49) [~~(44)~~] Single-dose container--A single-unit container for articles or preparations intended for parenteral administration only. It is intended for a single use. A single-dose container is labeled as such. Examples of single-dose containers include pre-filled syringes, cartridges, fusion-sealed containers, and closure-sealed containers when so labeled.

(50) [~~(45)~~] SOPs--Standard operating procedures.

(51) [~~(46)~~] Sterilizing grade membranes [~~Grade Membranes~~]--Membranes that are documented to retain 100% of a culture of 10^7 [~~107~~] 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-micron or 0.2 micron [~~0.22-micrometer or 0.2-micrometer~~] nominal pore size, depending on the manufacturer's practice.

(52) [~~(47)~~] Sterilization by filtration [~~Filtration~~]--Passage of a fluid or solution through a sterilizing grade membrane to produce a sterile filtrate [~~effluent~~].

(53) [~~(48)~~] Terminal sterilization [~~Sterilization~~]--The application of a lethal process, e.g., steam under pressure or autoclaving, to sealed final preparation containers for the purpose of achieving a predetermined sterility assurance level of usually less than 10^-6 [~~10-6~~] or a probability of less than one in one million of a non-sterile unit.

(54) [~~(49)~~] Unidirectional airflow [~~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.

(55) [~~(50)~~] USP/NF--The current edition of the United States Pharmacopeia/National Formulary.

(c) Personnel.

(1) Pharmacist-in-charge.

(A) General. The pharmacy shall have a pharmacist-in-charge in compliance with the specific license classification of the pharmacy.

(B) Responsibilities. In addition to the responsibilities for the specific class of pharmacy, the pharmacist-in-charge shall have the responsibility for, at a minimum, the following concerning the compounding of sterile preparations:

(i) developing a system to ensure that all pharmacy personnel responsible for compounding and/or supervising the compounding of sterile preparations within the pharmacy receive appropriate education and training and competency evaluation;

(ii) determining that all personnel involved in compounding sterile preparations obtain continuing education appropriate for the type of compounding done by the personnel;

(iii) supervising a system to ensure appropriate procurement of drugs and devices and storage of all pharmaceutical materials including pharmaceuticals, components used in the compounding of sterile preparations, and drug delivery devices;

(iv) ensuring that the equipment used in compounding is properly maintained;

(v) developing a system for the disposal and distribution of drugs from the pharmacy;

(vi) developing a system for bulk compounding or batch preparation of drugs;

(vii) developing a system for the compounding, sterility assurance, quality assurance, and quality control of sterile preparations; and

(viii) if applicable, ensuring that the pharmacy has a system to dispose of hazardous waste in a manner so as not to endanger the public health.

(2) Pharmacists.

(A) General.

(i) A pharmacist is responsible for ensuring that compounded sterile preparations are accurately identified, measured, diluted, and mixed and are correctly purified, sterilized, packaged, sealed, labeled, stored, dispensed, and distributed.

(ii) A pharmacist shall inspect and approve all components, drug preparation containers, closures, labeling, and any other materials involved in the compounding process.

(iii) A pharmacist shall review all compounding records for accuracy and conduct periodic in-process checks as defined in the pharmacy's policy and procedures.

(iv) A pharmacist shall review all compounding records for accuracy and conduct a final check.

(v) A pharmacist is responsible for ensuring the proper maintenance, cleanliness, and use of all equipment used in the compounding process.

(vi) A pharmacist shall be accessible at all times, 24 hours a day, to respond to patients' and other health professionals' questions and needs.

(B) Initial training and continuing education.

(i) All pharmacists who compound sterile preparations or supervise pharmacy technicians and pharmacy technician trainees compounding sterile preparations shall comply with the following:

(I) complete through a single course, a minimum of 20 hours of instruction and experience in the areas listed in paragraph (4)(D) of this subsection. Such training shall be obtained through completion of a recognized course in an accredited college of pharmacy or a course sponsored by an ACPE accredited provider;

(II) complete a structured on-the-job didactic and experiential training program at this pharmacy which provides sufficient hours of instruction and experience in the pharmacy's [~~facility's~~] sterile compounding processes and procedures. Such training may not be transferred to another pharmacy unless the pharmacies are under common ownership and control and use a common training program; and

(III) possess knowledge about:

(-a-) aseptic processing;

(-b-) quality control and quality assurance as related to environmental, component, and finished preparation release checks and tests;

(-c-) chemical, pharmaceutical, and clinical properties of drugs;

(-d-) container, equipment, and closure system selection; and

(-e-) sterilization techniques.

(ii) The required experiential portion of the training programs specified in this subparagraph shall [~~must~~] be supervised by an individual who is actively engaged in performing sterile compounding and is qualified and has completed training as specified in this paragraph or paragraph (3) of this subsection.

(iii) In order to renew a license to practice pharmacy, during the previous licensure period, a pharmacist engaged in sterile compounding shall complete a minimum of:

(I) two hours of ACPE-accredited continuing education relating to one or more of the areas listed in paragraph (4)(D) of this subsection if the pharmacist is engaged in compounding Category 1 or Category 2 compounded [~~low and medium risk~~] sterile preparations; or

(II) four hours of ACPE-accredited continuing education relating to one or more of the areas listed in paragraph (4)(D) of this subsection if the pharmacist is engaged in compounding Category 2 prepared from any non-sterile starting component or Category 3 compounded [~~high risk~~] sterile preparations.

(3) Pharmacy technicians and pharmacy technician trainees.

(A) General. All pharmacy technicians and pharmacy technician trainees shall meet the training requirements specified in §297.6 of this title (relating to Pharmacy Technician and Pharmacy Technician Trainee Training).

(B) Initial training and continuing education.

(i) Pharmacy technicians and pharmacy technician trainees may compound sterile preparations provided the pharmacy technicians and/or pharmacy technician trainees are supervised by a pharmacist as specified in paragraph (2) of this subsection.

(ii) All pharmacy technicians and pharmacy technician trainees who compound sterile preparations for administration to patients shall:

(I) have initial training obtained either through completion of:

(-a-) a single course, a minimum of 40 hours of instruction and experience in the areas listed in paragraph (4)(D) of this subsection. Such training shall be obtained through completion of a course sponsored by an ACPE accredited provider which provides 40 hours of instruction and experience; or

(-b-) a training program which is accredited by the American Society of Health-System Pharmacists.

(II) and

(-a-) complete a structured on-the-job didactic and experiential training program at this pharmacy which provides sufficient hours of instruction and experience in the pharmacy's [~~facility's~~] sterile compounding processes and procedures. Such training may not be transferred to another pharmacy unless the pharmacies are under common ownership and control and use a common training program; and

(-b-) possess knowledge about:

(-1-) aseptic processing;

(-2-) quality control and quality assurance as related to environmental, component, and finished preparation release checks and tests;

(-3-) chemical, pharmaceutical, and clinical properties of drugs;

(-4-) container, equipment, and closure system selection; and

(-5-) sterilization techniques.

(iii) Individuals enrolled in training programs accredited by the American Society of Health-System Pharmacists may compound sterile preparations in a licensed pharmacy provided the:

(I) compounding occurs only during times the individual is assigned to a pharmacy as a part of the experiential component of the American Society of Health-System Pharmacists training program;

(II) individual is under the direct supervision of and responsible to a pharmacist who has completed training as specified in paragraph (2) of this subsection;

(III) supervising pharmacist conducts periodic in-process checks as defined in the pharmacy's policy and procedures; and

(IV) supervising pharmacist conducts a final check.

(iv) The required experiential portion of the training programs specified in this subparagraph shall [~~must~~] be supervised by an individual who is actively engaged in performing sterile compounding, is qualified and has completed training as specified in paragraph (2) of this subsection or this paragraph.

(v) In order to renew a registration as a pharmacy technician, during the previous registration period, a pharmacy technician engaged in sterile compounding shall complete a minimum of:

(I) two hours of ACPE accredited continuing education relating to one or more of the areas listed in paragraph (4)(D) of this subsection if the pharmacy technician is engaged in compounding Category 1 or Category 2 compounded [~~low and medium risk~~] sterile preparations; or

(II) four hours of ACPE accredited continuing education relating to one or more of the areas listed in paragraph (4)(D) of this subsection if the pharmacy technician is engaged in compounding Category 2 prepared from any non-sterile starting component or Category 3 compounded [~~high risk~~] sterile preparations.

(4) Evaluation and testing requirements.

(A) All persons who perform or oversee compounding or support activities shall be trained in the pharmacy's SOPs. All pharmacy personnel preparing sterile preparations shall be trained conscientiously and skillfully by expert personnel through multimedia instructional sources and professional publications in the theoretical principles and practical skills of aseptic manipulations, garbing procedures, aseptic work practices, achieving and maintaining ISO Class 5 environmental conditions, and cleaning and disinfection procedures before beginning to prepare compounded sterile preparations.

(B) All pharmacy personnel preparing sterile preparations shall perform didactic review and pass written [~~and media-fill~~] testing of aseptic manipulative skills initially and every 12 months. [~~followed by:~~]

~~*[(i)* every 12 months for low- and medium-risk level compounding; and]~~

~~*[(ii)* every six months for high-risk level compounding.]~~

(C) Pharmacy personnel who fail written tests or whose media-fill tests result in gross microbial colonization shall:

(i) be immediately re-instructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies; and

(ii) not be allowed to compound sterile preparations for patient use until passing results are achieved.

(D) The didactic and experiential training shall include instruction, experience, and demonstrated proficiency in the following areas:

(i) aseptic technique;

(ii) critical area contamination factors;

(iii) environmental monitoring;

(iv) structure and engineering controls related to facilities;

(v) equipment and supplies;

(vi) sterile preparation calculations and terminology;

(vii) sterile preparation compounding documentation;

(viii) quality assurance procedures;

(ix) aseptic preparation procedures including proper gowning and gloving technique;

(x) handling of hazardous drugs, if applicable;

(xi) cleaning procedures; and

(xii) general conduct in the clean room.

(E) The aseptic technique of all compounding personnel and personnel who have direct oversight of compounding personnel but do not compound [~~each person compounding or responsible for the direct supervision of personnel compounding sterile preparations~~] shall be observed and evaluated by expert personnel as satisfactory through written and practical tests, and media-fill [~~challenge~~] testing, and such evaluation documented. Compounding personnel shall not evaluate their own aseptic technique or results of their own media-fill [~~challenge~~] testing. The pharmacy's SOPs shall define the aseptic technique evaluation for personnel who do not compound nor have direct oversight of compounding personnel such as personnel who restock or clean and disinfect the sterile compounding area, personnel who perform in-process checks or final verification of compounded sterile preparations, and others (e.g., maintenance personnel, certifiers, contractors, inspectors, surveyors).

(F) Media-fill tests shall [~~must~~] be conducted at each pharmacy where an individual compounds Category 1 or Category 2 [~~low or medium risk~~] sterile preparations. If pharmacies are under common ownership and control, the media-fill testing may be conducted at only one of the pharmacies provided each of the pharmacies are operated under equivalent policies and procedures and the testing is conducted under the most challenging or stressful conditions. In addition, each pharmacy shall [~~must~~] maintain documentation of the media-fill test. No preparation intended for patient use shall be compounded by an individual until the on-site media-fill tests indicate that the individual can competently perform aseptic procedures, except that a pharmacist may temporarily compound sterile preparations and supervise pharmacy technicians compounding sterile preparations without media-fill tests provided the pharmacist completes the on-site media-fill tests within seven days of commencing work at the pharmacy.

(G) Media-fill tests shall [~~must~~] be conducted at each pharmacy where an individual compounds Category 2 prepared from any non-sterile starting component or Category 3 [~~high risk~~] sterile preparations. No preparation intended for patient use shall be compounded by an individual until the on-site media-fill tests indicate that the individual can competently perform aseptic procedures, except that a pharmacist may temporarily compound sterile preparations and supervise pharmacy technicians compounding sterile preparations without media-fill tests provided the pharmacist completes the on-site media-fill tests within seven days of commencing work at the pharmacy.

(H) For media-fill testing of compounds using only sterile starting components, the components shall be manipulated in a manner that simulates sterile-to-sterile compounding activities. The sterile soybean-casein digest media shall be transferred into the same types of container closure systems commonly used at the pharmacy.

[~~(H) Media-fill testing procedures for assessing the preparation of specific types of sterile preparations shall be representative of the most challenging or stressful conditions encountered by the pharmacy personnel being evaluated and, if applicable, for sterilizing high-risk level compounded sterile preparations.~~]

(I) For media-fill testing of compounds using any non-sterile starting components, a commercially available non-sterile soybean-casein digest powder shall be dissolved in non-bacteriostatic water to make a 3.0% non-sterile solution. The components shall be manipulated in a manner that simulates non-sterile-to-sterile compounding activities. At least one container shall be prepared as the positive control to demonstrate growth promotion, as indicated by visible turbidity upon incubation.

[~~(I) Media-fill challenge tests simulating high-risk level compounding shall be used to verify the capability of the compounding environment and process to produce a sterile preparation.~~]

(J) Final containers shall be incubated in an incubator at 20 to 25 degrees Celsius and 30 to 35 degrees Celsius for a minimum of 7 days at each temperature band to detect a broad spectrum of microorganisms. The order of the incubation temperatures shall be described in the pharmacy's SOPs. Failure is indicated by visible turbidity or other visual manifestations of growth in the media in one or more container closure unit(s) on or before the end of the incubation period.

[~~(J) Commercially available sterile fluid culture media for low and medium risk level compounding or non-sterile fluid culture media for high risk level compounding shall be able to promote exponential colonization of bacteria that are most likely to be transmitted to compounding sterile preparations from the compounding personnel and environment. Media-filled vials are generally incubated at 20 to 25 degrees Celsius or at 30 to 35 degrees Celsius for a minimum of 14 days. If two temperatures are used for incubation of media-filled samples, then these filled containers should be incubated for at least 7 days at each temperature. Failure is indicated by visible turbidity in the medium on or before 14 days.~~]

(K) The pharmacist-in-charge shall ensure continuing competency of pharmacy personnel through in-service education, training, and media-fill tests to supplement initial training. Personnel competency shall be evaluated:

(i) during orientation and training prior to the regular performance of those tasks;

(ii) whenever the quality assurance program yields an unacceptable result;

(iii) whenever unacceptable techniques are observed; and

(iv) at least every 12 months, with the exception of media-fill testing which shall be completed every six months for compounding personnel [~~on an annual basis for low- and medium-risk level compounding, and every six months for high-risk level compounding~~].

(L) The pharmacist-in-charge shall ensure that proper hand hygiene and garbing practices of all compounding personnel and personnel who have direct oversight of compounding personnel but do not compound are evaluated prior to compounding, supervising, or verifying sterile preparations intended for patient use and whenever an aseptic media-fill [~~media fill~~] is performed.

(i) Gloved fingertip sampling shall be performed for all [~~Sampling of~~] compounding personnel and personnel who have direct oversight of compounding personnel but do not compound [~~glove fingertips shall be performed for all risk level compounding~~]. If pharmacies are under common ownership and control, the gloved fingertip and thumb sampling may be conducted at only one of the pharmacies provided each of the pharmacies are operated under equivalent policies and procedures and the testing is conducted under the most challenging or stressful conditions. In addition, each pharmacy shall [~~must~~] maintain documentation of the gloved fingertip and thumb sampling [~~of all compounding personnel~~].

