COMMONWEALTH OF VIRGINIA
Meeting of the Board of Pharmacy

Perimeter Center, 9960 Mayland Drive, Third Floor **(804) 367-4456 (Tel)**
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Tentative Agenda of Regulation Committee Meeting
May 23, 2023
9AM

TOPIC	PAGES
Call to Order: Kris Ratliff, DPh, Committee Chairman	
• Welcome & Introductions	
Call for Public Comment: The Board will receive public comment at this time. The Board will not receive comment on any regulation process for which a public comment period has closed or any pending disciplinary matters.	
Regulatory/Guidance: Erin Barrett, JD/Caroline Juran, RPh	
• Chart of Regulatory Actions	**2-4**
• Update on transfer of medical cannabis program to Virginia Cannabis Control Authority	
• Amend guidance on hydrocarbon solvents	**5-20**
○ Presentation on butane and propane, Becky Hobden, Lab Director, Green Analytics Virginia	**21-29**
• Adopt guidance regarding cannabis advertising regulations as applied to packaging	**30-31**
• Reconsider amendment of 18VAC110-20-555	**32-47**
• Discuss number and location of pharmacy permits in recent years	**48-50**
• Legislative proposals:	**51-77**
○ Pharmacy technicians accepting refill authorizations for Schedules III-VI prescriptions and clarification of quantity/refills for Schedule VI prescriptions	
○ Requiring federal criminal background check for resident and nonresident wholesale distributors and third-party logistics providers	
○ Clarifying compounding of essentially copies of commercially available drug product	
• Amend Guidance Documents 110-36 and 110-9 regarding USP revisions	**78-115**
• Discuss monetary penalties in GD 110-9 as compared to other states	**116-144**
• Discuss acceptance of outsourcing facility inspections performed by other states	**145-163**
Adjourn	

****The Board will have a working lunch at approximately 12pm.****

Board of Pharmacy
Current Regulatory Actions
As of May 2, 2023

In the Governor's Office

VAC	Stage	Subject Matter	Date submitted*	Office; time in office	Notes
18VAC110-20	Final	Prohibition against incentives to transfer prescriptions	5/23/2018	Governor 1,805 days; 6.1 years since submission for executive branch review	Addresses a patient safety concern.
18VAC110-20	Emergency/ NOIRA	Pharmacy working conditions	2/27/2023	Governor 64 days	Implements emergency regulations related to work environments for pharmacy personnel

In the Secretary's Office

VAC	Stage	Subject Matter	Date submitted*	Office; time in office	Notes
18VAC110-20	NOIRA	Implementation of 2021 Periodic Review	4/3/2022	Secretary 394 days	Implementation of changes identified during 2021 periodic review of regulations governing the practice of pharmacy
18VAC110-21	NOIRA	Implementation of 2021 Periodic Review	4/3/2022	Secretary 394 days	Implementation of changes identified during 2021 periodic review of regulations governing the licensure of pharmacists and

					registration of pharmacy technicians
18VAC110-20	Proposed	Centralized warehouser or wholesale distributor verification of Schedule VI drugs for ADDs in hospitals	8/31/2022	Secretary 244 days	Permits centralized warehousers or wholesale distributors to verify Schedule VI drugs for ADDs in hospitals

At DPB/OAG

VAC	Stage	Subject Matter	Date submitted*	Office; time in office	Notes
18VAC110-20	Final	Implementation of 2021 legislation for pharmacists initiating treatment	4/18/2023	DPB 14 days	Final regulatory action to replace 2021 emergency regulations for pharmacists initiating treatment
18VAC110-20	Exempt/ Final	March 2023 scheduling of chemicals in Schedule I	4/18/2023	OAG 14 days	Adds chemicals to Schedule I per DFS recommendation
18VAC110-20	Exempt/ Final	March 2023 scheduling and de-scheduling of drugs and chemicals pursuant to federal scheduling actions July 7, 2022 – February 3, 2023	5/2/2023	OAG 1 day	Scheduling action pursuant to federal changes
18VAC110-21	Emergency/ NOIRA	2023 pharmacists initiating treatment	4/18/2023	OAG 14 days	Changes in pharmacists initiating treatment pursuant to legislation

18VAC110-21	Fast-track	Repeal of outdated sections	4/18/2023	OAG 14 days	Repeals outdated regulations regarding pharmacy technician registration
18VAC110-30	Proposed	Implementation of 2021 periodic review	4/18/2023	OAG 14 days	Implements changes identified during the periodic review process
18VAC110-60	Exempt/ Final	Pharmaceutical processor regulations	10/5/2022	OAG 209 days	Implements changes to processor regulations pursuant to 2022 legislation

* Date submitted to current location

Recently effective or awaiting publication

VAC	Stage	Subject Matter	Publication date	Effective date
18VAC110-20	Exempt/ Final	December 2022 scheduling of chemicals in Schedule I	3/13/2023	4/12/2023
18VAC110-21	Emergency	2022 pharmacists initiating treatment	3/13/2023	2/21/2023

Agenda Topic: Amend guidance on hydrocarbon solvents

Included in Agenda Packet:

- Board-adopted draft guidance document *Approved Chemicals for use as Hydrocarbon or Other Flammable Solvents by Pharmaceutical Processors*
- Board-adopted emergency regulations regarding hydrocarbon-solvents
- Correspondence between Becky Hobden and Board staff
- Excerpt from American Herbal Pharmacopeia

Note from Staff:

- Becky Hobden, Lab Director, Green Analytics Virginia will provide presentation regarding use of butane and propane.

Action Needed:

- Motion to recommend to full board that it amend guidance document to include butane and propane; or
- Motion to recommend to full board that it not amend guidance document to include butane and propane.

Virginia Board of Pharmacy

Approved Chemicals for use as Hydrocarbon or Other Flammable Solvents by Pharmaceutical Processors

Pursuant to 18VAC110-60-281(H), the Board approves the following chemicals for use as hydrocarbon or other flammable solvents in the cultivation, extraction, production, or manufacturing of cannabis products. These approvals are based on the availability of testing for residual material of individual solvents.

- Ethanol
- Ethyl acetate
- Ethyl ether
- Heptane
- Hexane
- Pentane
- 2-propanol (IPA)

Project 7283 - Final

Board of Pharmacy

Pharmaceutical processor regulation changes pursuant to 2022 legislation

18VAC110-60-281. Use of hydrocarbon-based solvents or other flammable solvents.

A. The following words and phrases used in this section have the following meaning:

1. "Closed-loop system" means machinery in which volatile hydrocarbon substances are self-contained without the loss or escape of those substances.

2. "Flammable solvent" means a liquid that has a flash point below 100 degrees Fahrenheit. Flammable solvents include, but are not limited to, hydrocarbon-based solvents.

3. "Hydrocarbon-based solvent" means a type of solvent composed of hydrogen and carbon compounds, such as N-butane, isobutene, propane, or any isomer or combination thereof.

B. Hydrocarbon-based solvents may be used in the cultivation, extraction, production, or manufacturing of cannabis products provided that:

1. A pharmaceutical processor complies with all requirements in this section.

2. A pharmaceutical processor using hydrocarbon-based solvents in general industrial use as promulgated by the Occupational Safety and Health Administration and published in 29 C.F.R. § 1910 or any subsequent regulation governing such use, including, but not limited to, regulations governing:

a. ventilation requirements;

b. air contaminants; and

c. hazard communication.

3. A pharmaceutical processor using hydrocarbon-based solvents shall comply with any requirements issued by the Virginia Department of Labor and Industry regarding use of hydrocarbon-based solvents.

4. A pharmaceutical processor using hydrocarbon-based solvents shall comply with any requirements issued by the Virginia Department of Environmental Quality regarding use of hydrocarbon-based solvents.

5. A pharmaceutical processor using hydrocarbon-based solvents maintains sole responsibility for any adverse outcomes or violations of federal or Virginia state laws or regulations caused by such use.

6. A pharmaceutical processor using hydrocarbon-based solvents shall ensure that all equipment, counters, and surfaces used in the cultivation, extraction, production, or manufacturing of cannabis products are food-grade and do not react adversely with any hydrocarbon solvent used. All counters and surface areas shall be constructed in a manner that reduces the potential development of microbials, molds, and fungi and can be easily cleaned.

7. A pharmaceutical processor using hydrocarbon-based solvents shall ensure that any room in which hydrocarbon-based solvents will be used contains an emergency eye-wash station.

8. A pharmaceutical processor using hydrocarbon-based solvents shall ensure that a professional grade, closed-loop extraction system capable of recovering solvent is used in the cultivation, extraction, production, or manufacturing of cannabis products.

a. Closed-loop extraction systems must be commercially manufactured and bear a permanently affixed and visible serial number.

b. A pharmaceutical processor using a closed-loop extraction system must obtain a certification from a licensed engineer that certifies that the system was commercially manufactured, is safe for its intended use, and built to codes of recognized and generally accepted good engineering practices, such as: (i) the American Society of Mechanical Engineers ("ASME"); (ii) American National Standards Institute ("ANSI"); (iii) Underwriters Laboratories ("UL"); or (iv) the American Society for Testing and Materials ("ASTM").

c. The certification must contain the signature and stamp of a professional engineer and include the serial number of the extraction unit certified.

9. A pharmaceutical processor using hydrocarbon-based solvents shall obtain a safety data sheet for each hydrocarbon-based solvent used and store such data sheet on the premises. All such records shall be subject to inspection by the board.

10. A pharmaceutical processor using hydrocarbon-based solvents shall develop standard operating procedures, good manufacturing practices, and a training plan prior to using such solvents. Standard operating procedures shall specifically address the following:

a. Safe and proper handling and use of hydrocarbon-based solvents;

b. Safe and proper operation of machinery and equipment;

c. Adequate cleaning and maintenance of machinery and equipment;

d. Incident reporting for any instances where the operator does not follow the stated standard operating procedures which identifies: (i) the operator's name; (ii) the date and time of the incident; (iii) the supervising employees to which the incident report will be sent; and (iv) an incident summary, which includes whether any cannabis products or other substances escaped from the closed-loop system, the amount of

escaped material, whether the material was destroyed, and how the incident was resolved; and

e. Safe and proper disposal of waste created during processes using hydrocarbon-based solvents.

11. A pharmaceutical processor using hydrocarbon-based solvents shall ensure that any person using such solvents in a closed-loop system:

a. Is fully trained on how to use the system;

b. Has direct access to applicable material safety data sheets; and

c. Handles and stores the solvents safely.

C. If a pharmaceutical processor intends to use a flammable solvent, then a designated industrial hygienist or professional engineer that is not an employee of the pharmaceutical processor must:

1. Establish a maximum amount of flammable solvents and other flammable materials that may be stored within the pharmaceutical processor facility in accordance with applicable laws and regulations;

2. Determine what type of electrical equipment must be installed within the room or rooms in which flammable solvents are to be stored in accordance with applicable laws and regulations;

3. Determine whether a gas monitoring system must be installed within the room in which flammable solvents are to be used or stored, and, if required, the system's specifications in accordance with applicable laws and regulations;

4. Determine whether a fire suppression system must be installed within the room in which the flammable solvents are to be used or stored, and, if required, the system's specifications in accordance with applicable laws and regulations; and

5. Determine whether a fume vent hood or exhaust system must be installed within the room or rooms in which a flammable solvent will be used, and, if required, the system's specifications in accordance with applicable laws and regulations.

D. If a pharmaceutical processor makes a material change to its use of flammable solvents in any part of the manufacturing process, a designated industrial hygienist or professional engineer that is not an employee of the pharmaceutical processor must re-certify the standard operating procedures for use of flammable solvents determined under subsection C.

E. A pharmaceutical processor shall maintain copies of all reports generated by or received from the designated industrial hygienist or professional engineer for inspection by the board.

F. A pharmaceutical processor shall not store an amount of flammable solvents on site which exceeds the maximum amount allowable as identified by the designated industrial hygienist or professional engineer.

G. A pharmaceutical processor shall ensure that all appropriate safety and sanitary equipment, including personal protective equipment, is provided to, and appropriately used by, each employee handling a flammable solvent.

H. The board shall approve chemicals for use as hydrocarbon or other flammable solvents in the cultivation, extraction, production, or manufacturing of cannabis products based on availability of testing for residual material of individual solvents.

American Herbal Pharmacopoeia®

Cannabis Inflorescence
Cannabis spp.

Standards of Identity, Analysis, and Quality Control

Revision 2014

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Table 11 Metal limits recommended for herbal products in the US

Contaminating metal	Limit, µg/daily dose
Inorganic arsenic	10
Cadmium	4.1
Lead	6
Methyl mercury	2.0

Source: AHPA (2008).

ents have broad use sites that could allow for their use on cannabis. Additionally, some states, (e.g., Massachusetts, Washington, and Colorado) are formulating guidelines for pesticide use in cannabis cultivation, whose ingredients are approved in that state for organic production, or are listed by the Organic Materials Review Institute (OMRI). Use of unapproved pesticides in those states that allow for OMRI-listed or exempt pesticides represents a public safety license violation and can result in the cancellation of a cannabis producer's license. State allowance for pesticide use on cannabis may be in conflict with federal pesticide regulations.

Presence and Testing of Pesticides in Cannabis

Specialty agricultural supply stores for the cannabis industry, have proliferated across the US, many of which are categorized as "hydroponic". This aspect of the industry lacks any meaningful regulation or guidance. Products found in such stores have been reported to contain banned substances, and often fail to accurately disclose ingredients or provide adequate information for proper use. For example, the California Department of Food and Agriculture (CDFA) in 2011 issued cease and desist orders against the sale of a number of popular cannabis cultivation products due to their inclusion of a number of banned plant growth regulators including daminozide (Alar) and paclobutrazol (CDFA 2011). A number of these products are labeled as "organic" though they may not be compliant under the National Organics Program of the United States Department of Agriculture (USDA).

The use of such agents on cannabis crops is widespread. Daley et al. (2013) compiled a list of 148 pesticide products used in cannabis cultivation, based on a survey of California growers. Insecticides and miticides are often used on cannabis grown indoors, while fungicides are used on both indoor and outdoor crops. Inappropriate use of insecticides, miticides, and fungicides (such as improper product selection, application rate, concentration, and/or timing) can lead to pests becoming resistant and/or medical users being exposed to inappropriate residue levels.

Appropriate testing methodologies, as recommended by the Environmental Protection Agency (EPA Residue Analytical Methods [RAM]) or those of the Food and Drug Administration (FDA Pesticide Analytical Manual [PAM]), should be employed when appropriate. However, as these tests were developed for commodity food products, the amount of sample needed may be prohibitive to apply to the cannabis industry. Alternatively, The food testing QuEChERS screen uses smaller quantities and may be more applicable to a variety, though not all, of cannabis products (Schoen 2013, personal communication to AHP, unreferenced).

In the cannabis industry today, the most commonly used screening technology for organophosphates, organochlorines, carbamates, and ethylenediaminetetraacetic acid (EDTA) are immunoassays (e.g., enzyme-linked immunosorbent assays [ELISA]) and broad spectrum field tests that may or may not be validated for use on cannabis. Similarly, immunoassays for a broad range of PGRs and fungicides commonly used in cannabis cultivation are not available. Because of their relative inexpense, immunoassays are routinely used by analytical labs specializing in cannabis testing and are at high risk of not detecting pesticide residues and reporting samples to be "pesticide-free" or "non-detected". Before commercial use, any immunoassay should be validated against a standard testing methodology.

Table 10 provides a list of the most common pesticides (including acaricides, insecticides, fungicides, and plant growth regulators) used in cannabis production.

Solvent Residues

Limits on solvents used in the manufacture of botanical products are established by the International Conference on Harmonization (ICH) (ICH 2011), with exceptions made for ethanol and acetic acid in products formulated to contain these substances (e.g., tinctures and vinegars). According to the ICH guideline, solvents are categorized in 3 classes. Class 1 includes known carcinogens, toxic substances, and environmental hazards such as benzene, carbon tetrachloride, 1,2-dichloroethane, 1,1-dichloroethene, and 1,1,1-trichloroethane. These are to be avoided in the manufacture of herbal and/or pharmaceutical products. Class 2 and 3 solvents (Table 12) are distinguished based on their relative toxicity level. Limits established for permissible daily exposures (PDE) are determined individually for Class 2 solvents. Limits for Class 3 solvents are set at a general limit of 50 mg/day. In addition, the ICH guideline lists solvents for which no adequate toxicological data was found (Table 13) and requires manufacturers of pharmaceutical products that choose to use these solvents to supply justification for residual levels of these solvents in their final products. Petroleum ether, found in this group, is reportedly used in the production of hash oil (UNODC 2009).

Solvent extracted products made with Class 3 or other solvents, are not to exceed 0.5% residual solvent by weight or 5000 parts per million (PPM) per 10 gram of solvent-based product and are to be quantified according to the United States Pharmacopeia (USP <467>), Residual Solvents, Option 1. Higher concentrations may also be acceptable provided they are realistic in relation to safety, manufacturing, and good manufacturing practices.

Table 12 Permissable and restricted solvents in the manufacture of cannabis preparations

Class 2 solvents		Class 3 solvents Permissible daily exposure: 50 mg/day
Solvent	Permissible daily exposure, mg/day	
Acetonitrile	4.1	Acetic acid†
Chlorobenzene	3.6	Acetone
Chloroform*	0.6	Anisole
Cyclohexane	38.8	1-Butanol
1,2-Dichlorothene	18.7	2-Butanol
Dichloromethane*	6.0	Butyl acetate
1,2-Dimethoxyethane	1.0	tert-Butylmethylether
N,N-Dimethylacetamide*	10.9	Cumene*
N,N-Dimethylformamide	8.8	Dimethyl sulfoxide
1,4-Dioxane*	3.8	Ethanol*†
2-Ethoxyethanol	1.6	Ethyl acetate
Ethyleneglycol	6.2	Ethyl ether
Formamide	2.2	Ethyl formate
Hexane	2.9	Formic acid
Methanol*	30.0	Heptane
2-Methoxyethanol	0.5	Isobutyl acetate
Methylbutyl ketone	0.5	Isopropyl acetate
Methylcyclohexane	11.8	Methyl acetate
N-Methylpyrrolidone*	5.3	3-Methyl-1-butanol
Nitromethane*	0.5	Methylethyl ketone
Pyridine*	2.0	Methylisobutyl ketone
Sulfolane	1.6	2-Methyl-1-propanol
Tetrahydrofuran	7.2	Pentane
Tetralin	1.0	1-Pentanol
Toluene*	8.9	1-Propanol
1,1,2-Trichloroethene	0.8	2-Propanol
Xylene	21.7	Propyl acetate

* Listed as chemicals known to the state of California to cause cancer or reproductive toxicity under Proposition 65 (CAEPA 2013).
Source: AHPA (2008); CAEPA (2013); ICH (2011); United States Pharmacopeia (USP 30-NF 25 2007).

Table 13 Solvents for which no adequate toxicological data was found

1,1-Diethoxypropane	Methylisopropyl ketone
1,1-Dimethoxymethane	Methyltetrahydrofuran
2,2-Dimethoxypropane	Petroleum ether
Isooctane	Trichloroacetic acid
Isopropyl ether	Trifluoroacetic acid

Source: ICH (2011).

Re: Residual Solvents Testing for Hydrocarbons

Becky Hobden <becky.hobden@greenanalyticsllc.com>
Wed 3/22/2023 10:07 AM
To: Juran, Caroline (DHP) <Caroline.Juran@DHP.VIRGINIA.GOV>
Cc: Barrett, Erin (DHP) <Erin.Barrett@dhp.virginia.gov>;Kelley, Annette (DHP) <Annette.Kelley@dhp.virginia.gov>

3 attachments (1 MB)
oha-8964-technical-report-marijuana-contaminant-testing.pdf; ICH_Q3C-R8_Guideline_Step4_2021_0422_1 (3).pdf; USP 467.pdf;

Hi Caroline, Annette, and Erin,

Hope you are all enjoying the start of Spring! I am following up on the questions Caroline sent last week. May 23 is on my schedule to present an overview and answer any questions from the BOP.

The table that I sent you in the previous email addresses the specific question that was brought up at the Dec 6, 2022, full Board of Pharmacy meeting regarding what other states that have marijuana programs (medical and/or recreational) allow the use of butane and/or propane in their production. The concern from the BOP was that butane and propane are not specifically listed on Table 12 in the AHP, which references the International Conference on Harmonization (ICH) for the establishment of the solvents and limits. The table from my previous email came from looking at other states' lists of permissible solvents and their limits to highlight that most, if not all, other states with cannabis programs do allow butane and propane in their production.

Often, as in Table 12, you will see the listed solvents and their Permissible Daily Exposure (PDE), rather than Acceptable Concentration/Limits (ppm). The conversion from PDE (mg/day) to Acceptance Limits is found USP <467> (attached), which is referenced in the ICH, Section 3.3 (pg. 3):

The dose of 10g/day is used as a conservative maximum daily dose. As a reference point, Virginia has a limit of 10mg of THC per dose. A patient would have to consume 1000 doses in one day to reach a 10g dose.

For example, a solvent like ethanol (and all other Class 3 solvents), which has a PDE of 50mg per day, the calculation for acceptable concentration in a product is below:

Acceptance Limit (ppm) = (1000 x 50mg per day) / 10 g per day
Acceptance Limit (ppm) = 5000ppm

This calculation is also referenced, perhaps more succinctly, in a Technical Report from the Oregon Health Authority titled "Oregon Health Authority's Process To Determine Which Types of Contaminants to Test For in Cannabis Products, and Levels for Action" (attached to this email). Pages 9-10 give a good description of solvents use and limits in cannabis production and speaks specifically to butane and propane giving a justification for considering them a Class 3 solvent with a PDE of 50mg/day and an Acceptance Limit of 5000ppm:

"Butane, propane… are short-chain alkanes similar to pentane. Pentane falls into a class of solvents designated as class 3 by ICH Q3C. Class 3 solvents are less toxic and default to a health-based action level of 5,000 ppm for butane [and] propane"

I am not sure why some states have chosen other Acceptance Limits. Speaking with my colleagues in Massachusetts, where the limits are very low, there is significant on-going efforts to increase those limits.

Because butane and propane both fall into the definition in the ICH for a Class 3 solvent, my recommendation is to include them in the VA list of permissible solvents with the limits of a Class 3 solvent (5000 ppm).

To address the question of setting separate limits for inhalable products, the Oregon Technical Report addresses this question as well on pg.10, second bullet point, which states "… the ICH Q3C does assume 100% absorption by any exposure route. This covers inhalation, which is how some pharmaceuticals are administered".

Hope that helps, let me know if you have additional questions.

Thanks,
Becky Hobden
Lab Director
Green Analytics Virginia
540-682-3765 (lab)
828-279-2765 (direct)

On Fri, Mar 10, 2023 at 4:51 PM Juran, Caroline (DHP) <Caroline.Juran@dhp.virginia.gov> wrote:

> Hi, Becky -
>
> Circling back around to this issue. Greatly appreciate your providing us with your research below but I do have a few questions.
>
> 1. Would you be willing to provide a brief overview of the subject and answer board member questions at the May 23rd Regulation Committee meeting? I think this subject is going to require a deeper dive to ensure the board is educated and comfortable with the decision-making.
> 2. I'm trying understand your chart compared to Table 12 in the AHP Cannabis Inflorescence document. I noticed the table for Class 3 solvents uses a header of "Permissible Daily Exposure: 50mg/day", but your chart appears to reference Parts per Million. How do I compare or reconcile PDE to PPM?
> 3. Do you have a specific recommendation for limits? I see that most states have adopted 5,000 for both butane and propane but other states have landed on several different limits, and I note that Colorado with its longstanding cannabis program has set 1,000 as its limit for both solvents. What's the rationale for why the limits vary from 500 to 5,000? I read the pertinent sections of the National Academies of Science document you previously forwarded but some of the states' numbers feel somewhat arbitrary.
> 4. Do you recommend separating out limits for inhaled products vs. non-inhaled products as three states have done?
>
> Thank you, again, for your assistance with this subject. Have a nice weekend.
>
> Best,
> Caroline
>
> Caroline D. Juran, RPh
> Executive Director
> Virginia Board of Pharmacy
>
> **From:** Becky Hobden <becky.hobden@greenanalyticsllc.com>
> **Sent:** Tuesday, December 20, 2022 5:17 PM
> **To:** Juran, Caroline (DHP) <Caroline.Juran@DHP.VIRGINIA.GOV>

Cc: Kelley, Annette (DHP) <Annette.Kelley@dhp.virginia.gov>; Barrett, Erin (DHP) <Erin.Barrett@dhp.virginia.gov>
Subject: Re: Residual Solvents Testing for Hydrocarbons

Hi Caroline, Erin, and Annette,

Continuing the conversation about butane and propane, I did a thorough search of regulations around residual solvents in states where cannabis is regulated. I could find a list for almost all states either written in the regulations or as guidance documents from the regulatory body in the state. Almost all states test for butane and propane and I have included the limits in the table below. Many of these state regulations reference the *American Herbal Pharmacopoeia on Cannabis* and/or the *International Conference on Harmonization*, which is the guiding document for the AHP on residual solvents testing.

I would like to present this to the Board of Pharmacy and whatever additional documentation is needed to get the list updated to include butane and propane. Those hydrocarbons are widely used in cannabis production and are often preferred solvents because of their ability to retain the terpenes, which benefits patients and processors. We can currently test for both of those solvents. Let me know if you have any questions and the best path forward to amending the guidance document from the BOP.

Happy Holidays!

Becky Hobden
Lab Director
Green Analytics Virginia
540-682-3765 (lab)
828-279-2765 (direct)

State	Status	Butane	Propane
Alaska	medical & recreational	800	not tested
Arizona	medical & recreational	5000	5000
Arkansas	medical	5000	5000
California	medical & recreational	5000	5000
Colorado	medical & recreational	1000	1000
Connecticut	medical & recreational	residual solvents not tested at all	residual solvents not tested at all
Florida	medical	800	2100
Hawaii	medical	800	not tested
Illinois	medical & recreational	10	10
Louisiana	medical	800	not tested
Maine	medical & recreational	5000	5000
Maryland	medical & recreational	5000	5000
Massachusetts	medical & recreational	1	1
Michigan	medical & recreational	800 (inhaled products); 5000 (non-inhaled)	2100 (inhaled products); 5000 (non-inhaled)
Minnesota	medical	800 (inhaled products); 5000 (non-inhaled)	2100 (inhaled products); 5000 (non-inhaled)
Mississippi	medical	5000	5000
Missouri	medical & recreational	800 (inhaled products); 5000 (non-inhaled)	2100 (inhaled products); 5000 (non-inhaled)
Montana	medical & recreational	5000	5000
Nevada	medical & recreational	500	500

New Hampshire	medical	500	500
New Jersey	medical & recreational	5000	5000
New Mexico	medical & recreational	800	800
New York	medical & recreational	5000	5000
North Dakota	medical	5000	5000
Ohio	medical	5000	5000
Oklahoma	medical	1000	1000
Oregon	medical & recreational	5000	5000
Pennsylvania	medical	5000	not tested
Rhode Island	medical & recreational	5000	5000
South Dakota	medical	800	2100
Utah	medical	5000	5000
Vermont	medical & recreational	5000	5000
Washington	medical & recreational	5000	5000
Washington, DC	medical & recreational	5000	5000
West Virginia	medical	5000	5000
Alabama	medical	could not find limits	could not find limits
Delaware	medical	could not find limits	could not find limits

On Tue, Dec 6, 2022 at 8:44 AM Juran, Caroline (DHP) <Caroline.Juran@dhp.virginia.gov> wrote:

Becky -

Thank you for the additional information.

Caroline D. Juran, RPh
Executive Director
Virginia Board of Pharmacy

From: Becky Hobden <becky.hobden@greenanalyticsllc.com>
Sent: Tuesday, December 6, 2022 7:42 AM
To: Juran, Caroline (DHP) <Caroline.Juran@DHP.VIRGINIA.GOV>
Cc: Kelley, Annette (DHP) <Annette.Kelley@dhp.virginia.gov>; Barrett, Erin (DHP) <Erin.Barrett@dhp.virginia.gov>
Subject: Re: Residual Solvents Testing for Hydrocarbons

Hi Caroline,

Thanks for your email. The list of solvents in the AHP was pulled directly from the International Conference on Harmonization (ICH) in their published document I*CH Harmonised Guidelines*, *Impurities: Guidelines for Residual Solvents Q3C.* I've attached the most recent version (8) of that document to this email. In the 'Introduction' of that document, it states that the list presented is not exhaustive.