(ii) All compounding personnel and personnel who have direct oversight of compounding personnel but do not compound shall demonstrate competency in proper hand hygiene and garbing procedures and in aseptic work practices (e.g., disinfection of component surfaces, routine disinfection of gloved hands).

(iii) Sterile sampling media devices [~~contact agar plates~~] shall be used to sample the gloved fingertips of compounding personnel and personnel who have direct oversight of compounding personnel but do not compound after garbing in order to assess garbing competency and after completing the media-fill preparation (without applying sterile 70% IPA).

(iv) The visual observation shall be documented and maintained to provide a permanent record and long-term assessment of personnel competency.

(v) All compounding personnel and personnel who have direct oversight of compounding personnel but do not compound shall successfully complete an initial competency evaluation and gloved fingertip and thumb [~~fingertip/thumb~~] sampling procedure no less than three times before initially being allowed to compound sterile preparations for patient use. Immediately after the [~~compounding~~] personnel completes the hand hygiene and garbing procedure (i.e., after donning of sterile gloves and before any disinfecting with sterile 70% IPA), the evaluator will collect a gloved fingertip and thumb sample from both hands of the compounding personnel onto contact plates or swabs by having the individual lightly touching each fingertip onto the testing medium. Samples shall be incubated in an incubator. The media device shall be incubated at 30 to 35 degrees Celsius for no less than 48 hours and then at 20 to 25 degrees Celsius for no less than five additional days. Alternatively, to shorten the overall incubation period, two sampling media devices may be incubated concurrently in separate incubators with one media device incubated at 30 to 35 degrees Celsius for no less than 48 hours and the other media device incubated at 20 to 25 degrees Celsius for no less than five days. Media devices shall be handled and stored so as to avoid contamination and prevent condensate from dropping onto the agar during incubation and affecting the accuracy of the cfu reading (e.g., invert containers) [~~The contact plates or swabs will be incubated for the appropriate incubation period and at the appropriate temperature~~]. Action levels for

gloved fingertip and thumb sampling are based on the total cfu count from both hands. Results of the initial gloved fingertip and thumb sampling evaluations after garbing shall indicate not greater than zero colony-forming units (0 cfu) [~~(0 CFU)~~] growth on the contact plates or swabs, or the test shall be considered a failure. Results of the initial gloved fingertip evaluations after media-fill testing shall indicate not greater than three colony-forming units (3 cfus) growth on the contact plates or swabs, or the test shall be considered a failure. In the event of a failed gloved fingertip and thumb test, the evaluation shall be repeated until the individual can successfully don sterile gloves and pass the gloved fingertip and thumb sampling evaluation, defined as zero cfus [~~CFUs~~] growth. Surface sampling of the direct compounding area shall be performed. No preparation intended for patient use shall be compounded by an individual until the results of the initial gloved fingertip and thumb and surface sampling evaluations [~~evaluation~~] indicate that the individual can competently perform aseptic procedures except that a pharmacist may temporarily physically supervise pharmacy technicians compounding sterile preparations before the results of the evaluation have been received for no more than three days from the date of the test.

(vi) Re-evaluation of all compounding personnel shall occur at least every six months [~~annually for compounding personnel who compound low and medium risk level preparations and every six months for compounding personnel who compound high risk level preparations~~]. Re-evaluation of personnel who have direct oversight of compounding personnel but do not compound shall occur at least every 12 months. Results of gloved fingertip and thumb tests conducted immediately after compounding personnel complete a compounding procedure shall indicate no more than 3 cfus [~~CFUs~~] growth, or the test shall be considered a failure, in which case, the evaluation shall be repeated until an acceptable test can be achieved (i.e., the results indicated no more than 3 cfus [~~CFUs~~] growth).

(vii) Personnel who have direct oversight of compounding personnel but do not compound shall complete a garbing competency evaluation every 12 months. The pharmacy's SOPs shall define the garbing competency evaluation for personnel who do not compound nor have direct oversight of compounding personnel such as personnel who restock or clean and disinfect the sterile compounding area, personnel who perform in-process checks or final verification of compounded sterile preparations, and others (e.g., maintenance personnel, certifiers, contractors, inspectors, surveyors).

(M) The pharmacist-in-charge shall ensure surface sampling shall be conducted in all ISO classified areas on a periodic basis. Sampling shall be accomplished using contact plates or swabs at the conclusion of compounding. The sample area shall be gently touched with the agar surface by rolling the plate across the surface to be sampled.

(i) Each classified area, including each room and the interior of each ISO Class 5 primary engineering control (PEC) and pass-through chambers connecting to classified areas (e.g., equipment contained within the PEC, staging or work area(s) near the PEC, frequently touched areas), shall be sampled for microbial contamination using a risk-based approach.

(ii) For pharmacies compounding Category 1 or Category 2 compounded sterile preparations, surface sampling of all classified areas and pass-through chambers connecting to classified areas shall be conducted at least monthly. For pharmacies compounding any Category 3 compounded sterile preparations, surface sampling of all classified areas and pass-through chambers connecting to classified areas shall be completed prior to assigning a beyond-use-date longer than the limits established for Category 2 compounded sterile preparations and at least weekly on a regularly scheduled basis regardless of the frequency of compounding Category 3 compounded sterile preparations.

(iii) (iii) The following action levels for surface sampling apply:

(I) for ISO Class 5, greater than 3 cfus per media device;

(II) for ISO Class 7, greater than 5 cfus per media device; and

(III) for ISO Class 8, greater than 50 cfus per media device.

(iv) If levels measured during surface sampling exceed the levels in clause (iii) of this subparagraph for the ISO classification levels of the area sampled, the cause shall be investigated and corrective action shall be taken. Data collected in response to corrective actions shall be reviewed to confirm that the actions taken have been effective. The corrective action plan shall be dependent on the cfu count and the microorganism recovered. The corrective action plan shall be documented. If levels measured during surface sampling exceed the levels in clause (iii) of this subparagraph, an attempt shall be made to identify any microorganism recovered to the genus level with the assistance of a competent microbiologist.

(N) Personnel who only perform restocking or cleaning and disinfecting duties outside of the primary engineering control shall complete ongoing training as required by the pharmacy's SOPs.

(5) Documentation of training [~~Training~~]. The pharmacy shall maintain a record of the training and continuing education on each person who compounds sterile preparations. The record shall contain, at a minimum, a written record of initial and in-service training, education, and the results of written and practical testing and media-fill testing of pharmacy personnel. The record shall be maintained and available for inspection by the board and contain the following information:

(A) name of the person receiving the training or completing the testing or media-fill tests;

(B) date(s) of the training, testing, or media-fill [~~challenge~~] testing;

(C) general description of the topics covered in the training or testing or of the process validated;

(D) name of the person supervising the training, testing, or media-fill [~~challenge~~] testing; and

(E) signature or initials of the person receiving the training or completing the testing or media-fill [~~challenge~~] testing and the pharmacist-in-charge or other pharmacist employed by the pharmacy and designated by the pharmacist-in-charge as responsible for training, testing, or media-fill [~~challenge~~] testing of personnel.

(d) Operational standards [~~Standards~~].

(1) General requirements [~~Requirements~~].

(A) Sterile preparations may be compounded:

(i) upon presentation of a practitioner's prescription drug or medication order based on a valid pharmacist/patient/prescriber relationship;

(ii) in anticipation of future prescription drug or medication orders based on routine, regularly observed prescribing patterns; or

(iii) in reasonable quantities for office use by a practitioner and for use by a veterinarian.

(B) Sterile compounding in anticipation of future prescription drug or medication orders shall [~~must~~] be based upon a history of receiving valid prescriptions issued within an established pharmacist/patient/prescriber relationship, provided that in the pharmacist's professional judgment the quantity prepared is stable for the anticipated shelf time. The maximum batch size for all preparations requiring sterility testing shall be limited to 750 final yield units.

(i) The pharmacist's professional judgment shall be based on the criteria used to determine a beyond-use date outlined in paragraph (8)(J) [~~(6)(G)~~] of this subsection.

(ii) Documentation of the criteria used to determine the stability for the anticipated shelf time shall [~~must~~] be maintained and be available for inspection.

(iii) Any preparation compounded in anticipation of future prescription drug or medication orders shall be labeled. Such label shall contain:

(I) name and strength of the compounded preparation or list of the active ingredients and strengths;

(II) facility's lot number;

(III) beyond-use date as determined by the pharmacist using appropriate documented criteria as outlined in paragraph (8)(J) [~~(6)(G)~~] of this subsection;

(IV) quantity or amount in the container;

(V) appropriate ancillary instructions, such as storage instructions or cautionary statements, including hazardous drug warning labels where appropriate; and

(VI) device-specific instructions, where appropriate.

(C) Commercially available products may be compounded for dispensing to individual patients or for office use provided the following conditions are met:

(i) the commercial product is not reasonably available from normal distribution channels in a timely manner to meet individual patient's needs;

(ii) the pharmacy maintains documentation that the product is not reasonably available due to a drug shortage or unavailability from the manufacturer; and

(iii) the prescribing practitioner has requested that the drug be compounded as described in subparagraph (D) of this paragraph.

(D) A pharmacy may not compound preparations that are essentially copies of commercially available products (e.g., the preparation is dispensed in a strength that is only slightly different from a commercially available product) unless the prescribing practitioner specifically orders the strength or dosage form and specifies why the individual patient needs the particular strength or dosage form of the preparation or why the preparation for office use is needed in the particular strength or dosage form of the preparation. The prescribing practitioner shall provide documentation of a patient specific medical need and the preparation produces a clinically significant therapeutic response (e.g., the physician requests an alternate preparation due to hypersensitivity to excipients or preservative in the FDA-approved product, or the physician requests an effective alternate dosage form) or if the drug product is not commercially available. The unavailability of such drug product shall [~~must~~] be documented prior to compounding. The methodology for documenting unavailability includes maintaining a copy of the wholesaler's notification showing back-ordered, discontinued, or out-of-stock items. This documentation shall [~~must~~] be available in hard-copy or electronic format for inspection by the board.

(E) A pharmacy may enter into an agreement to compound and dispense prescription drug or medication orders for another pharmacy provided the pharmacy complies with the provisions of §291.125 of this title (relating to Centralized Prescription Dispensing).

(F) Compounding pharmacies/pharmacists may advertise and promote the fact that they provide sterile prescription compounding services, which may include specific drug preparations and classes of drugs.

(G) A pharmacy may not compound veterinary preparations for use in food producing animals except in accordance with federal guidelines.

(H) Compounded sterile preparations, including hazardous drugs and radiopharmaceuticals, shall be prepared only under conditions that protect the pharmacy personnel in the preparation and storage areas.

(2) Compounded sterile preparation categories. Category 1, Category 2, and Category 3 are primarily based on the state of environmental control under which they are compounded, the probability for microbial growth during the time they will be stored, and the time period within which they must be used.

(A) A Category 1 compounded sterile preparation is a compounded sterile preparation that is assigned a beyond-use date in accordance with paragraph (8)(J)(ii)(I) of this subsection and all applicable requirements of this section for Category 1 compounded sterile preparations.

(B) A Category 2 compounded sterile preparation is a compounded sterile preparation that is assigned a beyond-use date in accordance with paragraph (8)(J)(ii)(II) of this subsection and all applicable requirements of this section for Category 2 compounded sterile preparations.

(C) A Category 3 compounded sterile preparation is a compounded sterile preparation that is assigned a beyond-use date in accordance with paragraph (8)(J)(ii)(III) of this subsection and all applicable requirements of this section for Category 3 compounded sterile preparations.

[~~(2) Microbial Contamination Risk Levels. Risk Levels for sterile compounded preparations shall be as outlined in Chapter 797, Pharmacy Compounding--Sterile Preparations of the USP/NF and as listed in this paragraph.~~]

[~~(A) Low-risk level compounded sterile preparations.~~]

~~*(i)* Low-Risk conditions. Low-risk level compounded sterile preparations are those compounded under all of the following conditions:~~]

~~*(I)* The compounded sterile preparations are compounded with aseptic manipulations entirely within ISO Class 5 or better air quality using only sterile ingredients, products, components, and devices;~~]

~~*(II)* The compounding involves only transfer, measuring, and mixing manipulations using not more than three commercially manufactured packages of sterile products and not more than two entries into any one sterile container or package (e.g., bag, vial) of sterile product or administration container/device to prepare the compounded sterile preparation;~~]

[(III) Manipulations are limited to aseptically opening ampules, penetrating disinfected 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;]

[(IV) For a low-risk level preparation, in the absence of passing a sterility test the storage periods cannot exceed the following time periods: before administration, the compounded sterile preparation is stored properly and are exposed for not more than 48 hours at controlled room temperature, for not more than 14 days if stored at a cold temperature, and for 45 days if stored in a frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius. For delayed activation device systems, the storage period begins when the device is activated.]

[(ii) Examples of Low-Risk Level Compounding. Examples of low-risk level compounding include the following:]

[(I) Single volume transfers of sterile dosage forms from ampules, bottles, bags, and vials using sterile syringes with sterile needles, other administration devices, and other sterile containers. The solution content of ampules shall be passed through a sterile filter to remove any particles;]

[(II) Simple aseptic measuring and transferring with not more than three packages of manufactured sterile products, including an infusion or diluent solution to compound drug admixtures and nutritional solutions.]

[(B) Low-Risk Level compounded sterile preparations with 12-hour or less beyond-use date. Low-risk level compounded sterile preparations are those compounded pursuant to a physician's order for a specific patient under all of the following conditions:]

[(i) The compounded sterile preparations are compounded in compounding aseptic isolator or compounding aseptic containment isolator that does not meet the requirements described in paragraph (7)(C) or (D) of this subsection (relating to Primary Engineering Control Device) or the compounded sterile preparations are compounded in laminar airflow workbench or a biological safety cabinet that cannot be located within the buffer area;]

[(ii) The primary engineering control device shall be certified and maintain ISO Class 5 for exposure of critical sites and shall be located in a segregated compounding area restricted to sterile compounding activities that minimizes the risk of contamination of the compounded sterile preparation;]

[(iii) 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.]

[(iv) For a low-risk level preparation compounded as described in clauses (i) - (iii) of this subparagraph, administration of such compounded sterile preparations must commence within 12 hours of preparation or as recommended in the manufacturers' package insert, whichever is less. However, the administration of sterile radiopharmaceuticals, with documented testing of chemical stability, may be administered beyond 12 hours of preparation.]

[(C) Medium-risk level compounded sterile preparations.]

[(i) Medium-Risk Conditions. Medium-risk level compounded sterile preparations, are those compounded aseptically under low-risk conditions and one or more of the following conditions exists:]

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

[(II) The compounding process includes complex aseptic manipulations other than the single-volume transfer;]

[(III) The compounding process requires unusually long duration, such as that required to complete the dissolution or homogenous mixing (e.g., reconstitution of intravenous immunoglobulin or other intravenous protein products);]

[(IV) The compounded sterile preparations do not contain broad spectrum bacteriostatic substances and they are administered over several days (e.g., an externally worn infusion device); or]

[(V) For a medium-risk level preparation, in the absence of passing a sterility test the storage periods cannot exceed the following time periods: before administration, the compounded sterile preparations are properly stored and are exposed for not more than 30 hours at controlled room temperature, for not more than 9 days at a cold temperature, and for 45 days in solid frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius.]