> The lists [of Class 1, 2, and 3 solvents] are not exhaustive and other solvents can be used and later added to the lists. Recommended limits of Class 1 and 2 solvents or classification of solvents may change as new safety data becomes available. Supporting safety data in a marketing application for a new drug product containing a new solvent may be based on concepts in this guideline or the concept of qualification of impurities as expressed in the guideline for drug substance (Q3A, Impurities in New Drug Substances) or drug product (Q3B, Impurities in New Drug Products), or all three guidelines. (pg. 7)

In a precursory review of safety data for butane and propane, there is a good amount of published data available. The National Library of Medicine has published data in A*cute Exposure Guideline Levels for Selected*

Airborne Chemicals: Vol. 12 that includes acute exposure data for butane (pg. 13-47) and propane (pg. 288-315). That document is attached.

Butane and Propane are often preferred solvents in cannabis production because of their ability to retain the cannabis terpenes, a benefit to patients and processes alike. They are widely used in other states safely and effectively. One example of this is Maryland where in the Maryland Medical Cannabis Commission's Testing Regulations published June 2019, they refer specifically to the same ICH guidelines and include in their list of acceptable solvents both butane and propane. They are listed as Class 3 solvents with a limit of 5,000 ppm.

Becky Hobden
Lab Director
Green Analytics Virginia
540-682-3765 (lab)
828-279-2765 (direct)

On Mon, Dec 5, 2022 at 4:01 PM Juran, Caroline (DHP) <Caroline.Juran@dhp.virginia.gov> wrote:

Becky -

Thank you for the email, however, I don't think we can include butane and propane in the guidance document. Regulation 18VAC110-60-300(G)(6) states "6. For the purposes of the residual solvent test, a sample of the cannabis oil product shall be deemed to have passed if it meets the standards and limits recommended by the American Herbal Pharmacopia for Cannabis Inflorescence." Butane and propane do not appear to be listed in the AHP.

Please let me know if I am overlooking something.

Kindest regards,
Caroline

Caroline D. Juran, RPh
Executive Director
Virginia Board of Pharmacy

From: Becky Hobden <becky.hobden@greenanalyticsllc.com>
Sent: Thursday, December 1, 2022 8:09 AM
To: Kelley, Annette (DHP) <Annette.Kelley@dhp.virginia.gov>; Barrett, Erin (DHP) <Erin.Barrett@dhp.virginia.gov>; Juran, Caroline (DHP) <Caroline.Juran@DHP.VIRGINIA.GOV>
Subject: Re: Residual Solvents Testing for Hydrocarbons

Dear Caroline, Erin, Annette, and Members of the Board of Pharmacy,

Thank you for taking into consideration the public comments addressing residual solvents testing that were submitted by Green Analytics Virginia during the recent comment period for the Proposed Regulations Governing Pharmaceutical Processors. The regulation for approving hydrocarbons “based on availability of testing for residual material of individual solvents” ensures all potential residual solvents left from processing are detectable before product approval.

In addition to the solvents approved by the VA Board of Pharmacy, Green Analytics has the capability to test for butane and propane. These hydrocarbons are widely used in cannabis production and have proven to be effective, efficient, and safe technologies. Green Analytics is currently testing for propane and butane for our customers in other states where they are not restricted. Including butane and propane in the list of approved hydrocarbons would be within the boundaries of the regulations.

Thank you for your time and consideration in this matter. Please reach out with any questions.

Becky Hobden
Lab Director
Green Analytics Virginia
540-682-3765 (lab)
828-279-2765 (direct)

Residual Solvents Testing in Cannabis

Becky Hobden
Lab Director, Green Analytics Virginia

Green Analytics

Green Analytics Virginia is an ISO 17025 accredited cannabis testing laboratory located in Ashland, VA. We were the first cannabis testing lab in the state of Virginia. **Our mission is to reliably provide our customers with accurate results on the safety and quality of their plants and products.**

A2LA ACCREDITED
CERTIFICATE NUMBER 5748.01

Why Test for Residual Solvents?

Long history in Pharmaceutical and Food Manufacturing

United States Pharmacopeia <467> RESIDUAL SOLVENTS

Residual solvents in pharmaceuticals are defined as organic volatile chemicals that are used or produced in the manufacture of drug substances or excipients, or in the preparation of drug products. The solvents are not completely removed by practical manufacturing techniques… Because residual solvents do not provide therapeutic benefit, they should be removed, to the extent possible, to meet ingredient and product specifications, good manufacturing practices, or other quality-based requirements.

And in Cannabis Processing

- In the manufacture of medical cannabis, solvents are used to extract cannabinoids and terpenes from plant material.
- Manufacturers and processors select extraction method and solvent choice on safety, extraction efficiency, and cost.
- The solvents most widely used in the processing of cannabis are ethanol, butane, CO_2, heptane, pentane, IPA, hexane.

Guidance for Testing Residual Solvents

USP <467>

Classifies and defines limits for residual solvents likely to be present as a result of the manufacturing process. **These tables and the list are not exhaustive.**

Table 1. Classification of Residual Solvents and Their Assessments

Residual Solvent Classes	Assessment
Class 1 (solvents to be avoided)	Known human carcinogens
	Strongly suspected human carcinogens
	Solvents particularly known to have ozone-depleting properties
Class 2 (solvents to be limited)	Nongenotoxic animal carcinogens or possible causative agents of other irreversible toxicity, such as neurotoxicity or teratogenicity
	Solvents suspected of other significant but reversible toxicities
Class 3 (solvents with low toxic potential)	Solvents with low toxic potential to humans; no health-based exposure limit is needed

International Conference on Harmonization,
Impurities: Guideline For Residual Solvents Q3C(R8)

The objective of this guideline is to recommend acceptable amounts for residual solvents in pharmaceuticals for the safety of the patient. The guideline recommends use of less toxic solvents and describes levels considered to be toxicologically acceptable for some residual solvents. Ideally, less toxic solvents (Class 3, Table 3) should be used where practical. The complete list of solvents included in this guideline is given in Appendix 1. ***The lists are not exhaustive and other solvents can be used and later added to the lists.***

Guidance for Testing Residual Solvent in Cannabis

American Herbal Pharmacopeia for Cannabis Inflorescence (AHP)

Limits on solvents used in the manufacture of botanical products are established by the International Conference on Harmonization (ICH 2011).

Solvent extracted products made with Class 3 or other solvents, are not to exceed 0.5% residual solvents by weight or 5000 parts per million (ppm) per 10 gram of solvent-based product and are to be quantified according to the United States Pharmacopeia (USP <467>)…

Table 12 Permissable and restricted solvents in the manufacture of cannabis preparations

Class 2 solvents		Class 3 solvents Permissible daily exposure: 50 mg/day
Solvent	Permissible daily exposure, mg/day	
Acetonitrile	4.1	Acetic acid[†]
Chlorobenzene	3.6	Acetone
Chloroform*	0.6	Anisole
Cyclohexane	38.8	1-Butanol
1,2-Dichlorothene	18.7	2-Butanol
Dichloromethane*	6.0	Butyl acetate
1,2-Dimethoxyethane	1.0	tert-Butylmethylether
N,N-Dimethylacetamide*	10.9	Cumene*
N,N-Dimethylformamide	8.8	Dimethyl sulfoxide
1,4-Dioxane*	3.8	Ethanol*[†]
2-Ethoxyethanol	1.6	Ethyl acetate
Ethyleneglycol	6.2	Ethyl ether
Formamide	2.2	Ethyl formate
Hexane	2.9	Formic acid
Methanol*	30.0	Heptane
2-Methoxyethanol	0.5	Isobutyl acetate
Methylbutyl ketone	0.5	Isopropyl acetate
Methylcyclohexane	11.8	Methyl acetate
N-Methylpyrrolidone*	5.3	3-Methyl-1-butanol
Nitromethane*	0.5	Methylethyl ketone
Pyridine*	2.0	Methylisobutyl ketone
Sulfolane	1.6	2-Methyl-1-propanol
Tetrahydrofuran	7.2	Pentane
Tetralin	1.0	1-Pentanol
Toluene*	8.9	1-Propanol
1,1,2-Trichloroethene	0.8	2-Propanol
Xylene	21.7	Propyl acetate

* Listed as chemicals known to the state of California to cause cancer or reproductive toxicity under Proposition 65 (CAEPA 2013).
Source: AHPA (2008); CAEPA (2013); ICH (2011); United States Pharmacopeia (USP 30-NF 25 2007).

Permissible Daily Exposure (PDE) to Acceptable Concentration (PPM)

The conversion from PDE (mg/day) to Acceptance Limits is below:

$$\text{Concentration (ppm)} = \frac{1000 \text{ x PDE}}{\text{dose}} \qquad (1)$$

Here, PDE is given in terms of mg/day and dose is given in g/day.

The dose of 10g/day is used as a conservative maximum daily dose. Virginia has a limit of 10mg of THC per dose. A patient would have to consume 1000 doses in one day to reach a 10g dose.

For a solvent like ethanol (and all other Class 3 solvents), which has a PDE of 50mg per day, the calculation for acceptable concentration in a product is below:

Acceptance Limit (ppm) = (1000 x 50mg per day) / 10 g per day
Acceptance Limit (ppm) = 5000ppm

For Class 2 solvents, this same calculation can be used where the PDE will vary depending on exposure limits.

Virginia's Regulations for Testing Residual Solvents in Cannabis Products

Regulations Governing Pharmaceutical Processors

18-VAC110-60-300(G)(6)
For the purpose of the residual solvents test, a sample of the cannabis oil product shall be deemed to have passed if it meets the standards and limits recommended by the American Herbal Pharmacopeia for Cannabis Inflorescence.

As a result of HB933/SB671 (2022)

18VAC110-60-281(H)
The board shall approve chemicals for use as hydrocarbon or other flammable solvents in the cultivation, extraction, production, or manufacturing of cannabis products based on availability of testing for residual material of individual solvents.

Guidance Document 110-45: Approved Chemicals for use as Hydrocarbon or Other Flammable Solvents by Pharmaceutical Processors.
Pursuant to 18VAC110-60-281(H), the Board approves the following chemicals for use as hydrocarbon or other flammable solvents in the cultivation, extraction, production, or manufacturing of cannabis products. These approvals are based on the availability of testing for residual material of individual solvents.

Ethanol, Ethyl acetate, Ethyl ether, Heptane, Hexane, Pentane, 2-propanol (IPA)

Pros: Defined list
Cons: What about other widely used, effective, safe hydrocarbons?

Butane & Propane

Can it be tested?

Green Analytics Virginia has a validated method that is currently being reviewed for addition to our ISO 17025 Scope of Accreditation. Green Analytics additionally has used these validated methods for testing butane and propane in other states for several years.

Are we following Virginia laws and regulations?

Based on the language in USP <467>, ICH, and the AHP, the list of solvents in each of those documents explicitly states the list is not exhaustive, therefore butane and propane should not be excluded based on those lists.

Is it established to be safe and effective in the industry?

Reviewing cannabis regulations in other states, both butane and propane are widely used.

What are appropriate Acceptance Concentrations (PPM)?

Oregon Health Authority's Process To Determine Which Types of Contaminants to Test For in Cannabis Products, and Levels for Action

The… solvents commonly used in the cannabis industry for which no action levels have been established are butane, propane… [They] are short-chain alkanes similar to pentane. Pentane falls into a class of solvents designated as class 3 by ICH Q3C. Class 3 solvents are less toxic and default to a health-based action level of 5,000 ppm for butane [and] propane.

Butane & Propane Testing by State

State	Status	Butane	Propane
Alaska	full	800	not tested
Arizona	full	5000	5000
Arkansas	medical	5000	5000
California	full	5000	5000
Colorado	full	1000	1000
Florida	medical	800	2100
Hawaii	medical	800	not tested
Illinois	full	10	10
Louisiana	medical	800	not tested
Maine	full	5000	5000
Maryland	full	5000	5000
Massachusetts	full	12	12
Michigan	full	800 (inhaled products); 5000 (non-inhaled)	2100 (inhaled products); 5000 (non-inhaled)
Minnesota	medical	800 (inhaled products); 5000 (non-inhaled)	2100 (inhaled products); 5000 (non-inhaled)
Mississippi	medical	5000	5000
Missouri	full	800 (inhaled products); 5000 (non-inhaled)	2100 (inhaled products); 5000 (non-inhaled)
Montana	full	5000	5000

State	Status	Butane	Propane
Nevada	full	500	500
New Hampshire	medical	500	500
New Jersey	full	5000	5000
New Mexico	full	800	800
New York	full	5000	5000
North Dakota	medical	5000	5000
Ohio	medical	5000	5000
Oklahoma	medical	1000	1000
Oregon	full	5000	5000
Pennsylvania	medical	5000	not tested
Rhode Island	full	5000	5000
South Dakota	medical	800	2100
Utah	medical	5000	5000
Vermont	full	5000	5000
Washington	full	5000	5000
Washington, DC	full	5000	5000
West Virginia	medical	5000	5000

Questions

Becky Hobden

Lab Director, Green Analytics Virginia

becky.hobden@greenanalyticsllc.com

Agenda Topic: Adopt guidance regarding cannabis advertising regulations as applied to packaging

Included in Packet:

- Draft Guidance Document 110-50

Action Needed:

- Motion to recommend to full board adoption of guidance document as presented or amended; OR
- Motion to recommend to full board that no action be taken.

Virginia Board of Pharmacy

Cannabis Product Packaging Requirements

In addition to packaging and labeling requirements found in 18VAC110-60-210, 18VAC110-60-290, 18VAC110-60-310 and pursuant to § 54.1-3442.6 and 18VAC110-60-285, the Board of Pharmacy interprets the term "advertising" (18VAC110-60-10) to include packaging in which cannabis products are marketed and dispensed. Therefore, cannabis product packages, including the brand name assigned to the cannabis product and appearing on the package label, should comply with the advertisement requirements of 18VAC110-60-215. Additional guidance is provided below to clarify acceptable packaging requirements.

Packaging should not:

- Promote over consumption or consumption for other than medical purposes;
- Include neon colors;
- Include psychedelic design; or,
- Include any color or design combinations that could be misconstrued to encourage the recreational use of cannabis.

Brand names assigned to cannabis products and included on the package label may include strain names, including those developed by pharmaceutical processors, that do not violate 18VAC110-20-215 or that are associated with movies, fictional characters, video games, illegal activities, or include derogatory, slang, or racial nomenclature. Descriptors such as flavors, colors, or minerals would be acceptable. Names comprised of a combination of letters or numbers would also be acceptable.

References:

Va. Code § 54.1-3442.6
18VAC110-60-10
18VAC110-60-210
18VAC110-60-215
18VAC110-60-285
18VAC110-60-290
18VAC110-60-310

Agenda Topic: Reconsider amendment of 18VAC110-20-555

Included in Packet:

- NOIRA and public comments received
- Proposed regulatory action adopted in March 2023
- 2016 DEA letter to ASCP
- Excerpt from 2022 DEA Pharmacist's Manual

Background:

Board counsel has advised that the proposed regulatory action appears to violate federal requirements and therefore, may be inconsistent with the requirement in 18VAC110-20-555 (13) which requires a pharmacy to comply with a written policy and procedure for complying with federal regulations related to the storage and dispensing of the controlled substances.

Action Needed:

- Motion to recommend to the full board that it withdraw the March 2023 adoption of the proposed regulatory amendment of 18VAC110-20-555.

United States Department of Justice

Drug Enforcement Administration
Diversion Control Division

www.DEAdiversion.usdoj.gov

Pharmacist's Manual

An Informational Outline of the Controlled Substances Act

Revised 2022[1]

1 This manual replaces all previous editions of the Pharmacist's Manual issued by the Drug Enforcement Administration, both hard copy and electronic. Previous Version EO-DEA154, DEA-DC-046.

registered sites at the retail pharmacy or other approved central location. 21 CFR 1304.04(a)(2) and (b)(1).

DEA registered pharmacies wishing to operate an ADS at an LTCF must contact the DEA Office of Diversion Control, Registration and Program Support Section, at 1-800-882-9539 for registration instructions. An affidavit which meets the requirement of 21 CFR 1301.17(c) must also be submitted with DEA. 21 CFR 1301.27(a).

Emergency Kits for Long-Term Care Facilities

DEA has issued a policy statement which provides individual state licensing and regulatory boards with general guidelines for establishing specific rules concerning controlled substances used in emergency kits at LTCFs. 45 FR 24128 (Apr. 9, 1980) (See Appendix H, *Guidelines for Emergency Kits in Long-Term Care Facilities*.)

All emergency kits (whether or not they are electronic) remain subject to the policy statement in Appendix H, provided they satisfy the criteria of that policy statement at all times. 45 FR 24128 (Apr. 9, 1980). Among other things, it is crucial to bear in mind that an emergency kit is for use in emergencies as defined by the state. It also bears emphasis that, in accordance with the CSA and DEA regulations, a controlled substance may only be dispensed for emergency purposes (or otherwise) pursuant to a valid prescription or medical order. 21 U.S.C. 841(a)(1), 21 CFR 1306.04(a), 21 CFR 1300.01(b) ("*prescriptions*"). Thus, where the kit is maintained at the LTCF by a pharmacy, controlled substances may not be dispensed from the kit for emergencies prior to receipt by the pharmacist of a valid prescription in accordance with the requirements of 21 CFR 1306.11, 1306.21. As these sections of the regulations indicate, such prescriptions may, depending on the circumstances, be issued in writing (paper or electronic in accordance with Part 1311), orally, or by fax. In addition, to be valid, a prescription for a controlled substance must be issued for a legitimate medical purpose by a practitioner acting in the usual course of his professional practice, and the pharmacist bears a corresponding responsibility therefor. 21 CFR 1306.04(a). If, at any time, a kit is used to administer or dispense controlled substances for a purpose other than in emergencies as defined by the state, the kit thereafter ceases to be an emergency kit and, as a result, the separate registration requirement applies.

Opioid (Narcotic) Addiction Treatment Programs

The Narcotic Addict Treatment Act of 1974, the Drug Addiction Treatment Act (DATA) of 2000, the Comprehensive Addiction and Recovery Act of 2016 (CARA) and the SUPPORT for Patients and Communities Act of 2018 amended the CSA with respect to the use of controlled substances in the medical treatment of opioid addiction. These laws established the procedures for approving and licensing practitioners involved in the treatment of opioid addiction as well as improving the quality and delivery of that treatment to the segment of society in need.

U. S. Department of Justice
Drug Enforcement Administration
8701 Morrissette Drive
Springfield, Virginia 22152

www.dea.gov

NOV 30 2016

Arnold E. Clayman, PD, FASCP
Vice President of Pharmacy Practice & Government Affairs
American Society of Consultant Pharmacists
1321 Duke Street
Alexandria, Virginia 22314-3563

Dear Mr. Clayman:

This responds to your letter dated June 9, 2016, to the Drug Enforcement Administration (DEA), which was submitted as a follow-up to a meeting between the DEA and the American Society of Consultant Pharmacists (ASCP) on May 25, 2016, regarding the use of electronic emergency kits in Long Term Care Facilities (LTCFs). In your letter, you ask whether electronic emergency kits at LTCFs require a separate registration. The DEA appreciates the opportunity to address your inquiry.

As your letter points out, DEA issued a policy statement in 1980 addressing the use of emergency kits in LTCFs. 70 FR 24128 (April 9, 1980). In that document, DEA took the position that an emergency kit containing controlled substances may be placed in a "non-federal registered" LTCF if certain conditions were met. As DEA has not issued any Federal Register document rescinding that policy statement, it remains effective.

Your letter also refers to the DEA regulations relating to an Automated Dispensing System (ADS). As set forth in 21 CFR § 1301.27, a retail pharmacy that installs and operates an ADS at an LTCF must maintain a separate registration at that location.

All emergency kits – whether or not they are electronic – remain subject to the 1980 policy statement (and thus need not be separately registered), *provided they satisfy the criteria of the 1980 policy statement at all times.* Among other things, it is crucial to bear in mind that an emergency kit is only an emergency kit if it is used *exclusively for emergencies*. It also bears emphasis that, in accordance with the CSA and DEA regulations, a controlled substance may only be dispensed for emergency purposes (or otherwise) pursuant to a valid prescription. Thus, where, as in the scenario described in your letter, the kit is maintained at the LTCF by a pharmacy, controlled substances may not be dispensed from the kit for emergencies prior to receipt by the pharmacist of a valid prescription in accordance with the requirements of in 21 CFR §§ 1306.11 and 1306.21. As these sections of the regulations indicate, such prescription may, depending on the circumstances, be issued in writing (paper or electronic in accordance with part 1311), orally, or by fax. In addition, as you know, to be valid, a prescription for a controlled substance must be issued for a legitimate medical purpose by a practitioner acting in the usual course of his professional practice, and the pharmacist bears a corresponding responsibility therefor. 21 CFR § 1306.04(a).

If, at any time, a kit is used to administer or dispense controlled substances for a purpose other than an emergency, the kit thereafter ceases to be an emergency kit and, as a result, the separate registration requirement applies.

We trust this letter adequately addresses your inquiry. For information regarding the DEA Diversion Control Division, please visit www.DEAdiversion.usdoj.gov. If you have any additional questions on this issue, please contact the Diversion Control Division Liaison and Policy Section at (202) 307-7297.

Sincerely,

Louis J. Milione
Assistant Administrator
Diversion Control Division

townhall.virginia.gov

Notice of Intended Regulatory Action (NOIRA) Agency Background Document

Agency name	Board of Pharmacy, Department of Health Professions
Virginia Administrative Code (VAC) Chapter citation(s)	18VAC110-20
VAC Chapter title(s)	Regulations Governing the Practice of Pharmacy
Action title	Exemption of automated dispensing devices stocked solely with emergency or stat use medications from certain requirements of 18VAC110-20-555
Date this document prepared	June 6, 2022

This information is required for executive branch review and the Virginia Registrar of Regulations, pursuant to the Virginia Administrative Process Act (APA), Executive Order 14 (as amended, July 16, 2018), the Regulations for Filing and Publishing Agency Regulations (1VAC7-10), and the *Form and Style Requirements for the Virginia Register of Regulations and Virginia Administrative Code*.

Brief Summary

Provide a brief summary (preferably no more than 2 or 3 paragraphs) of the subject matter, intent, and goals of this this regulatory change (i.e., new regulation, amendments to an existing regulation, or repeal of an existing regulation.

In response to a petition for rulemaking, the Board is issuing a Notice of Intended Regulatory Action to consider an amendment to section 555 to exempt an automated dispensing device ("ADD") from the requirements of 18VAC110-20-555 when that ADD is exclusively stocked with certain drugs that may be kept in a stat-drug box pursuant to 18VAC110-20-550 or an emergency drug kit pursuant to 18VAC110-20-540 and are solely administered for stat or emergency use.

Acronyms and Definitions

Define all acronyms or technical definitions used in this form.

ADD = automated dispensing device

Mandate and Impetus

Identify the mandate for this regulatory change and any other impetus that specifically prompted its initiation (e.g., new or modified mandate, petition for rulemaking, periodic review, or board decision). For purposes of executive branch review, "mandate" has the same meaning as defined in Executive Order 14 (as amended, July 16, 2018), "a directive from the General Assembly, the federal government, or a court that requires that a regulation be promulgated, amended, or repealed in whole or part."

The impetus for change is a petition for rulemaking requesting an amendment to regulations for ADDs stocked solely with stat or emergency use drugs. As presented by the petitioner, it would be more secure for such drugs to be stored in an ADD than a "tackle-box" style mechanism which is currently used.

Legal Basis

Identify (1) the promulgating agency, and (2) the state and/or federal legal authority for the regulatory change, including the most relevant citations to the Code of Virginia and Acts of Assembly chapter number(s), if applicable. Your citation must include a specific provision, if any, authorizing the promulgating agency to regulate this specific subject or program, as well as a reference to the agency's overall regulatory authority.

Regulations of the Board of Pharmacy are promulgated under the general authority of Chapter 24 of Title 54.1 of the Code of Virginia. Virginia Code § 54.1-2400(6) specifically states that the general powers and duties of health regulatory boards shall be "[t]o promulgate regulations in accordance with the Administrative Process Act (§ 2.2-4000 et seq.) that are reasonable and necessary to administer effectively the regulatory system."

Purpose

Describe the specific reasons why the agency has determined that this regulation is essential to protect the health, safety, or welfare of citizens. In addition, explain any potential issues that may need to be addressed as the regulation is developed.

The Board determined that the petitioner correctly identified a potential hazard in storage of stat or emergency use only medications under 18VAC110-20-540 or 18VAC110-20-550. Stat or emergency use drugs stored in an ADD would contain an electronic record of access to those drugs, while the current tackle-box style storage systems do not. For some facilities, such as nursing homes, ADDs are not used because the only drugs stored on the premises are stat or emergency use medication. Patient and drug security may be increased through utilization of ADDs when exempted from certain requirements that would unacceptably delay the administration of life-saving drugs for patients.

Substance

Briefly identify and explain the new substantive provisions that are being considered, the substantive changes to existing sections that are being considered, or both.

An amendment to 18VAC110-20-555 would exempt ADDs exclusively stocked with drugs that would be kept in an emergency drug kit pursuant to 18VAC110-20-540 or a stat-drug box pursuant to 18VAC110-20-550 and are solely administered for stat or emergency use from the requirements of 18VAC110-20-555(1), (4)(a), and (4)(b).

Alternatives to Regulation

Describe any viable alternatives to the regulatory change that were considered, and the rationale used by the agency to select the least burdensome or intrusive alternative that meets the essential purpose of the regulatory change. Also, include discussion of less intrusive or less costly alternatives for small businesses, as defined in § 2.2-4007.1 of the Code of Virginia, of achieving the purpose of the regulatory change.

The Board of Pharmacy regulates both the use of ADDs and the use of emergency or stat drugs. There is no alternative to regulation to create this exemption.

Periodic Review and Small Business Impact Review Announcement

This NOIRA is not being used to announce a periodic review or a small business impact review.

Public Participation

Indicate how the public should contact the agency to submit comments on this regulation, and whether a public hearing will be held, by completing the text below. In addition, as required by § 2.2-4007.02 of the Code of Virginia describe any other means that will be used to identify and notify interested parties and seek their input, such as regulatory advisory panels or general notices.

The Board of Pharmacy is providing an opportunity for comments on this regulatory proposal, including but not limited to (i) the costs and benefits of the regulatory proposal, (ii) any alternative approaches, and (iii) the potential impacts of the regulation.

Anyone wishing to submit written comments for the public comment file may do so through the Public Comment Forums feature of the Virginia Regulatory Town Hall web site at: https://townhall.virginia.gov. Comments may also be submitted by mail, email or fax to Erin Barrett, 9960 Mayland Drive, Suite 300, Henrico, Virginia 23233, erin.barrett@dhp.virginia.gov, or by fax at (804) 915-0382. In order to be considered, comments must be received by 11:59 pm on the last day of the public comment period.

A public hearing will not be held following the publication of the proposed stage of this regulatory action.

Commenter: Ben Traynham, Hancock, Daniel & Johnson, P.C.

Comments by PharmScript, LLC

Dear Mr. St. Clair:

Please accept this letter on behalf of PharmScript, LLC as comments on the proposed rulemaking to exempt automated dispensing devices stocked solely with emergency or stat-use medications from certain requirements of 18VAC110-20-555. PharmScript supports the rulemaking because it will eliminate a hurdle to speedy patient care and ultimately lower risk of patient harm.

PharmScript is one of several long-term care pharmacy services companies who provide remote pharmacy services such as distributing and dispensing emergency and stat-use pre-packaged drugs via automated dispensing devices (ADDs) to nursing homes in Virginia.

18VAC110-20-555 presents an issue that is unique to our operation in Virginia, and that is the required extra-step pharmacist authorization (PV1 order verification) of stat-drugs being dispensed from an ADD. Requiring the pharmacist to review and electronically authorize each stat-drug *prior* to administration is a time-consuming and unnecessary task during a critical period in patient care when the patient needs medication.

PharmScript operates in twenty-three states and the District of Columbia, and Virginia is the only jurisdiction that requires this authorization prior to administration. Other states, including neighbors DC, Maryland, Tennessee, and North Carolina, allow for the pharmacist verification of stat drugs (also referred to as "starter drugs" or "emergency drugs") after administration, usually within 24 hours.

Stat-drugs, synonymous and used as a term interchangeable with emergency drugs, are drugs that should be administered immediately to avoid or reduce patient harm. Stat-drug boxes contain pre-packaged drugs that are ready for administration. The risk of improper administration by the caregiver accessing the ADD is extremely low to nonexistent as there are many safeguards, including electronic controlled access, already built into the ADD system.

In short, the net effect of this requirement is delayed patient care. Delayed care increases the risk of harm to the patient. The increased risk of harm due to delayed care significantly outweighs any potential risk associated with eliminating the PV1 authorization prior to removing stat drugs from an ADD.

Accordingly, PharmScript strongly supports the proposed rulemaking as it would provide patients faster access to the medication they need while reducing potential risk of harm. Please feel free to contact me if you or any Board member wishes to discuss the operational effect of this regulation further.

Sincerely,

John Camperlengo
Chief Legal Officer, PharmScript LLC
CommentID: 206471

12/7/22 1:42 pm

Commenter: Brad McDaniel, Virginia Society of Health-system Pharmacists

Emergent Medication Access vis ADCs

VSHP supports the access to medications that are required in emergent circumstances and waiting for a pharmacist to review the order could adversely impact the patient's condition. The Institute for Safe Medication Practice's "Guidelines for the Safe Use of Automated Dispensing Cabinets" includes that such circumstances would include antidotes, rescue agents, and reversal agents, life-sustaining medications, and urgent comfort medications such as managing acute pain or intractable nausea and vomiting.

Condition 1. VSHP requests that the Board consider the following exemptions to support timely access to medications outside of pharmacy service hours, when access to medications from a STAT box is needed:

- Outside of pharmacy service hours

- Nurse removes the medication under a patient profile (meaning that the ADC is configured as a "profiled" machine) – this is called an "override" function in the ADC

- Medications provided for this indication are for emergent use (such as criteria outlined in ISMP's guidelines)

- Overrides are assessed periodically by the pharmacy provider for appropriate use of emergent medications

We believe these exemptions will support after-hours emergent access to medications and still allow for pharmacist review and verification of orders during pharmacy service hours.

Conditions 4(a) and 4(b) are appropriate exemptions to accomplish this objective.

Brad McDaniel, PharmD, MBA, BCCCP

Chair, Legislative Affairs Committee

Virginia Society of Health-systems Pharmacists

Project 7251 - Proposed

Board of Pharmacy

Exemption of automated dispensing devices stocked solely with emergency or stat-use medications from certain requirements of 18VAC110-20-555

Chapter 20

Regulations Governing the Practice of Pharmacy

18VAC110-20-555. Use of automated dispensing devices.

Nursing homes licensed pursuant to Chapter 5 (§ 32.1-123 et seq.) of Title 32.1 of the Code of Virginia may use automated drug dispensing systems, as defined in § 54.1-3401 of the Code of Virginia, upon meeting the following conditions:

1. Drugs placed in an automated drug dispensing system in a nursing home shall be under the control of the pharmacy providing services to the nursing home, the pharmacy shall have online communication with and control of the automated drug dispensing system, and access to any drug for a patient shall be controlled by the pharmacy.

2. A nursing home without an in-house pharmacy shall obtain a controlled substances registration prior to using an automated dispensing system, unless the system is exclusively stocked with drugs that would be kept in a stat-drug box pursuant to 18VAC110-20-550 or an emergency drug kit pursuant to 18VAC110-20-540 and are solely administered for stat or emergency administration.

3. For facilities not required to obtain a controlled substance registration, access to the automated dispensing device shall be restricted to a licensed nurse, pharmacist, or prescriber, or a registered pharmacy technician for the purpose of stocking or reloading.

4. Removal of drugs from any automated drug dispensing system for administration to patients can only be made pursuant to a valid prescription or lawful order of a prescriber under the following conditions:

a. ~~A drug, including a drug that would be stocked in a stat-drug box pursuant to subsection B of 18VAC110-20-550,~~ Except for automated dispensing devices exclusively stocked with drugs that would be stored in an emergency drug kit or stat-drug box for emergency or stat administration, a drug may not be administered to a patient from an automated dispensing device until a pharmacist has reviewed the prescription order and electronically authorized the access of that drug for that particular patient in accordance with the order.

b. The PIC of the provider pharmacy shall ensure that a pharmacist who has online access to the system is available at all times to review a prescription order as needed and authorize administering pursuant to the order reviewed.

c. Drugs that would be stocked in an emergency drug kit pursuant to 18VAC110-20-540 may be accessed prior to receiving electronic authorization from the pharmacist provided that the absence of the drugs would threaten the survival of the patients.

d. Automated dispensing devices shall be capable of producing a hard-copy record of distribution that shall show patient name, drug name and strength, dose withdrawn, dose to be administered, date and time of withdrawal from the device, and identity of person withdrawing the drug.

5. Drugs placed in automated dispensing devices shall be in the manufacturer's sealed original unit dose or unit-of-use packaging or in repackaged unit-dose containers in compliance with the requirements of 18VAC110-20-355 relating to repackaging, labeling, and records.

6. Prior to the removal of drugs from the pharmacy, a delivery record shall be generated for all drugs to be placed in an automated dispensing device, which shall include the date; drug name, dosage form, and strength; quantity; nursing home; a unique identifier for the specific device receiving drugs; and initials of the pharmacist checking the order of drugs to be removed from the pharmacy and the records of distribution for accuracy.

7. At the direction of the PIC, drugs may be loaded in the device by a pharmacist or a pharmacy technician adequately trained in the proper loading of the system.

8. At the time of loading, the delivery record for all Schedules II through VI drugs shall be signed by a nurse or other person authorized to administer drugs from that specific device, and the record returned to the pharmacy.

9. At the time of loading any Schedules II through V drug, the person loading will verify that the count of that drug in the automated dispensing device is correct. Any discrepancy noted shall be recorded on the delivery record and immediately reported to the PIC, who shall be responsible for reconciliation of the discrepancy or the proper reporting of a loss.

10. The PIC of the provider pharmacy or his designee shall conduct at least a monthly audit to review distribution and administration of Schedules II through V drugs from each automated dispensing device as follows:

a. The audit shall reconcile records of all quantities of Schedules II through V drugs dispensed from the pharmacy with records of all quantities loaded into each device to detect whether any drugs recorded as removed from the pharmacy were diverted rather than being placed in the proper device.

b. A discrepancy report shall be generated for each discrepancy in the count of a drug on hand in the device. Each such report shall be resolved by the PIC or his

designee within 72 hours of the time the discrepancy was discovered or, if determined to be a theft or an unusual loss of drugs, shall be immediately reported to the board in accordance with § 54.1-3404 E of the Drug Control Act.

c. The audit shall include a review of a sample of administration records from each device per month for possible diversion by fraudulent charting. A sample shall include all Schedules II through V drugs administered for a time period of not less than 24 consecutive hours during the audit period.

d. The audit shall include a check of medical records to ensure that a valid order exists for a random sample of doses recorded as administered.

e. The audit shall also check for compliance with written procedures for security and use of the automated dispensing devices, accuracy of distribution from the device, and proper recordkeeping.

f. The hard copy distribution and administration records printed out and reviewed in the audit shall be initialed and dated by the person conducting the audit. If nonpharmacist personnel conduct the audit, a pharmacist shall review the record and shall initial and date the record.

11. Automated dispensing devices shall be inspected monthly by pharmacy personnel to verify proper storage, proper location of drugs within the device, expiration dates, the security of drugs and validity of access codes.

12. Personnel allowed access to an automated dispensing device shall have a specific access code which records the identity of the person accessing the device.

13. The PIC of the pharmacy providing services to the nursing home shall establish, maintain, and assure compliance with written policy and procedure for the accurate stocking and proper storage of drugs in the automated drug dispensing system,

accountability for and security of all drugs maintained in the automated drug dispensing system, preventing unauthorized access to the system, tracking access to the system, complying with federal and state regulations related to the storage and dispensing of controlled substances, maintaining patient confidentiality, maintaining required records, and assuring compliance with the requirements of this chapter. The manual shall be capable of being accessed at both the pharmacy and the nursing home.

14. All records required by this section shall be filed in chronological order from date of issue and maintained for a period of not less than two years. Records shall be maintained at the address of the pharmacy providing services to the nursing home except:

a. Manual Schedule VI distribution records may be maintained in offsite storage or electronically as an electronic image that provides an exact image of the document that is clearly legible provided such offsite or electronic storage is retrievable and made available for inspection or audit within 48 hours of a request by the board or an authorized agent.

b. Distribution and delivery records and required signatures may be generated or maintained electronically provided:

(1) The system being used has the capability of recording an electronic signature that is a unique identifier and restricted to the individual required to initial or sign the record.

(2) The records are maintained in a read-only format that cannot be altered after the information is recorded.

(3) The system used is capable of producing a hard-copy printout of the records upon request.

c. Schedules II through V distribution and delivery records may only be stored offsite or electronically as described in subdivisions 14 a and 14 b of this section if authorized by DEA or in federal law or regulation.

d. Hard-copy distribution and administration records that are printed and reviewed in conducting required audits may be maintained offsite or electronically provided they can be readily retrieved upon request; provided they are maintained in a read-only format that does not allow alteration of the records; and provided a separate log is maintained for a period of two years showing dates of audit and review, the identity of the automated dispensing device being audited, the time period covered by the audit and review, and the initials of all reviewers.

Agenda Topic: Discuss number and location of pharmacy permits in recent years

Included in Agenda Packet:

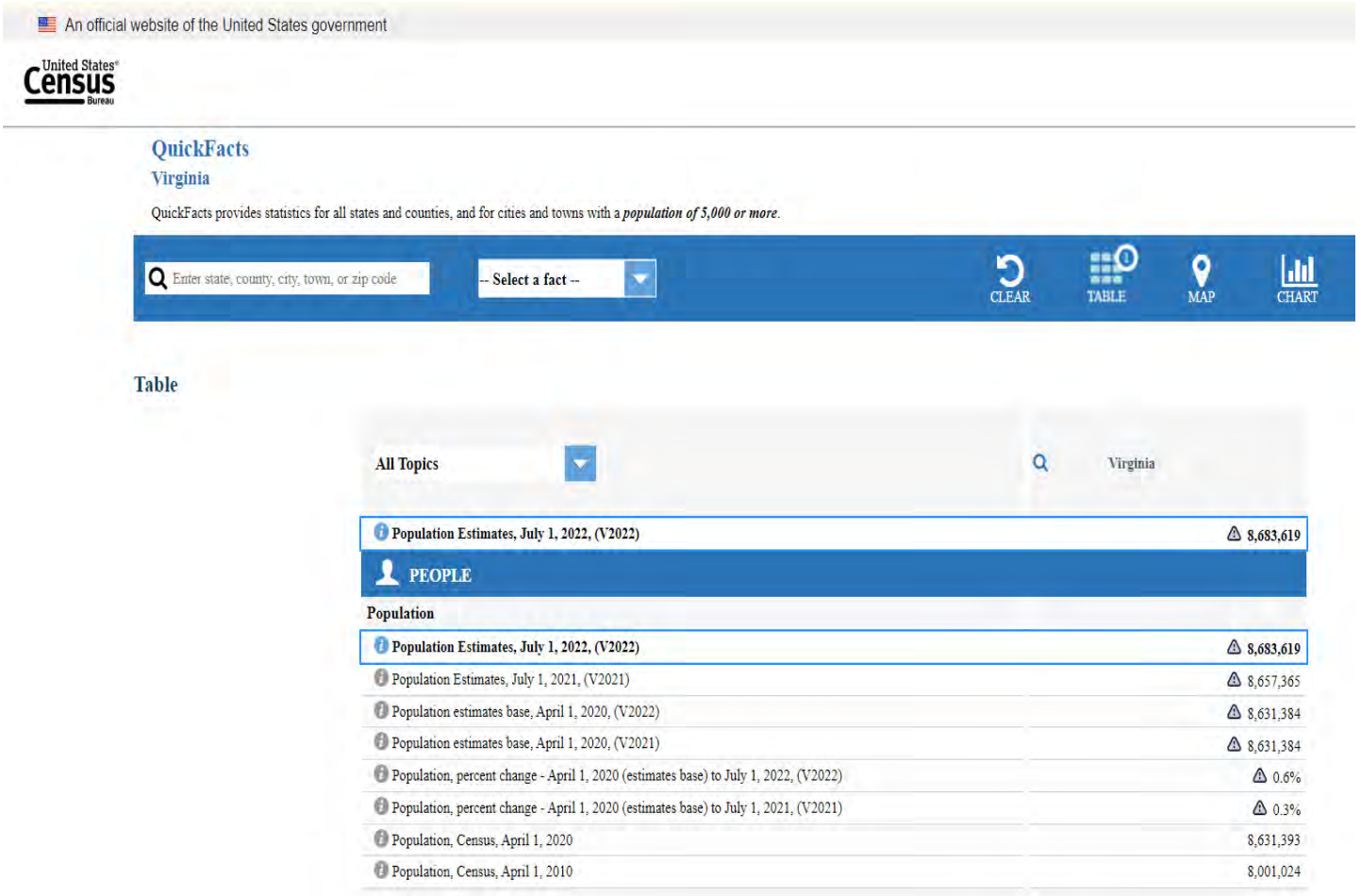
- Excerpt from 2022 DHP Biennial Report regarding number of current active pharmacy permits between 2012 and 2022
- U.S. Census Data, population in Virginia in 2010 and 2022
- Geo-mapping of current active pharmacy permits (to be provided as a handout)

Action Needed:

- Discussion.

Appendix A – Licenses

Board	Occupation	2012 30-Jun	2014 30-Jun	2016 30-Jun	2018 30-Jun	2020 30-Jun	2022 30-Jun	Percent Change 20-22
Pharmacy	Pharmacy	1,754	1,796	1,854	1,822	1,771	1,768	-0.17%
	Pharmacy Intern	1,797	2,092	2,058	1,865	1,649	1,312	-20.44%
	Pharmacy Technician	12,413	13,610	13,719	13,773	13,162	12,924	-1.81%
	Pharmacy Technician Training Program	86	103	120	143	130	126	-3.08%
	Pharmacy Technician Trainee						6,258	-
	Physician Selling Controlled Substances	500	664	666	708	626	571	-8.79%
	Physician Selling Drugs Location	-	255	222	157	174	160	-8.05%
	Pilot Programs	-	6	18	10	22	25	13.64%
	Registered Agent for Medical Cannabis					7	179	2457.14%
	Registered Practitioner For CBD/THCA Oil						873	-
	Registered Par/Guard For Medical Cannab					51	262	413.73%
	Registered Patient For Medical Cannabis					3,978	52,903	1229.89%
	Registered Product						1,566	-
	Registered Physician for CBD/THC Oil	-	-	-	-	401	-	-
	Repackaging Training Program	-	1	-	2	2	2	0.00%
	Restricted Manufacturer	77	75	69	55	44	36	-18.18%
	Third Party Logistics Provider †	-	-	-	5	6	7	16.67%
	Warehouser	46	42	47	86	112	121	8.04%
	Wholesale Distributor	112	122	120	79	65	62	-4.62%
Pharmacy Total		**30,666**	**34,398**	**35,972**	**36,968**	**41,676**	**99,376**	**138.45%**


An official website of the United States government
United States Census Bureau
QuickFacts
Virginia
QuickFacts provides statistics for all states and counties, and for cities and towns with a population of 5,000 or more.
Enter state, county, city, town, or zip code
-- Select a fact --
CLEAR
TABLE
MAP
CHART
Table
All Topics
Virginia
Population Estimates, July 1, 2022, (V2022) 8,683,619
PEOPLE
Population
Population Estimates, July 1, 2022, (V2022) 8,683,619
Population Estimates, July 1, 2021, (V2021) 8,657,365
Population estimates base, April 1, 2020, (V2022) 8,631,384
Population estimates base, April 1, 2020, (V2021) 8,631,384
Population, percent change - April 1, 2020 (estimates base) to July 1, 2022, (V2022) 0.6%
Population, percent change - April 1, 2020 (estimates base) to July 1, 2021, (V2021) 0.3%
Population, Census, April 1, 2020 8,631,393
Population, Census, April 1, 2010 8,001,024

Agenda Topic: 2024 Legislative proposals

- Authorization of pharmacy technicians to clarify refills and quantity of certain prescriptions
- Clarifying compounding of essentially copies of commercially available drug product
- Requiring federal criminal background check for resident and nonresident wholesale distributors and third-party logistics providers

Staff Note:

Legislative proposals for 2024 must be adopted by the Board in June for consideration by the DHP Director, Secretary of HHR, and Governor for possible inclusion in the Governor's packet of legislation introduced during the 2024 General Assembly Session.

Included in packet:

- Draft proposal regarding pharmacy technicians resulting from 2021 work group
- Draft proposal regarding compounding
- FDA guidance on compounding
- Regulation 18VAC110-50-80 requiring federal background report

Action Needed:

- Recommend the full board adopt the legislative proposals as presented or amended; OR
- Recommend the full board take no action.

Department of Health Professions

Authorization of pharmacy technicians to clarify refills and quantity of certain prescriptions

A BILL to amend the *Code of Virginia* by amending §§ 54.1-3320 and 54.1-3321 of the Code of Virginia relating to permissible acts of pharmacy technicians.

Be it enacted by the General Assembly of Virginia:

1. **That § 54.1-3320 and 54.1-3321 of the *Code of Virginia* are amended and reenacted as follows:**

§ 54.1-3320. Acts restricted to pharmacists.

A. Within the practice of pharmacy as defined in § 54.1-3300, the following acts shall be performed by pharmacists, except as provided in subsection B:

1. The review of a prescription, in conformance with this chapter and Chapter 34 (§ 54.1-3400 et seq.) of this title and with current practices in pharmacy, for its completeness, validity, safety, and drug-therapy appropriateness, including, but not limited to, interactions, contraindications, adverse effects, incorrect dosage or duration of treatment, clinical misuse or abuse, and noncompliance and duplication of therapy;

2. The receipt of an oral prescription from a practitioner or his authorized agent;

3. The conduct of a prospective drug review and counseling as required by § 54.1-3319 prior to the dispensing or refilling of any prescription;

4. The provision of information to the public or to a practitioner concerning the therapeutic value and use of drugs in the treatment and prevention of disease;

5. The communication with the prescriber, or the prescriber's agent, involving any modification other than refill authorization of a prescription or of any drug therapy in Schedules III-VI or clarification of quantity or refill of a prescription issued for a Schedule VI drug, resolution of any drug therapy problem, or the substitution of any drug prescribed;

6. The verification of the accuracy of a completed prescription prior to dispensing the prescription;

7. The supervision of pharmacy interns and pharmacy technicians; and

8. Any other activity required by regulation to be performed by a pharmacist.

B. A pharmacy intern may engage in the acts to be performed by a pharmacist as set forth in subsection A or the Drug Control Act (§ 54.1-3400 et seq.) for the purpose of obtaining practical

experience required for licensure as a pharmacist, if the supervising pharmacist is directly monitoring these activities.

C. A registered pharmacy technician, working under the direct supervision of a qualified nuclear pharmacist, as defined by regulations of the Board, may accept oral prescriptions for diagnostic, nonpatient specific radiopharmaceuticals in accordance with subsection C of § 54.1-3410.1.

D. Consistent with patient safety, a pharmacist shall exercise sole authority in determining the maximum number of pharmacy technicians that he shall supervise; however, no pharmacist shall supervise more pharmacy technicians than allowed by Board regulations.

§ 54.1-3321. Registration of pharmacy technicians.

A. No person shall perform the duties of a pharmacy technician without first being registered as a pharmacy technician with the Board. Upon being registered with the Board as a pharmacy technician, the following tasks may be performed:

1. The entry of prescription information and drug history into a data system or other record keeping system;

2. The preparation of prescription labels or patient information;

3. The removal of the drug to be dispensed from inventory;

4. The counting, measuring, or compounding of the drug to be dispensed;

5. The packaging and labeling of the drug to be dispensed and the repackaging thereof;

6. The stocking or loading of automated dispensing devices or other devices used in the dispensing process;

7. The acceptance of refill authorization of a prescription for a Schedule III-VI drug, or clarification of quantity and refills for a prescription issued for a Schedule VI drug from a prescriber or his authorized ~~agency~~ agent, so long as there is no other change to the original prescription;

8. Under the supervision of a pharmacist, meaning the supervising pharmacist is at the same physical location of the technician or pharmacy intern, and consistent with the requirements of § 54.1-3303.1, administration of the following drugs and devices to persons three years of age or older as set forth in regulations of the Board: vaccines included on the Immunization Schedule published by the Centers for Disease Control and Prevention and vaccines for COVID-19; and

9. The performance of any other task restricted to pharmacy technicians by the Board's regulations.

B. To be registered as a pharmacy technician, a person shall submit:

1. An application and fee specified in regulations of the Board;

2. Evidence that he has successfully completed a training program that is (i) an accredited training program, including an accredited training program operated through the Department of Education's Career and Technical Education program or approved by the Board, or (ii) operated through a federal agency or branch of the military; and

3. Evidence that he has successfully passed a national certification examination administered by the Pharmacy Technician Certification Board or the National Healthcareer Association.

C. The Board shall promulgate regulations establishing requirements for:

1. Issuance of a registration as a pharmacy technician to a person who, prior to the effective date of such regulations, (i) successfully completed or was enrolled in a Board-approved pharmacy technician training program or (ii) passed a national certification examination required by the Board but did not complete a Board-approved pharmacy technician training program;

2. Issuance of a registration as a pharmacy technician to a person who (i) has previously practiced as a pharmacy technician in another U.S. jurisdiction and (ii) has passed a national certification examination required by the Board; and

3. Evidence of continued competency as a condition of renewal of a registration as a pharmacy technician.

D. The Board shall waive the initial registration fee for a pharmacy technician applicant who works as a pharmacy technician exclusively in a free clinic pharmacy. A person registered pursuant to this subsection shall be issued a limited-use registration. A pharmacy technician with a limited-use registration shall not perform pharmacy technician tasks in any setting other than a free clinic pharmacy. The Board shall also waive renewal fees for such limited-use registrations. A pharmacy technician with a limited-use registration may convert to an unlimited registration by paying the current renewal fee.

E. Any person registered as a pharmacy technician prior to the effective date of regulations implementing the provisions of this section shall not be required to comply with the requirements of subsection B in order to maintain or renew registration as a pharmacy technician.

F. A pharmacy technician trainee enrolled in a training program for pharmacy technicians described in subdivision B 2 may engage in the acts set forth in subsection A for the purpose of obtaining practical experience required for completion of the training program, so long as such activities are directly monitored by a supervising pharmacist.

G. To be registered as a pharmacy technician trainee, a person shall submit an application and a fee specified in regulations of the Board. Such registration shall only be valid while the person is enrolled in a pharmacy technician training program described in subsection B and actively progressing toward completion of such program. A registration card issued pursuant to this section shall be invalid and shall be returned to the Board if such person fails to enroll in a pharmacy technician training program described in subsection B.

H. A pharmacy intern may perform the duties set forth for pharmacy technicians in subsection A when registered with the Board for the purpose of gaining the practical experience required to apply for licensure as a pharmacist.

I. A registered nurse or licensed practical nurse practicing at an opioid treatment program pharmacy may perform the duties set forth for pharmacy technicians in subsection A, provided that all take-home medication doses are verified for accuracy by a pharmacist prior to dispensing.

Board of Pharmacy

2024 Session of the General Assembly

A BILL to amend the *Code of Virginia* by amending § 54.1-3410.2, relating to the compounding of commercially available products.

Be it enacted by the General Assembly of Virginia:

1. That § 54.1-3410.2 of the *Code of Virginia* is amended and reenacted as follows:

§ 54.1-3410.2. Compounding; pharmacists' authority to compound under certain conditions; labeling and record maintenance requirements.

A. A pharmacist may engage in compounding of drug products when the dispensing of such compounded products is (i) pursuant to valid prescriptions for specific patients and (ii) consistent with the provisions of § 54.1-3303 relating to the issuance of prescriptions and the dispensing of drugs.

Pharmacists shall label all compounded drug products that are dispensed pursuant to a prescription in accordance with this chapter and the Board's regulations, and shall include on the labeling an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding.

B. A pharmacist may also engage in compounding of drug products in anticipation of receipt of prescriptions based on a routine, regularly observed prescribing pattern.

Pharmacists shall label all products compounded prior to dispensing with (i) the name and strength of the compounded medication or a list of the active ingredients and strengths; (ii) the pharmacy's assigned control number that corresponds with the compounding record; (iii) an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding; and (iv) the quantity.

C. In accordance with the conditions set forth in subsections A and B, pharmacists shall not distribute compounded drug products for subsequent distribution or sale to other persons or to commercial entities, including distribution to pharmacies or other entities under common ownership or control with the facility in which such compounding takes place; however, a pharmacist may distribute to a veterinarian in accordance with federal law.

Compounded products for companion animals, as defined in regulations promulgated by the Board of Veterinary Medicine, and distributed by a pharmacy to a veterinarian for further distribution or sale to his own patients shall be limited to drugs necessary to treat an emergent condition when timely access to a compounding pharmacy is not available as determined by the prescribing veterinarian.

A pharmacist may, however, deliver compounded products dispensed pursuant to valid prescriptions to alternate delivery locations pursuant to § 54.1-3420.2.

A pharmacist may provide a reasonable amount of compounded products to practitioners of medicine, osteopathy, podiatry, or dentistry to administer to their patients, either personally or under their direct and immediate supervision, if there is a critical need to treat an emergency condition, or as allowed by federal law or regulations. A pharmacist may also provide compounded products to practitioners of veterinary medicine for office-based administration to their patients.

Pharmacists who provide compounded products for office-based administration for treatment of an emergency condition or as allowed by federal law or regulations shall label all compounded products distributed to practitioners other than veterinarians for administration to their patients with (i) the statement "For Administering in Prescriber Practice Location Only"; (ii) the name and strength of the compounded medication or list of the active ingredients and strengths; (iii) the facility's control number; (iv) an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding; (v) the name and address of the pharmacy; and (vi) the quantity.

Pharmacists shall label all compounded products for companion animals, as defined in regulations promulgated by the Board of Veterinary Medicine, and distributed to a veterinarian for either further distribution or sale to his own patient or administration to his own patient with (a) the name and strength of the compounded medication or list of the active ingredients and strengths; (b) the facility's control number; (c) an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding; (d) the name and address of the pharmacy; and (e) the quantity.

D. Pharmacists shall personally perform or personally supervise the compounding process, which shall include a final check for accuracy and conformity to the formula of the product being prepared, correct ingredients and calculations, accurate and precise measurements, appropriate conditions and procedures, and appearance of the final product.

E. Pharmacists shall ensure compliance with USP-NF standards for both sterile and non-sterile compounding.

F. Pharmacists may use bulk drug substances in compounding when such bulk drug substances:

1. Comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if such monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding; or are drug substances that are components of drugs approved by the FDA for use in the United States; or are otherwise approved by the FDA; or are manufactured by an establishment that is registered by the FDA; and

2. Are distributed by a licensed wholesale distributor or registered nonresident wholesale distributor, or are distributed by a supplier otherwise approved by the Board and the FDA to distribute bulk drug substances if the pharmacist can establish purity and safety by reasonable means, such as lot analysis, manufacturer reputation, or reliability of the source.

G. Pharmacists may compound using ingredients that are not considered drug products in accordance with the USP-NF standards and guidance on pharmacy compounding.

H. Pharmacists shall not engage in the following:

1. The compounding for human use of a drug product that has been withdrawn or removed from the market by the FDA because such drug product or a component of such drug product has been found to be unsafe. However, this prohibition shall be limited to the scope of the FDA withdrawal;

2. The regular compounding or the compounding of inordinate amounts of any drug products that are essentially copies of commercially available drug products. However, this prohibition shall not include (i) the compounding of any commercially available product when there is a change in the product ordered by the prescriber for an individual patient which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product and such determination is documented on the prescription (ii) the compounding of a commercially manufactured drug only during times when the product is not available from the manufacturer or supplier, (iii) the compounding of a commercially manufactured drug whose manufacturer has notified the FDA that the drug is unavailable due to a current drug shortage, or (iv) the compounding of a commercially manufactured drug when the prescriber has indicated in the oral or written prescription for an individual patient that there is an emergent need for a drug that is not readily available within the time medically necessary, ~~or (v) the mixing of two or more commercially available products regardless of whether the end product is a commercially available product;~~ or

3. The compounding of inordinate amounts of any preparation in cases in which there is no observed historical pattern of prescriptions and dispensing to support an expectation of receiving a valid prescription for the preparation. The compounding of an inordinate amount of a preparation in such cases shall constitute manufacturing of drugs.

I. Pharmacists shall maintain records of all compounded drug products as part of the prescription, formula record, formula book, or other log or record. Records may be maintained electronically, manually, in a combination of both, or by any other readily retrievable method.