[(ii) Examples of medium-risk compounding. Examples of medium-risk compounding include the following:]

[(I) Compounding of total parenteral nutrition fluids using a manual or automated device during which there are multiple injections, detachments, and attachments of nutrient source products to the device or machine to deliver all nutritional components to a final sterile container;]

[(II) Filling of reservoirs of injection and infusion devices with more than three sterile drug products and evacuations of air from those reservoirs before the filled device is dispensed;]

[(III) Filling of reservoirs of injection and infusion devices with volumes of sterile drug solutions that will be administered over several days at ambient temperatures between 25 and 40 degrees Celsius (77 and 104 degrees Fahrenheit); and]

[(IV) Transfer of volumes from multiple ampules or vials into a single, final sterile container or product.]

[(D) High-risk level compounded sterile preparations.]

[(i) High-risk Conditions. High-risk level compounded sterile preparations are those compounded under any of the following conditions:]

[(I) Non-sterile ingredients, including manufactured products not intended for sterile routes of administration (e.g., oral) are incorporated or a non-sterile device is employed before terminal sterilization.]

[(II) Any of the following are exposed to air quality worse than ISO Class 5 for more than 1 hour:]

[(-a-) sterile contents of commercially manufactured products;]

[(-b-) CSPs that lack effective antimicrobial preservatives; and]

[(-c-) sterile surfaces of devices and containers for the preparation, transfer, sterilization, and packaging of CSPs;]

[(III) Compounding personnel are improperly garbed and gloved;]

[(IV) Non-sterile water-containing preparations are exposed no more than 6 hours before being sterilized;]

[(V) 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;]

[(VI) For a sterilized high-risk level preparation, in the absence of passing a sterility test, the storage periods cannot exceed the following time periods: before administration, the compounded sterile preparations are properly stored and are exposed for not more than 24 hours at controlled room temperature, for not more than 3 days at a cold temperature, and for 45 days in solid frozen state between minus 25 degrees Celsius and minus 10 degrees Celsius; or]

[(VII) All non-sterile measuring, mixing, and purifying devices are rinsed thoroughly with pyrogen-free or depyrogenated sterile water, and then thoroughly drained or dried immediately before use for high-risk compounding. All high-risk compounded sterile solutions subjected to terminal sterilization are prefiltered by passing through a filter with a nominal pore size not larger than 1.2 micron preceding or during filling into their final containers to remove particulate matter. Sterilization of high-risk level compounded sterile preparations by filtration shall be performed with a sterile 0.2 micrometer or 0.22 micrometer nominal pore size filter entirely within an ISO Class 5 or superior air quality environment.]

[(ii) Examples of high-risk compounding. Examples of high-risk compounding include the following.]

[(I) Dissolving non-sterile bulk drug powders to make solutions, which will be terminally sterilized;]

(II) Exposing the sterile ingredients and components used to prepare and package compounded sterile preparations to room air quality worse than ISO Class 5 for more than one hour;

[(III) Measuring and mixing sterile ingredients in non-sterile devices before sterilization is performed; and]

[(IV) Assuming, without appropriate evidence or direct determination, that packages of bulk ingredients contain at least 95% by weight of their active chemical moiety and have not been contaminated or adulterated between uses.]

(3) Depyrogenation. Dry heat depyrogenation shall be used to render glassware, metal, and other thermostable containers and components pyrogen free. The duration of the exposure period shall include sufficient time for the items to reach the depyrogenation temperature. The items shall remain at the depyrogenation temperature for the duration of the depyrogenation period. The effectiveness of the dry heat depyrogenation cycle shall be established initially and verified annually using endotoxin challenge vials to demonstrate that the cycle is capable of achieving a greater than or equal to 3-log reduction in endotoxins. The effectiveness of the depyrogenation cycle shall be re-established if there are changes to the depyrogenation cycle described in the pharmacy's SOPs (e.g., changes in load conditions, duration, or temperature). This verification shall be documented.

(4) [(3)] Immediate use compounded sterile preparations [Use Compounded Sterile Preparations]. When all of the following conditions are met, compounding of compounded sterile preparations for direct and immediate administration is not subject to the requirements for Category 1, Category 2, or Category 3 compounded sterile preparations: [For the purpose of emergency or immediate patient care, such situations may include cardiopulmonary resuscitation, emergency room treatment, preparation of diagnostic agents, or critical therapy where the preparation of the compounded sterile preparation under low-risk level conditions would subject the patient to additional risk due to delays in therapy. Compounded sterile preparations are exempted from the requirements described in this paragraph for low-risk level compounded sterile preparations when all of the following criteria are met:]

(A) Only simple aseptic measuring and transfer manipulations are performed with not more than three different sterile [non-hazardous commercial drug and diagnostic radiopharmaceutical] drug products, including an infusion or diluent solution, from the manufacturers' original containers and not more than two entries into any one container or package of sterile infusion solution or administration container/device;

(B) Unless required for the preparation, the compounding procedure occurs continuously without delays or interruptions and does not exceed 1 hour;

(C) During preparation, aseptic technique is followed and, if not immediately administered, the finished compounded sterile preparation is under continuous supervision to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter of biological fluids, mix-ups with other compounded sterile preparations, and direct contact with outside surfaces;

(D) Administration begins not later than four hours [one hour] following the start [completion] of preparing the compounded sterile preparation;

(E) When the compounded sterile preparation [preparations] is not administered by the person who prepared it, or its administration is not witnessed by the person who prepared it, the compounded sterile preparation shall bear a label listing patient identification information such as name and identification number(s), the names and amounts of all ingredients, the name or initials of the person who prepared the compounded sterile preparation, and the exact 4-hour [1-hour] beyond-use time and date;

(F) If administration has not begun within four hours [one hour] following the completion of preparing the compounded sterile preparation, the compounded sterile preparation is promptly and safely discarded. Immediate use compounded sterile preparations shall not be stored for later use; [and]

(G) Hazardous drugs shall not be prepared as immediate use compounded sterile preparations; and[.]

(H) Personnel are trained and demonstrate competency in aseptic processes as they relate to assigned tasks and the pharmacy's SOPs.

(5) [(4)] Single-dose and multiple-dose [multiple dose] containers.

(A) Opened or needle punctured single-dose containers, such as bags bottles, syringes, and vials of sterile products shall be used within one hour if opened in worse than ISO Class 5 air quality. Any remaining contents shall [must] be discarded.

(B) If a single-dose vial is entered or punctured only in ISO Class 5 or cleaner air, it may be used up to 12 hours after initial entry or puncture as long as the labeled storage requirements during that 12 hour period are maintained [Single-dose containers, including single-dose large volume parenteral solutions and single-dose vials, exposed to ISO Class 5 or cleaner air may be used up to six hours after initial needle puncture].

(C) Open single-dose ampules shall not be stored for any time period [Opened single-dose fusion sealed containers shall not be stored for any time period].

(D) Once initially entering or puncturing a multiple-dose container, the multiple-dose container shall not be used for

more than 28 days unless otherwise specified by the manufacturer on the labeling [~~Multiple-dose containers may be used up to 28 days after initial needle puncture unless otherwise specified by the manufacturer~~].

(E) Conventionally manufactured pharmacy bulk packages shall be restricted to the sterile preparation of admixtures for infusion or, through a sterile transfer device, for the filling of empty sterile containers. The pharmacy bulk package shall be used according to the manufacturer's labeling and entered or punctured only in an ISO Class 5 primary engineering control.

(F) Multiple-dose compounded sterile preparations shall meet the criteria for antimicrobial effectiveness testing and the requirements of subparagraph (G) of this paragraph. Multiple-dose compounded sterile preparations shall be stored under conditions upon which the beyond-use date is based (e.g., refrigerator or controlled room temperature). After a multiple-dose compounded sterile preparation is initially entered or punctured, the multiple-dose compounded sterile preparation shall not be used for longer than the assigned beyond-use date or 28 days, whichever is shorter.

(G) A multiple-dose compounded sterile preparation shall be prepared as a Category 2 or Category 3 compounded sterile preparation. An aqueous multiple-dose compounded sterile preparation shall additionally pass antimicrobial effectiveness testing. In the absence of supporting documentation or data, compounding personnel may rely on antimicrobial effectiveness testing conducted or contracted for once for each formulation in the particular container closure system in which it will be packaged.

(H) In the absence of container closure data, the container closure system used to package the multiple-dose compounded sterile preparation shall be evaluated for and conform to container closure integrity. The container closure integrity test shall be conducted only once on each formulation and on fill volume in the particular container closure system in which the multiple-dose compounded sterile preparation shall be packaged.

(I) Multiple-dose, nonpreserved, aqueous topical, and topical ophthalmic compounded sterile preparations. Antimicrobial effectiveness testing under subparagraph (G) of this paragraph is not required if the preparation is prepared as a Category 2 or Category 3 compounded sterile preparation, for use by a single patient, and labeled to indicate that once opened, it shall be discarded after 24 hours when stored at controlled room temperature, 72 hours when stored under refrigeration, or 90 days when frozen if based on documented published stability and effectiveness data.

(J) When a single-dose compounded sterile preparation or compounded sterile preparation stock solution is used as a component to compound additional compounded sterile preparations, the original single-dose compounded sterile preparation or compounded sterile preparation stock solution shall be entered or punctured in ISO Class 5 or cleaner air and stored under the conditions upon which its beyond-use date is based (e.g., refrigerator or controlled room temperature). The component compounded sterile preparation may be used for sterile compounding for up to 12 hours once accessed or its assigned beyond-use date, whichever is shorter, and any remainder shall be discarded.

(6) Proprietary bag and vial systems. Docking and activation of proprietary bag and vial systems in accordance with the manufacturer's labeling for immediate administration to an individual patient is not considered compounding and may be performed outside of an ISO Class 5 environment. Docking of the proprietary bag and vial system for future activation and administration is considered compounding and shall be performed in an ISO Class 5 environment. Beyond-use dates for proprietary bag and vial systems shall not be longer than those specified in the manufacturer's labeling.

(7) [~~(5)~~] Library. In addition to the library requirements of the pharmacy's specific license classification, a pharmacy shall maintain current or updated copies in hard-copy or electronic format of each of the following:

(A) a reference text on injectable drug preparations, such as Handbook on Injectable Drug Products;

(B) a specialty reference text appropriate for the scope of pharmacy services provided by the pharmacy, e.g., if the pharmacy prepares hazardous drugs, a reference text on the preparation of hazardous drugs;

(C) the United States Pharmacopeia/National Formulary containing USP Chapter 71, Sterility Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding--Nonsterile Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--Sterile Preparations, and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding; and

(D) any additional USP/NF chapters applicable to the practice of the pharmacy (e.g., USP Chapter 800, Hazardous Drugs--Handling in Healthcare Settings, USP Chapter 823, Positron Emission Tomography Drugs for Compounding, Investigational, and Research Uses).

(8) [~~(6)~~] Environment. Compounding facilities shall be physically designed and environmentally controlled to minimize airborne contamination from contacting critical sites.

(A) Air exchange requirements. For cleanroom suites, adequate HEPA-filtered airflow to the buffer room(s) and anteroom(s) is required to maintain appropriate ISO classification during compounding activities. Airflow is measured in terms of the number of air changes per hour (ACPH).

(i) Unclassified sterile compounding area. No requirement for ACPH.

(ii) ISO Class 7 room(s). A minimum of 30 total HEPA-filtered ACPH shall be supplied to ISO Class 7 rooms. At least 15 ACPH of the total air change rate in a room shall come from the HVAC through HEPA filters located in the ceiling. The ACPH from HVAC, ACPH contributed from the PEC, and the total ACPH shall be documented on the certification report.

(iii) ISO Class 8 room(s). A minimum of 20 total HEPA-filtered ACPH shall be supplied to ISO Class 8 rooms. At least 15 ACPH of the total air change rate in a room shall come from the HVAC through HEPA filters located in the ceiling. The total ACPH shall be documented on the certification report.

(B) Cleanroom suite. Seals and sweeps should not be installed at doors between buffer rooms and anterooms. Access doors should be hands-free. Tacky mats shall not be placed within ISO-classified areas.

(C) [~~(A)~~] Category 1 and Category 2 preparations [~~Low and Medium Risk Preparations~~]. A pharmacy that prepares Category 1 compounded sterile preparations outside of a segregated compounding area or Category 2 compounded sterile [~~low- and medium-risk~~] preparations shall have a clean room for the compounding of sterile preparations that is constructed to minimize the opportunities for particulate and microbial contamination. The clean room shall:

(i) be clean, well lit, and of sufficient size to support sterile compounding activities;

(ii) be maintained at a temperature of 20 degrees Celsius or cooler and at a humidity of 60% or below [~~60%~~];

(iii) be used only for the compounding of sterile preparations;

(iv) be designed such that hand sanitizing and gowning occurs outside the buffer room [~~area~~] but allows hands-free access by compounding personnel to the buffer room [~~area~~];

(v) have non-porous and washable floors or floor covering to enable regular disinfection;

(vi) be ventilated in a manner to avoid disruption from the HVAC system and room cross-drafts;

(vii) have walls, ceilings, floors, fixtures, shelving, counters, and cabinets that are smooth, impervious, free from cracks and crevices (e.g., coved), non-shedding and resistant to damage by disinfectant agents;

(viii) have junctures of ceilings to walls coved or caulked to avoid cracks and crevices;

(ix) have drugs and supplies stored on shelving areas above the floor to permit adequate floor cleaning;

(x) contain only the appropriate compounding supplies and not be used for bulk storage for supplies and materials. Objects that shed particles shall not be brought into the clean room. A Class B pharmacy may use low-linting absorbent materials in the primary engineering control device;

(xi) contain an anteroom [~~ante-area~~] that contains a sink with hot and cold running water that enables hands-free use with a closed system of soap dispensing to minimize the risk of extrinsic contamination. A Class B pharmacy may have a sink with hot and cold running water that enables hands-free use with a closed system of soap dispensing immediately outside the anteroom [~~ante-area~~] if antiseptic hand cleansing is performed using a waterless alcohol-based surgical hand scrub with persistent activity following manufacturers' recommendations once inside the anteroom [~~ante-area~~]; and

(xii) contain a buffer room [~~area~~]. The following is applicable for the buffer room [~~area~~]:

(I) There shall be some demarcation designation that delineates the anteroom [~~ante-area~~] from the buffer room [~~area~~]. The demarcation shall be such that it does not create conditions that could adversely affect the cleanliness of the room [~~area~~];

(II) The buffer room [~~area~~] shall be segregated from surrounding, unclassified spaces to reduce the risk of contaminants being blown, dragged, or otherwise introduced into the filtered unidirectional airflow environment, and this segregation should be continuously monitored;

(III) A buffer room [~~area~~] that is not physically separated from the anteroom [~~ante-area~~] shall employ the principle of displacement airflow as defined in Chapter 797, Pharmaceutical Compounding--Sterile Preparations, of the USP/NF, with limited access to personnel; and

(IV) The buffer room [~~area~~] shall not contain sources of water (i.e., sinks) or floor drains other than distilled or sterile water introduced for facilitating the use of heat block wells for radiopharmaceuticals.