1. In addition to other requirements for prescription records, records for products compounded pursuant to a prescription order for a single patient where only manufacturers' finished products are used as components shall include the name and quantity of all components, the date of compounding and dispensing, the prescription number or other identifier of the prescription order, the total quantity of finished product, the signature or initials of the pharmacist or pharmacy technician performing the compounding, and the signature or initials of the pharmacist responsible for supervising the pharmacy technician and verifying the accuracy and integrity of compounded products.

2. In addition to the requirements of subdivision I 1, records for products compounded in bulk or batch in advance of dispensing or when bulk drug substances are used shall include: the generic name and the name of the manufacturer of each component or the brand name of each component; the manufacturer's lot number and expiration date for each component or when the original

manufacturer's lot number and expiration date are unknown, the source of acquisition of the component; the assigned lot number if subdivided, the unit or package size and the number of units or packages prepared; and the beyond-use date. The criteria for establishing the beyond-use date shall be available for inspection by the Board.

3. A complete compounding formula listing all procedures, necessary equipment, necessary environmental considerations, and other factors in detail shall be maintained where such instructions are necessary to replicate a compounded product or where the compounding is difficult or complex and must be done by a certain process in order to ensure the integrity of the finished product.

4. A formal written quality assurance plan shall be maintained that describes specific monitoring and evaluation of compounding activities in accordance with USP-NF standards. Records shall be maintained showing compliance with monitoring and evaluation requirements of the plan to include training and initial and periodic competence assessment of personnel involved in compounding, monitoring of environmental controls and equipment calibration, and any end-product testing, if applicable.

J. Practitioners who may lawfully compound drugs for administering or dispensing to their own patients pursuant to §§ 54.1-3301, 54.1-3304, and 54.1-3304.1 shall comply with all provisions of this section and the relevant Board regulations.

K. Every pharmacist-in-charge or owner of a permitted pharmacy or a registered nonresident pharmacy engaging in sterile compounding shall notify the Board of its intention to dispense or otherwise deliver a sterile compounded drug product into the Commonwealth. Upon renewal of its permit or registration, a pharmacy or nonresident pharmacy shall notify the Board of its intention to continue dispensing or otherwise delivering sterile compounded drug products into the Commonwealth. Failure to provide notification to the Board shall constitute a violation of Chapter 33 (§ 54.1-3300 et seq.) or Chapter 34 (§ 54.1-3400 et seq.). The Board shall maintain this information in a manner that will allow the production of a list identifying all such sterile compounding pharmacies.

Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance/OUDLC

January 2018
Compounding

Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance/OUDLC

January 2018
Compounding

TABLE OF CONTENTS

Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act
Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or the Agency) on this topic. It does not create any rights for any person and is not binding on FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed in the title page.

I. INTRODUCTION AND SCOPE

To qualify for exemptions under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act), a drug product must be compounded by a licensed pharmacist or physician who does not compound regularly or in inordinate amounts any drug products that are essentially copies of a commercially available drug product, among other conditions. This guidance sets forth FDA's policies regarding this provision of section 503A, including the terms *commercially available*, *essentially a copy of a commercially available drug product*, and *regularly or in inordinate amounts*.[2]

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

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[1] This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research, in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

[2] This guidance does not apply to drugs compounded for use in animals, to biological products subject to licensure in a biologics license application, or to repackaged drug products. For policies pertaining to mixing, diluting, and repackaging biological products, see FDA's guidance, *Mixing, Diluting, and Repackaging Biological Products Outside the Scope of an Approved Biologics License Application.* For policies pertaining to repackaged drug products, see FDA's guidance, *Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities*.

All FDA guidances are available on the FDA guidance web page. FDA updates guidances regularly. To make sure you have the most recent version of a guidance, always consult the guidance web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

II. BACKGROUND

A. Section 503A of the FD&C Act

Section 503A, added to the FD&C Act by the Food and Drug Administration Modernization Act of 1997 and amended by the Drug Quality and Security Act in 2013, describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State-licensed pharmacy or Federal facility, or by a licensed physician, to qualify for exemptions from the following three sections of the FD&C Act:[3]

- Section 501(a)(2)(B) (concerning current good manufacturing practice (CGMP) requirements)
- Section 502(f)(1) (concerning the labeling of drugs with adequate directions for use)
- Section 505 (concerning the approval of drugs under new drug applications (NDAs) or abbreviated new drug applications (ANDAs))

One of the conditions that must be met for a compounded drug product to qualify for the exemptions under section 503A of the FD&C Act is that it must be compounded by a licensed pharmacist or a licensed physician that "does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product."[4]

The statute further states that "the term 'essentially a copy of a commercially available drug product' does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug."[5]

A complete list of the conditions that must be met for a compounded drug product to qualify for the exemptions in section 503A appears in the FDA guidance, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*.

B. Compounding, Generally

Compounded drug products serve an important role for patients whose clinical needs cannot be met by an FDA-approved drug product, such as a patient who has an allergy and needs a medication to be made without a certain dye, an elderly patient who cannot swallow a pill and needs a medicine in a liquid form that is not otherwise available, or a child who needs a drug in a strength that is lower than that of the commercially available product. Drug products for identified individual patients can be compounded by licensed pharmacists in state-licensed

[3] In addition, under section 581(13) of the FD&C Act, the term "product," for purposes of pharmaceutical supply chain security requirements, does not include a drug compounded in compliance with section 503A.

[4] See section 503A(b)(1)(D).

[5] See section 503A(b)(2).

pharmacies and Federal facilities and by licensed physicians operating under section 503A of the FD&C Act. Drug products can also be compounded by outsourcing facilities under section 503B of the FD&C Act for identified individual patients pursuant to prescriptions or for distribution to health care practitioners without first receiving a prescription.[6] Both sections 503A and 503B restrict compounding drug products that are essentially a copy of a commercially available drug product (section 503A) or an approved drug product (section 503B).

C. Risks Associated with Compounded Drug Products

Although compounded drugs can serve an important need, they can also pose a higher risk to patients than FDA-approved drugs. Compounded drug products are not FDA-approved, which means they have not undergone FDA premarket review for safety, effectiveness, and quality. In addition, licensed pharmacists and licensed physicians who compound drug products in accordance with section 503A are not required to comply with CGMP requirements. Furthermore, FDA does not interact with the vast majority of licensed pharmacists and licensed physicians who compound drug products and seek to qualify for the exemptions under section 503A of the FD&C Act for the drug products that they compound because these compounders are not licensed by FDA and generally do not register their compounding facilities with FDA. Therefore, FDA is often not aware of potential problems with their compounded drug products or compounding practices unless it receives a complaint, such as a report of a serious adverse event or visible contamination.

FDA has investigated numerous serious adverse events associated with compounded drug products that were contaminated or otherwise compounded improperly, including the adverse events associated with the 2012 fungal meningitis outbreak in which contaminated injectable drug products resulted in more than 60 deaths and 750 cases of infection. FDA has also identified many pharmacies that compounded drug products under insanitary conditions such that the drug products may have been contaminated with filth or rendered injurious to health and that shipped the compounded drug products made under these conditions to patients and health care practitioners across the country, sometimes in large amounts.

D. Compounded Drugs That Are Essentially Copies of Commercially Available Drug Products

Section 503A provides exemptions from new drug approval, labeling with adequate directions for use, and CGMP requirements of the FD&C Act, so that drug products can be compounded as customized therapies for identified individual patients whose medical needs cannot be met by commercially available drug products. The restrictions on making drugs that are essentially copies ensure that pharmacists and physicians do not compound drug products under the exemptions for patients who could use a commercially available drug product. Such a practice would create significant public health risks because patients would be unnecessarily exposed to drug products that have not been shown to be safe and effective and that may have been prepared

[6] Section 503B of the FD&C Act describes the conditions that must be met for a human drug product compounded by an outsourcing facility to qualify for exemptions from sections 505, 502(f)(1), and 582 (concerning drug supply chain security requirements) of the FD&C Act. The conditions applicable to outsourcing facilities are discussed in separate guidances applicable to those facilities.

under substandard manufacturing conditions. FDA has investigated serious adverse events in patients who received contaminated compounded drugs when a comparable approved drug, made in a facility subject to CGMP requirements, was available.

In addition to these immediate public health risks, section 503A's limitations on producing a drug product that is essentially a copy of a commercially available drug product protects the integrity and effectiveness of the new drug and abbreviated new drug approval processes that Congress put in place to protect patients from unsafe, ineffective, or poor quality drugs. Furthermore, sponsors may be less likely to invest in and seek approval of innovative, life-saving medications if a compounder could, after a drug is approved, compound "substitutes" that may be less expensive because they have not had to demonstrate safety and effectiveness and are not produced in accordance with CGMP requirements or labeled with adequate directions for use.

Sponsors might also be less likely to seek approval of an ANDA for a generic drug if compounders were permitted to compound drugs that are essentially copies of commercially available drugs without going through the ANDA process. An ANDA must include data to demonstrate that the drug has the same active ingredient and is bioequivalent to an approved drug. FDA also conducts premarketing inspections of proposed manufacturing facilities.

The copies restriction also protects FDA's drug monograph process. FDA has an ongoing process for evaluating the safety and effectiveness of certain over-the-counter (OTC) medications, and if the Agency determines that an OTC drug meets certain conditions and is generally recognized as safe and effective, it will publish a final monograph specifying those conditions. Products that comply with a final monograph may be marketed, but manufacturers are required to meet CGMP standards. Restrictions in section 503A prevent compounders from producing drugs without having to comply with monograph standards, or CGMP requirements.

III. POLICY

As stated above, to qualify for the exemptions under section 503A of the FD&C Act, a drug must be compounded by a licensed pharmacist or a licensed physician that does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product.[7] This means that a compounded drug product is not eligible for the exemptions in section 503A if it is (1) essentially a copy of a commercially available drug product, and (2) compounded regularly or in inordinate amounts. Accordingly, and as discussed below, when evaluating whether a drug product meets the condition in section 503A regarding essentially copies, FDA intends to determine whether a compounded drug product is *essentially a copy of a commercially available drug product:* if it is, FDA intends to determine whether the drug product was compounded regularly or in inordinate amounts.[8]

[7] See section 503A(b)(1)(D).

[8] FDA is considering the applicability of the policies described in this guidance to hospitals and health systems and intends to address these issues in separate guidance or rulemaking. FDA regards a health system as collection of hospitals that are owned and operated by the same entity and that share access to databases with drug order information for their patients. There is no definition of "health system" that applies to all sections of the FD&C Act.

FDA's policies with regard to the terms (1) *commercially available drug product*, (2) *essentially a copy of a commercially available drug product*, and (3) *regularly or in inordinate amounts*, are as follows:

A. Commercially Available Drug Product

For purposes of this guidance, a drug product is commercially available if it is a marketed drug product.

We do not consider a drug product to be commercially available if

- the drug product has been discontinued and is no longer marketed[9] or
- the drug product appears on the FDA drug shortage list in effect under section 506E of the FD&C Act.[10] A drug "appears on the drug shortage list in effect under section 506E" if the drug is in "currently in shortage" status (and not in "resolved" status) in FDA's drug shortage database.

Commercially available drugs are available on the market, and they are generally subject to FD&C Act requirements relating to approval, labeling, and CGMP requirements, and the copies restriction applies to all such drugs because section 503A is not intended to provide a means for compounders to produce compounded drugs exempt from the Act's requirements that are essentially copies of commercially available drug products.

B. Essentially a Copy of a Commercially Available Drug Product

1. What is Essentially a Copy?

FDA intends to consider a compounded drug product to be essentially a copy of a commercially available drug product if:

- the compounded drug product has the same active pharmaceutical ingredient(s) (API) as the commercially available drug product;
- the API(s) have the same, similar, or an easily substitutable dosage strength; and

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However, this is the definition of a "health system" used in section 506F of the Act concerning hospital repackaging of drugs in shortage.

[9] FDA maintains a list of approved drug products that sponsors have indicated are not marketed in the discontinued section of the list of Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book). See http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm. Specifically, the list includes approved drug products that have never been marketed, are for exportation, are for military use, have been discontinued from marketing and we have not determined were withdrawn for safety or effectiveness reasons, or have had their approvals withdrawn for reasons other than safety or effectiveness subsequent to being discontinued from marketing.

[10] See http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.

- the commercially available drug product can be used by the same route of administration as prescribed for the compounded drug,

unless, as provided by section 503A(b)(2), a prescriber determines that there is a change, made for an identified individual patient, which produces, for that patient, a significant difference from the commercially available drug product.

The limitations in section 503A(b)(1)(D) apply to the compounding of drug products that are *essentially* copies of a commercially available drug product – not only to drugs that are exact copies or even to drugs that are nearly identical. This is to ensure that compounders do not evade the limits in this section by making relatively small changes to a compounded drug product and then offering the drug to the general public without regard to whether a prescribing practitioner has determined that the change produces for the patient a significant difference. For example, Congress contemplated that a compounded drug may be essentially a copy of a commercially available drug if "minor changes in strength (such as from .08% to .09%) are made that are not known to be significant . . ." for the patient for whom the drug was prescribed.[11]

a. Same API

With regard to the characteristics listed above, an API is the substance in a drug product that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or function of the body.[12] When a compounded drug product offers the same API as a commercially available drug product, in the same, similar, or easily substitutable dosage strength and for use through the same route of administration, we generally intend to consider such a drug product *essentially a copy,* unless a prescriber determines that there is a change, made for an identified individual patient, that will produce a significant difference for that patient.

We recognize that, for some patients, a drug product that has the same API, strength, and route of administration may include a change that produces a significant difference for a particular patient. For example, a drug product compounded without a particular inactive ingredient may produce a significant difference for a patient who has an allergy to the inactive ingredient in the commercially available drug product. However, for other patients, this change may produce no difference at all. Congress did not intend for compounders to use, for example, the fact that some patients may have allergies as a basis to compound a drug without the inactive ingredient for other patients who do not have the allergy under the exemptions in section 503A (i.e., without meeting requirements for premarket approval, labeling with adequate directions for use, or

[11] U.S. House. Food and Drug Administration Modernization Act of 1997, *Conference Report* (to Accompany S. 830). (105 H. Rpt. 399).

[12] Section 503A refers to bulk drug substances. A *bulk drug substance* is defined as any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body. It does not include intermediates used in the synthesis of the substance. This definition is the same as the definition of active pharmaceutical ingredient. See 21 CFR 207.1, 207.3.

CGMP requirements).[13] In the context of compounding and consistent with the statute, we generally intend to consider such a drug essentially a copy unless a prescriber determines that there is a change that will produce a significant difference for the patient for whom it is prescribed.

b. Same, Similar or Easily Substitutable Strength

FDA generally intends to consider two drugs to have a similar dosage strength if the dosage strength of the compounded drug is within 10% of the dosage strength of the commercially available drug product.

With regard to the concept of easily substitutable strength, in some cases, the same or similar dosage strength can be achieved by administration of fractional or multiple doses of a drug product. For example, if FDA-approved Drug X tablets have a dosage strength of 25 mg and a patient needs 50 mg of Drug X, FDA would generally consider a compounded Drug X 50 mg tablet to have an easily substitutable strength because the patient could take two Drug X 25 mg tablets to achieve the required dose.[14]

c. Same Route of Administration

Route of administration is a way of administering a drug to a site in a patient (e.g., topical, intravenous, oral).[15] In general, FDA does not intend to consider a compounded drug product with the same API and similar or easily substitutable strength to be essentially a copy of a commercially available drug product if the compounded drug product and the commercially available drug product have different routes of administration (e.g., if the commercially available drug product is oral and the compounded drug product is topical). However, if the compounded drug product has the same API and similar or easily substitutable strength as the commercially available drug product and the commercially available drug product can be used (regardless of how it is labeled) by the route of administration prescribed for the compounded drug, FDA generally intends to consider the compounded drug to be essentially a copy of the commercially available drug. In this case, the compounded drug product generally would not produce a significant difference for an identified individual patient relative to the commercially available drug product.

For example, if the commercially available drug is an injectable drug sold in a vial that is labeled for intra-muscular use, but the drug also can be drawn from the vial by a smaller needle for subcutaneous administration, a compounded drug product with the same API and similar or

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[13] *See* note 11.

[14] If a commercially available tablet must be split to achieve the prescribed dosage strength, and such tablet is not suitable for splitting, FDA would not consider the compounded drug made to the prescribed dosage strength to have an easily substitutable strength. For example, some tablets may be too small or crumble too easily when split, making splitting an inappropriate option. Information regarding tablet splitting may be printed in the "HOW SUPPLIED" section of the professional label insert and in the patient package insert of an approved drug product.

[15] See http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/DataStandardsManualmonographs/ucm071667.htm.

easily substitutable strength prescribed for sub-cutaneous administration would generally be considered to be essentially a copy, unless the prescriber documents on the prescription that the compounded drug product produces a significant difference for the identified individual patient.

d. Same Characteristics as Two or More Commercially Available Drug Products

FDA intends to consider a compounded drug product to be essentially a copy of a commercially available drug product if the compounded drug product contains the same APIs as two or more commercially available drug products in the same, similar, or easily substitutable strength and if the commercially available drug products can be used (regardless of how they are labeled) by the same route of administration prescribed for the compounded drug, unless there is documentation as described in section III.B.2. Such drug products present the same kinds of concerns as drug products that have a single API and in some respects may be more dangerous because of the potential for unintended drug interactions or formulation issues. For example, if drug X and drug Y are commercially available oral drug products, FDA generally intends to consider a compounded oral drug product that combines drug X and drug Y in strengths that are within 10% of the strengths of the respective commercially available products to be essentially a copy of the commercially available drug product, unless a prescriber determination of a significant difference has been documented.

2. Statement of Significant Difference

Pursuant to section 503A(b)(2) of the FD&C Act, a compounded drug product is not essentially a copy of a commercially available drug product if a change is made for an identified individual patient, and the prescribing practitioner has determined that the change will produce a significant difference for that patient. If a compounder intends to rely on such a determination to establish that a compounded drug is not essentially a copy of a commercially available drug product, the compounder should ensure that the determination is documented on the prescription.

FDA does not believe that a particular format is needed to document the determination, provided that the prescription makes clear that the prescriber identified the relevant change and the significant difference that the change will produce for the patient. For example, the following would be sufficient:

- "No Dye X, patient allergy" (if the comparable drug contains the dye)
- "Liquid form, patient can't swallow tablet" (if the comparable drug is a tablet)
- "6 mg, patient needs higher dose" (if the comparable drug is only available in 5 mg dose)

However, if a prescription identifies only a patient name and drug product formulation, this would not be sufficient to establish that the prescriber made the determination described by section 503A(b)(2). Note also that the significant benefit that the prescriber identifies must be produced by the change the compounder will make to a commercially available drug product (i.e., a change in drug product formulation). Other factors, such as a lower price, are not

sufficient to establish that the compounded drug product is not essentially a copy of the commercially available drug product.[16]

If a prescription does not make clear that the prescriber made the determination required by section 503A(b)(2), or a compounded drug is substituted for the commercially available drug product, the compounder can contact the prescriber and if the prescriber confirms it, make a notation on the prescription that the compounded drug product contains a change that makes a significant difference for the patient. The notations should be as specific as those described above, and the date of the conversation with the prescriber should be included on the prescription.[17]

It is not possible to offer exhaustive guidance about when a difference will be "significant" to an identified individual patient. At this time, FDA generally does not intend to question prescriber determinations that are documented in a prescription or notation. However, we do intend to consider whether a prescription or notation relied upon by a compounder to establish that a drug is not essentially a copy documents that the determination was made.

If the compounder produces drugs in anticipation of receiving valid prescriptions for identified individual patients, and the compounder obtains the statement of significant difference from the prescriber when it receives the prescription for the compounded drug, prior to distribution, FDA does not intend to consider the compounded drug that is then distributed to be essentially a copy.

3. Documentation of Shortage

If the drug was compounded because the approved drug product was not commercially available because it was on the FDA drug shortage list, the prescriber or compounder should include a notation on the prescription that it was on the drug shortage list and the date the list was checked.[18]

4. Regularly or in Inordinate Amounts

A drug product is not eligible for the exemptions in section 503A if it is prepared by a pharmacist or physician who compounds "regularly or in inordinate amounts (as defined by the Secretary)" any drug products that are essentially copies of a commercially available drug

[16] Congress noted that "where it is readily apparent, based on the circumstances, that the 'significant difference' is a mere pretext to allow compounding of products that are essentially copies of commercially available products, such compounding would be considered copying of commercially available products and would not qualify for the compounding exemptions if it is done regularly or in inordinate amounts. Such circumstances may include, for example, instances in which minor changes in strength (such as from .08% to .09%) are made that are not known to be significant or instances in which the prescribing physician is receiving financial remuneration or other financial incentives to write prescriptions for compounded products." *See* the U.S. House. Food and Drug Administration Modernization Act of 1997*, Conference Report* (to Accompany S. 830). (105 H. Rpt. 399).

[17] See section IV of this guidance.

[18] See section IV of this guidance.

product.[19] FDA interprets this to mean that, in order to be compounded in accordance with section 503A, a drug product that is essentially a copy of a commercially available drug product cannot be compounded regularly – i.e., it cannot be compounded at regular times or intervals, usually, or very often. Nor can the amounts compounded be inordinate, in light of the purpose of section 503A.

Section 503A is intended to protect patients from the public health risks of providing compounded drugs to patients whose medical needs could be met by commercially available drug products and to protect the integrity and efficiency of the drug approval process. Under the statutory scheme, only very rarely should a compounded drug product that is essentially a copy of a commercially available drug product be offered to a patient. We conclude, therefore, that a drug product that is essentially a copy of a commercially available drug product is compounded regularly or in inordinate amounts if it is compounded more frequently than needed to address unanticipated, emergency circumstances, or in more than the small quantities needed to address unanticipated, emergency circumstances.

It is important to note that the regularly or in inordinate amounts provision is not implicated if the compounded drug is not essentially a copy of a commercially available drug product. For example, a compounded drug product that has the same API, dosage strength, and route of administration as a drug product on FDA's shortage list would not be considered essentially a copy of a commercially available drug because a drug product is not considered *commercially available* if it is on FDA's drug shortage list. In addition, a compounded drug product is not essentially a copy of a commercially available drug product if a prescriber has determined that the compounded drug has a change that produces a significant difference for a patient.
Once it has been determined that a compounded drug is essentially a copy of a commercially available drug product as described above, the following are examples of factors that may be the basis for concluding that it has been compounded regularly or in inordinate amounts:

- The compounded drug product amounts to more than a small number of prescriptions or a small percentage of the compounded drug products that a compounder prepares.
- The compounder routinely substitutes compounded drugs that are essentially copies of commercially available drugs upon receiving prescriptions for patients.
- The compounder offers pre-printed prescription pads that a prescriber can use to write a prescription for the drug product that is essentially a copy without making a determination that there is a change that will produce a significant difference for a patient.
- The compounded drug product is not compounded on an as-needed basis, but on a routine or pre-set schedule.

The foregoing list is not intended to be exhaustive. Other factors may be appropriate for consideration in a particular case.

To focus enforcement on the most significant cases, as a matter of policy, at this time FDA does not intend to take action against a compounder for compounding a drug product that is

[19] See section 503A(b)(1)(D).

essentially a copy of a commercially available drug product regularly or in inordinate amounts if the compounder fills four or fewer prescriptions for the relevant compounded drug product in a calendar month.[20] As noted above, a compounded drug product is not essentially a copy of a commercially available drug product if a prescriber has determined that the compounded drug has a change that produces a significant difference for a patient; thus, a prescription that documents such a prescriber determination would not be counted towards the four prescriptions.

Compounders may produce a limited amount of drugs in anticipation of receiving valid prescriptions for identified individual patients. See section 503A(a)(2). FDA generally intends to consider whether such drugs are essentially a copy at the time the drug is distributed rather than the time it is produced.

5. Recordkeeping

A licensed pharmacist or physician seeking to compound a drug product under section 503A should maintain records to demonstrate compliance with section 503A(b)(1)(D). For example, records should be kept of notations on prescriptions for identified individual patients that a prescriber has determined that the compounded drug has a change that produces a significant difference for the identified patient.

Compounders under section 503A should also maintain records of the frequency in which they have compounded drug products that are essentially copies of commercially available drug products and the number of prescriptions that they have filled for compounded drug products that are essentially copies of commercially available drug products to document that such compounding has not been done regularly or in inordinate amounts.[21]

FDA recommends that compounders maintain the records described above for a period of at least three years.

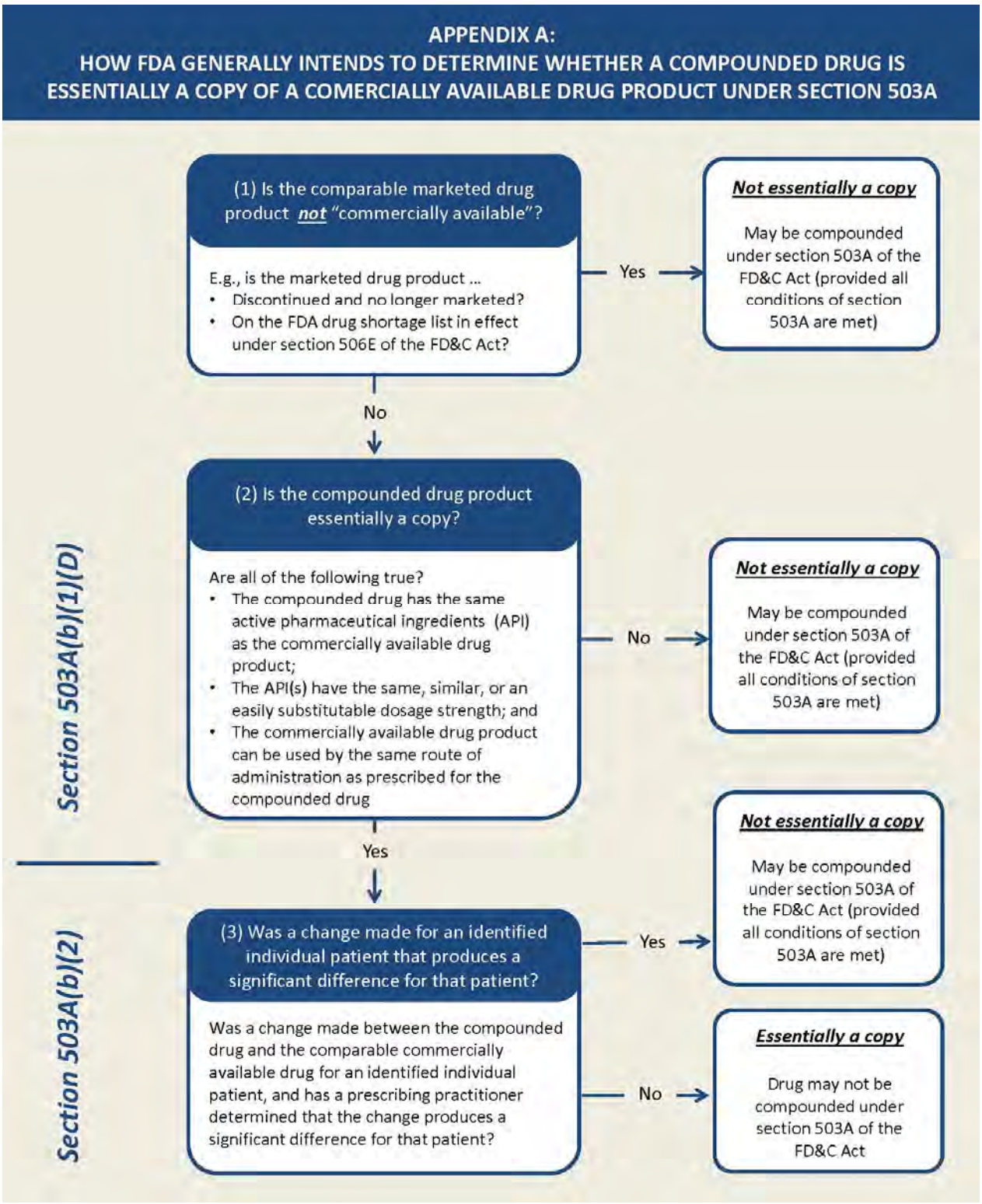
IV. PAPERWORK REDUCTION ACT

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). See footnotes 17, 18, and 21. These provisions require review and are not in effect until they display a currently valid OMB control number. The information collection provisions in this guidance have been submitted to OMB for review as required by section 3507(d) of the Paperwork Reduction Act of 1995. FDA will publish a notice in the *Federal Register* announcing OMB's decision regarding the information collection provisions in this guidance.