(D) [~~(B)~~] Category 2 prepared from any non-sterile starting component and Category 3 preparations [~~High-risk Preparations~~].

(i) In addition to the requirements in subparagraph (C) [~~(A)~~] of this paragraph, when Category 2 prepared from any non-sterile starting component or Category 3 compounded sterile [~~high-risk~~] preparations are compounded, the primary engineering control shall be located in a buffer room [~~area~~] that provides a physical separation, through the use of walls, doors and pass-throughs and has a minimum differential positive pressure of 0.02 [~~to 0.05~~] inches water column.

(ii) Presterilization procedures for Category 2 prepared from any non-sterile starting component or Category 3 [~~high-risk level~~] compounded sterile preparations, such as weighing and mixing, shall be completed in no worse than an ISO Class 8 environment using depyrogenated equipment.

(E) [~~(C)~~] Automated compounding device.

(i) General. If automated compounding devices are used, the pharmacy shall have a method to calibrate and verify the accuracy of automated compounding devices used in aseptic processing and document the calibration and verification on a daily basis, based on the manufacturer's recommendations, and review the results at least weekly.

(ii) Loading bulk drugs into automated compounding devices.

(I) Automated compounding devices may be loaded with bulk drugs only by a pharmacist or by pharmacy technicians or pharmacy technician trainees under the direction and direct supervision of a pharmacist.

(II) The label of an automated compounding device container shall indicate the brand name and strength of the drug; or if no brand name, then the generic name, strength, and name of the manufacturer or distributor.

(III) Records of loading bulk drugs into an automated compounding device shall be maintained to show:

(-a-) name of the drug, strength, and dosage form;

(-b-) manufacturer or distributor;

(-c-) manufacturer's lot number;

(-d-) manufacturer's expiration date;

(-e-) quantity added to the automated compounding device;

(-f-) date of loading;

(-g-) name, initials, or electronic signature of the person loading the automated compounding device; and

(-h-) name, initials, or electronic signature of the responsible pharmacist.

(IV) The automated compounding device shall not be used until a pharmacist verifies that the system is properly loaded and affixes his or her signature or electronic signature to the record specified in subclause (III) of this clause.

(F) [~~(D)~~] Hazardous drugs. If the preparation is hazardous, the following is also applicable:

(i) Hazardous drugs shall be prepared only under conditions that protect personnel during preparation and storage;

(ii) Hazardous drugs shall be stored separately from other inventory in a manner to prevent contamination and personnel exposure;

(iii) All personnel involved in the compounding of hazardous drugs shall wear appropriate protective apparel, such as gowns, face masks, eye protection, hair covers, shoe covers or

dedicated shoes, and appropriate gloving at all times when handling hazardous drugs, including receiving, distribution, stocking, inventorying, preparation, for administration and disposal;

(iv) Appropriate safety and containment techniques for compounding hazardous drugs shall be used in conjunction with aseptic techniques required for preparing sterile preparations;

(v) Disposal of hazardous waste shall comply with all applicable local, state, and federal requirements;

(vi) Prepared doses of hazardous drugs shall [~~must~~] be dispensed, labeled with proper precautions inside and outside, and distributed in a manner to minimize patient contact with hazardous agents.

(G) [~~(E)~~] Blood-labeling procedures. When compounding activities require the manipulation of a patient's blood-derived material (e.g., radiolabeling a patient's or donor's white blood cells), the manipulations shall be performed in an [~~a~~] ISO Class 5 biological safety cabinet located in a buffer room [~~area~~] and shall be clearly separated from routine material-handling procedures and equipment used in preparation activities to avoid any cross-contamination. The preparations shall not require sterilization.

(H) [~~(F)~~] Cleaning and disinfecting the sterile compounding areas. The following cleaning and disinfecting practices and frequencies apply to direct and contiguous compounding areas, which include ISO Class 5 compounding areas for exposure of critical sites as well as buffer rooms [~~areas~~], anterooms [~~ante-areas~~], and segregated compounding areas.

(i) The pharmacist-in-charge is responsible for developing written standard operating procedures (SOPs) for cleaning and disinfecting the direct and contiguous compounding areas and assuring the procedures are followed.

(ii) In a PEC, sterile 70% IPA shall be applied after cleaning and disinfecting, or after the application of a one-step disinfectant cleaner or sporicidal disinfectant, to remove any residue. Sterile 70% IPA shall also be applied immediately before initiating compounding. During the compounding process sterile 70% IPA shall be applied to the horizontal work surface, including any removable work trays, of the PEC at least every 30 minutes if the compounding process takes 30 minutes or less. If the compounding process takes more than 30 minutes, compounding shall not be disrupted and the work surface of the PEC shall be disinfected immediately after compounding [~~These procedures shall be conducted at the beginning of each work shift, before each batch preparation is started, when there are spills, and when surface contamination is known or suspected resulting from procedural breaches, and every 30 minutes during continuous compounding of individual compounded sterile preparations, unless a particular compounding procedure requires more than 30 minutes to complete, in which case, the direct compounding area is to be cleaned immediately after the compounding activity is completed~~].

(iii) Surfaces shall be cleaned prior to being disinfected unless a one-step disinfectant cleaner is used to accomplish both the cleaning and disinfection in one step. The manufacturer's directions or published data for the minimum contact time shall be followed for each of the cleaning, disinfecting, and sporicidal disinfectants used. When sterile 70% IPA is used, it shall be allowed to dry. [~~Before compounding is performed, all items shall be removed from the direct and contiguous compounding areas and all surfaces are cleaned by removing loose material and residue from spills, followed by an application of a residue-free disinfecting agent (e.g., IPA), which is allowed to dry before compounding begins~~]. In a Class B pharmacy, objects used in preparing sterile radiopharmaceuticals (e.g., dose calibrator) which cannot be reasonably removed from the compounding area shall be sterilized with an application of a residue-free disinfection agent.

(iv) Surfaces in classified areas used to prepare Category 1, Category 2, and Category 3 compounded sterile preparations shall be cleaned, disinfected, and sporicidal disinfectants applied in accordance with the following:

(I) PEC(s) and equipment inside PEC(s).

(-a-) Equipment and all interior surfaces of the PEC shall be cleaned daily on days when compounding occurs and when surface contamination is known or suspected. Equipment and all interior surfaces of the PEC shall be disinfected on days when compounding occurs and when surface contamination is known or suspected. Sporicidal disinfectants shall be applied monthly for pharmacies compounding Category 1 or Category 2 compounded sterile preparations and weekly for pharmacies compounding Category 3 compounded sterile preparations.

(-b-) Cleaning and disinfecting agents, with the exception of sporicidal disinfectants, used within the PEC shall be sterile. When diluting concentrated cleaning and disinfecting agents for use in the PEC, sterile water shall be used.

(II) Removable work tray of the PEC, when applicable. Work surfaces of the tray shall be cleaned daily on days when compounding occurs and all surfaces and the area underneath the work tray shall be cleaned monthly. Work surfaces of the tray shall be disinfected on days when compounding occurs and all surfaces and the area underneath the work tray shall be disinfected monthly. Sporicidal disinfectants shall be applied monthly on work surfaces of the tray, all surfaces, and the area underneath the work tray monthly.

(III) Pass-through chambers. Pass-through chambers shall be cleaned daily on days when compounding occurs and disinfected daily on days when compounding occurs. Sporicidal disinfectants shall be applied monthly for pharmacies compounding Category 1 or Category 2 compounded sterile preparations and weekly for pharmacies compounding Category 3 compounded sterile preparations.

(IV) Work surface(s) outside the PEC. Work surfaces outside the PEC shall be cleaned daily on days when compounding occurs and disinfected daily on days when compounding occurs. Sporicidal disinfectants shall be applied monthly for pharmacies compounding Category 1 or Category 2 compounded sterile preparations and weekly for pharmacies compounding Category 3 compounded sterile preparations.

(V) Floor(s). Floors shall be cleaned daily on days when compounding occurs and disinfected daily on days when compounding occurs. Sporicidal disinfectants shall be applied monthly for pharmacies compounding Category 1 or Category 2 compounded sterile preparations and weekly for pharmacies compounding Category 3 compounded sterile preparations.

(VI) Wall(s), door(s), door frame(s), storage shelving and bin(s), and equipment outside of the PEC(s). Walls, doors, door frames, storage shelving and bins, and equipment outside of the PECs shall be cleaned, disinfected, and sporicidal disinfectants applied on a monthly basis.

(VII) Ceiling(s). Ceilings of the classified areas shall be cleaned, disinfected, and sporicidal disinfectant applied on a monthly basis. Ceilings of the segregated compounding area shall be cleaned, disinfected, and sporicidal disinfectants applied when visibly soiled and when surface contamination is known or suspected.

~~(iv)~~ ~~Work surfaces in the buffer areas and ante-areas, as well as segregated compounding areas, shall be cleaned and~~

disinfected at least daily. Dust and debris shall be removed when necessary from storage sites for compounding ingredients and supplies using a method that does not degrade the ISO Class 7 or 8 air quality.]

[(v) Floors in the buffer area, ante-area, and segregated compounding area shall be cleaned by mopping with a cleaning and disinfecting agent at least once daily when no aseptic operations are in progress. Mopping shall be performed by trained personnel using approved agents and procedures described in the written SOPs. It is incumbent on compounding personnel to ensure that such cleaning is performed properly.]

[(vi) In the buffer area, ante-area, and segregated compounding area, walls, ceilings, and shelving shall be cleaned and disinfected monthly. Cleaning and disinfecting agents shall be used with careful consideration of compatibilities, effectiveness, and inappropriate or toxic residues.]

(v) [(vii)] All cleaning materials, such as wipers, sponges, and mops, shall be non-shedding, and dedicated to use in the buffer room [area], anteroom [ante-area], and segregated compounding areas and shall not be removed from these areas except for disposal. Floor mops may be used in both the buffer room [area] and anteroom [ante-area], but only in that order. If cleaning materials are reused, procedures shall be developed that ensure that the effectiveness of the cleaning device is maintained and that repeated use does not add to the bio-burden of the area being cleaned.

(vi) [(viii)] Supplies and equipment removed from shipping cartons shall [must] be wiped with a disinfecting agent, such as sterile IPA. After the disinfectant is sprayed or wiped on a surface to be disinfected, the disinfectant shall be allowed to dry, during which time the item shall not be used for compounding purposes. However, if sterile supplies are received in sealed pouches, the pouches may be removed as the supplies are introduced into the ISO Class 5 area without the need to disinfect the individual sterile supply items. No shipping or other external cartons may be taken into the buffer room [area] or segregated compounding area.

(vii) Before any item is introduced into the clean side of the anteroom(s), placed into pass-through chamber(s), or brought into the segregated compounding area, providing that packaging integrity will not be compromised, the item shall be wiped with a sporicidal disinfectant, EPA-registered disinfectant, or sterile 70% IPA using low-lint wipers by personnel wearing gloves. If an EPA-registered disinfectant or sporicidal disinfectant is used, the agent shall be allowed to dwell the minimum contact time specified by the manufacturer. If sterile 70% IPA is used, it shall be allowed to dry. The wiping procedure should not compromise the packaging integrity or render the product label unreadable.

(viii) Immediately before any item is introduced into the PEC, it shall be wiped with sterile 70% IPA using sterile low-lint wipers and allowed to dry before use. When sterile items are received in sealed containers designed to keep them sterile until opening, the sterile items may be removed from the covering as the supplies are introduced into the ISO Class 5 PEC without the need to wipe the individual sterile supply items with sterile 70% IPA. The wiping procedure shall not render the product label unreadable.

(ix) Critical sites (e.g., vial stoppers, ampule necks, and intravenous bag septums) shall be wiped with sterile 70% IPA in the PEC to provide both chemical and mechanical actions to remove contaminants. The sterile 70% IPA shall be allowed to dry before personnel enter or puncture stoppers and septums or break the necks of ampules.

[(ix) Storage shelving emptied of all supplies, walls, and ceilings shall be cleaned and disinfected at planned intervals, monthly, if not more frequently.]

(x) Cleaning shall [must] be done by personnel trained in appropriate cleaning techniques.

(xi) Proper documentation and frequency of cleaning shall [must] be maintained and shall contain the following:

(I) date [and time] of cleaning;

(II) type of cleaning performed; and

(III) name of individual who performed the cleaning.

(I) [(G)] Security requirements. The pharmacist-in-charge may authorize personnel to gain access to that area of the pharmacy containing dispensed sterile preparations, in the absence of the pharmacist, for the purpose of retrieving dispensed prescriptions to deliver to patients. If the pharmacy allows such after-hours access, the area containing the dispensed sterile preparations shall be an enclosed and lockable area separate from the area containing undispensed prescription drugs. A list of the authorized personnel having such access shall be in the pharmacy's policy and procedure manual.

(J) [(H)] Storage requirements and beyond-use dating.

(i) Storage requirements. All drugs shall be stored at the proper temperature and conditions, as defined in the USP/NF and in §291.15 of this title (relating to Storage of Drugs).

(ii) Beyond-use dating. When assigning a beyond-use date, compounding personnel shall consult and apply drug-specific and general stability documentation and literature where available, and they should consider the nature of the drug and its degradation mechanism, the container in which it is packaged, the expected storage conditions, and the intended duration of therapy. A shorter beyond-use date shall be assigned when the physical and chemical stability of the preparation is less than the beyond-use date limits provided in subclauses (I) - (III) of this clause.

(I) Beyond-use date limits for Category 1 compounded sterile preparations. Category 1 compounded sterile preparations shall be prepared in a segregated compounding area or cleanroom suite and have a beyond-use date of not more than 12 hours when stored at controlled room temperature or 24 hours when stored in a refrigerator.

[(I) Beyond-use dates for compounded sterile preparations shall be assigned based on professional experience, which shall include careful interpretation of appropriate information sources for the same or similar formulations.]

(II) Beyond-use date limits for Category 2 compounded sterile preparations. Category 2 compounded sterile preparations shall be prepared in a cleanroom suite.

(-a-) Aseptically processed compounded sterile preparations without sterility testing performed and passed.

(-1-) If prepared from one or more non-sterile starting component(s), the preparation shall have a beyond-use date of not more than one day when stored at controlled room temperature, four days when stored in a refrigerator, or 45 days when stored in a freezer.

(-2-) If prepared from only sterile starting component(s), the preparation shall have a beyond-use date of not more than four days when stored at controlled room tempera-

ture, 10 days when stored in a refrigerator, or 45 days when stored in a freezer.

(-b-) Terminally sterilized compounded sterile preparations without sterility testing performed and passed shall have a beyond-use date of not more than 14 days when stored at controlled room temperature, 28 days when stored in a refrigerator, or 45 days when stored in a freezer.

(-c-) If sterility testing is performed and passed, aseptically processed or terminally sterilized compounded sterile preparations shall have a beyond-use date of not more than 45 days when stored at controlled room temperature, 60 days when stored in a refrigerator, or 90 days when stored in a freezer.

~~*[(II)* Beyond-use dates for compounded sterile preparations that are prepared strictly in accordance with manufacturers' product labeling must be those specified in that labeling, or from appropriate literature sources or direct testing.]~~

(III) Beyond-use date limits for Category 3 compounded sterile preparations. Category 3 compounded sterile preparations shall be prepared in a cleanroom suite.

(-a-) Aseptically processed compounded sterile preparations that are sterility tested and passed all applicable tests for Category 3 compounded sterile preparations shall have a beyond-use date of not more than 60 days when stored at controlled room temperature, 90 days when stored in a refrigerator, or 120 days when stored in a freezer.

(-b-) Terminally sterilized compounded sterile preparations that are sterility tested and passed all applicable tests for Category 3 compounded sterile preparations shall have a beyond-use date of not more than 90 days when stored at controlled room temperature, 120 days when stored in a refrigerator, or 180 days when stored in a freezer.

(-c-) A Category 3 compounded sterile preparation in a nonaqueous dosage form (i.e., water activity level less than 0.6) may have a beyond-use date of not more than 180 days if based on documented current literature supporting stability and sterility.

(-d-) Additional requirements to assign Category 3 beyond-use dates to compounded sterile preparations.

(-1-) Category 3 personnel competency requirements as specified in subsection (c)(4)(L) of this section apply to personnel who participate in or oversee the compounding of Category 3 compounded sterile preparations.

(-2-) Category 3 garbing requirements as specified in paragraph (15)(C)(iv)(II) of this subsection apply to all personnel entering the buffer room where Category 3 compounded sterile preparations are compounded and apply at all times regardless of whether Category 3 compounded sterile preparations are being compounded on a given day.

(-3-) Increased environmental monitoring requirements as specified in subsection (c)(4)(M) of this section and paragraph (16)(C)(vi) of this subsection apply to all classified areas where Category 3 compounded sterile preparations are compounded and apply at all times regardless of whether Category 3 compound sterile preparations are being compounded on a given day.

(-4-) The frequency of application of sporicidal disinfectants as specified in paragraph (8)(H)(iv) of this subsection applies to all classified areas where Category 3 compounded sterile preparations are compounded and applies at all times regardless of whether Category 3 compounded sterile preparations are being compounded on a given day.

~~*[(III)* When assigning a beyond-use date, compounding personnel shall consult and apply drug-specific and general stability documentation and literature where available, and they should consider the nature of the drug and its degradation mechanism, the container in which it is packaged, the expected storage conditions, and the intended duration of therapy.]~~

~~*[(IV)* The sterility and storage and stability beyond-use date for attached and activated container pairs of drug products for intravascular administration shall be applied as indicated by the manufacturer.]~~

(9) [~~(7)~~] Primary engineering control device. The pharmacy shall prepare sterile preparations in a primary engineering control device (PEC), such as a laminar air flow hood, biological safety cabinet, compounding aseptic isolator (CAI), or compounding aseptic containment isolator (CACI) which is capable of maintaining at least ISO Class 5 conditions for 0.5 micron and larger [~~micrometer~~] particles while compounding sterile preparations.

(A) Laminar air flow hood. If the pharmacy is using a laminar air flow hood as its PEC, the laminar air flow hood shall:

(i) be located in the buffer room [~~area~~] and placed in the buffer room [~~area~~] in a manner as to avoid conditions that could adversely affect its operation such as strong air currents from opened doors, personnel traffic, or air streams from the heating, ventilating and air condition system;

(ii) be certified for operational efficiency using certification procedures, such as those outlined in the Certification Guide for Sterile Compounding Facilities (CAG-003-2022) [~~(CAG-003-2006)~~], which shall be performed by a qualified independent individual initially and no less than every six months and whenever the device or room is relocated or altered or major service to the pharmacy [~~facility~~] is performed;

(iii) have pre-filters inspected periodically and replaced as needed, in accordance with written policies and procedures and the manufacturer's specification, and the inspection and/or replacement date documented; and

(iv) be located in a buffer room [~~area~~] that has a minimum differential positive pressure of 0.02 [~~to 0.05~~] inches water column. A buffer room [~~area~~] that is not physically separated from the anteroom [~~ante-area~~] shall employ the principle of displacement airflow as defined in Chapter 797, Pharmaceutical Compounding--Sterile Preparations, of the USP/NF, with limited access to personnel.

(B) Biological safety cabinet.

(i) If the pharmacy is using a biological safety cabinet (BSC) as its PEC for the preparation of hazardous sterile compounded preparations, the biological safety cabinet shall be a Class II or III vertical flow biological safety cabinet located in an ISO Class 7 area that is physically separated from other preparation areas. The area for preparation of sterile chemotherapeutic preparations shall:

(I) have not less than 0.01 inches water column negative pressure to the adjacent positive pressure ISO Class 7 or better anteroom [~~ante-area~~]; and

(II) have a pressure indicator that can be readily monitored for correct room pressurization.

(ii) Pharmacies that prepare a low volume of hazardous drugs, are not required to comply with the provisions of clause (i) of this subparagraph if the pharmacy uses a device that provides two tiers of containment (e.g., closed-system vial transfer device within a BSC).

(iii) If the pharmacy is using a biological safety cabinet as its PEC for the preparation of non-hazardous sterile compounded preparations, the biological safety cabinet shall:

(I) be located in the buffer room [~~area~~] and placed in the buffer room [~~area~~] in a manner as to avoid conditions that could adversely affect its operation such as strong air currents from opened doors, personnel traffic, or air streams from the heating, ventilating and air condition system;

(II) be certified for operational efficiency using certification procedures, such as those outlined in the Certification Guide for Sterile Compounding Facilities (CAG-003-2022) [~~(CAG-003-2006)~~], which shall be performed by a qualified independent individual initially and no less than every six months and whenever the device or room is relocated or altered or major service to the pharmacy [~~facility~~] is performed;

(III) have pre-filters inspected periodically and replaced as needed, in accordance with written policies and procedures and the manufacturer's specification, and the inspection and/or replacement date documented; and

(IV) be located in a buffer room [~~area~~] that has a minimum differential positive pressure of 0.02 [~~to 0.05~~] inches water column.

(C) Compounding aseptic isolator.

(i) If the pharmacy is using a compounding aseptic isolator (CAI) as its PEC, the CAI shall provide unidirectional airflow within the main processing and antechambers, and be placed in an ISO Class 7 buffer room [~~area~~] unless the isolator meets all of the following conditions:

(I) The isolator shall [~~must~~] provide isolation from the room and maintain ISO Class 5 during dynamic operating conditions including transferring ingredients, components, and devices into and out of the isolator and during preparation of compounded sterile preparations;

(II) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site shall [~~must~~] maintain ISO Class 5 levels during compounding operations;

(III) The CAI shall [~~must~~] be certified for operational efficiency using certification procedures, such as those outlined in the Certification Guide for Sterile Compounding Facilities (CAG-003-2022) [~~(CAG-003-2006)~~], which shall be performed by a qualified independent individual initially and no less than every six months and whenever the device or room is relocated or altered or major service to the pharmacy [~~facility~~] is performed; and

(IV) The pharmacy shall maintain documentation from the manufacturer that the isolator meets this standard when located in worse than ISO Class 7 environments.

(ii) If the isolator meets the requirements in clause (i) of this subparagraph, the CAI may be placed in a non-ISO classified area of the pharmacy; however, the area shall be segregated from other areas of the pharmacy and shall:

(I) be clean, well lit, and of sufficient size;

(II) be used only for the compounding of Category 1 or Category 2 [~~low- and medium-risk,~~] non-hazardous sterile preparations;

(III) be located in an area of the pharmacy with non-porous and washable floors or floor covering to enable regular disinfection; and

(IV) be an area in which the CAI is placed in a manner as to avoid conditions that could adversely affect its operation.

(iii) In addition to the requirements specified in clauses (i) and (ii) of this subparagraph, if the CAI is used in the compounding of Category 2 prepared from any non-sterile starting component or Category 3 [~~high-risk~~] non-hazardous preparations, the CAI shall be placed in an area or room with at least ISO Class 7 [~~8~~] quality air so that high-risk powders weighed in at least ISO Class 7 [~~ISO-8~~] air quality conditions, compounding utensils for measuring and other compounding equipment are not exposed to lesser air quality prior to the completion of compounding and packaging of the Category 2 prepared from any non-sterile starting component or Category 3 [~~high-risk~~] preparation.

(D) Compounding aseptic containment isolator.

(i) If the pharmacy is using a compounding aseptic containment isolator (CACI) as its PEC for the preparation of Category 1 or Category 2 [~~low- and medium-risk~~] hazardous drugs, the CACI shall be located in a separate room away from other areas of the pharmacy and shall:

(I) provide at least 0.01 inches water column negative pressure compared to the other areas of the pharmacy;

(II) provide unidirectional airflow within the main processing and antechambers, and be placed in an ISO Class 7 room [~~area~~], unless the CACI meets all of the following conditions;

(-a-) The isolator shall [~~must~~] provide isolation from the room and maintain ISO Class 5 during dynamic operating conditions including transferring ingredients, components, and devices into and out of the isolator and during preparation of compounded sterile preparations;

(-b-) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site shall [~~must~~] maintain ISO Class 5 levels during compounding operations;

(-c-) The CACI shall [~~must~~] be certified for operational efficiency using certification procedures, such as those outlined in the Certification Guide for Sterile Compounding Facilities (CAG-003-2022) [~~(CAG-003-2006)~~], which shall be performed by a qualified independent individual initially and no less than every six months and whenever the device or room is relocated or altered or major service to the pharmacy [~~facility~~] is performed; and

(-d-) The pharmacy shall maintain documentation from the manufacturer that the isolator meets this standard when located in worse than ISO Class 7 environments.

(ii) If the CACI meets all conditions specified in clause (i) of this subparagraph, the CACI shall not be located in the same room as a CAI, but shall be located in a separate room in the pharmacy, that is not required to maintain ISO classified air. The room in which the CACI is located shall provide a minimum of 0.01 inches water column negative pressure compared with the other areas of the pharmacy and shall meet the following requirements:

(I) be clean, well lit, and of sufficient size;

(II) be maintained at a temperature of 20 degrees Celsius or cooler and a humidity of 60% or below [~~60%~~];

(III) be used only for the compounding of Category 1 or Category 2 hazardous sterile preparations;

(IV) be located in an area of the pharmacy with walls, ceilings, floors, fixtures, shelving, counters, and cabinets that are smooth, impervious, free from cracks and crevices, non-shedding and resistant to damage by disinfectant agents; and

(V) have non-porous and washable floors or floor covering to enable regular disinfection.

(iii) If the CACI is used in the compounding of Category 2 prepared from any non-sterile starting component or Category 3 [~~high-risk~~] hazardous preparations, the CACI shall be placed in an area or room with at least ISO Class 7 [~~8~~] quality air so that high-risk powders, weighed in at least ISO Class 7 [~~ISO-8~~] air quality conditions, are not exposed to lesser air quality prior to the completion of compounding and packaging of the Category 2 prepared from any non-sterile starting component or Category 3 [~~high-risk~~] preparation.

(iv) Pharmacies that prepare a low volume of hazardous drugs, are not required to comply with the provisions of clauses (i) and (iii) of this subparagraph if the pharmacy uses a device that provides two tiers of containment (e.g., CACI that is located in a non-negative pressure room).

(10) [~~(8)~~] Additional Equipment and Supplies. Pharmacies compounding sterile preparations shall have the following equipment and supplies:

(A) a calibrated system or device (i.e., thermometer) to monitor the temperature to ensure that proper storage requirements are met, if sterile preparations are stored in the refrigerator;

(B) a calibrated system or device to monitor the temperature where bulk chemicals are stored;

(C) a temperature-sensing mechanism suitably placed in the controlled temperature storage space to reflect accurately the true temperature;

(D) if applicable, a Class A prescription balance, or analytical balance and weights. Such balance shall be properly maintained and subject to periodic inspection by the Texas State Board of Pharmacy;

(E) equipment and utensils necessary for the proper compounding of sterile preparations. Such equipment and utensils used in the compounding process shall be:

(i) of appropriate design, appropriate capacity, and be operated within designed operational limits;

(ii) 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 preparation beyond the desired result;

(iii) cleaned and sanitized immediately prior to and after each use; and

(iv) routinely inspected, calibrated (if necessary), or checked to ensure proper performance;

(F) appropriate disposal containers for used needles, syringes, etc., and if applicable, hazardous waste from the preparation of hazardous drugs and/or biohazardous waste;

(G) appropriate packaging or delivery containers to maintain proper storage conditions for sterile preparations;

(H) infusion devices, if applicable; and

(I) all necessary supplies, including:

(i) disposable needles, syringes, and other supplies for aseptic mixing;

(ii) disinfectant cleaning solutions;

(iii) sterile 70% isopropyl alcohol;

(iv) sterile gloves, both for hazardous and non-hazardous drug compounding;

(v) sterile alcohol-based or water-less alcohol based surgical scrub;

(vi) hand washing agents with bactericidal action;

(vii) disposable, lint free towels or wipes;

(viii) appropriate filters and filtration equipment;

(ix) hazardous spill kits, if applicable; and

(x) masks, caps, coveralls or gowns with tight cuffs, shoe covers, and gloves, as applicable.

(11) [~~(9)~~] Labeling.

(A) Prescription drug or medication orders. In addition to the labeling requirements for the pharmacy's specific license classification, the label dispensed or distributed pursuant to a prescription drug or medication order shall contain the following:

(i) the generic name(s) or the official name(s) of the principal active ingredient(s) of the compounded sterile preparation;

(ii) for outpatient prescription orders other than sterile radiopharmaceuticals, a statement that the compounded sterile preparation has been compounded by the pharmacy. (An auxiliary label may be used on the container to meet this requirement); and

(iii) a beyond-use date. The beyond-use date shall be determined as outlined in Chapter 797, Pharmacy Compounding--Sterile Preparations of the USP/NF, and paragraph (8)(J) [~~(7)(G)~~] of this subsection;

(B) Batch. If the sterile preparation is compounded in a batch, the following shall also be included on the batch label:

(i) unique lot number assigned to the batch;

(ii) quantity;

(iii) appropriate ancillary instructions, such as storage instructions or cautionary statements, including hazardous drug warning labels where appropriate; and

(iv) device-specific instructions, where appropriate.

(C) Pharmacy bulk package. The label of a pharmacy bulk package shall:

(i) state prominently "Pharmacy Bulk Package--Not for Direct Infusion;"

(ii) contain or refer to information on proper techniques to help ensure safe use of the preparation; and

(iii) bear 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.

(12) [~~(10)~~] Written drug information for prescription drug orders only. Written information about the compounded preparation or its major active ingredient(s) shall be given to the patient at the time of dispensing a prescription drug order. A statement which indicates that the preparation was compounded by the pharmacy shall [~~must~~] be included in this written information. If there is no written information available, the patient shall be advised that the drug has been compounded and how to contact a pharmacist, and if appropriate, the prescriber, concerning the drug. This paragraph does not apply to the preparation of radiopharmaceuticals.

(13) [~~(11)~~] Pharmaceutical care services [~~Care Services~~]. In addition to the pharmaceutical care requirements for the pharmacy's specific license classification, the following requirements for sterile preparations compounded pursuant to prescription drug orders shall [~~must~~] be met. This paragraph does not apply to the preparation of radiopharmaceuticals.

(A) Primary provider. There shall be a designated physician primarily responsible for the patient's medical care. There shall be a clear understanding between the physician, the patient, and the pharmacy of the responsibilities of each in the areas of the delivery of care, and the monitoring of the patient. This shall be documented in the patient medication record (PMR).