[20] For purposes of this policy, FDA intends to consider each refill of a prescription as an additional prescription.

[21] See section IV of this guidance.

APPENDIX A.


APPENDIX A:
HOW FDA GENERALLY INTENDS TO DETERMINE WHETHER A COMPOUNDED DRUG IS ESSENTIALLY A COPY OF A COMERCIALLY AVAILABLE DRUG PRODUCT UNDER SECTION 503A
Section 503A(b)(1)(D)
Section 503A(b)(2)
(1) Is the comparable marketed drug product not "commercially available"?
E.g., is the marketed drug product ...
• Discontinued and no longer marketed?
• On the FDA drug shortage list in effect under section 506E of the FD&C Act?
Yes
Not essentially a copy
May be compounded under section 503A of the FD&C Act (provided all conditions of section 503A are met)
No
(2) Is the compounded drug product essentially a copy?
Are all of the following true?
• The compounded drug has the same active pharmaceutical ingredients (API) as the commercially available drug product;
• The API(s) have the same, similar, or an easily substitutable dosage strength; and
• The commercially available drug product can be used by the same route of administration as prescribed for the compounded drug
No
Not essentially a copy
May be compounded under section 503A of the FD&C Act (provided all conditions of section 503A are met)
Yes
(3) Was a change made for an identified individual patient that produces a significant difference for that patient?
Was a change made between the compounded drug and the comparable commercially available drug for an identified individual patient, and has a prescribing practitioner determined that the change produces a significant difference for that patient?
Yes
Not essentially a copy
May be compounded under section 503A of the FD&C Act (provided all conditions of section 503A are met)
No
Essentially a copy
Drug may not be compounded under section 503A of the FD&C Act

18VAC110-50-80. Minimum licensure and permitting qualifications and eligibility; responsible party.

A. The board shall use the following factors in determining the eligibility for licensure of wholesale distributors, registration of nonresident wholesale distributors or nonresident third-party logistics providers, and permitting of third-party logistics providers:

1. The existence of grounds to deny an application as set forth in § 54.1-3435.1 of the Code of Virginia;

2. The applicant's past experience in the manufacture or distribution of drugs or devices;

3. Compliance with the recordkeeping requirements;

4. Prior disciplinary action by a regulatory authority, prior criminal convictions, or ongoing investigations related to the manufacturing, distribution, prescribing, or dispensing of drugs by the responsible party or immediate family members of the responsible party, and owners, directors, or officers; and

5. The responsible party's credentials as set forth in subsection B of this section.

B. Requirements for the person named as the responsible party.

1. The responsible party shall be the primary contact person for the board as designated by the wholesale distributor, nonresident wholesale distributor, third-party logistics provider, or nonresident third-party logistics provider, who shall be responsible for managing the wholesale distribution operations at that location;

2. The responsible party shall have a minimum of two years of verifiable experience in a pharmacy or wholesale distributor or third-party logistics provider licensed, registered, or permitted in Virginia or another state where the person's responsibilities included managing or supervising the recordkeeping, storage, and shipment for drugs or devices;

3. A person may only serve as the responsible party for one wholesale distributor license, nonresident wholesale distributor registration, third-party logistics provider permit, or nonresident third-party logistics provider registration at any one time;

4. The responsible party shall be employed full time in a managerial position and actively engaged in daily operations of the wholesale distributor, nonresident

wholesale distributor, third-party logistics provider, or nonresident third-party logistics provider;

5. The responsible party shall be present on a full-time basis at the location of the wholesale distributor, nonresident wholesale distributor, third-party logistics provider, or nonresident third-party logistics provider during normal business hours, except for time periods when absent due to illness, family illness or death, vacation, or other authorized absence; and

6. The responsible party shall be aware of, and knowledgeable about, all policies and procedures pertaining to the operations of the wholesale distributor, nonresident wholesale distributor, third-party logistics provider, or nonresident third-party logistics provider and all applicable state and federal laws related to wholesale distribution of prescription drugs or the legal acts of a third-party logistics provider.

C. The person named as the responsible party on the application shall submit the following with the application:

1. A passport size and quality photograph taken within 30 days of submission of the application;

2. A resume listing employment, occupations, or offices held for the past seven years including names, addresses, and telephone numbers of the places listed;

3. An attestation disclosing whether the person has a criminal conviction or is the subject of any pending criminal charges within or outside the Commonwealth;

4. A federal criminal history record check; and

5. A description of any involvement by the person with any business, including any investments, other than the ownership of stock in a publicly traded company or mutual fund, during the past seven years, that manufactured, administered, prescribed, distributed, or stored drugs and devices and any lawsuits, regulatory actions, or criminal convictions related to drug laws or laws concerning third-party logistics providers or wholesale distribution of prescription drugs in which such businesses were named as a party.

D. Responsibilities of the responsible party.

1. Ensuring that any employee engaged in operations is adequately trained in the requirements for the lawful and appropriate wholesale distribution of prescription drugs or the legal acts of a third-party logistics provider;

2. Requiring any employee who has access to prescription drugs to attest that the employee has not been convicted of a violation of any federal or state drug law or any law relating to third-party logistics providers or to the manufacture, distribution, or dispensing of prescription drugs;

3. Maintaining current working knowledge of requirements for wholesale distributors or third-party logistics providers and assuring continued training for employees;

4. Maintaining proper security, storage, and shipping conditions for all prescription drugs; and

5. Maintaining all required records.

E. Each nonresident wholesale distributor or nonresident third-party logistics provider shall designate a registered agent in Virginia for service of any notice or other legal document. Any nonresident wholesale distributor or nonresident third-party logistics provider that does not designate a registered agent shall be deemed to have designated the Secretary of the Commonwealth to be its true and lawful agent, upon whom may be served all legal process in any action or proceeding against such nonresident wholesale distributor or nonresident third-party logistics provider. A copy of any such service of legal documents shall be mailed to the nonresident wholesale distributor or nonresident third-party logistics provider by the board by certified mail at the address of record.

Agenda Topic: Amend Guidance Documents 110-36 and 110-9 regarding USP revisions

Staff Note: Revisions to the United States Pharmacopeia Chapters <795> and <797> become effective on November 1, 2023. Staff will provide a handout of these two documents, highlighting potential areas for amendment.

Action Needed:

- Motion to recommend that the full board amend Guidance Documents 110-36 and 110-9 as presented, amended, or discussed.

Virginia Board of Pharmacy

COMPLIANCE WITH USP STANDARDS FOR COMPOUNDING

§54.1-3410.2 of the Code of Virginia and Regulation 18VAC110-20-321 requires pharmacies performing sterile or non-sterile compounding to comply with USP Standards. USP standards for sterile and non-sterile compounding may be found in the current editions of the USP-NF. In accordance with 18VAC110-20-170, the Board requires a pharmacy to maintain references consistent with the pharmacy's scope of practice and with public safety.

USP Chapter 795 lists the requirements for non-sterile compounding including information about the compounding environment, equipment, stability criteria and beyond-use dating and records. USP Chapter 797 lists requirements for policies and procedures, training and evaluation of personnel performing sterile compounding, determining risk levels and the physical standards for the sterile compounding area. The Board expects that the requirements of Chapters 795 and 797 will be found in compliance at time of inspection. USP Chapter 800 describes practice and quality standards for handling hazardous drugs to promote patient safety, worker safety, and environmental protection. ~~USP first published Chapter 800 in 2014. It was first published as an official standard in February 2016 with a delayed implementation date of July 1, 2018. On September 27, 2017, USP published a notification of intent to revise the effective date of chapter <800> to December 1, 2019.~~ While full compliance with Chapter 800 is encouraged, only those requirements related to compounding are legally required.

~~The terms "annually" and "semiannually" as used in USP Chapters 795 and 797 are defined to mean every 12 months and every 6 months, respectively. Records associated with annual and semiannual requirements shall be maintained in accordance with USP standards. Such records may be maintained as an electronic image that provides an exact image of the document that is clearly legible provided such electronic image is retrievable and made available at the time of inspection or audit by the Board or an authorized agent.~~

~~*NOTE: On September 23, 2019, USP published a Notice of Intent to Revise which stated Chapters 795, 797, and 825 were under appeal and that "USP's Bylaws provide that the official date of a standard under appeal must be postponed while an appeal is pending. Therefore, USP is postponing the official dates of the revised <795> and <797>, and the new general chapter <825> until further notice. In the interim, the currently official chapters of <795> (last revised in 2014) and <797> (last revised in 2008) including the section Radiopharmaceuticals as CSPs will remain official. General Chapter <800> is not subject to any pending appeals and will become official on December 1, 2019. During the postponement and pending resolution of the appeals of <795> and <797>, <800> is informational and not compendially applicable." While USP and the Board encourages utilization of <800> in the interest of advancing public health, the Board cannot legally require compliance with requirements in 800 related to compounding until the appeals of 795 and 797 are resolved and the revised chapters become effective.*~~

USP often updates and adds to their Frequently Asked Questions site for the general chapters. Please visit the following links to the USP website for frequently asked questions on the following applicable chapters:

Chapter <795> - https://go.usp.org/USP_GC_795_FAQs
Chapter <797> - https://go.usp.org/USP_GC_797_FAQs
Chapter <800> - https://go.usp.org/General-Chapter-800-FAQ
Chapter <825> - https://www.usp.org/frequently-asked-questions/radiopharmaceuticals

1. ***Where may information regarding USP-NF standards for compounding be located?***

   A subscription to the current version of USP-NF Chapters may be purchased at https://store.usp.org/usp-nf-online/category/USP-3110. ~~"USP on Compounding: A Guide for the Compounding Practitioner" may be purchased at http://www.usp.org/store/products-services/usp-compounding This guide provides access to all compounding-related General Chapters from the USP-NF and is updated with the release of each new USP-NF edition and supplement~~.

2. ***Does the law require compliance only with Chapter <797>?***

   No, the law requires compliance with all applicable chapters within USP-NF. Regarding sterile compounding, pharmacists should pay particularly close attention to General Chapters: <1> Injections, <71> Sterility Testing, <85> Bacterial Endotoxin Testing, <659> Packaging and Storage Requirements, and <797> Pharmaceutical Compounding- Sterile Preparations.

~~**3. *Are there specific educational and training requirements regarding personnel?***~~

~~Yes. In USP chapter <797>, compounding personnel are required to be adequately skilled, educated, instructed, and trained to correctly perform and document the following activities in their sterile compounding duties: perform aseptic hand cleansing and disinfection of nonsterile compounding surfaces; select and apropriately don protective garb; maintain or achieve sterility of compounded sterile products in ISO class 5 environments; identify, weigh, and measure ingredients; manipulate sterile products aseptically; sterilize high-risk level compounded sterile products and label; and, inspect the quality of compounded sterile products. Personnel must also sucessfully complete a site-specific training program as required in Regulation 18VAC110-20-111.~~

~~***3. In the absence of sterility testing, what beyond use dates (BUDs) must be used?***~~

~~When sterility testing has not been performed, the assigned BUD must not exceed the following allowances:~~

	~~Controlled Room Temperature~~	~~Refrigerator~~	~~Freezer~~
~~Low-risk~~	~~48 hours~~	~~14 days~~	~~45 days~~
~~Medium-risk~~	~~30 hours~~	~~9 days~~	~~45 days~~
~~High-risk~~	~~24 hours~~	~~3 days~~	~~45 days~~

4. ~~***What BUD must be assigned to a single dose vial used in preparing a compounded sterile product?***~~

- ~~If the single dose vial is punctured outside of an ISO Class 5 environment, the assigned BUD shall not exceed 1 hour, unless specified otherwise by the manufacturer;~~
- ~~If the single dose vial is puntured within and stored within an ISO Class 5 environment, the assigned BUD shall not exceed 6 hours;~~
- ~~A puntured single dose vial that is removed from the ISO Class 5 environment such as for final verification purposes shall not exceed 1 hour from being removed from the ISO Class 5 environment or the originally assigned BUD of 6 hours within the ISO Class 5 environment, whichever is shorter (reference the Center For Disease Control (CDC) and USP Appendix);~~
- ~~A closed system transfer device (CSTD) should not be used to extend the BUD of a single dose vial to exceed the 1 hour BUD when punctured outside of an ISO Class 5 environment or the 6 hour BUD when punctured within and not removed from an ISO Class 5 environment.~~

~~**5. *Is it appropriate to assign a BUD of 90 days in the absence of sterility testing if there is literature indicating the stability of the drug is assured for 90 days?***~~

~~No, it is inappropriate and a violation of law to assign a BUD which exceeds the USP default BUDs in the absence of sterility testing. Drug stability should not be confused with drug sterility.~~

~~***6. How may stability information be taken into consideration when assigning a BUD?***~~

~~Stability information for multiple drugs may be considered when combining the drugs in a compound, assuming the shortest BUD is used to assign stability to the compound. Peer-review or reference source literature shall be consulted and the professional judgement of the pharmacist exercised when assigning the BUD of a compound containing multiple drugs. Any extended BUD must also comply with the applicable USP Chapter <795> or <797>.~~

~~***7. What concepts, at a minimum, should be taken into consideration when determining drug stability?***~~

~~Pharmacists should use professional judgment to determine appropriate references of chemical stability information and note that sterile and non-sterile drug stability is formulation specific. Existing stability information may only be used when the compound has been prepared using the same formulation (USP-NF equivalent ingredients) as used in either at least one peer-reviewed article or other reliable reference source. The process used by the pharmacist to determine drug stability should be well-documented and maintained for inspector review.~~

~~Additionally, stability may be estimated for an aqueous or non-aqueous compound under the following conditions:~~

~~Stability information exists in peer-reviewed articles or reference sources indicating stability at a low concentration and high concentration and therefore, stability for concentrations in-between could be estimated;~~
~~Stability of the drug is not concentration-dependent; and,~~
~~The drug is compounded using the same formulation (USP-NF equivalent ingredients) as used in the peer-reviewed articles or reference sources.~~

8. ~~***What is skip lot testing and may skip lot testing be used to perform sterility testing of compounded sterile products?***~~

~~Skip lot testing is a process that only tests a fraction of the drugs compounded. It is NOT appropriate for sterility testing. It may only be used for ensuring consistency and drug strength (potency). Because skip lot testing is complex and requires a robust program, it may not be possible for a pharmacy to properly implement. Information regarding skip lot testing may be accessed at~~ http://www.itl.nist.gov/div898/handbook/pmc/section2/pmc27.htm

~~***9. How may a hospital pharmacy "batch-producing" limited quantity of CSPs for IN-HOUSE use extend the BUD past the default dating in Chapter <797>?***~~

~~EACH BATCH must undergo sterility testing in accordance with USP Chapter <71> in order to extend the BUD past the default dating in Chapter <797> and the appropriate documentation to support an extended BUD must be kept on file for presentation upon inspection.~~

~~***10. Do batches less than 25 require sterility testing to be performed?***~~

~~No, however, the batches may not be assigned a BUD which exceeds the default BUDs in USP Chapter <797>. The chapter requires sterility testing according to USP <71> before CSPs are dispensed or administered when:~~

- ~~high-risk level CSPs that are prepared in groups of more than 25 identical individual single-dose packages (e.g., ampuls, bags, syringes, vials) or~~
- ~~in multiple-dose vials (MDVs) for administration to multiple patients or~~
- ~~CSPs that are exposed longer than 12 hours at 2 to 8 C and longer than 6 hours at warmer than 8 C before they are sterilized.~~

~~***11. How often must the primary engineering control, e.g., laminar airflow workbench and secondary engineering control, e.g., ante and buffer rooms be certified?***~~

~~Certification of the primary and secondary engineering controls shall be performed no less than every six months and whenever the device or room is relocated, altered, or major service to the facility is performed. The certification must be performed no later than *the last day of the sixth month*, following the previous certification.~~
~~***Note~~ this guidance reflects a change to Major Deficiencies 22 and 23 in Guidance Document 110-9 which was amended at the March 2013 full board meeting.~~

3. Must compounding personnel who work in multiple pharmacies, to include pharmacy interns on rotations, pass a media-fill test at each pharmacy where they will prepare CSPs?

Yes, all compounding personnel working in multiple pharmacies, to include pharmacy interns on rotations, must pass a media-fill test at each pharmacy prior to performing sterile compounding.

~~***4. How often must media-fill testing be performed?***~~

~~Media-fill testing of all compounding personnel shall be performed initially prior to beginning sterile compounding and at least annually thereafter for low and medium-risk compounding, and semiannually for high-risk level compounding. ***Note – the terms "annually" and "semi-annually" are defined within this guidance document to mean every 12 months and every 6 months, respectively. Annual media-fill testing must be performed no later than the last day of the twelfth month from the date the previous media-fill test was initiated. Semiannual media-fill testing must be performed no later than the last day of the sixth month from the date the previous media-fill test was initiated.~~

~~***5. If compounding personnel fail a media-fill test, may they continue preparing compounded sterile products?***~~

~~No, compounding personnel who failed a media-fill test may not be allowed to prepare compounded sterile products (low, medium, or high-risk) prior to retraining and receipt of a passing media-fill test. ***Note- this guidance reflects a change to Major Deficiency 26a in Guidance Document 110-9 which was amended at the March 2013 full board meeting.~~

~~***6. Because batches less than 25 do not require sterility testing to be performed, may the CSP which may have been autoclaved be assigned an extended BUD based on stability data?***~~

~~Per USP, sterility testing is not required for autoclaved CSP prepared in batches less than 25 and if the storage times for high-risk CSPs are not exceeded. If the storage times of high-risk CSPs are exceeded, sterility testing is required. Once sterility testing is successfully completed, a longer BUD may be assigned based on the criteria described in the chapter (e.g., based on stability studies).~~

~~***7. Does USP-NF address how long a CSP may hang for infusion?***~~

~~No, USP-NF does not address how long a CSP may hang for infusion. Refer to facility policy on this issue. USP-NF, however, does require the administration of CSPs to begin prior to the assigned BUD.~~

~~***8. May a pharmacist repackage Avastin for office administration not pursuant to a patient-specific prescription?***~~

~~No. While pharmacists may repackage a drug product when dispensing a drug pursuant to patient-specific prescription, a pharmacist may not repackage a drug for another entity. The board has historically interpreted the repackaging of a drug for distribution purposes as an act restricted to a manufacturer, defined in Va Code §54.1-3401. This interpretation appears consistent with recent warning letters from the US Food and Drug Administration (FDA). The~~

~~allowance in Va Code §54.1-3401 for a pharmacist to provide compounded drugs to a physician for office administration does not apply. Repackaging Avastin does not constitute compounding as it does not involve the mixing of two of more substances.~~

~~9. May a pharmacist repackage Avastin pursuant to a patient-specific prescription?~~

~~Yes, a pharmacist may repackage a drug as part of the dispensing process pursuant to a patient-specific prescription.~~

~~10. What concepts, at a minimum, should be taken into consideration when performing sterility testing of CSPs?~~

- ~~Maintain a written policy and procedure manual clearly identifying sterility testing procedures used by the pharmacy and processes for assigning BUDs.~~
- ~~Prior to using an outside testing company to perform sterility testing, evaluate the company to determine if it performs testing in full compliance with USP Chapter <71>. This may be done by reviewing 483 reports issued by the FDA to the testing company and which may be available on the FDA website. Alternatively, request copies of the 483 reports directly from the testing company. The observed deficiencies noted on the 483 reports will assist the pharmacist in evaluating the testing company's level of compliance. Also, request written documentation from the testing company which explains the sterility testing processes used and how it complies with USP Chapter <71> in its totality. This documentation should contain, at a minimum, specific details regarding the method of testing, method suitability associated with each sterility testing process to ensure the drug being tested will not interfere with the test, identification of testing method (membrane filtration is the preferred method of testing), two growth media, and number of days of incubation. Have this documentation readily available for inspector review.~~
- ~~When performing sterility testing in-house, document in the written policy and procedure manual, at a minimum, specific details regarding the method of testing, method suitability associated with each sterility testing process to ensure the drug being tested will not interfere with the test, identification of two growth media, and number of days of incubation.~~
- ~~Vendors providing products for in-house testing must describe all conditions and limitations to their testing products. Ensure the appropriate filtration volume and sample size is being tested.~~
- ~~When determining an appropriate sterility testing process, note that the preferred method per USP is membrane filtration. The Board strongly recommends that written documentation justifying the use of direct inoculation be available for inspection~~
- ~~Ensure the sterility testing incorporates two media for growth.~~
- ~~The sample size used for testing must comply with USP Chapter <71>, tables 2 and 3.~~
- ~~Maintain robust recordkeeping, e.g., chart the dates, temperatures, growth associated with the two media incubations, and employee signatures. Do not simply indicate "no growth" without indicating which growth media was used and the number of days incubated.~~

~~11. Must sterility testing be performed on all batches of CSPs?~~

~~Sterility testing is not required of low and medium-risk level batched CSPs if the BUDs do not exceed the default BUDs found in USP Chapter <797>. If the low or medium-risk level batched CSP is to be assigned an extended BUD, then sterility testing must be performed. Sterility testing must always be performed of high-risk level CSPs in batches greater than 25. See Response to Q#7~~

~~12. What is the definition of a "batch"?~~

~~USP does not currently define the term "batch". In 21CFR210.3, FDA defines "batch" to mean a specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.~~

~~22. How should a dilution or stock bag for pediatrics be treated?~~

~~USP does not currently address this issue, however, the Board advises that the dilution or stock bag should be treated as a single dose container/vial with the remains being discarded within 6 hours of compounding.~~

~~23. What are some important considerations regarding membrane filtration and filter integrity testing, aka bubble point testing?~~

~~Membrane filtration may be accomplished using a 0.22 micron filter. It is important to note that sterility testing cannot be accomplished by simply performing membrane filtration. Filter integrity testing, also known as a bubble point test, must be performed to verify that the filter was successful in its application. Smaller disc filters may have filter volume limitations which must be taken into consideration. Because it is known that filtration has not always been successful in preventing the passing through of microorganisms, pharmacists must always build quality processes into their sterile compounding to minimize the risk and the introduction of contamination.~~

~~24. What are some best practices for performing required media fill testing and gloved fingertip sampling?~~

~~Persons performing high-risk level CSPs must successfully pass media-fill testing prior to initially compounding sterile products and semi-annually (within 6 months of the last testing). Persons performing low or medium-risk level CSPs must successfully pass media-fill testing prior to initially compounding sterile products and annually (within 12 months of the last testing). Persons who fail a media-fill test may not perform sterile compounding prior to retraining and receipt of a passing media-fill test.~~

~~Media fill testing should mimic the most challenging sterile compounding activity performed by those persons. Robust documentation regarding the media-fill testing process and individual~~

~~testing must be maintained which documents, at a minimum, the media growth to include lot and expiration date, number of days in incubator, incubator temperature, name of person being tested, dates testing performed, results of growth. Blanks in the form used to document media fill testing should be evaluated and corrected to ensure an accurate testing process.~~

~~Glove finger tip testing verifies the person can properly don gloves without contaminating them and is routinely disinfecting them. To improve compliance with required testing, pharmacists should consider performing media-fill testing and glove finger tip testing around the same time that environments are being certified. Employees who use isolators must also perform gloved fingertip sampling by donning sterile gloves within the ISO Class 5 main chamber and testing those gloves.~~

~~25. How often must air and surface sampling be performed?~~

~~USP requires air sampling to be performed at least every 6 months. Air sampling shall be conducted using volumetric air sampling equipment and the appropriate media (bacterial sampling for all risk levels and fungi sampling for high-risk level compounding operations). USP requires surface sampling to be performed "periodically". The Board advises that surface sampling should be performed at least quarterly. It may be performed by pharmacy personnel or outsourced.~~

~~26. What minimally should be taken into consideration when having primary and secondary engineering controls certified?~~

~~Certification and testing of primary (LAFWs, BSCs, CAIs and CACIs) and secondary engineering controls (buffer and ante areas) shall be performed by a qualified individual no less than every six months and whenever the device or room is relocated, altered, or major service to the facility is performed. Certification procedures such as those outlined in the CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006) shall be used. Pharmacists shall request written documentation from the certifying company explaining how the company's certifying processes fully comply with these standards. This shall include written acknowledgement that certification testing will be performed under dynamic conditions. Certifications issued shall specifically indicate the ISO standard for each primary and secondary engineering control and not simply indicate "passed".~~

~~27. What minimally should be taken into consideration when compounding multidose vials?~~

~~Currently USP Chapter <797> does not contain specific requirements for compounding multiple-dose containers, such as the need for a preservative, nor requirements for testing, labeling, and container closures for compounded multiple-dose containers. Chapter <797> references Chapter <51> for informational purposes as the source of the 28-day BUD after initially entering or opening a multiple-dose container, unless otherwise specified by the manufacturer.~~

~~28. What BUDs are recommended for non-sterile compounded products?~~

~~USP Chapter <795> makes the following recommendations for assigned BUDs of non-sterile compounded products:~~

~~**Nonaqueous formulations** – The BUD is not later than the time remaining until the earliest expiration date of any API or 6 months, whichever is earlier.~~
~~**Water-Containing Oral Formulations** – The BUD is not later than 14 days when stored at controlled cold temperatures.~~
~~**Water-Containing Topical/Dermal and Mucosal Liquid and Semisolid Formulations** – The BUD is not later than 30 days.~~

~~These maximum BUDs are recommended for nonsterile compounded drug preparations in the absence of stability information that is applicable to a specific drug or preparation. The BUD shall not be later than the expiration date on the container of any component.~~

~~29. May a non-sterile compounded product be assigned an extended BUD beyond the recommendations in USP Chapter <795>?~~

~~The Board advises that non-sterile compounded products should not be assigned an extended BUD unless the pharmacist maintains full documentation to justify the appropriateness of the extended BUD.~~

~~30. Under what conditions may a glove box be used to perform sterile compounding?~~

~~The glove box, referred to as an isolator (CAI/CACI) in Chapter <797>, must be placed in an ISO 7 buffer area UNLESS it meets all of the following conditions listed in USP Chapter 797:~~

- ~~The isolator shall 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 CSPs.~~
- ~~Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations.~~
- ~~Not more than 3520 particles (0.5 µm and larger) per m^3 shall be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing the transfer.~~[8]

~~It is incumbent upon the compounding personnel to obtain documentation from the manufacturer that the CAI/CACI will meet this standard when located in environments where the background particle counts exceed ISO Class 8 for 0.5-µm and larger particles. When isolators are used for sterile compounding, the recovery time to achieve ISO Class 5 air quality shall be documented and internal procedures developed to ensure that adequate recovery time is allowed after material transfer before and during compounding operations.~~

~~If the primary engineering control (PEC) is a CAI or CACI that does not meet the requirements above or is a LAFW or BSC that cannot be located within an ISO Class 7 buffer area, then only low-risk level nonhazardous and radiopharmaceutical CSPs pursuant to a physician order for a~~

~~specific patient may be prepared, and administration of the CSP shall commence within 12 hours of preparation or as recommended in the manufacturer's package insert, whichever is less.~~

~~The weighing of chemicals must occur in at least ISO Class 8 conditions. An isolator used to compound hazardous drugs (with exception of "low volume") must be located in a separate negative pressure room and exhausted outside.~~

~~31. May hazardous sterile products be compounded in the same hood as non-hazardous sterile drugs?~~

~~No. Hazardous sterile products may not be compounded in the same hood as non-hazardous CSPs.~~

~~32. Under what conditions may hazardous drugs be compounded in a cleanroom with positive air pressure?~~

~~USP allows a "low volume" of hazardous CSPs to be compounded in a cleanroom with positive air pressure, however, USP does not currently define the term "low volume". The "low volume" hazardous CSPs must be compounded under two tiers of containment, the isolator or biologic safety cabinet and closed system transfer device.~~

4~~33~~. Must a compounding pharmacy using Schedule II powders comply with the perpetual inventory requirements of Regulation 18VAC110-20-240?

Yes.

~~34. Must bladder irrigation fluids and irrigations for wounds be prepared in a sterile manner in compliance with USP-NF requirements?~~

~~Yes.~~

~~35. In addition to bladder irrigation and irrigations for wounds, what other types of drugs must be prepared in a sterile manner in compliance with USP-NF requirements?~~

~~USP Chapter <797> states that for the purposes of the chapter, a compounded sterile product includes any of the following: compounded biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals, including but not limited to the following dosage forms that must be sterile when they are administered to patients: aqueous bronchial and nasal inhalations for the lungs, baths and soaks for live organs and tissues, injections (e.g., colloidal dispersions, emulsions, solutions, suspensions), irrigations for wounds and body cavities, ophthalmic drops and ointments, and tissue implants. Note: Nasal sprays and irrigations for the nasal passages may be prepared as non-sterile compounds.~~

5~~36~~. May a pharmacist provide a compounded drug to another pharmacy or veterinarian who will then dispense the drug to his client?

No. Va Code §54.1-3410.2 indicates pharmacists shall not distribute compounded drug products for subsequent distribution or sale to other persons or to commercial entities, including distribution to pharmacies or other entities under common ownership or control with the facility in which such compounding takes place.

VA Code §54.1-3410.2 does authorize pharmacists to provide compounded drug to practitioners of medicine, osteopathy, podiatry, dentistry, or veterinary medicine to administer to their patients in the course of their professional practice, either personally or under their direct and immediate supervision. The compounded drug must be labeled with (i) the statement "For Administering in Prescriber Practice Location Only"; (ii) the name and strength of the compounded medication or list of the active ingredients and strengths; (iii) the facility's control number; (iv) an appropriate beyond-use date as determined by the pharmacist in compliance with USP-NF standards for pharmacy compounding; and (v) quantity.

6~~37~~. May a prescriber or patient obtain a patient-specific compounded sterile product from an out-of-state pharmacy that is not registered by the Virginia Board of Pharmacy as a nonresident pharmacy?

No, only nonresident pharmacies registered by the Virginia Board of Pharmacy may ship compounded sterile products into Virginia. Verification of registration may be determined at https://dhp.virginiainteractive.org/Lookup/Index~~t~~
~~https://secure01.virginiainteractive.org/dhp/cgi-bin/search_publicdb.cgi~~ by searching the business name and choosing the occupation of "non-resident pharmacy".

7. May a pharmacy or prescriber obtain a compounded sterile product from an out-of-state outsourcing facility that is not registered by the Virginia Board of Pharmacy as a nonresident outsourcing facility?

No, only nonresident outsourcing facilities registered by the Virginia Board of Pharmacy may ship compounded sterile products into Virginia. Verification of registration may be determined at https://dhp.virginiainteractive.org/Lookup/Index by searching the business name and choosing the occupation of "nonresident outsourcing facility".

~~***38. What risk-level is associated with repackaging an undiluted multi-dose vial?***~~

~~The repackaging of an undiluted multi-dose vial, e.g., insulin, into multiple syringes is a medium-risk level manipulation when puncturing the vial more than 3 times. Note: this guidance addresses repackaging, not administration.~~

~~***39. May a microbiological method alternative to compendial methods be used?***~~

~~Regarding sterility testing, USP Chapter <797> states, "The *Membrane Filtration* method is the method of choice where feasible (e.g., components are compatible with the membrane). A method not described in the *USP* may be used if verification results demonstrate that the alternative is at least as effective and reliable as the *USP Membrane Filtration* method or the *USP Direct Inoculation of the Culture Medium* method where the *Membrane Filtration* method~~

is not feasible." Additionally, USP General Chapter <1223> "provides guidance on the selection, evaluation, and use of microbiological methods as alternatives to compendial methods. To properly implement alternative methods, one must consider a number of important issues before selecting the analytical technology and qualifying that method with the actual product. These issues include, but are not limited to, identification of suitable alternative methodology, development of user specifications for equipment selection, demonstration of the applicability of the method as a replacement for a standard compendial method, and qualification of the method in the laboratory…..*General Notices and Requirements* in the *USP* states, "Alternative methods and/or procedures may be used if they provide advantages in terms of accuracy, sensitivity, precision, selectivity, or adaptability to automation or computerized data reduction, or in other special circumstances." General Chapter <1223> also makes reference to 21 CFR Part 211.194 stating, "This subsection of the regulations also recognizes the legal basis of *USP* and the *National Formulary (NF)* standards and makes it clear that it is the responsibility of the user to validate methods or procedures that differ from those standardized in the compendia." Refer to *USP* for additional guidance.

40. Does the December 1, 2019 official date of <800> impact my current or early adoption of the general chapter?

Per USP, no. USP encourages adoption and implementation of General Chapter <800> to help ensure a quality environment and protection of healthcare workers and patients when hazardous drugs are handled.

41. How do I adopt USP General Chapter <800> if sections are not harmonized with USP General Chapter <797>?

Per USP, two sections that are not harmonized between the two chapters are: Segregated Compounding Area and 'Low volume' hazardous drug compounding. Below please find guidance on how to adopt USP <800> until the revised USP <797> is published.

Segregated Compounding Area (SCA)

- USP <797> only allows low-risk level nonhazardous and radiopharmaceutical Compounded Sterile Preparations (CSPs) with 12 hour or less beyond-use date (BUD) to be prepared in an unclassified segregated compounding area (SCA).
- USP <800> allows low and medium risk level hazardous drug CSPs to be prepared in an unclassified containment segregated compounding area (C-SCA). The C-SCA is required to have fixed walls, be externally vented with 30 ACPH and have a negative pressure between 0.01 and 0.03 inches of water column relative to the adjacent areas.
- Note the differences in terminology and requirements in the SCA in USP <797> and C-SCA in <800>.
    - For early adoption of <800>, low- and medium- risk level HDs may be prepared in a C-SCA provided it meets the requirements in the chapter and the CSP is assigned a BUD of 12 hours or less.

- For facilities that have not yet adopted <800>, the standards in USP <797> would apply. Only low-risk level nonhazardous and radiopharmaceutical CSPs with 12 hour or less BUD may be prepared in a SCA.

-

~~"Low volume" hazardous drug compounding~~

- ~~USP <797> allows facilities that prepare a "low volume" of HDs to compound these drugs in a non-negative pressure room if "two tiers of containment (e.g., CSTD within a BSC or CACI that is located in a non-negative pressure room)" are used.~~
- ~~USP <800> requires facilities that prepare HDs to have a containment secondary engineering control (C-SEC) that is externally vented, physically separated, have appropriate air exchange, and have a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas.~~
- ~~For early adoption of <800>, HDs must be prepared in a C-SEC meeting the requirements in the chapter.~~
- ~~For facilities that have not yet adopted <800>, the standards in <797> would apply. Facilities preparing a low volume of HDs may continue to compound these CSPs outside a negative pressure room if two tiers of containment (e.g., CSTD within a BSC or CACI that is located in a non-negative pressure room)" are used.~~

~~42. What are the hazardous drugs (HD) that USP Chapter <800> oversees?~~

~~Refer to the most current National Institute for Occupational Safety and Health (NIOSH) list at www.cdc.gov. Note: Chapter <800> defines HDs are those on the NIOSH list, not the EPA hazardous materials list. Some drugs on the Environmental Protection Agency (EPA) list may not be on the NIOSH list, e.g., epinephrine.~~

~~43. In general, how are drugs grouped within the NIOSH list?~~

~~Hazardous drugs are categorized into three tables:~~

- ~~Antineoplastic drugs, e.g., cisplatin, methotrexate~~
- ~~Non-antineoplastic drugs, e.g., carbamazepine, estrogen/progesterone combinations~~
- ~~Non-antineoplastic drugs that have adverse reproductive effects, e.g., temazepam, warfarin~~
- ~~***What drugs MUST comply with all USP Chapter <800> containment requirements?***~~
- ~~Drugs on the NIOSH list that will be involved in compounding must follow the requirements in this chapter include:~~
- ~~Any HD active pharmaceutical ingredient (API) on any of the three tables, and~~
- ~~Any antineoplastic requiring manipulation other than counting or repackaging.~~
- ~~***How should a pharmacist determine how to comply with 800?***~~
- ~~Pharmacists should ask themselves the following questions, at a minimum:~~
- ~~Do I perform nonsterile or sterile compounding? If no compounding is performed, then the requirements of chapter <800> are recommended, but not required.~~

- ~~What drugs do I receive, store, dispense that are deemed hazardous pursuant to the NIOSH list and are used in compounding products? If no hazardous drugs are used in compounding, then the requirements of chapter <800> are recommended, but not required.~~
- ~~If hazardous drugs are used in compounding, then:~~
  - ~~Must those drugs comply with all containment requirements or do some qualify for performing an assessment of risk?~~
  - ~~What changes will I need to make to my facility in order to comply with Chapter <800>?~~
  - ~~What personnel training is needed to meet compliance?~~
  - ~~What cleaning processes must be implemented or changed to meet compliance?~~
  - ~~What activities do I perform with these hazardous drugs, e.g., compounding, administration, etc.?~~

~~46. If the pharmacy does not compound with hazardous drugs, but does split tablets of hazardous drugs, must the pharmacy comply with the requirements of Chapter <800>?~~

~~No. <795> states that splitting tablets is out of the scope of the chapter:~~

~~**Splitting tablets:** Breaking or cutting a tablet into smaller portions is not required to meet the standards in this chapter.~~

~~Thus, while <800> may speak about splitting tablet, it is not "compendially applicable" since it is not in scope of <795>.~~

~~47. If it is determined that the pharmacy stocks HDs, what options exist for the pharmacy?~~

~~The pharmacy may treat all dosage forms of all HDs that are used in compounding products the same and follow all containment requirements in Chapter <800> or it may perform an assessment of risk to identify and use alternative containment strategies and/or work practices for specific dosage forms of HDs that are not antineoplastic agents or not API.~~

~~48. What hazardous drugs may be considered during an assessment of risk?~~

- ~~Antineoplastics that only need to be counted or packaged~~
- ~~Non-antineoplastics~~
- ~~Reproductive-only hazards~~

~~49. What should be considered, at a minimum, during an assessment of risk?~~

- ~~Type of HD, dosage form, risk of exposure, packaging, manipulation to be performed~~
- ~~Alternative containment strategies and/or work practices should be documented~~
- ~~The assessment of risk shall be reviewed every 12 months and documented.~~

~~50. What minimal questions and/or information will an inspector for the Board of Pharmacy be asking during an inspection? Note: Refer to page 1 regarding enforcement of Chapter <800>.~~

- ~~Does the pharmacy perform sterile or non-sterile compounding?~~
- ~~Does the pharmacy stock HDs that are used in compounding products? The list of HDs that are used in compounding products that the pharmacy stocks must be provided for inspector review.~~
- ~~Are all HDs that are used in compounding products contained in a manner consistent with USP Chapter <800> or was an assessment of risk performed to identify and use alternative containment strategies and/or work practices for specific dosage forms of HDs that are not antineoplastic agents or not API. The assessment of risk must be provided for inspector review.~~
- ~~Who is the 'designated person' for the pharmacy who is responsible for the continuing to evaluate the fundamental practices and precautions for handling HDs?~~
- ~~Documentation of required training.~~
- ~~Appropriate personnel equipment.~~
- ~~Appropriate engineering controls.~~
- ~~Standard operating procedures for safe handling of HDs that are used in compounding products for all situations in which the HDs are used throughout the facility.~~

***~~51.~~* ~~What does USP Chapter <800> list as the general engineering control requirements for performing non-sterile HD compounding?~~**

~~Table 2. Engineering Controls for Nonsterile HD Compounding~~

~~Containment Primary Engineering Control (C-PEC)~~	~~Containment Secondary Engineering Control (C-SEC)~~
~~Externally vented (preferred) or redundant-HEPA filtered in series~~ ~~Examples: CVE, Class I or II BSC, CACI~~	~~Externally vented~~ ~~12 air changes per hour (ACPH)~~ ~~Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas~~ ~~Fixed walls~~

~~52. What does USP Chapter <800> list as the general engineering control requirements for performing sterile HD compounding?~~

~~Table 3. Engineering Controls for Sterile HD Compounding~~

~~Configuration~~	~~C-PEC~~	~~C-SEC~~	~~Maximum BUD~~
~~ISO Class 7 buffer room with an ISO Class 7 ante-room~~	~~Externally vented~~ ~~Examples: Class II BSC or CACI~~	~~Externally vented~~ ~~30 air changes per hour-ACPH~~ ~~Negative pressure between 0.01 and 0.03 inches of~~	~~As described in (797~~

		water colum relative to adjacent areas	
Unclassified C-SCA	• Externally vented • Examples: Class II BSC or CACI	• Externally vented • 12 ACPH • Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas	As described in (797) for CSPs prepared in a segregated compounding area

53. Where may a list of recommended personal protective equipment by type of drug formulation and engineering controls for working with HDs in a healthcare setting be found?

Table 5 of the NIOSH list.

54. Regarding the Segregated Compounding Area (SCA) definition, Chapter <797> states an SCA may be a designated space, room or demarcated area. Chapter <800> states SCA requires fixed walls and removes the "space or demarcated area". Please clarify the Board's expectations on this issue.

Per USP, please note the differences in terminology in <797> and <800>. General Chapter <800> specifies that this is a containment segregated compounding area (C-SCA). For hazardous drug compounding, the C-SCA must have fixed walls. For nonhazardous drug sterile compounding, the SCA may be in an unclassified area (and not necessarily have fixed walls). For the C-SCA, fixed are also necessary to maintain negative pressure.

55. Regarding low-risk level compounding with 12 hour or less beyond use dating (hood within a non-ISO Class 7 area), Chapter <797> states that this configuration does not allow hazardous compounding. Chapter <800> states that it is allowed, but only low and medium risk HDs may be prepared and beyond use dating (BUD) that cannot exceed <797> for being prepared in a SCA. Please clarify the Board's understanding on this issue.

Per USP, the intent of <800> is to apply a 12-hour or less BUD to low- and medium- risk level compounded sterile products prepared in a containment segregated compounding area (C-SCA). USP is aware of the conflict and is in the process of revising <797> to align with the requirements in <800>.

56. Chapter <797> also allows for placement of an isolator outside of an ISO Class 7 buffer room with meeting of specification requirements and allowance of full BUD. Chapter <800> states if the containment primary engineering control (C-PEC) is placed in a containment segregated compounding area (C-SCA), then the BUD of all compounded sterile products must be limited as described in <797>. Again, Chapter <797> states that this configuration does not allow hazardous compounding. Please clarify the Board's understanding on this issue.

~~Per USP, the intent of <800> is to apply a 12-hour or less BUD to low- and medium- risk level compounded sterile products prepared in a C-SCA. USP is aware of the conflict and is in the process of revising <797> to align with the requirements in <800>.~~

~~57. With the implementation of Chapter <800>, will USP continue to allow compounding aseptic isolators (CAI) placed outside of a classified area to be used to compound sterile products and assigned a full BUD as authorized in <797>?~~

~~Yes, Chapter <797> still allows for a compounding aseptic isolator (CAI) placed outside of a classified area to be used to compound sterile products and assigned the full storage period BUD provided the conditions specified in the chapter are met. Note, for compounding sterile hazardous drugs, the compounding aseptic containment isolator (CACI) must be placed in a negative pressure containment secondary engineering control (C-SEC) with adequate air changes per hour (ACPH).~~

~~58. Does Chapter <800> recommend wipe sampling and medical surveillance?~~

~~Yes, Chapter <800> states that "environmental wipe sampling for HD surface residue should be performed routinely." Medical surveillance is also a recommendation of the chapter. The chapter states that "healthcare workers who handle HDs as a regular part of their job assignment should be enrolled in a medical surveillance program." Note, both of these issues are recommendations of Chapter <800> and not a requirement.~~

~~59. USP <797> and USP <800> recommend the use of closed-system drug-transfer devices (CSTD). Is there guidance on the proper evaluation of the available technologies?~~

~~USP currently recommends the use of CSTDs for compounding HDs. Per USP, it is not a requirement as there is no published universal performance standard for evaluation of CSTD containment. NIOSH is currently working on developing such a protocol.~~

~~60. Is a line of demarcation for doffing personal protective equipment (PPE) required for all hazardous containment secondary engineering controls?~~

~~USP <800> *requires* a doffing area if the negative-pressure hazardous drug (HD) buffer room is entered through the positive-pressure non-hazardous drug buffer room. Additionally, it states a designated doffing area *should* be indicated within all containment secondary engineering controls (C-SEC). Other than the line of demarcation mentioned in section 5.3.2, General Chapter <800> does not specify where doffing should occur. However, this is entity dependent and should additionally follow garbing requirements in <797>.~~

~~61. USP <800>, within Section 5.3, indicates that an eyewash station and/or other emergency or safety precautions that meet applicable laws and regulations must be readily available. Are there applicable laws and regulations in Virginia regarding eyewash stations and/or other emergency or safety precautions?~~

~~The Board is not currently aware of laws and regulations in Virginia related to use of eyewash stations or other safety precautions related to this issue.~~

~~62. May a laminar airflow workbench (LAFW) or a compounding aseptic isolator (CAI) be used for compounding with an antineoplastic hazardous drug (HD)?~~

~~No.~~

~~63. Is it required to compound all sterile hazardous drugs within an externally vented containment primary engineering control (biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI))?~~

~~No, dosage forms of non-antineoplastic and reproductive risk hazardous drugs may be handled and compounded under an assessment of risk. If, however, bulk active pharmaceutical ingredients (API) of these drugs are used as starting ingredients, all of the containment requirements in <800> would apply. Refer to Box 1 within USP Chapter <800>.~~

~~64. What are the specifications required of a pass through chamber? Is it required be interlocking and HEPA filtered purged? Between what areas may these chambers be utilized?~~

~~General Chapter <800> defines a pass-through as "an enclosure with interlocking doors that is positioned between two spaces for the purpose of reducing particulate transfer while moving materials from one space to another. A pass-through serving negative pressure rooms needs to be equipped with sealed doors. The chapter does not require the pass-through to be HEPA filter purged and does not limit where these pass-throughs may be placed. General Chapter <800> additionally states that refrigerator pass-throughs must not be used.~~

~~65. Chapter <800> states sterile and nonsterile HDs may be stored together, but HDs used for nonsterile compounding should not be stored in areas designated for sterile compounding to minimize traffic into the sterile compounding area. What is the intent of this statement?~~

~~The intent of prohibiting the storage of nonsterile compounding materials in sterile compounding areas is to minimize traffic flow into the sterile classified areas.~~

~~66. May bulk active pharmaceutical ingredients (API) used for sterile compounding be stored in the negative pressure C-SEC?~~

~~Yes. Refer also to USP's frequently asked question #16 found at http://www.usp.org/frequently-asked-questions/hazardous-drugs-handling-healthcare-settings~~

~~67. Where must manipulation of non-sterile, non-antineoplastic and reproductive risk hazardous drugs (that are not bulk active pharmaceutical ingredients (API)) occur?~~

~~The location where manipulation occurs should follow an assessment of risk for non-antineoplastic and reproductive risk hazardous drugs (that are not bulk APIs). Facilities should determine their own strategies based on its assessment of risk.~~

~~68. Does Chapter <800> address whether scrubs that are worn within the hazardous compounding/storage area may be allowed to be taken home?~~

~~No. General Chapter <800> does not specify best practices for clothing under the gown. However, section 7.2 does require gowns to be disposable and shown to resist permeability by HDs.~~

~~69. What is the best practice for receiving hazardous drugs (HD)?~~

~~USP <800>, within Section 5.1, states antineoplastic HDs and all HD active pharmaceutical ingredients (API) must be unpacked (i.e., removal from external shipping containers) in an area that is neutral/normal or negative pressure relative to the surrounding areas. HDs must not be unpacked from their external shipping containers in sterile compounding areas or in positive pressure areas. Best practice is to unpack the hazardous drugs from the delivery tote, and leave packaged in a zip-locked plastic bag. From there, the unopened plastic bags should be moved to HD storage room, where the HDs can be removed from the bags and received into inventory. HDs should never be withdrawn from the plastic transport bags in any room other than the HD storage room.~~

~~70. If the C-PEC vents externally and the room is able to maintain appropriate negative pressure and air exchanges, does the C-SEC need to be vented?~~

~~No.~~

~~For more information regarding USP Chapter <800>, an extensive list of frequently asked questions published by USP may be accessed at http://www.usp.org/frequently-asked-questions/hazardous-drugs-handling-healthcare-settings.~~

Virginia Board of Pharmacy
Pharmacy Inspection Deficiency Monetary Penalty Guide

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
1. No Pharmacist-in-Charge or Pharmacist-in-Charge not fully engaged in practice at pharmacy location	54.1-3434 and 18VAC110-20-110	must have documentation	2000
2. Pharmacist-in-Charge in place, inventory taken, but application not filed with Board within the required timeframe	54.1-3434 and 18VAC110-20-110		1000
3. Unregistered persons performing duties restricted to pharmacy technician without first becoming registered as a pharmacy technician trainee	54.1-3321 and 18VAC110-20-111	per individual	First documented occurrence = no penalty Repeat = $ penalty 250
4. Pharmacists/pharmacy technicians/pharmacy interns/pharmacy technician trainees performing duties on an expired license/registration	18VAC110-21-60, 18VAC110-21-110, 18VAC110-21-141, and 18VAC110-21-170.	per individual	First documented occurrence = no penalty Repeat = $ penalty 100

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
5. Pharmacy technicians, pharmacy interns, or pharmacy technician trainees performing duties without monitoring by a pharmacist, or unlicensed persons engaging in acts restricted to pharmacists	54.1-3320 18VAC110-20-112		500
6. Exceeds pharmacist to pharmacy technician ratio	54.1-3320 18VAC110-20-112	per each technician over the ratio	First documented occurrence = no penalty Repeat = $ penalty 100
7. Change of location or remodel of pharmacy without submitting application or Board approval	18VAC110-20-140	must submit an application and fee	250
8. Refrigerator/freezer temperature out of range greater than +/- 4 degrees Fahrenheit.	18VAC110-20-150 and 18VAC110-20-10	determined using inspector's or pharmacy's calibrated thermometer	First documented occurrence = no penalty; drugs may be embargoed Repeat = $ penalty 100 Drugs may be embargoed
9. The alarm is not operational. The enclosure is not locked at all times when a pharmacist is not on duty. The alarm is not set at all times when the pharmacist is not on duty.	18VAC110-20-180 and 18VAC110-20-190		1000

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
9a. Alarm incapable of sending an alarm signal to the monitoring entity when breached if the communication line is not operational. Alarm is operational but does not fully protect the prescription department and/or is not capable of detecting breaking by any means when activated. The alarm system does not include a feature by which any breach shall be communicated to the PIC or a pharmacist working at the pharmacy.	18VAC110-20-180		250
10. Unauthorized access to alarm or locking device to the prescription department	18VAC110-20-180 and 18VAC110-20-190		1000
11. Insufficient enclosures or locking devices.	18VAC110-20-190		First documented occurrence and no drug loss = no penalty Drug loss or repeat = $ penalty 500
12. Storage of prescription drugs not in the prescription department	18VAC110-20-190		500

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
12a. Schedule II drugs are not dispersed with other schedules of drugs or maintained in a securely locked cabinet, drawer, or safe, or maintained in a manner that combines the two methods.	18VAC110-20-200		First documented occurrence and no drug loss of Schedule II = no penalty Drug loss or repeat = $ penalty 250
13. No biennial inventory, or over 30 days late, or substantially incomplete, i.e., did not include all drugs in Schedules II-V.	54.1-3404 and 18VAC110-20-240	Cite Deficiency 113 if only expired drugs not included in inventory.	Over 30 days late and first documented occurrence = no penalty Over 30 days late and repeat = $ penalty 500
14. No incoming change of Pharmacist-in-Charge inventory, inventory taken or over 5 days late, or substantially incomplete, i.e., did not include all drugs in Schedules II-V	54.1-3434 and 18VAC110-20-240	Per occurrence. Cite Deficiency 113 if only expired drugs not included in inventory.	500

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
15. Perpetual inventory not being maintained as required as it does not: • Include all Schedule II drugs received or dispensed; • Accurately indicate the physical count of each Schedule II drug "on-hand" at the time of performing the inventory; • Include a reconciliation of each Schedule II drug at least monthly; or • Include a written explanation of any difference between the physical count and the theoretical count. Monthly perpetual inventory is performed more than 7 days prior or more than 7 days after designated calendar month for which an inventory is required.	18VAC110-20-240	Review 10 drugs for six consecutive months. Includes expired drugs. Deficiency if more than 5 drugs not compliant.	250
16. Theft/unusual loss of drugs not reported to the Board as required	54.1-3404 and 18VAC110-20-240	per report/theft-loss	250
17. Hard copy prescriptions not maintained or retrievable as required (i.e. hard copy of fax for Schedule II, III, IV & V drugs and refill authorizations)	54.1-3404 and 18VAC110-20-240		250
18. Records of dispensing not maintained as required	54.1-3404, 18VAC110-20-240, 18VAC110-20-250, 18VAC110-20-420, and 18VAC110-20-425		250

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
19. Pharmacists not verifying or failing to document verification of accuracy of dispensed prescriptions	18VAC110-20-270, 18VAC110-20-420 and 18VAC110-20-425	10% threshold for documentation	500
20. Pharmacist not checking and documenting repackaging or bulk packaging	54.1-3410.2, 18VAC110-20-355 and 18VAC110-20-425	Review all entries for 5 drugs for six consecutive months. Deficiency if 10% or more are not compliant.	250
20a. Pharmacist not documenting verification of accuracy of non-sterile compounding process and integrity of compounded products	54.1-3410.2, 18VAC110-20-355	10% threshold	500
20b. Pharmacist not documenting verification of accuracy of sterile compounding process and integrity of compounded products	54.1-3410.2, 18VAC110-20-355		5000
21. No clean room	54.1-3410.2		10000
21a. Performing sterile compounding outside of a clean room.	54.1-3410.2	Compliant clean room present but not utilized for preparation of compounded sterile drug products.	3000

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
21b. Presterilization procedures for Category 2 or Category 3~~high-risk level~~ CSPs, such as weighing and mixing, are completed in areas not classified as ISO Class 8 or better.	54.1-3410.2		500
22. Certification of the direct compounding area (DCA) for compounded sterile preparations indicating ISO Class 5 not performed by a qualified individual no less than every 6 months,~~ and~~ whenever there are changes to the area such as redesign, construction, replacement or relocation of any PEC, or alteration in the configuration of the room that could affect airflow or air quality, ~~the device or room is relocated, altered, or major service to the facility is performed.~~and/or certification does not include airflow testing, HEPA filter integrity testing, total particle count testing, and dynamic airflow smoke pattern test.	54.1-3410.2	Review 2 most recent reports; certification must be performed no later than the last day of the sixth month from the previous certification	3000

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
23. Certification of the buffer or clean room and ante room indicating ISO Class 7 / ISO Class 8 or better not performed by a qualified individual no less than every six months, ~~and~~ whenever there are changes to the area such as redesign, construction, replacement or relocation of any PEC, or alteration in the configuration of the room that could affect airflow or air quality, ~~the device or room is relocated, altered, or major service to the facility is performed.~~and/or certification does not include airflow testing, HEPA filter integrity testing, total particle count testing, and dynamic airflow smoke pattern test.	54.1-3410.2	Review 2 most recent reports; certification must be performed no later than the last day of the sixth month from the previous certification	1000
24. Sterile compounding of hazardous drugs performed in an area not physically separated from other preparation areas	54.1-3410.2		2000
25. No documentation of sterilization methods or endotoxin ~~pyrogen~~ testing for ~~high risk level~~Category 2 CSPs ~~compounded sterile preparations~~ and/or ~~high risk~~Category 3 CSPs ~~compounded sterile preparations~~ assigned inappropriate beyond use date (BUD)	54.1-3410.2		5000

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
25a. No documentation of initial and at least every ~~semi-annual (6~~3 months~~)~~ media-fill testing or gloved fingertip testing for persons performing compounding of ~~high-risk level~~Category 3 CSPs ~~compounding of sterile preparations~~.	54.1-3410.2	Review 2 most recent reports. Media-fill testing and gloved fingertip testing must be performed no later than the last day of the ~~sixth~~third month from the date the previous media-fill test and gloved fingertip testing was initiated.*	5000
25b. ~~High-risk~~Category 3 compounded sterile preparations intended for use are improperly stored	54.1-3410.2		5000
25c. Documentation that a person who failed a media-fill test or gloved fingertip test has performed ~~high-risk level~~ compounding of Category 3 CSPs~~sterile preparations~~ after receipt of the failed test result and prior to retraining and receipt of passing media-fill and gloved fingertip test	54.1-3410.2		5000

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
26. No documentation of initial and at least every ~~annual (12~~6 months~~)~~ media-fill testing or gloved fingertip testing for persons performing ~~low and medium-risk level~~ compounding of Category 1 and Category 2 CSPs ~~sterile preparations~~.	54.1-3410.2	Review 2 most recent reports. Media-fill testing and gloved finger-tip testing must be performed no later than the last day of the ~~twelfth~~sixth month from the date the previous media-fill test and gloved fingertip testing was initiated.*	500
26a. Documentation that a person who failed a media-fill test or gloved fingertip test has performed ~~low or medium risk level~~ compounding of Category 1 or Category 2 CSPs~~sterile preparations~~ after receipt of the failed test result and prior to retraining and receipt of passing media-fill and gloved fingertip test	54.1-3410.2		500
27. Compounding using ingredients in violation of 54.1-3410.2.	54.1-3410.2		1000

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
28. Compounding copies of commercially available products	54.1-3410.2	per Rx dispensed up to maximum of 100 RX or $5000	50
29. Unlawful compounding for further distribution by other entities	54.1-3410.2		500
30. Security of after-hours stock not in compliance	18VAC110-20-450		First documented occurrence and no drug loss = no penalty Drug loss or repeat = $ penalty 500
31. Drugs removed and administered to a patient from an automated dispensing device in a nursing home prior to review of the order and authorization by a pharmacist.	18VAC110-20-555	Except for drugs that would be stocked in an emergency drug kit as allowed by 18VAC110-20-555 (3)(C)	First documented occurrence and no known patient harm = no penalty Repeat = $ penalty 250
32. Have clean room, but not all physical standards in compliance, e.g., flooring, ceiling	54.1-3410.2		2000
33. ~~Low or medium risk~~Category 1 or Category 2 CSPs ~~compounded sterile preparations~~ assigned inappropriate beyond use date (BUD)	54.1-3410.2		1000
34. Combined with Deficiency 142 – 12/2013.			