(B) Patient training. The pharmacist-in-charge shall develop policies to ensure that the patient and/or patient's caregiver receives information regarding drugs and their safe and appropriate use, including instruction when applicable, regarding:

(i) appropriate disposition of hazardous solutions and ancillary supplies;

(ii) proper disposition of controlled substances in the home;

(iii) self-administration of drugs, where appropriate;

(iv) emergency procedures, including how to contact an appropriate individual in the event of problems or emergencies related to drug therapy; and

(v) if the patient or patient's caregiver prepares sterile preparations in the home, the following additional information shall be provided:

(I) safeguards against microbial contamination, including aseptic techniques for compounding intravenous admixtures and aseptic techniques for injecting additives to premixed intravenous solutions;

(II) appropriate storage methods, including storage durations for sterile pharmaceuticals and expirations of self-mixed solutions;

(III) handling and disposition of premixed and self-mixed intravenous admixtures; and

(IV) proper disposition of intravenous admixture compounding supplies such as syringes, vials, ampules, and intravenous solution containers.

(C) Pharmacist-patient relationship. It is imperative that a pharmacist-patient relationship be established and maintained throughout the patient's course of therapy. This shall be documented in the patient's medication record (PMR).

(D) Patient monitoring. The pharmacist-in-charge shall develop policies to ensure that:

(i) the patient's response to drug therapy is monitored and conveyed to the appropriate health care provider;

(ii) the first dose of any new drug therapy is administered in the presence of an individual qualified to monitor for and respond to adverse drug reactions; and

(iii) reports of adverse events with a compounded sterile preparation are reviewed promptly and thoroughly to correct and prevent future occurrences.

(14) [~~(12)~~] Drugs, components, and materials used in sterile compounding.

(A) Drugs used in sterile compounding shall be [~~a~~] USP/NF grade substances manufactured in an FDA-registered facility.

(B) If USP/NF grade substances are not available, substances used in sterile compounding shall be of a chemical grade in one of the following categories:

(i) Chemically Pure (CP);

(ii) Analytical Reagent (AR);

(iii) American Chemical Society (ACS); or

(iv) Food Chemical Codex.

(C) If a drug, component or material is not purchased from a FDA-registered facility, the pharmacist shall establish purity and stability by obtaining a Certificate of Analysis from the supplier and the pharmacist shall compare the monograph of drugs in a similar class to the Certificate of Analysis.

(D) All components shall:

(i) be manufactured in an FDA-registered facility; or

(ii) in the professional judgment of the pharmacist, be of high quality and obtained from acceptable and reliable alternative sources; and

(iii) be stored in properly labeled containers in a clean, dry place [~~area~~], under proper temperatures.

(E) Drug preparation containers and closures shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the compounded drug preparation beyond the desired result.

(F) Components, drug preparation containers, and closures shall be rotated so that the oldest stock is used first.

(G) Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the compounded drug preparation.

(H) A pharmacy may not compound a preparation that contains ingredients appearing on a federal Food and Drug Administration list of drug products withdrawn or removed from the market for safety reasons.

(15) [~~(13)~~] Compounding process.

(A) Standard operating procedures (SOPs). All significant procedures performed in the compounding area shall be covered by written SOPs designed to ensure accountability, accuracy, quality, safety, and uniformity in the compounding process. At a minimum, SOPs shall be developed and implemented for:

(i) the pharmacy [~~facility~~];

(ii) equipment;

(iii) personnel;

(iv) preparation evaluation;

(v) quality assurance;

(vi) preparation recall;

(vii) packaging; and

(viii) storage of compounded sterile preparations.

(B) USP/NF. Any compounded formulation with an official monograph in the USP/NF shall be compounded, labeled, and packaged in conformity with the USP/NF monograph for the drug.

(C) Personnel cleansing and garbing [~~Cleansing and Garbing~~].

(i) Any person with an apparent illness or open lesion, including rashes, sunburn, weeping sores, conjunctivitis, and active respiratory infection, that may adversely affect the safety or quality of a drug preparation being compounded shall be excluded from working in ISO Class 5, ISO Class 7, and ISO Class 8 compounding areas until the condition is remedied.

(ii) Before entering the buffer room [~~area~~], compounding personnel shall [~~must remove the following~~]:

(I) remove personal outer garments (e.g., bandanas, coats, hats, jackets, scarves, sweaters, vests);

(II) remove all cosmetics;[~~, because they shed flakes and particles; and~~]

(III) remove all hand, wrist, and other body jewelry or piercings (e.g., earrings, lip or eyebrow piercings) that can interfere with the effectiveness of personal protective equipment (e.g., fit of gloves and cuffs of sleeves); and[~~.~~]

(IV) wipe eyeglasses, if worn.

(iii) The wearing of artificial nails or extenders is prohibited while working in the sterile compounding environment. Natural nails shall be kept neat and trimmed.

(iv) Personnel shall [~~don personal protective equipment and~~] perform hand hygiene and garbing in an order determined by the pharmacy depending on the placement of the sink. The order of garbing shall be documented in the pharmacy's SOPs. Garb shall be donned and doffed in an order that reduces the risk of contamination. Donning and doffing garb shall not occur in the same area at the same time. [~~that proceeds from the dirtiest to the cleanest activities as follows:~~]

(I) The minimum garbing requirements for preparing Category 1 or Category 2 compounded sterile preparations include the following:

(-a-) low-lint garment with sleeves that fit snugly around the wrists and an enclosed neck (e.g., gown or coverall);

(-b-) low-lint covers for shoes;

(-c-) low-lint cover for head that covers the hair and ears, and if appliable, cover for facial hair;

(-d-) low-lint face mask;

(-e-) sterile powder-free gloves; and

(-f-) if using a restricted-access barrier system (i.e., a compounding aseptic isolator or compounding aseptic containment isolator), disposable gloves should be worn inside the gloves attached to the restricted-access barrier system sleeves. Sterile gloves shall be worn over the gloves attached to the restricted-access barrier system sleeve.

~~*[(I)* Activities considered the dirtiest include donning of dedicated shoes or shoe covers, head and facial hair covers (e.g., beard covers in addition to face masks), and face mask/eye shield. Eye shields are optional unless working with irritants like germicidal disinfecting agents or when preparing hazardous drugs.]~~

(II) The following additional garbing requirements shall be followed in the buffer room where Category 3 compounded sterile preparations are prepared for all personnel regardless of whether Category 3 compounded sterile preparations are compounded on a given day:

(-a-) skin may not be exposed in the buffer room (i.e., face and neck shall be covered);

(-b-) all low-lint outer garb shall be sterile, including the use of sterile sleeves over gauntlet sleeves when a restricted-access barrier system is used;

(-c-) disposable garbing items shall not be reused and any laundered garb shall not be reused without being laundered and resterilized with a validated cycle; and

(-d-) the pharmacy's SOPs shall describe disinfection procedures for reusing goggles, respirators, and other reusable equipment. If compounding a hazardous drug, appropriate personal protective equipment shall be worn.

(III) [~~(II)~~] After donning dedicated shoes or shoe covers, head and facial hair covers, and face masks, personnel shall perform a hand hygiene procedure by removing debris from underneath fingernails using a nail cleaner under running warm water followed by vigorous hand washing. Personnel shall begin washing arms at the hands and continue washing to elbows for at least 30 seconds with either a plain (non-antimicrobial) soap, or antimicrobial soap, and water while in the anteroom [~~ante-area~~]. Disposable soap containers shall not be refilled or topped off. Brushes shall not be used for hand hygiene. Hands and forearms to the elbows shall be completely dried using lint-free disposable towels, an electronic hands-free hand dryer, or a HEPA filtered hand dryer.

(IV) [~~(III)~~] After completion of hand washing, personnel shall don clean non-shedding gowns with sleeves that fit snugly around the wrists and enclosed at the neck.

(V) [~~(IV)~~] Once inside the buffer room [~~area~~] or segregated compounding area, and prior to donning sterile powder-free gloves, antiseptic hand cleansing shall be performed using an alcohol-based hand rub [~~a waterless alcohol-based surgical hand scrub with persistent activity following manufacturers' recommendations~~]. Hands shall be allowed to dry thoroughly before donning sterile gloves.

(VI) [~~(V)~~] Sterile gloves that form a continuous barrier with the gown shall be the last item donned before compounding begins. Sterile gloves shall be donned in a classified area or segregated compounding area using proper technique to ensure the sterility of the glove is not compromised while donning. The cuff of the sterile glove shall cover the cuff of the gown at the wrist. When preparing hazardous preparations, the compounder shall double glove or shall use single gloves ensuring that the gloves are sterile powder-free chemotherapy-rated gloves. Routine application of sterile 70% IPA shall occur throughout the compounding day and whenever non-sterile surfaces are touched.

(v) Garb shall be replaced immediately if it becomes visibly soiled or if its integrity is compromised. Gowns and other garb shall be stored in a manner that minimizes contamination (e.g., away from sinks to avoid splashing). If compounding Category 1 or Category 2 compounded sterile preparations, gowns may be reused within the same shift by the same person if the gown is maintained in a classified area or adjacent to, or within, the segregated compounding area in a manner that prevents contamination. When personnel exit the compounding area, garb, except for gowns, may not be reused and shall be discarded or laundered before use. The pharmacy's SOPs shall describe disinfection procedures for reusing goggle, respirators, and other reusable equipment. [~~When compounding personnel shall temporarily exit the buffer area during a work shift, the exterior gown, if not visibly soiled, may be removed and retained in the ante-area, to be re-donned during that same work shift only. However, shoe covers, hair and facial hair covers, face mask/eye shield, and gloves shall be replaced with new ones before re-entering the buffer area along with performing proper hand hygiene.~~]

(vi) During [~~high-risk level~~] compounding activities that precede terminal sterilization, such as weighing and mixing of non-sterile ingredients, compounding personnel shall be garbed and gloved the same as when performing compounding in an ISO Class 5 environment. Properly garbed and gloved compounding personnel who are exposed to air quality that is either known or suspected to be worse than ISO Class 7 shall re-garb personal protective equipment along with washing their hands properly, performing antiseptic hand cleansing with a sterile 70% IPA-based or another suitable sterile alcohol-based surgical hand scrub, and donning sterile gloves upon re-entering the ISO Class 7 buffer room [~~area~~].

(vii) When compounding aseptic isolators or compounding aseptic containment isolators are the source of the ISO Class 5 environment, at the start of each new compounding procedure, a new pair of sterile gloves shall be donned within the CAI or CACI. In addition, the compounding personnel should follow the requirements as specified in this subparagraph, unless the isolator manufacturer can provide written documentation based on validated environmental testing that any components of personal protective equipment or cleansing are not required.

(16) [~~(14)~~] Quality assurance [~~Assurance~~].

(A) Initial formula validation [~~Formula Validation~~]. Prior to routine compounding of a sterile preparation, a pharmacy shall conduct an evaluation that shows that the pharmacy is capable of compounding a preparation that is sterile and that contains the stated amount of active ingredient(s).

~~*(i)* Low risk level preparations.]~~

(i) [~~(I)~~] Quality assurance practices include, but are not limited to the following:

(I) [~~(-a-)~~] Routine disinfection and air quality testing of the direct compounding environment to minimize microbial surface contamination and maintain ISO Class 5 air quality;

(II) [~~(-b-)~~] Visual confirmation that compounding personnel are properly donning and wearing appropriate items and types of protective garments and goggles;

(III) Confirmation that media-fill tests indicate that compounding personnel and personnel who have direct oversight of compounding personnel but do not compound can competently perform aseptic procedures;

(IV) [~~(-c-)~~] Review of all orders and packages of ingredients to ensure that the correct identity and amounts of ingredients were compounded; and

(V) [~~(-d-)~~] Visual inspection of compounded sterile preparations, except for sterile radiopharmaceuticals, to ensure the absence of particulate matter in solutions, the absence of leakage from vials and bags, and the accuracy and thoroughness of labeling.

~~*(II)* Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least annually by each person authorized to compound in a low-risk level under conditions that closely simulate the most challenging or stressful conditions encountered during compounding of low-risk level sterile preparations. Once begun, this test is completed without interruption within an ISO Class 5 air quality environment. Three sets of four 5-milliliter aliquots of sterile fluid culture media are transferred with the same sterile 10-milliliter syringe and vented needle combination into separate sealed, empty, sterile 30-milliliter clear vials (i.e., four 5-milliliter aliquots into each of three 30-milliliter vials). Sterile adhesive seals are aseptically affixed to the rubber closures on the three filled vials. The vials are incubated within a range of 20 - 35 degrees Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the medium on or before 14 days. The media-fill test must include a positive-control sample.]~~

~~*(ii)* Medium risk level preparations.]~~

~~*(I)* Quality assurance procedures for medium-risk level compounded sterile preparations include all those for low-risk level compounded sterile preparations, as well as a more challenging media-fill test passed annually, or more frequently.]~~

~~*(II)* Example of a Media-Fill Test Procedure. This, or an equivalent test, is performed at least annually under conditions that closely simulate the most challenging or stressful conditions encountered during compounding. This test is completed without interruption within an ISO Class 5 air quality environment. Six 100-milliliter aliquots of sterile Soybean-Casein Digest Medium are aseptically transferred by gravity through separate tubing sets into separate evacuated sterile containers. The six containers are then arranged as three pairs, and a sterile 10-milliliter syringe and 18-gauge needle combination is used to exchange two 5-milliliter aliquots of medium from one container to the other container in the pair. For example, after a 5-milliliter aliquot from the first container is added to the second container in the pair, the second container is agitated for 10 seconds, then a 5-milliliter aliquot is removed and returned to the first container in the pair. The first container is then agitated for 10 seconds, and the next 5-milliliter aliquot is transferred from it back to the second container in the pair. Following the two 5-milliliter aliquot exchanges in each pair of containers, a 5-milliliter aliquot of medium from each container is aseptically injected into a sealed, empty, sterile 10-milliliter clear vial, using a sterile 10-milliliter syringe and vented needle. Sterile adhesive seals are aseptically affixed to the rubber closures on the three filled vials. The vials are incubated within a range of 20 - 35 degrees Celsius for a minimum of 14 days. Failure is indicated by visible turbidity in the medium on or before 14 days. The media-fill test must include a positive-control sample.]~~

~~*(iii)* High risk level preparations.]~~

~~*(I)* Procedures for high-risk level compounded sterile preparations include all those for low-risk level compounded sterile preparations. In addition, a media-fill test that represents high-risk level compounding is performed twice a year by each person authorized to compound high-risk level compounded sterile preparations.]~~

~~*(II)* Example of a Media-Fill Test Procedure for Compounded Sterile Preparations Sterilized by Filtration. This test, or an equivalent test, is performed under conditions that closely simulate the most challenging or stressful conditions encountered when compounding high-risk level compounded sterile preparations. Note: Sterility tests for autoclaved compounded sterile preparations are not required unless they are prepared in batches of more than 25 units. This test is completed without interruption in the following sequence:]~~

~~[(-a-) Dissolve 3 grams of non-sterile commercially available fluid culture media in 100 milliliters of non-bacteriostatic water to make a 3% non-sterile solution.]~~

~~[(-b-) Draw 25 milliliters of the medium into each of three 30-milliliter sterile syringes. Transfer 5 milliliters from each syringe into separate sterile 10-milliliter vials. These vials are the positive controls to generate exponential microbial growth, which is indicated by visible turbidity upon incubation.]~~

~~[(-c-) Under aseptic conditions and using aseptic techniques, affix a sterile 0.2-micron porosity filter unit and a 20-gauge needle to each syringe. Inject the next 10 milliliters from each syringe into three separate 10-milliliter sterile vials. Repeat the process for three more vials. Label all vials, affix sterile adhesive seals to the closure of the nine vials, and incubate them at 20 to 35~~

degrees Celsius for a minimum of 14 days. Inspect for microbial growth over 14 days as described in Chapter 797 Pharmaceutical Compounding--Sterile Preparations, of the USP/NF.]

(ii) [(III)] Filter integrity testing [Integrity Testing]. Filters shall [need to] undergo testing to evaluate the integrity of filters used to sterilize Category 2 prepared from any non-sterile starting component or Category 3 compounded sterile [high-risk] preparations, such as bubble point testing [Bubble Point Testing] or comparable filter integrity testing. Such testing is not a replacement for sterility testing and shall not be interpreted as such. Such test shall be performed after a sterilization procedure on all filters used to sterilize each Category 2 prepared from any non-sterile starting component or Category 3 compounded sterile [high-risk] preparation or batch preparation and the results documented. The results should be compared with the filter manufacturer's specification for the specific filter used. If a filter fails the integrity test, the preparation or batch shall [must] be sterilized again using new unused filters.

(B) Finished preparation release checks and tests.

(i) Each time a Category 3 compounded sterile preparation is prepared, it shall be tested for sterility and meet the requirements of Chapter 71, Sterility Tests of the USP/NF, or a validated alternative method that is noninferior to Chapter 71 testing. Each time a Category 2 injectable compounded sterile preparation compounded from one or more non-sterile components and assigned a beyond-use date that requires sterility testing is prepared, the preparation shall be tested to ensure that it does not contain excessive bacterial endotoxins. Each time a Category 3 injectable compounded sterile preparation compounded from one or more non-sterile components is prepared, the preparation shall be tested to ensure that it does not contain excessive bacterial endotoxins. [All high-risk level compounded sterile preparations that are prepared in groups of more than 25 identical individual single-dose packages (such as ampules, bags, syringes, and vials), or in multiple dose vials for administration to multiple patients, or are exposed longer than 12 hours at 2 - 8 degrees Celsius and longer than six hours at warmer than 8 degrees Celsius before they are sterilized shall be tested to ensure they are sterile and do not contain excessive bacterial endotoxins as specified in Chapter 71, Sterility Tests of the USP/NF before being dispensed or administered.]

(ii) All compounded sterile preparations, except for sterile radiopharmaceuticals, that are intended to be solutions shall [must] be visually examined for the presence of particulate matter and not administered or dispensed when such matter is observed.

(iii) The prescription drug and medication orders, written compounding procedure, preparation records, and expended materials used to make compounded sterile preparations [at all contamination risk levels] shall be inspected for accuracy of correct identities and amounts of ingredients, aseptic mixing and sterilization, packaging, labeling, and expected physical appearance before they are dispensed or administered.

(iv) Written procedures for checking compounding accuracy shall be followed for every compounded sterile preparation during preparation, in accordance with pharmacy's policies and procedures, and immediately prior to release, including label accuracy and the accuracy of the addition of all drug products or ingredients used to prepare the finished preparation and their volumes or quantities. A pharmacist shall ensure that components used in compounding are accurately weighed, measured, or subdivided as appropriate to conform to the formula being prepared.

(C) Environmental testing [Testing].

(i) Viable and nonviable environmental sampling testing. Environmental sampling shall occur, at a minimum, every six months as part of a comprehensive quality management program and under any of the following conditions:

(I) as part of the commissioning and certification of new facilities and equipment;

(II) following any servicing of facilities and equipment;

(III) as part of the re-certification of facilities and equipment;

(IV) in response to identified problems with end products or staff technique; or

(V) in response to issues with compounded sterile preparations, observed compounding personnel work practices, or patient-related infections (where the compounded sterile preparation is being considered as a potential source of the infection).

(ii) Total particle counts. Certification that each ISO classified area (e.g., ISO Class 5, 7, and 8), is within established guidelines shall be performed no less than every six months and whenever the equipment is relocated or the physical structure of the buffer room [area] or anteroom [ante-area] has been altered. All certification records shall be maintained and reviewed to ensure that the controlled environments comply with the proper air cleanliness, room pressures, and air changes per hour. These certification records shall [must] include acceptance criteria and be made available upon inspection by the Board. Testing shall be performed by qualified operators using current, state-of-the-art equipment, with results of the following:

(I) ISO Class 5 - not more than 3,520 [3520] particles 0.5 microns [micrometer] and larger in diameter [size] per cubic meter of air;

(II) ISO Class 7 - not more than 352,000 particles of 0.5 microns [micrometer] and larger in diameter [size] per cubic meter of air for any buffer room [area]; and

(III) ISO Class 8 - not more than 3,520,000 particles of 0.5 microns [micrometer] and larger in diameter [size] per cubic meter of air for any anteroom [ante-area].

(iii) Pressure differential monitoring. A pressure gauge or velocity meter shall be installed to monitor the pressure differential or airflow between the buffer room [area] and the anteroom [ante-area] and between the anteroom [ante-area] and the general environment outside the compounding area. The results shall be reviewed and documented on a log at least every work shift (minimum frequency shall be at least daily) or by a continuous recording device. The pressure between the ISO Class 7 or ISO Class 8 and the general pharmacy area shall not be less than 0.02 inch water column.

(iv) Sampling plan. An appropriate environmental sampling plan shall be developed for airborne viable particles based on a risk assessment of compounding activities performed. Selected sampling sites shall include locations within each ISO Class 5 environment and in the ISO Class 7 and 8 areas and in the segregated compounding areas at greatest risk of contamination. The plan shall include sample location, method of collection, frequency of sampling, volume of air sampled, and time of day as related to activity in the compounding area and action levels.

(v) Viable air sampling. Evaluation of airborne microorganisms using volumetric collection methods in the controlled air environments shall be performed by properly trained individuals for all compounded sterile preparations [compounding risk levels].

Volumetric active air sampling of all active classified areas using an impaction air sampler shall be conducted in each classified area (e.g., ISO Class 5 PEC and ISO Class 7 and 8 room(s)) during dynamic operating conditions. For entities compounding Category 1 or Category 2 compounded sterile preparations, this shall be completed at least every six months. For entities compounding any Category 3 compounded sterile preparations, this shall be completed within 30 days prior to the commencement of any Category 3 compounding and at least every three months thereafter regardless of the frequency of compounding Category 3 compounded sterile preparations. Air sampling sites shall be selected in all classified areas. [~~For low-, medium-, and high-risk level compounding, air sampling shall be performed at locations that are prone to contamination during compounding activities and during other activities such as staging, labeling, gowning, and cleaning. Locations shall include zones of air backwash turbulence within the laminar airflow workbench and other areas where air backwash turbulence may enter the compounding area. For low-risk level compounded sterile preparations within 12-hour or less beyond-use-date prepared in a primary engineering control that maintains an ISO Class 5, air sampling shall be performed at locations inside the ISO Class 5 environment and other areas that are in close proximity to the ISO Class 5 environment during the certification of the primary engineering control.~~]

(vi) Air sampling [~~frequency and~~] process. [~~Air sampling shall be performed at least every 6 months as a part of the re-certification of facilities and equipment.~~]

(I) A sufficient volume of air shall be sampled [~~and the manufacturer's guidelines for use of the electronic air sampling equipment followed~~]. Follow the manufacturer's instructions for operation of the impaction air sampler, including placement of media device(s). Using the impaction air sampler, test at least 1 cubic meter or 1,000 liters of air from each location sampled. At the end of each sampling period, retrieve the media device and cover it. Handle and store media devices to avoid contamination and prevent condensate from dropping onto the agar during incubation and affecting the accuracy of the cfu reading (e.g., invert plates). At the end of the designated sampling or exposure period for air sampling activities, the microbial growth media plates are recovered and their covers secured and they are inverted and incubated pursuant to the procedures in subclause (II) of this clause [~~at a temperature and for a time period conducive to multiplication of microorganisms~~]. Sampling data shall be collected and reviewed on a periodic basis as a means of evaluating the overall control of the compounding environment.

(II) Incubation procedures.

(-a-) Incubate the media device at 30 to 35 degrees Celsius for no less than 48 hours. Examine for growth. Record the total number of discrete colonies of microorganisms on each media device as cfu per cubic meter of air on an environmental sampling form based on sample type (i.e., viable air), sample location, and sample date.

(-b-) Then incubate the media at 20 to 25 degrees Celsius for no less than five additional days. Examine for growth. Record the total number of discrete colonies of microorganisms on each media device as cfu per cubic meter of air on an environmental sampling form based on sample type (i.e., viable air), sample location, and sample date.

(-c-) Alternatively, to shorten the overall incubation period, two sampling media devices may be collected for each sample location and incubated concurrently.

(-1-) The media devices shall either both be trypticase soy agar or shall be one trypticase soy agar and the other fungal media (e.g., malt extract agar or Sabouraud dextrose agar).

(-2-) Incubate each media device in a separate incubator. Incubate one media device at 30 to 35 degrees Celsius for no less than 48 hours, and incubate the other media device at 20 to 25 degrees Celsius for no less than five days. If fungal media are used as one of the samples, incubate the fungal media sample at 20 to 25 degrees Celsius for no less than five days.

(-3-) Count the total number of discrete colonies of microorganisms on each media device, and record these results as cfu per cubic meter of air.

(-4-) Record the results of the sampling on an environmental sampling form based on sample type (i.e., viable air), and include the sample location and sample date.

(III) The following action levels for viable air sampling apply: a [~~If an activity consistently shows elevated levels of microbial growth, competent microbiology or infection control personnel shall be consulted. A~~] colony forming unit (cfu) count greater than 1 cfu per cubic meter of air for ISO Class 5, greater than 10 cfus [~~cfu~~] per cubic meter of air for ISO Class 7, and greater than 100 cfus [~~cfu~~] per cubic meter of air for ISO Class 8. If levels measured during viable air sampling exceed the action levels in this subclause for the ISO classification levels of the area sampled, the cause shall be investigated and corrective action shall be taken. Data collected in response to corrective actions shall be reviewed to confirm that the actions taken have been effective. The corrective action plan shall be dependent on the cfu count and the microorganism recovered. The corrective action plan shall be documented. If levels measured during viable air sampling exceed the action levels in this subclause, an attempt shall be made to identify any microorganism recovered to the genus level with the assistance of a competent microbiologist. [~~or worse should prompt a re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within the aseptic compounding location. An investigation into the source of the contamination shall be conducted. The source of the problem shall be eliminated, the affected area cleaned, and resampling performed. Counts of cfu are to be used as an approximate measure of the environmental microbial bioburden. Action levels are determined on the basis of cfu data gathered at each sampling location and trended over time. Regardless of the number of cfu identified in the pharmacy, further corrective actions will be dictated by the identification of microorganisms recovered by an appropriate credentialed laboratory of any microbial bioburden captured as a cfu using an impaction air sampler. Highly pathogenic microorganisms (e.g., gram-negative rods, coagulase positive staphylococcus, molds and yeasts) can be potentially fatal to patient receiving compounded sterile preparations and must be immediately remedied, regardless of colony forming unit count, with the assistance, if needed, of a competent microbiologist, infection control professional, or industrial hygienist.~~]

(vii) Compounding accuracy checks. Written procedures for checking compounding accuracy shall be followed for every compounded sterile preparation during preparation and immediately prior to release, including label accuracy and the accuracy of the addition of all drug products or ingredients used to prepare the finished preparation and their volumes or quantities. At each step of the compounding process, the pharmacist shall ensure that components used in compounding are accurately weighed, measured, or subdivided as appropriate to conform to the formula being prepared.

(17) [~~(15)~~] Quality control.

(A) Quality control procedures. The pharmacy shall follow established quality control procedures to monitor the compounding environment and quality of compounded drug preparations for conformity with the quality indicators established for the prepara-

tion. When developing these procedures, pharmacy personnel shall consider the provisions of USP Chapter 71, Sterility Tests, USP Chapter 85, Bacterial Endotoxins Test, Pharmaceutical Compounding-Non-sterile Preparations, USP Chapter 795, USP Chapter 797, Pharmaceutical Compounding--Sterile Preparations, USP Chapter 800, Hazardous Drugs--Handling in Healthcare Settings, USP Chapter 823, Positron Emission Tomography Drugs for Compounding, Investigational, and Research Uses, USP Chapter 1160, Pharmaceutical Calculations in Prescription Compounding, and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding of the current USP/NF. Such procedures shall be documented and be available for inspection.

(B) Verification of compounding accuracy and sterility.

(i) The accuracy of identities, concentrations, amounts, and purities of ingredients in compounded sterile preparations shall be confirmed by reviewing labels on packages, observing and documenting correct measurements with approved and correctly standardized devices, and reviewing information in labeling and certificates of analysis provided by suppliers.

(ii) If the correct identity, purity, strength, and sterility of ingredients and components of compounded sterile preparations cannot be confirmed such ingredients and components shall be discarded immediately. Any compounded sterile preparation that fails sterility testing following sterilization by one method (e.g., filtration) is to be discarded and not subjected to a second method of sterilization.

(iii) If individual ingredients, such as bulk drug substances, are not labeled with expiration dates, when the drug substances are stable indefinitely in their commercial packages under labeled storage conditions, such ingredients may gain or lose moisture during storage and use and shall require testing to determine the correct amount to weigh for accurate content of active chemical moieties in compounded sterile preparations.

(C) Sterility testing. Sterility testing shall be performed on a number of units equal to 5% of the number of compounded sterile preparations prepared, rounded up to the next whole number. Sterility tests resulting in failure shall prompt an investigation into the possible causes of the failure and shall include identification of the microorganism and an evaluation of the sterility testing procedure, compounding facility, process, and personnel that may have contributed to the failure. The sources of the contamination, if identified, shall be corrected and the pharmacy shall determine whether the conditions causing the sterility failure affect other compounded sterile preparations. The investigation and resulting corrective actions shall be documented.

(e) Records. Any testing, cleaning, procedures, or other activities required in this subsection shall be documented and such documentation shall be maintained by the pharmacy.

(1) Maintenance of records. Every record required under this section shall [~~must~~] be:

(A) kept by the pharmacy and be available, for at least two years for inspecting and copying by the board or its representative and to other authorized local, state, or federal law enforcement agencies; and

(B) supplied by the pharmacy within 72 hours, if requested by an authorized agent of the Texas State Board of Pharmacy. If the pharmacy maintains the records in an electronic format, the requested records shall [~~must~~] be provided in an electronic format. Failure to provide the records set out in this section, either on site or within 72 hours, constitutes prima facie evidence of failure to keep and maintain records in violation of the Act.

(2) Compounding records.