Deficiency	Law/Reg Cite	Conditions	$ Monetary Penalty
35. Schedule II through VI drugs are being purchased from a wholesale distributor or warehouse not licensed or registered by the board or from another pharmacy in a non-compliant manner	18VAC110-20-395		250

Other Deficiencies

If five (5) or more deficiencies in this category are cited, a $250 monetary penalty shall be imposed. Another $100 monetary penalty will be added for each additional deficiency cited in this category, over the initial five.

Deficiency	Law/Regulation Cite	Conditions
101. Repealed 6/2011		
102. Special/limited-use scope being exceeded without approval	18VAC110-20-120	
103. Repealed 12/2013		
104. Sink with hot and cold running water not available within the prescription department.	18VAC110-20-150	
105. No thermometer or non-functioning thermometer in refrigerator/freezer, but temperature within range, +/-4 degrees Fahrenheit. Temperature not being recorded daily or record of such not maintained properly.	18VAC110-20-150 and 18VAC110-20-10	determined using inspector's calibrated thermometer
106. Prescription department substantially not clean and sanitary and in good repair	18VAC110-20-160	must have picture documentation

Deficiency	Law/Regulation Cite	Conditions
107. Current dispensing reference not maintained	18VAC110-20-170	
108. Emergency access alarm code/key not maintained in compliance	18VAC110-20-190	
109. Expired drugs in working stock, dispensed drugs being returned to stock not in compliance, dispensed drugs returned to stock container or automated counting device not in compliance. (i.e. appropriate expiration date not placed on label of returned drug, mixing lot numbers in stock container)	54.1-3457 18VAC110-20-200 18VAC110-20-355	10% threshold
110. Storage of paraphernalia/Rx devices not in compliance	18VAC110-20-200	

Deficiency	Law/Regulation Cite	Conditions
111. Storage of prescriptions awaiting delivery outside of the prescription department not in compliance	18VAC110-20-200	
112. Biennial taken late but within 30 days	54.1-3404 and 18VAC110-20-240	
113. Inventories taken on time, but not in compliance, i.e., no signature, date, opening or close, Schedule II drugs not separate, failure to include expired drugs.	54.1-3404, 54.1-3434 and 18VAC110-20-240	
114. Records of receipt (e.g. invoices) not on site or retrievable	54.1-3404 and 18VAC110-20-240	
115. Other records of distributions not maintained as required	54.1-3404 and 18VAC110-20-240	
116. Prescriptions do not include required information. Prescriptions not transmitted as required (written, oral, fax, electronic, etc.)	54.1-3408.01, 54.1-3408.02, 54.1-3410, 18VAC110-20-280 and 18VAC110-20-285 18VAC110-20-270	10% threshold
117. Deficiency 117 combined with Deficiency 116 – 6/2011		
118. Schedule II emergency oral prescriptions not dispensed in compliance	54.1-3410 and 18VAC110-20-290	>3
119. Not properly documenting partial filling of prescriptions	54.1-3412, 18VAC110-20-255,18VAC110-20-310, and 18VAC110-20-320	
120. Offer to counsel not made as required	54.1-3319	

Deficiency	Law/Regulation Cite	Conditions
121. Prospective drug review not performed as required	54.1-3319	
122. Engaging in alternate delivery not in compliance	18VAC110-20-275	
123. Engaging in remote processing not in compliance	18VAC110-20-276 and 18VAC110-20-515	
124. Labels do not include all required information	54.1-3410, 54.1-3411 and 18VAC110-20-330	10% Threshold Review 25 prescriptions
125. Compliance packaging or labeling does not comply with USP-NF standards for customized patient medication packages	18VAC110-20-340	
126. Special packaging not used or no documentation of request for non-special packaging	54.1-3426, 54.1-3427 and 18VAC110-20-350	10% threshold Review 25 prescriptions
127. Repackaging records and labeling not kept as required or in compliance	18VAC110-20-355	10% threshold
128. Unit dose procedures or records not in compliance	18VAC110-20-420	
129. Robotic pharmacy systems not in compliance	18VAC110-20-425	
130. Required compounding/dispensing/distribution records not complete and properly maintained	54.1-3410.2	
130a Compounded products not properly labeled	54.1-3410.2	

Deficiency	Law/Regulation Cite	Conditions
131. Required "other documents" for USP-NF 797 listed on the pharmacy inspection report are not appropriately maintained	54.1-3410.2	
132. Personnel preparing compounded sterile preparations and/or who have direct oversight of compounding personnel, but do not compound, do not comply with cleansing and garbing requirements	54.1-3410.2	
133. Compounding facilities and equipment used in performing non-sterile compounds not in compliance with 54.1-3410.2	54.1-3410.2	
134. Policies and procedures for proper storage, security and dispensing of drugs in hospital not established or assured	18VAC110-20-440	
135. Policies and procedures for drug therapy reviews not maintained or followed	18VAC110-20-440	
136. After hours access to a supply of drugs or -records not in compliance	18VAC110-20-450	10% threshold
137. Floor stock records not in compliance, pharmacist not checking, required reconciliations not being done	18VAC110-20-460	10% threshold
138. Automated dispensing device loading, records, and monitoring/reconciliation not in compliance	54.1-3434.02, 18VAC110-20-490 and 18VAC110-20-555	Cite if no documentation of monitoring. Review ADD in areas that do not utilize patient specific profile. Review 3 months of records – 30% threshold. Cite if exceeds threshold. Describe in comment section steps pharmacy is taking to comply. Educate regarding requirements.

Deficiency	Law/Regulation Cite	Conditions
139. Emergency medical services procedures or records not in compliance	18VAC110-20-500	10% threshold
140. Emergency kit or stat-drug box procedures or records not in compliance	18VAC110-20-540 and 18VAC110-20-550	10 % threshold
141. Maintaining floor stock in a long-term care facility when not authorized	18VAC110-20-520 and 18VAC110-20-560	
142. No record maintained and available for 12 months from date of analysis of dispensing errors or submission to patient safety organization	18VAC110-20-418	
143. Repealed 6/21/2018		
144. Repealed 6/21/2018		
145. Repealed 6/21/2018		
146. Repealed 6/21/2018		
147. Particle counts, environmental sampling, and smoke pattern testing not performed under dynamic conditions.	54.1-3410.2	
148. Theft/unusual loss of drugs reported to board but report not maintained by pharmacy	54.1-3404 and 18VAC110-20-240	

NOTE: A "repeat" deficiency is a deficiency that was cited during the routine or focused inspection performed immediately prior to the current routine inspection and after July 1, 2018.

Examples:
Routine inspection on 7/1/18 – Cited for Deficiency 3. No monetary penalty.
Routine inspection on 7/1/20. Cited for Deficiency 3. Monetary penalty.

Routine inspection on 7/1/18 – Cited for deficiency 3. No monetary penalty.
Routine inspection on 7/1/20 – No deficiency.
Routine inspection on 7/1/22 – Cited for deficiency 3. No monetary penalty.
Routine inspection on 7/1/24 – Cited for deficiency 3. Monetary penalty.

Agenda Topic: Discuss monetary penalties in Guidance Document 110-9 as compared to other states.

Included in Agenda Packet:

- Guidance Document 110-9 revised March 30, 2023 and under Administrative Review
- Fees provided by the District of Columbia, Tennessee, and Pennsylvania

Action Needed:

- Discussion

Virginia Board of Pharmacy
Pharmacy Inspection Deficiency Monetary Penalty Guide

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
1. No Pharmacist-in-Charge or Pharmacist-in-Charge not fully engaged in practice at pharmacy location	54.1-3434 and 18VAC110-20-110	must have documentation	2000
2. Pharmacist-in-Charge in place, inventory taken, but application not filed with Board within the required timeframe	54.1-3434 and 18VAC110-20-110		1000
3. Unregistered persons performing duties restricted to pharmacy technician without first becoming registered as a pharmacy technician trainee	54.1-3321 and 18VAC110-20-111	per individual	First documented occurrence = no penalty Repeat = $ penalty 250
4. Pharmacists/pharmacy technicians/pharmacy interns/pharmacy technician trainees performing duties on an expired license/registration	18VAC110-21-60, 18VAC110-21-110, 18VAC110-21-141, and 18VAC110-21-170.	per individual	First documented occurrence = no penalty Repeat = $ penalty 100

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
5. Pharmacy technicians, pharmacy interns, or pharmacy technician trainees performing duties without monitoring by a pharmacist, or unlicensed persons engaging in acts restricted to pharmacists	54.1-3320 18VAC110-20-112		500
6. Exceeds pharmacist to pharmacy technician ratio	54.1-3320 18VAC110-20-112	per each technician over the ratio	First documented occurrence = no penalty Repeat = $ penalty 100
7. Change of location or remodel of pharmacy without submitting application or Board approval	18VAC110-20-140	must submit an application and fee	250
8. Refrigerator/freezer temperature out of range greater than +/- 4 degrees Fahrenheit.	18VAC110-20-150 and 18VAC110-20-10	determined using inspector's or pharmacy's calibrated thermometer	First documented occurrence = no penalty; drugs may be embargoed Repeat = $ penalty 100 Drugs may be embargoed
9. The alarm is not operational. The enclosure is not locked at all times when a pharmacist is not on duty. The alarm is not set at all times when the pharmacist is not on duty.	18VAC110-20-180 and 18VAC110-20-190		1000

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
9a. Alarm incapable of sending an alarm signal to the monitoring entity when breached if the communication line is not operational. Alarm is operational but does not fully protect the prescription department and/or is not capable of detecting breaking by any means when activated. The alarm system does not include a feature by which any breach shall be communicated to the PIC or a pharmacist working at the pharmacy.	18VAC110-20-180		250
10. Unauthorized access to alarm or locking device to the prescription department	18VAC110-20-180 and 18VAC110-20-190		1000
11. Insufficient enclosures or locking devices	18VAC110-20-190		First documented occurrence and no drug loss = no penalty Drug loss or repeat = $ penalty 500
12. Storage of prescription drugs not in the prescription department	18VAC110-20-190		500

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
12a. Schedule II drugs are not dispersed with other schedules of drugs or maintained in a securely locked cabinet, drawer, or safe, or maintained in a manner that combines the two methods.	18VAC110-20-200		First documented occurrence and no drug loss of Schedule II = no penalty Drug loss or repeat = $ penalty 250
13. No biennial inventory, or over 30 days late, or substantially incomplete, i.e., did not include all drugs in Schedules II-V.	54.1-3404 and 18VAC110-20-240	Cite Deficiency 113 if only expired drugs not included in inventory.	Over 30 days late and first documented occurrence = no penalty Over 30 days late and repeat = $ penalty 500
14. No incoming change of Pharmacist-in-Charge inventory, inventory taken or over 5 days late, or substantially incomplete, i.e., did not include all drugs in Schedules II-V	54.1-3434 and 18VAC110-20-240	Per occurrence. Cite Deficiency 113 if only expired drugs not included in inventory.	500

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
15. Perpetual inventory not being maintained as required as it does not: • Include all Schedule II drugs received or dispensed; • Accurately indicate the physical count of each Schedule II drug "on-hand" at the time of performing the inventory; • Include a reconciliation of each Schedule II drug at least monthly; or • Include a written explanation of any difference between the physical count and the theoretical count. Monthly perpetual inventory is performed more than 7 days prior or more than 7 days after designated calendar month for which an inventory is required.	18VAC110-20-240	Review 10 drugs for six consecutive months. Includes expired drugs. Deficiency if more than 5 drugs not compliant.	250
16. Theft/unusual loss of drugs not reported to the Board as required	54.1-3404 and 18VAC110-20-240	per report/theft-loss	250
17. Hard copy prescriptions not maintained or retrievable as required (i.e. hard copy of fax for Schedule II, III, IV & V drugs and refill authorizations)	54.1-3404 and 18VAC110-20-240		250
18. Records of dispensing not maintained as required	54.1-3404, 18VAC110-20-240, 18VAC110-20-250, 18VAC110-20-420, and 18VAC110-20-425		250

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
19. Pharmacists not verifying or failing to document verification of accuracy of dispensed prescriptions	18VAC110-20-270, 18VAC110-20-420 and 18VAC110-20-425	10% threshold for documentation	500
20. Pharmacist not checking and documenting repackaging or bulk packaging	54.1-3410.2, 18VAC110-20-355 and 18VAC110-20-425	Review all entries for 5 drugs for six consecutive months. Deficiency if 10% or more are not compliant.	250
20a. Pharmacist not documenting verification of accuracy of non-sterile compounding process and integrity of compounded products	54.1-3410.2, 18VAC110-20-355	10% threshold	500
20b. Pharmacist not documenting verification of accuracy of sterile compounding process and integrity of compounded products	54.1-3410.2, 18VAC110-20-355		5000
21. No clean room	54.1-3410.2		10000
21a. Performing sterile compounding outside of a clean room.	54.1-3410.2	Compliant clean room present but not utilized for preparation of compounded sterile drug products.	3000

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
21b. Presterilization procedures for high-risk level CSPs, such as weighing and mixing, are completed in areas not classified as ISO Class 8 or better.	54.1-3410.2		500
22. Certification of the direct compounding area (DCA) for compounded sterile preparations indicating ISO Class 5 not performed by a qualified individual no less than every 6 months and whenever the device or room is relocated, altered, or major service to the facility is performed.	54.1-3410.2	Review 2 most recent reports; certification must be performed no later than the last day of the sixth month from the previous certification	3000
23. Certification of the buffer or clean room and ante room indicating ISO Class 7 / ISO Class 8 or better not performed by a qualified individual no less than every six months and whenever the device or room is relocated, altered, or major service to the facility is performed.	54.1-3410.2	Review 2 most recent reports; certification must be performed no later than the last day of the sixth month from the previous certification	1000
24. Sterile compounding of hazardous drugs performed in an area not physically separated from other preparation areas	54.1-3410.2		2000
25. No documentation of sterilization methods or endotoxin pyrogen testing for high-risk level compounded sterile preparations or high risk compounded sterile preparations assigned inappropriate beyond use date (BUD)	54.1-3410.2		5000

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
25a. No documentation of initial and semi-annual (6 months) media-fill testing or gloved fingertip testing for persons performing high-risk level compounding of sterile preparations.	54.1-3410.2	Review 2 most recent reports. Media-fill testing and gloved fingertip testing must be performed no later than the last day of the sixth month from the date the previous media-fill test and gloved fingertip testing was initiated.	5000
25b. High-risk compounded sterile preparations intended for use are improperly stored	54.1-3410.2		5000
25c. Documentation that a person who failed a media-fill test or gloved fingertip test has performed high-risk level compounding of sterile preparations after receipt of the failed test result and prior to retraining and receipt of passing media-fill and gloved fingertip test	54.1-3410.2		5000

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
26. No documentation of initial and annual (12 months) media-fill testing or gloved fingertip testing for persons performing low and medium-risk level compounding of sterile preparations.	54.1-3410.2	Review 2 most recent reports. Media-fill testing and gloved finger-tip testing must be performed no later than the last day of the twelfth month from the date the previous media-fill test and gloved fingertip testing was initiated.	500
26a. Documentation that a person who failed a media-fill test or gloved fingertip test has performed low or medium risk level compounding of sterile preparations after receipt of the failed test result and prior to retraining and receipt of passing media-fill and gloved fingertip test	54.1-3410.2		500
27. Compounding using ingredients in violation of 54.1-3410.2.	54.1-3410.2		1000
28. Compounding copies of commercially available products	54.1-3410.2	per Rx dispensed up to maximum of 100 RX or $5000	50

Deficiency	Law / Reg Cite	Conditions	$ Monetary Penalty
29. Unlawful compounding for further distribution by other entities	54.1-3410.2		500
30. Security of after-hours stock not in compliance	18VAC110-20-450		First documented occurrence and no drug loss = no penalty Drug loss or repeat = $ penalty 500
31. Drugs removed and administered to a patient from an automated dispensing device in a nursing home prior to review of the order and authorization by a pharmacist.	18VAC110-20-555	Except for drugs that would be stocked in an emergency drug kit as allowed by 18VAC110-20-555 (3)(C)	First documented occurrence and no known patient harm = no penalty Repeat = $ penalty 250
32. Have clean room, but not all physical standards in compliance, e.g., flooring, ceiling	54.1-3410.2		2000
33. Low or medium-risk compounded sterile preparations assigned inappropriate beyond use date (BUD)	54.1-3410.2		1000
34. Combined with Deficiency 142 – 12/2013.			
35. Schedule II through VI drugs are being purchased from a wholesale distributor or warehouse not licensed or registered by the board or from another pharmacy in a non-compliant manner	18VAC110-20-395		250

Other Deficiencies

If five (5) or more deficiencies in this category are cited, a $250 monetary penalty shall be imposed. Another $100 monetary penalty will be added for each additional deficiency cited in this category, over the initial five.

Deficiency	Law/Regulation Cite	Conditions
101. Repealed 6/2011		
102. Special/limited-use scope being exceeded without approval	18VAC110-20-120	
103. Repealed 12/2013		
104. Sink with hot and cold running water not available within the prescription department.	18VAC110-20-150	
105. No thermometer or non-functioning thermometer in refrigerator/freezer, but temperature within range, +/-4 degrees Fahrenheit. Temperature not being recorded daily or record of such not maintained properly.	18VAC110-20-150 and 18VAC110-20-10	determined using inspector's calibrated thermometer
106. Prescription department substantially not clean and sanitary and in good repair	18VAC110-20-160	must have picture documentation
107. Current dispensing reference not maintained	18VAC110-20-170	
108. Emergency access alarm code/key not maintained in compliance	18VAC110-20-190	
109. Expired drugs in working stock, dispensed drugs being returned to stock not in compliance, dispensed drugs	54.1-3457 18VAC110-20-200	10% threshold

	Deficiency	Law/Regulation Cite	Conditions
	returned to stock container or automated counting device not in compliance. (i.e. appropriate expiration date not placed on label of returned drug, mixing lot numbers in stock container)	18VAC110-20-355	
110.	Storage of paraphernalia/Rx devices not in compliance	18VAC110-20-200	
111.	Storage of prescriptions awaiting delivery outside of the prescription department not in compliance	18VAC110-20-200	
112.	Biennial taken late but within 30 days	54.1-3404 and 18VAC110-20-240	
113.	Inventories taken on time, but not in compliance, i.e., no signature, date, opening or close, Schedule II drugs not separate, failure to include expired drugs.	54.1-3404, 54.1-3434 and 18VAC110-20-240	
114.	Records of receipt (e.g. invoices) not on site or retrievable	54.1-3404 and 18VAC110-20-240	
115.	Other records of distributions not maintained as required	54.1-3404 and 18VAC110-20-240	
116.	Prescriptions do not include required information. Prescriptions not transmitted as required (written, oral, fax, electronic, etc.)	54.1-3408.01, 54.1-3408.02, 54.1-3410, 18VAC110-20-280 and 18VAC110-20-285 18VAC110-20-270	10% threshold
117.	Deficiency 117 combined with Deficiency 116 – 6/2011		
118.	Schedule II emergency oral prescriptions not dispensed in compliance	54.1-3410 and 18VAC110-20-290	>3

Deficiency	Law/Regulation Cite	Conditions
119. Not properly documenting partial filling of prescriptions	54.1-3412, 18VAC110-20-255,18VAC110-20-310, and 18VAC110-20-320	
120. Offer to counsel not made as required	54.1-3319	
121. Prospective drug review not performed as required	54.1-3319	
122. Engaging in alternate delivery not in compliance	18VAC110-20-275	
123. Engaging in remote processing not in compliance	18VAC110-20-276 and 18VAC110-20-515	
124. Labels do not include all required information	54.1-3410, 54.1-3411 and 18VAC110-20-330	10% Threshold Review 25 prescriptions
125. Compliance packaging or labeling does not comply with USP-NF standards for customized patient medication packages	18VAC110-20-340	
126. Special packaging not used or no documentation of request for non-special packaging	54.1-3426, 54.1-3427 and 18VAC110-20-350	10% threshold Review 25 prescriptions
127. Repackaging records and labeling not kept as required or in compliance	18VAC110-20-355	10% threshold
128. Unit dose procedures or records not in compliance	18VAC110-20-420	
129. Robotic pharmacy systems not in compliance	18VAC110-20-425	

Deficiency	Law/Regulation Cite	Conditions
130. Required compounding/dispensing/distribution records not complete and properly maintained	54.1-3410.2	
130a Compounded products not properly labeled	54.1-3410.2	
131. Required "other documents" for USP-NF 797 listed on the pharmacy inspection report are not appropriately maintained	54.1-3410.2	
132. Personnel preparing compounded sterile preparations do not comply with cleansing and garbing requirements	54.1-3410.2	
133. Compounding facilities and equipment used in performing non-sterile compounds not in compliance with 54.1-3410.2	54.1-3410.2	
134. Policies and procedures for proper storage, security and dispensing of drugs in hospital not established or assured	18VAC110-20-440	
135. Policies and procedures for drug therapy reviews not maintained or followed	18VAC110-20-440	
136. After hours access to a supply of drugs or records not in compliance	18VAC110-20-450	10% threshold
137. Floor stock records not in compliance, pharmacist not checking, required reconciliations not being done	18VAC110-20-460	10% threshold
138. Automated dispensing device loading, records, and monitoring/reconciliation not in compliance	54.1-3434.02, 18VAC110-20-490 and 18VAC110-20-555	Cite if no documentation of monitoring. Review ADD in areas that do not utilize patient specific profile. Review 3 months of records – 30% threshold. Cite if exceeds threshold. Describe in

Deficiency	Law/Regulation Cite	Conditions
		comment section steps pharmacy is taking to comply. Educate regarding requirements.
139. Emergency medical services procedures or records not in compliance	18VAC110-20-500	10% threshold
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142. No record maintained and available for 12 months from date of analysis of dispensing errors or submission to patient safety organization	18VAC110-20-418	
143. Repealed 6/21/2018		
144. Repealed 6/21/2018		
145. Repealed 6/21/2018		
146. Repealed 6/21/2018		
147. Particle counts, environmental sampling, and smoke pattern testing not performed under dynamic conditions.	54.1-3410.2	

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Routine inspection on 7/1/24 – Cited for deficiency 3. Monetary penalty.

	Government of the District of Columbia Department of Health	Health Regulations and Licensing Administration Pharmaceutical Control Division Inspection FineSchedule	899 North Capitol St, NE, 2nd Floor Washington, DC 20002 202-724-8800 202-727-8677 (fax) www.hpla.doh.dc.gov
		PHARMACY INSPECTION FINE SCHEDULE	
	DCOC/ DCMR/ CFR Citation	**Conduct**	**Fine Amount**
	VIOLATIONS OF LICENSURE	**AND/OR DISPLAY REQUIREMENTS**	
	DCOC 47-2885.03(d)/ 22-B DCMR 1900.1	Operating a pharmacy without a valid license	$2,000.00
	D.C. Official Code § 47-2885.08(b)	Failure to renew a pharmacy license	$2,000.00
	DCOC 48-903.02(a)/ 22-B DCMR 1002.1	Expired DCCS registration or failure register.	$2,000.00
	22-B DCMR 1502.1/ 22-B DCMR 1000.2/ 21 CFR 1301.11(a)	Expired DEA registration or failure register	$2,000.00
	DCOC 47-2885.09(a)/ 22-B DCMR 1901.1	Unlicensed pharmacist on duty	$2,000.00
	DCOC 47-2885.09(a)/ 22-B DCMR 1901.2	Pharmacy open without Pharmacist being on duty	$2,000.00
	DCOC 47-2885.06, DCOC 3-1210.06(b)(4), and 17 DCMR 6509.3	Unregistered Pharmacy Intern on duty	$2,000.00
	DCOC 47-2885.09(a)/ 22-B DCMR 1901.3	Failure of pharmacist on duty to conspicuously post his or her pharmacist license.	$500.00
	22-B DCMR 1901.3	Failure to conspicuously post pharmacy license, occupancy permit, DEA or DCCS registrations, pharmacist licenses, or intern registrations.	$500.00
	DCOC 47-2885.09(a)/ 22-B DCMR 1901.3	Failure to properly display hours of operation	$500.00
	DCOC 48-801.03	Failure to post top 100 drugs pricing poster	$500.00
	DCOC 48-803.03a	Failure to prominently display sign regarding drug substitution.	$500.00

	DCOC/ DCMR/ CFR Citation	Conduct	Fine Amount
	VIOLATIONS OF	**OPERATIONS REQUIREMENTS**	
	DCOC 47-2885.08(c)	Using a pharmacy license for a location other than the one specified on the license, or under a different name, or transferring a pharmacy license.	$2,000.00
	22-B DCMR 1902.1 and 1902.12	Operating a pharmacy outside of the classification for which the license was issued; or failing to adhere to restrictions placed on the license.	$2,000.00
	22-B DCMR 1907.3	Operating a pharmacy in either a temporary or trailer-type facility without approval.	$2,000.00
	22-B DCMR 1900.3	Having drugs in a pharmacy before a pharmacy license has been obtained from the Director	$1,000.00
	22-B DCMR 1920	Failure of pharmacist-in-charge to comply with requirements and duties, to be physically present in the pharmacy to provide supervision and control; or serving as PIC for more than one pharmacy without approval.	$2,000.00
	DCOC 47-2885.09(b)	Failure of pharmacist on duty to control all professional aspects of the practice of pharmacy; or allowing any usurpation of his or her professional judgment by a non-pharmacist proprietor or personnel.	$1,000.00
	22-B DCMR 1902.8	Failure to notify the Director within thirty (30) days after a change in the pharmacist-in-charge, Director of Pharmacy, or Responsible Nuclear Pharmacist.	$1,000.00
	22-B DCMR 1905.4	Failure to notify the Director at least sixty (60) days prior to the change of proprietorship of a pharmacy; or to apply for a new license.	$1,000.00
	22-B DCMR 1906.1 through 1906.4	Failure to comply with the requirements for closing a pharmacy.	$1,000.00
	VIOLATIONS OF PHYSICAL	**STANDARDS AND EQUIPMENT**	
	22-B DCMR 1907.4(a)	Failure of pharmacy compounding and dispensing area to be a minimum of one-hundred and fifty (150) square feet	$1,000.00