(A) Compounding pursuant to patient specific prescription drug orders or medication orders not prepared from non-sterile ingredient(s). Compounding records for all compounded preparations shall be maintained by the pharmacy and shall include a complete formula, including methodology and necessary equipment which includes the brand name(s) of the raw materials, or if no brand name, the generic name(s) or official name and name(s) of the manufacturer(s) or distributor of the raw materials and the quantities of each; however, if the sterile preparation is compounded according to the manufacturer's labeling instructions, then documentation of the formula is not required.[~~:~~]

~~(i)~~ ~~the date and time of preparation;~~]

~~(ii)~~ ~~a complete formula, including methodology and necessary equipment which includes the brand name(s) of the raw materials, or if no brand name, the generic name(s) or official name and name(s) of the manufacturer(s) or distributor of the raw materials and the quantities of each; however, if the sterile preparation is compounded according to the manufacturer's labeling instructions, then documentation of the formula is not required;~~]

~~(iii)~~ ~~written or electronic signature or initials of the pharmacist or pharmacy technician or pharmacy technician trainee performing the compounding;~~]

~~(iv)~~ ~~written or electronic signature or initials of the pharmacist responsible for supervising pharmacy technicians or pharmacy technician trainees and conducting finals checks of compounded pharmaceuticals if pharmacy technicians or pharmacy technician trainees perform the compounding function;~~]

~~(v)~~ ~~the container used and the number of units of finished preparation prepared; and~~]

~~(vi)~~ ~~a reference to the location of the following documentation which may be maintained with other records, such as quality control records:~~]

~~(I)~~ ~~the criteria used to determine the beyond-use date; and~~]

~~(II)~~ ~~documentation of performance of quality control procedures.~~]

(B) Compounding records for compounded sterile preparations prepared from non-sterile ingredient(s) or prepared for more than one patient [~~when batch compounding or compounding in anticipation of future prescription drug or medication orders.~~]

(i) [~~Master work sheet~~]. A master formulation record [~~master work sheet~~] shall be created for compounded sterile preparations prepared from non-sterile ingredient(s) or prepared for more than one patient. Any changes or alterations to the master formulation record shall be approved and documented according to the pharmacy's SOPs. The master formulation record shall include at least the following information: [~~developed and approved by a pharmacist for preparations prepared in batch. Once approved, a duplicate of the master work sheet shall be used as the preparation work sheet from which each batch is prepared and on which all documentation for that batch occurs. The master work sheet shall contain at a minimum:~~]

(I) name, strength or activity, and dosage form of the compounded sterile preparation [~~the formula~~];

(II) identities and amounts of all ingredients and, if applicable, relevant characteristics or components (e.g., particle size, salt form, purity grade, solubility) [~~the components~~];

(III) type and size of container closure system(s) [~~the compounding directions~~];

(IV) complete instructions for preparing the compounded sterile preparation, including equipment, supplies, a description of the compounding steps, and any special precautions [~~a sample label~~];

(V) physical description of the final compounded sterile preparation [~~evaluation and testing requirements~~];

(VI) beyond-use date and storage requirements; [~~specific equipment used during preparation; and~~]

(VII) reference source to support the stability of the compounded sterile preparation; [~~storage requirements.~~]

(VIII) quality control procedures (e.g., pH testing, filter integrity testing); and

(IX) other information as needed to describe the compounding process and ensure repeatability (e.g., adjusting pH and tonicity; sterilization method, such as steam, dry heat, irradiation, or filter).

(ii) A compounding record that documents the compounding process shall be created for all compounded sterile preparations. The compounding record shall include at least the following information:

(I) name, strength or activity, and dosage form of the compounded sterile preparation;

(II) date and time of preparation of the compounded sterile preparation;

(III) assigned internal identification number (e.g., prescription, order, or lot number);

(IV) written or electronic signature or initials of the pharmacist or pharmacy technician or pharmacy technician trainee performing the compounding;

(V) written or electronic signature or initials of the pharmacist responsible for supervising pharmacy technicians or pharmacy technician trainees and conducting final checks of compounded preparations if pharmacy technicians or pharmacy technician trainees perform the compounding function;

(VI) name of each component;

(VII) vendor, lot number, and expiration date for each component for compounded sterile preparations prepared for more than one patient or prepared from non-sterile ingredient(s);

(VIII) weight or volume of each component;

(IX) strength or activity of each component;

(X) total quantity compounded;

(XI) final yield (e.g., quantity, containers, number of units);

(XII) assigned beyond-use date and storage requirements;

(XIII) results of quality control procedures (e.g., visual inspection, filter integrity testing, pH testing);

(XIV) if applicable, master formulation record for the compounded sterile preparation; and

(XV) if applicable, calculations made to determine and verify quantities or concentrations of components.

~~(ii)~~ ~~Preparation work sheet. The preparation work sheet for each batch of preparations shall document the following:~~]

~~(I)~~ ~~identity of all solutions and ingredients and their corresponding amounts, concentrations, or volumes;~~]

~~(II)~~ ~~lot number for each component;~~]

~~(III)~~ ~~component manufacturer/distributor or suitable identifying number;~~]

~~(IV)~~ ~~container specifications (e.g., syringe, pump cassette);~~]

~~(V)~~ ~~unique lot or control number assigned to batch;~~]

~~(VI)~~ ~~expiration date of batch-prepared preparations;~~]

~~(VII)~~ ~~date of preparation;~~]

~~(VIII)~~ ~~name, initials, or electronic signature of the person(s) involved in the preparation;~~]

~~(IX)~~ ~~name, initials, or electronic signature of the responsible pharmacist;~~]

~~(X)~~ ~~finished preparation evaluation and testing specifications, if applicable; and~~]

~~(XI)~~ ~~comparison of actual yield to anticipated or theoretical yield, when appropriate.~~]

(f) Office use compounding and distribution of sterile compounded preparations. [~~Use Compounding and Distribution of Sterile Compounded Preparations~~]

(1) General.

(A) A pharmacy may compound, dispense, deliver, and distribute a compounded sterile preparation as specified in Subchapter D, Texas Pharmacy Act Chapter 562.

(B) A Class A-S pharmacy is not required to register or be licensed under Chapter 431, Health and Safety Code, to distribute sterile compounded preparations to a Class C or Class C-S pharmacy.

(C) A Class C-S pharmacy is not required to register or be licensed under Chapter 431, Health and Safety Code, to distribute sterile compounded preparations that the Class C-S pharmacy has compounded for other Class C or Class C-S pharmacies under common ownership.

(D) To compound and deliver a compounded preparation under this subsection, a pharmacy shall [~~must~~]:

(i) verify the source of the raw materials to be used in a compounded drug;

(ii) comply with applicable United States Pharmacopoeia guidelines, including the testing requirements, and the Health Insurance Portability and Accountability Act of 1996 (Pub. L. No. 104-191);

(iii) enter into a written agreement with a practitioner for the practitioner's office use of a compounded preparation;

(iv) comply with all applicable competency and accrediting standards as determined by the board; and

(v) comply with the provisions of this subsection.

(E) This subsection does not apply to Class B pharmacies compounding sterile radiopharmaceuticals that are furnished for

departmental or physicians' use if such authorized users maintain a Texas radioactive materials license.

(2) Written Agreement. A pharmacy that provides sterile compounded preparations to practitioners for office use or to another pharmacy shall enter into a written agreement with the practitioner or pharmacy. The written agreement shall:

(A) address acceptable standards of practice for a compounding pharmacy and a practitioner and receiving pharmacy that enter into the agreement including a statement that the compounded drugs may only be administered to the patient and may not be dispensed to the patient or sold to any other person or entity except to a veterinarian as authorized by §563.054 of the Act;

(B) require the practitioner or receiving pharmacy to include on a patient's chart, medication order or medication administration record the lot number and beyond-use date of a compounded preparation administered to a patient; and

(C) describe the scope of services to be performed by the pharmacy and practitioner or receiving pharmacy, including a statement of the process for:

(i) a patient to report an adverse reaction or submit a complaint; and

(ii) the pharmacy to recall batches of compounded preparations.

(3) Recordkeeping.

(A) Maintenance of Records.

(i) Records of orders and distribution of sterile compounded preparations to a practitioner for office use or to an institutional pharmacy for administration to a patient shall:

(I) be kept by the pharmacy and be available, for at least two years from the date of the record, for inspecting and copying by the board or its representative and to other authorized local, state, or federal law enforcement agencies;

(II) be maintained separately from the records of preparations dispensed pursuant to a prescription or medication order; and

(III) be supplied by the pharmacy within 72 hours, if requested by an authorized agent of the Texas State Board of Pharmacy or its representative. If the pharmacy maintains the records in an electronic format, the requested records shall [~~must~~] be provided in an electronic format. Failure to provide the records set out in this subsection, either on site or within 72 hours for whatever reason, constitutes prima facie evidence of failure to keep and maintain records.

(ii) Records may be maintained in an alternative data retention system, such as a data processing system or direct imaging system provided the data processing system is capable of producing a hard copy of the record upon the request of the board, its representative, or other authorized local, state, or federal law enforcement or regulatory agencies.

(B) Orders. The pharmacy shall maintain a record of all sterile compounded preparations ordered by a practitioner for office use or by an institutional pharmacy for administration to a patient. The record shall include the following information:

(i) date of the order;

(ii) name, address, and phone number of the practitioner who ordered the preparation and if applicable, the name, address and phone number of the institutional pharmacy ordering the preparation; and

(iii) name, strength, and quantity of the preparation ordered.

(C) Distributions. The pharmacy shall maintain a record of all sterile compounded preparations distributed pursuant to an order to a practitioner for office use or by an institutional pharmacy for administration to a patient. The record shall include the following information:

(i) date the preparation was compounded;

(ii) date the preparation was distributed;

(iii) name, strength and quantity in each container of the preparation;

(iv) pharmacy's lot number;

(v) quantity of containers shipped; and

(vi) name, address, and phone number of the practitioner or institutional pharmacy to whom the preparation is distributed.

(D) Audit trail [~~Trail~~].

(i) The pharmacy shall store the order and distribution records of preparations for all sterile compounded preparations ordered by and or distributed to a practitioner for office use or by a pharmacy licensed to compound sterile preparations for administration to a patient in such a manner as to be able to provide an audit trail for all orders and distributions of any of the following during a specified time period:

(I) any strength and dosage form of a preparation (by either brand or generic name or both);

(II) any ingredient;

(III) any lot number;

(IV) any practitioner;

(V) any facility; and

(VI) any pharmacy, if applicable.

(ii) The audit trail shall contain the following information:

(I) date of order and date of the distribution;

(II) practitioner's name, address, and name of the institutional pharmacy, if applicable;

(III) name, strength and quantity of the preparation in each container of the preparation;

(IV) name and quantity of each active ingredient;

(V) quantity of containers distributed; and

(VI) pharmacy's lot number.

(4) Labeling. The pharmacy shall affix a label to the preparation containing the following information:

(A) name, address, and phone number of the compounding pharmacy;

(B) the statement: "For Institutional or Office Use Only--Not for Resale"; or if the preparation is distributed to a veterinarian the statement: "Compounded Preparation";

(C) name and strength of the preparation or list of the active ingredients and strengths;

(D) pharmacy's lot number;

(E) beyond-use date as determined by the pharmacist using appropriate documented criteria;

(F) quantity or amount in the container;

(G) appropriate ancillary instructions, such as storage instructions or cautionary statements, including hazardous drug warning labels where appropriate; and

(H) device-specific instructions, where appropriate.

(g) Recall procedures [~~Procedures~~].

(1) The pharmacy shall have SOPs [~~written procedures~~] for the recall of any compounded sterile preparation provided to a patient, to a practitioner for office use, or a pharmacy for administration. The SOPs [~~Written procedures~~] shall include, but not be limited to the requirements as specified in paragraph (3) of this subsection.

(2) The pharmacy shall immediately initiate a recall of any sterile preparation compounded by the pharmacy upon identification of a potential or confirmed harm to a patient.

(3) In the event of a recall, the pharmacist-in-charge shall ensure that:

(A) the distribution of any affected compounded sterile preparation is determined, including the date and quantity of distribution;

(B) [~~(A)~~] each practitioner, facility, and/or pharmacy to which the preparation was distributed is notified, in writing, of the recall;

(C) [~~(B)~~] each patient to whom the preparation was dispensed is notified, in writing, of the recall;

(D) [~~(C)~~] the board is notified of the recall, in writing, not later than 24 hours after the recall is issued;

(E) [~~(D)~~] if the preparation is distributed for office use, the Texas Department of State Health Services, Drugs and Medical Devices Group, is notified of the recall, in writing;

(F) [~~(E)~~] any unused dispensed compounded sterile preparations are recalled and any stock remaining in the pharmacy is quarantined [~~the preparation is quarantined~~]; and

(G) [~~(F)~~] the pharmacy keeps a written record of the recall including all actions taken to notify all parties and steps taken to ensure corrective measures.

(4) Recall of out-of-specification dispensed compounded sterile preparations.

(A) If a compounded sterile preparation is dispensed or administered before the results of testing are known, the pharmacy shall have SOPs in place to:

(i) immediately notify the prescriber of a failure of specifications with the potential to cause patient harm (e.g., sterility, strength, purity, bacterial endotoxin, or other quality attributes); and

(ii) investigate if other lots are affected and recall if necessary.

(B) SOPs for recall of out-of-specification dispensed compounded sterile preparations shall contain procedures to:

(i) determine the severity of the problem and the urgency for implementation and completion of the recall;

(ii) determine the disposal and documentation of the recalled compounded sterile preparation; and

(iii) investigate and document the reason for failure.

(5) [~~(4)~~] If a pharmacy fails to initiate a recall, the board may require a pharmacy to initiate a recall if there is potential for or confirmed harm to a patient.

(6) [~~(5)~~] A pharmacy that compounds sterile preparations shall notify the board immediately of any adverse effects reported to the pharmacy or that are known by the pharmacy to be potentially attributable to a sterile preparation compounded by the pharmacy.

The agency certifies that legal counsel has reviewed the proposal and found it to be within the state agency's legal authority to adopt.

Filed with the Office of the Secretary of State on December 16, 2024.

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Executive Director
Texas State Board of Pharmacy
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For further information, please call: (512) 305-8033

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TITLE 34. PUBLIC FINANCE

PART 1. COMPTROLLER OF PUBLIC ACCOUNTS

CHAPTER 7. PREPAID HIGHER EDUCATION TUITION PROGRAM

SUBCHAPTER N. TEXAS ACHIEVING A BETTER LIFE EXPERIENCE (ABLE) PROGRAM

34 TAC §7.198

The Comptroller of Public Accounts proposes amendments to §7.198, concerning ABLE program advisory committee. The legislation enacted within the last four years that provides the statutory authority for this proposal is Senate Bill 702, 87th Legislature, R.S., 2021.

The amendments to subsections (a) and (b) expand the categories of individuals eligible to serve on the committee to include representatives of the business, legal, or veteran community.

The amendment to subsection (e) allows the comptroller the flexibility of not appointing a replacement member to the committee provided the requirements of subsection (b) have been met.

The amendment to subsection (f) allows the presiding officer or comptroller flexibility in determining how frequently the committee meets.

The amendment to subsection (g) reduces the number of members required to be present to constitute a quorum.

Brad Reynolds, Chief Revenue Estimator, has determined that during the first five years that the proposed amended rule is in effect, the rule: will not create or eliminate a government program; will not require the creation or elimination of employee positions; will not require an increase or decrease in future legislative ap-