	DCOC/ DCMR/ CFR Citation	Conduct	Fine Amount
	22-B DCMR 1907.4(c)	Failure to have a confidential patient counseling area	$1,000.00
	22-B DCMR 1907.4(g)	Failure of pharmacy to have a goose-neck faucet; hot and cold water; soap or detergent; air driers or single-use towels	$1,000.00
	2-B DCMR 1907.4(i)	Failure to have refrigeration facilities exclusively for cold storage drugs storage	$1,000.00
	DCOC 47-2885.13(a)/22-B DCMR 1907.4(i)/ 22-B DCMR 1907.5	Failure to maintain pharmacy storage area temperature compatible with the proper storage of drugs with a	$1,000.00
	22-B DCMR 1909.2- 1909.5	Failure to maintain required equipment and references consistent with the pharmacy's scope of practice, the	$500.00
	VIOLATIONS OF SECURITY	**REQUIREMENTS**	
	DCOC 47-2885.09(d)/ 22-B DCMR 1901.8	Failure to report thefts, suspected diversions, significant losses of drug inventory or the inability to account for such	$2,000.00
	22-B DCMR 1907.4(d)/ D.C. Code 47-2885.09(c)(1)	Failure to have a barrier that renders pharmacy inaccessible to unauthorized persons	$1,000.00
	DCOC 47-2885.09(c)(1)/ 22-B DCMR 1910.4	Failure to keep controlled substances stored outside compounding and dispensing area in a locked storage area	$1,000.00
	22-B DCMR 1910.2/ 22-B DCMR 1910.7	Failure to have an operating security alarm system	$1,000.00
	DCOC 47-2885.09(c)(1)/ 22-B DCMR 1910.5/ 22-B DCMR 1910.7	Failure to securely enclose pharmacy area to prevent unauthorized access or diversion of drugs when the	$1,000.00
	22-B DCMR 1910.5/ 22-B DCMR 1910.7/ 47-2885.09(c)(3)	Failure to have doors capable of being locked; to securely lock the pharmacy; or to restrict pharmacy access to authorized persons	$1,000.00
	DCOC 47-2885.09(c)(4)/ 22-B DCMR 1910.8	Failure to keep the key or keys to the pharmacy areas under the control or in the possession of the pharmacy on	$1,000.00
	22-B DCMR 1910.9	Displaying or storing prohibited drugs in an area accessible to the public	$500.00
	VIOLATIONS OF SANITATION	**REQUIREMENTS**	
	22-B DCMR 1900.4	Failure to maintain written policies and procedures regarding sanitation standards	$2,000.00

	DCOC/ DCMR/ CFR Citation	Conduct	Fine Amount
	22-B DCMR 1908.2	Failure to keep pharmacy clean and in a sanitary condition; (i.e. dusty shelves, trash on the floor, food lying around on	$2,000.00
	22-B DCMR 1908.2	Failure to maintain clean and sanitary restroom facilities.	$2,000.00
	22-B DCMR 1908.2	Failure to keep pharmacy free of infestation by infested by rodents, birds, insects, or other vermin	$2,000.00
	22-B DCMR 1908.3	Failure to keep pharmacy and storage areas dry and well ventilated.	$2,000.00
	22-B DCMR 1908.4	Failure to keep equipment clean and in good operating condition.	$2,000.00
	22-B DCMR 1908.5	Failure to cover trash containers or use opaque trash bags	$2,000.00
	22-B DCMR 1908.6	Failure to remove trash in a timely and sanitary manner	$2,000.00
	22-B DCMR 1908.7	Failure of pharmacy to have restroom facilities in an area reasonably accessible to pharmacy personnel and supplied with a hand washing sink, soap or detergent, toilet paper, and air driers or single-service towels	$2,000.00
	22-B DCMR 1908.8	Failure to keep pharmacy plumbing facilities in good repair	$2,000.00
	22-B DCMR 1908.9	Permitting animals in the pharmacy or areas immediately adjacent to and under the control of the pharmacy except for guide dogs accompanying disabled persons.	$2,000.00
	DCOC 47-2885.11(b)(2)-(4)/ 22-B DCMR 1908.10	Failure of persons working in the pharmacy to follow hygienic practices	$2,000.00
	VIOLATIONS OF PACKAGING/ HANDLING AND DRUG LABELING REQUIREMENTS		
	22-B DCMR 1911.2	Failure to dispense drugs in new and clean containers or original manufacturer packaging	$2,000.00
	22-B DCMR 1911.3	Failure to dispense drugs in child-resistant containers without documentation of patient request.	$2,000.00

	DCOC/ DCMR/ CFR Citation	Conduct	Fine Amount
	22-B DCMR 1911.4	Reuse of manufacturer bottle or container	$2,000.00
	22-B DCMR 1911.5	Reuse of bottle or container that previously held toxic, adulterated, or misbranded substances	$2,000.00
	22-B DCMR 1911.6	Failure to obtain drugs from approved suppliers	$2,000.00
	22-B DCMR 1911.7	Failure to obtain drugs in original manufacturer or distributor container	$2,000.00
	22-B DCMR 1911.8	Failure of pharmacist to direct and supervise compounding, repackaging, or prepackaging of drugs	$2,000.00
	DCOC 47-2885.13(a)/ 22-B DCMR 1911.11	Failure to store all drugs and devices in a proper and safe manner, in an appropriate container, in a manner to insure accurate identification and in accordance with applicable federal and D.C. laws	$2,000.00
	DCOC 47-2885.10(a)(3)/ 22-B DCMR 1901.6	Storing misbranded drugs with currently dated products	$2,000.00
	DCOC 47-2885.14/	Failure to dispense a drug, except to hospital inpatients, in a suitable container appropriately labeled	$1,000.00
	22-B DCMR 1912		
	DCOC 48-903.08(e)/ 22-B DCMR 1308.1/22-B DCMR 1912.2	Failure to label written or emergency CS II substances as required by law	$1,000.00
	DCOC 48-903.08(e)/ 22-B DCMR 1312.1/ 22-B DCMR 1912.2	Failure to label CS III-V as required by law	$1,000.00
	22-B DCMR 1912.4	Failure to label prepackaged or repackaged container with label containing required information.	$1,000.00
	22-B DCMR 1912.6	Failure to place appropriate expiration date on multi-dose container after opening it	$1,000.00
	22-B DCMR 1325.6	Failure to affix a label to non-controlled substance prescription package	$2,000.00
	VIOLATIONS OF	**RECORDKEEPING REQUIREMENTS**	
	22-B DCMR 1503.1 and 22-B DCMR 1913	Failure to maintain prescription files in conformity with the requirements of 22 DCMR 1913.1 et. seq.	$2,000.00
	22-B DCMR 1502.1	Failure of registrant to keep records, maintain inventories and file reports as required by fed. law	$2,000.00

	DCOC/ DCMR/ CFR Citation	Conduct	Fine Amount
	22-B DCMR 1913.8	Failure to file CSII prescriptions separately from other pharmacy records	$2,000.00
	22-B DCMR 1306.3	Failure to cancel out CS II prescription by drawing a line through the entire prescription order, with date dispensed and initials of person who dispensed the drug	$2,000.00
	22-B DCMR 1310.3/ 22-B DCMR 1310.4/ 22-B DCMR 1310.8	Failure to record CSIII, IV, and V prescription refills in a readily retrievable record with the required information	$2,000.00
	22-B DCMR 1913.9	Failure to maintain separate file for CSIII, IV, and V prescriptions, or to mark in red letter "C"; unless an electronic recordkeeping system is used to identify by prescription number	$2,000.00
	22-B DCMR 1302.2	Failure to immediately reduce an oral prescription order to writing	$2,000.00
	22-B DCMR 1302.3 to 22-B DCMR 1302.9	Failure to include all required information on an oral prescription drug order	$2,000.00
	22-B DCMR 1303.6 to 22-B DCMR 1303.12	Failure of telephone facsimile orders to contain all required information	$2,000.00
	DCOC 47-2885.15(a)/ 22-B DCMR 1911.9	Failure to keep required log of compounded or repackaged or prepackaged drugs	$2,000.00
	DCOC 47-2885.15(b)(1)	Failure to maintain a record of over-the-counter CS V drugs sales	$500.00
	DCOC 47-2885.15(b)(2)(a)	Failure to maintain a record of hypodermic syringes, needles, or other medical devices which may be used in the administration of controlled substances	$500.00
	22-B DCMR 1913.11	Failure to maintain a patient record system with immediate retrieval of required patient information during pharmacy operating hours.	$2,000.00
	22-B DCMR 1301.6	Failure to document the pharmacist's name, initials or any changes on a prescription order	$20,000.00

	DCOC/ DCMR/ CFR Citation	Conduct	Fine Amount
	22-B DCMR 1301.7	Failure to document authorization for a substitution on the prescription order	$2,000.00
	22-B DCMR 1913.6	Failure to put in place systems to assign a secure identification for each pharmacist for use on verification of records, or to require manual signatures of pharmacists performing final verifications.	$500.00
	22 DCMR 1502.1/ 21 CFR 1305.12/ 21 CFR 1305.13(e)	Failure to execute DEA 222 Forms as required by law	$2,000.00
	22-B DCMR 1325.10	Failure to document and uniformly maintain in a readily retrievable record each refilling of a non-controlled substance.	$1,000.00
	22-B DCMR 1325.12	Failure to properly document the required refill authorization information on each refill of a non-controlled substance.	$1,000.00
	22-B DCMR 1325.15	Failure to properly document the partial filling of a prescription for a non-controlled substance	$1,000.00
	22-B DCMR 1300.7	Dispensing a medication or device pursuant to a prescription that the pharmacist knows is not based on a valid patient–practitioner relationship	$2,000.00
	22-B DCMR 1305.6	Dispensing a medication or device pursuant to a prescription that the pharmacist knows was not issued in the usual course of professional treatment or in legitimate and authorized research.	$2,000.00
	22-B DCMR 1306.2	CS II prescription filled more than thirty (30) days after the prescription was issued	$2,000.00
	22-B DCMR 1306.3	Refilled a CS II prescription.	$2,000.00
	22-B DCMR 1306.4	Failure to obtain the original written prescription before dispensing a CSII prescription that was transmitted via telephone facsimile	$2,000.00

	DCOC/ DCMR/ CFR Citation	Conduct	Fine Amount
	22-B DCMR 1306.5	Failure to comply with requirements for dispensing a CSII in an emergency situation	$2,000.00
	22-B DCMR 1306.7 to 22-B DCMR 1306.9	Failure to comply with requirements for dispensing a CSII via telephone facsimile	$2,000.00
	22-B DCMR 1310.1	Refilled a CS III through V prescription more than six months after issuance	$2,000.00
	22-B DCMR 1310.2	Refilled a CS III through V prescription more than five (5) times	$2,000.00
	DCOC 47-2885.10(a)(3)/ 22-B DCMR 1901.5	Selling, or offering for sale, adulterated or misbranded drugs or devices	$2,000.00
	DCOC 47-2885.13(a)/ 22-B DCMR 1901.6	Selling or dispensing expired drugs; or storing expired drugs with currently dated products	$2,000.00
	DCOC 47-2885.13(c)/ 22-B DCMR 1329.1	Placing in stock for reuse or resale, or accepting back to the pharmacy, a drug which has been returned after leaving the pharmacy.	$2,000.00
	22-B DCMR 1901.4	Stocking, selling, dispensing, or distributing non-FDA registered drugs, medical devices, or chemicals for compounding	$2,000.00
	22-B DCMR 1901.7	Obtaining drugs or medical devices from a non-registered entity.	$2,000.00
	DCOC 47-2885.13(b)	Selling drugs designated as “sample.”	$1,000.00
	22-B DCMR 1919	Failure to offer to counsel (all patients)	$500.00

Board of Pharmacy Civil Penalties

TENNESSEE BOARD OF PHARMACY

PENALTY MATRIX FOR CONSISTENCY OF DISCIPLINE

Category of violation	To	Civil Penalty
Counseling violation	Pharmacy	$1000 per violation with suspension of all but $1000 with plan of correction
Counseling violation	Pharmacist	$1,000
Counseling violation	PIC	Letter of Instruction
Counseling violation	Technician	$100 failure to notify DPh of need to counsel
Exceeding pharmacist/technician ratio	PIC	$100 per incidence
Expired registration - technician	Technician	$100
Failure to conduct CS inventory upon change in PIC	Pharmacy	$50 per month
Failure to notify BOP of change of address - wholesaler	Wholesaler	$100 per month ($50 if limited to oxygen distribution)
Failure to notify BOP of change of employment	Pharmacist	$100
Failure to notify BOP of change in PIC	Pharmacy	$100 per month
Misfill	Pharmacist	Letter of Warning to responsible pharmacist
Non-registered technician	PIC	$100 per month unregistered after 90 day grace period (determine if PIC was there during that time)
Stealing/diverting CS by technician	Technician	Revocation with authorization of formal hearing
Unlicensed activity - wholesaler	Wholesaler	$100 per month
Unlicensed activity - wholeslaer of oxygen only (or legend device)	Wholesaler	$100 per month
Failure to maintain sanitary conditions	Pharmacist	LOI
Filled prescription beyond 1 year from written date	Pharmacist	LOI
Privacy violation - another patient's medication attached	PIC	LOW
Pharmacist not on duty for > 1 hour, no sign	Pharmacist	LOW
Tech gave out prescriptions while pharmacist not in pharmacy	Technician	LOI
Dispensing Expired Medication		$100 per item 12/14/20
Unethical/unprofessional conduct	Pharmacist	LOW
Unlicensed activity - PIC	PIC	$1000 per month
Unlicensed activity opening - DME	Pharmacy	$50 per month
Unlicensed employee only person present in pharmacy w/key	PIC	LOI to PIC (was closed door pharmacy dispensing vaccines)
Key violation	PIC	7/12/17 CHANGED TO $1,000
Failure to report conviction		$1,000
Unlicensed pharmacy		$1,000
Records not retrievable Updated 1/27/2022		$1,000

Close Window

§ 43b.7. Schedule of civil penalties—pharmacists and pharmacies.

STATE BOARD OF PHARMACY

Violation under 35 P. S.	Title/Description	Civil Penalty
Section 637.6(a)(1)	Failure of a pharmacy permit holder to post a sign as required under section 4 of the Clean Indoor Air Act (35 P. S. § 637.4)	1st offense—$250 2nd offense (within 1 year of 1st offense)—$500 3rd offense (within 1 year of 2nd offense)—$1,000 Subsequent offenses (within 1 year of previous offense) —$1,000
Section 637.6(a)(2)	Pharmacy permit holder permitting smoking in the pharmacy in violation of the Clean Indoor Air Act (35 P. S. § § 637.1—637.11)	1st offense—$250 2nd offense (within 1 year of 1st offense)—$500 3rd offense (within 1 year of 2nd offense)—$1,000 Subsequent offenses (within 1 year of previous offense —$1,000
Section 637.6(a)(3)	Licensee of the Board smoking in a pharmacy in violation of the Clean Indoor Air Act	1st offense—$250 2nd offense (within 1 year of 1st offense)—$500 3rd offense (within 1 year of 2nd offense)—$1,000 Subsequent offenses (within 1 year of previous offense) —$1,000

Violation under 49 Pa. Code Chapter 27	Title/Description	Civil Penalty
Section 27.11	Pharmacy Permit—	
	(a) Lack of permit showing accurate and current information as to name and address of pharmacy and name of pharmacist manager	$100
	(b) Display, advertise or use a name other than registered name	1st offense—$100 2nd offense—$100
	(g) Failure to notify Board of change in pharmacist manager or operation of pharmacy without pharmacist manager.	1st offense—$50 per month or part of month; Formal action if no compliance within 60 days after receiving citation 2nd offense—same as 1st offense
Section 27.14	Supplies—	
	(b) Expired drugs	1st offense—Under 1 year old—$250 1st offense—Over 1 year old—$500 2nd offense—$1,000
	(c) Failure to maintain equipment and miscellaneous supplies	$100 each

Section 27.15	Sanitary standards	
	(a) Pharmacy not in good repair or not in clean and orderly condition.	$250
	(b) Violation of health and sanitation statutes of the Commonwealth and of the municipality and county where pharmacy is located.	$250
	(c) Waste disposal violations	$250
	(d) Prescription area not dry, well ventilated and well lighted; not free from rodents or insects	$250
	(e) Plumbing not functional	$250
	(f) Unauthorized items in prescription area	$250
Section 27.16	Construction requirements—	
	(b)(4) Lack of telephone	$250
	(5) Lack of required sanitary facilities	$250
	(7) Television set in prescription area not intended for pharmacy instructional use	$500
	(8) Drugs accessible to unauthorized persons; animals unrelated to pharmacy security in prescription area	$250
Section 27.18	Standards of practice—	
	(a) Unsuitable containers	$100
	(b) Lack of required information on prescriptions	$100
	(d) Lack of required information on container labels	$100
Section 27.31	Biennial renewal—(c) practicing on a lapsed license or permit	0-4 months—$50 per month; over 4 months—8 months—$100 per month; over 9 months—12 months—$200 per month; over 1 year—formal action

Violation under 28 Pa. Code Chapter 25	**Title/Description**	**Civil Penalty**
Section 25.55(d)	Improper generic substitution	
	Five to nine	$250
	10 or more	$500
Section 25.55(e)	Failure to refill prescription with the identical product without authorization from prescriber and patient	$100
Section 25.56(a)	Improper filing of Schedule II prescriptions	$100
Section 25.56(b)	Improper filing of Schedule III, IV, V prescriptions	$100
Section 25.63(b)	Inadequate security for controlled substances	$250
Section 25.92	Lack of lot numbers required on stock items	$100
Section 25.94	Lack of expiration date on label of dispensed drugs of less than 1 year's potency.	$100

Authority

The provisions of this § 43b.7 amended under the act of July 2, 1993 (P.L. 345, No. 48).

Source

The provisions of this § 43b.7 amended March 2, 2001, effective March 3, 2001, 31 Pa.B. 1227; amended December 21, 2012, effective December 22, 2012, 42 Pa.B. 7673. Immediately preceding text appears at serial pages (325189) to (325191).

Top

Agenda Topic: Discuss acceptance of outsourcing facility inspections performed by other states.

Included in Agenda Packet:

- Relevant law regarding qualifying inspection for outsourcing facilities and nonresident outsourcing facilities
- Excerpt from 2016 full board meeting minutes
- Florida inspection report for outsourcing facilities

Staff Note:

- Staff will provide information regarding California's inspection report during the meeting.

Action Needed:

- Motion to recommend to the full board that it approve acceptance of the Florida and/or California Board of Pharmacy inspection report for outsourcing facilities, in addition to Bestech GMP, if the outsourcing facility has not been inspected by the U.S. Food and Drug Administration within the required period; OR
- Motion to recommend to the full board that it take no action on this subject.

From *The Pharmacy Act and Drug Control Act with Related Statutes*, 7/1/2022

§ 54.1-3434.05. Permit to act as an outsourcing facility.

A. No person shall act as an outsourcing facility without first obtaining a permit from the Board.

B. Applications for a permit to act as an outsourcing facility shall be made on a form provided by the Board and signed by a pharmacist who will be in full and actual charge of the outsourcing facility and who will be fully engaged in the compounding performed at the location designated on the application. Such application shall be accompanied by a fee determined by the Board in regulation. All permits shall expire annually on a date determined by the Board in regulation. No permit shall be issued or renewed for an outsourcing facility unless the facility can demonstrate compliance with all applicable federal and state laws and regulations governing outsourcing facilities.

C. As a prerequisite to obtaining or renewing a permit from the Board, the outsourcing facility shall (i) register as an outsourcing facility with the U.S. Secretary of Health and Human Services in accordance with 21 U.S.C. § 353b and (ii) submit a copy of a current inspection report resulting from an inspection conducted by the U.S. Food and Drug Administration that indicates compliance with the requirements of state and federal law and regulations, including all applicable guidance documents and Current Good Manufacturing Practices published by the U.S. Food and Drug Administration.

The inspection report required pursuant to clause (ii) shall be deemed current for the purposes of this section if the inspection was conducted (a) no more than one year prior to the date of submission of an application for a permit to the Board or (b) no more than two years prior to the date of submission of an application for renewal of a permit to the Board. However, if the outsourcing facility has not been inspected by the U.S. Food and Drug Administration within the required period, the Board may accept an inspection report or other documentation from another entity that is satisfactory to the Board, or the Board may cause an inspection to be conducted by its duly authorized agent and may charge an inspection fee in an amount sufficient to cover the costs of the inspection.

D. Every outsourcing facility shall compound in compliance with the requirements of state and federal law and regulations except § 54.1-3410.2, to include all applicable guidance documents and Current Good Manufacturing Practices published by the U.S. Food and Drug Administration.

E. An outsourcing facility shall not engage in compounding of drug products to be dispensed pursuant to a valid prescription for a specific patient without first obtaining a permit to operate a pharmacy.

2015, c. 300.

§ 54.1-3434.5. Nonresident outsourcing facilities to register with the Board.

A. Any outsourcing facility located outside the Commonwealth that ships, mails, or delivers in any manner Schedule II through VI drugs or devices into the Commonwealth shall be considered a nonresident outsourcing facility and shall be registered with the Board.

B. Applications for registration to act as a non-resident outsourcing facility shall be made on a form provided by the Board and signed by a pharmacist who is licensed as a pharmacist in Virginia and who is in full and actual charge of the outsourcing facility, is fully engaged in the compounding performed at the location stated on the application, and is fully responsible for the outsourcing facility's compliance with state and federal law and regulations. Such application shall be accompanied by a fee determined by the Board in regulation. All registrations shall expire annually on a date determined by the Board in regulation.

C. As a prerequisite to registering or renewing a registration with the Board, the outsourcing facility shall (i) register as an outsourcing facility with the U.S. Secretary of Health and Human Services in accordance with 21 U.S.C. § 353b and (ii) submit a copy of a current inspection report resulting from an inspection conducted by the U.S. Food and Drug Administration that indicates compliance with the requirements of state and federal law and regulations, including all applicable guidance documents and Current Good Manufacturing Practices published by the U.S. Food and Drug Administration.

The inspection report required pursuant to clause (ii) shall be deemed current for the purposes of this section if the inspection was conducted (a) no more than one year prior to the date of submission of an application for registration with the Board or (b) no more than two years prior to the date of submission of an application for renewal of a registration with the Board. However, if the outsourcing facility has not been inspected by the U.S. Food and Drug Administration within the required period, the Board may accept an inspection report or other documentation from another entity that is satisfactory to the Board, or the Board may cause an inspection to be conducted by its duly authorized agent and may charge an inspection fee in an amount sufficient to cover the costs of the inspection.

D. A nonresident outsourcing facility shall not engage in compounding of drug products to be dispensed pursuant to a valid prescription for a specific patient without first obtaining a registration to operate a nonresident pharmacy. The nonresident pharmacy shall comply with all state and federal laws, regulations, and requirements except § 54.1-3410.2.

2015, c. 300.

Excerpt from 9/7/2016 Full Board Meeting Minutes:

OLD BUSINESS:

• Consideration for accepting inspection from Bestech GMP Contracting, Inc. in lieu of FDA inspection for outsourcing facility	Matthew Bestercy, Owner and Principal Consultant for Bestech GMP Contracting, Inc., provided a handout with additional information for board consideration in follow-up to the discussion during the June 2016 full board meeting. He is requesting the board to accept an inspection report of outsourcing facilities resulting from inspections performed by his company for satisfying the requirement for an outsourcing facility to submit a current inspection report when the FDA has not performed an inspection in the required timeframe as authorized in 54.1-3434.05 and 54.1-3434.5. Bestech would provide the board with the complete inspection report, collect a written corrective action plan from the outsourcing facility within 15 days of the inspection, and provide the board with a written opinion regarding the appropriateness of the written corrective action plan. Mr. Bestercy indicated his inspectors would be able to provide testimony during a disciplinary case, if necessary. It was stated that all inspection reports of outsourcing facilities resulting from an FDA inspection must be considered by the board and that an inspection from Bestech would not preclude this requirement. However, the board could consider accepting an inspection from Bestech for licensure purposes when the FDA had not performed an inspection in the required timeframe.
MOTION:	**The board voted 7 to 3 in support of accepting an inspection report from Bestech GMP Contracting, Inc. for licensure purposes of outsourcing facilities when the FDA has not performed an inspection within the required timeframe for a "current" inspection report pursuant to 54.1-3434.05 and 54.1-3434.5. (motion by Saenz, second by Shinaberry; M. Elliott, Boone, and S. Elliott opposed)**

STATE OF FLORIDA
DEPARTMENT OF HEALTH
INVESTIGATIVE SERVICES
503b Outsourcing Inspection

NAME	PERMIT NUMBER	DATE OF INSPECTION
DOING BUSINESS AS		
STREET ADDRESS	TELEPHONE #	EXT
CITY	COUNTY	STATE/ZIP

Pharmacy Affiliate	License #
Pharmacy Affiliate	License #

	License #

Quality - 21CFR part 211
subpart B

Firm has an independent Quality Control Unit.	
The QC unit has the authority and responsibility to approve or reject all components, drug product containers or closures, end process materials, packaging materials, labeling and drug products.	
QC unit reviews production records to assure that no errors have occurred, or if errors have occurred, that they have been fully investigated.	
Adequate laboratory facilities for the testing and approval (or rejection) of components, drug product containers, closures, packaging materials, in-process materials, and drug products are available to the quality control unit.	
The quality unit approves or rejects all procedures or specifications impacting the identity, strength, quality, and purity of the drug product.	
The responsibilities and procedures applicable to the QC unit are in writing and such procedures are followed.	
QC unit personnel are qualified through training and experience.	

INVESTIGATIONS

The QC Unit conducts a written and thorough investigations of any unexplained discrepancy, deviation, equipment malfunctions, and OOS (including a percentage of theoretical yield exceeding the maximum or minimum percentages established in master production and control records) or the failure of a batch or any of its components to meet any of its specifications whether or not the batch has already been distributed.	
Investigations are conducted within time limits specified per SOP.	
When investigations are not conducted, the written records include the reason the investigation was not deemed to be necessary and the name of the person that made that determination.	
Investigations are extended to other batches that may have been impacted by a failure or discrepancy	
Investigations include findings, conclusions and follow up.	
Record of investigations are maintained at the establishment where the investigation occurred.	

Personnel Qualification –
21CFR Subpart B

All personnel involved in the processing, packing, or holding of a drug product have the education, training and experience to enable the person to perform the assigned functions.	
Facility has a written training program that describes the required training, frequency of training and process for evaluating the performance of individuals involved in compounding.	
Facility has documentation that compounding personnel have the required skills necessary to perform their assigned functions.	
Prior to beginning to prepare CSP's personnel have completed training and have demonstrated proficiency in the principles and hands on skills of aseptic manipulations.	
CGMP trainers are qualified through experience and training	
Personnel receive ongoing periodic CGMP training by qualified trainers for the specific tasks they are authorized to perform.	
Personnel are qualified for the number of units they can compound and the processes they perform.	
Prior to beginning to prepare CSP's personnel have completed training and have demonstrated proficiency in the principles and hands on skills of aseptic manipulations.	

Personnel have been periodically trained in core competencies, visual observation is conducted to confirm personnel have necessary skills (i.e. Hand hygiene and garbing, aseptic manipulations, cleaning and disinfecting).	
Personnel sampling including GFT is conducted after compounding and documented on each batch record.	
Personnel have completed media fill simulations for all aseptic compounding processes under the most difficult and challenging conditions which include the most manipulations/units, most complex flow of material, longest time to compound and all breaks and interventions.	
Personnel are retrained and requalified after failure of media fill, GFT or batch failures.	
Firm has adequate written procedures for visual inspection.	
Personnel conducting visual inspection of the final product have been qualified through training in applicable SOPs and have annual eye exams.	
Personnel conducting visual inspections have been qualified for the number of units and amount of time they can inspect before taking a break.	
Significant defect categories are identified in the SOP and personnel conducting visual inspection have demonstrated competency in identifying common defects.	
Persons supervising the manufacture, processing, packing or holding of a drug product have the education, training, and experience to perform assigned functions in a manner to provide assurance of the safety, identity, strength, quality and purity of the drug product.	
Employees are required to report to their supervisor any health issues that might impact the quality, safety and purity of the product.	
Temporary employees are given the same orientations as permanent employees.	
The firm has records stating the name, address, and qualification of all consultants and the type of service they provide.	
Documentation of training personnel on use of equipment.	

Facilities and Equipment –

21CFR part 211 subpart C and subpart D

The facility design is suitable for compounding sterile products.	
The facility is designed to allow adequate flow of components, drug product containers, closures, labeling, in-process materials and drug products through the building to prevent contamination.	
The facility has the space, construction, and location to facilitate cleaning, maintenance, and proper operation.	
There is adequate space for the orderly placement of equipment and materials to prevent mixups between different components, containers, closures, labeling, in-process materials, or drug products and to prevent contamination.	
Facility had adequate space to quarantine incoming components, drug product containers, closures, and labeling pending the sampling, testing or examination by the quality control unit prior to release.	
Facility has space to hold rejected components, container, closures and labeling prior to disposition.	
There is a separate, defined area for quarantine storage before release of drug products.	
Compounding of hazardous drugs is clearly separated from non-hazardous drugs to prevent cross contamination.	
Beta lactams are separated to prevent cross contamination with other drug products.	
Certifications of primary and secondary engineering controls are current and are conducted under dynamic, worst case conditions with the maximum number of personnel allowed per SOP present.	
All HEPA filters are leak tested.	
Visual smoke studies have been conducted under operational conditions to demonstrate laminar flow air in all primary engineering controls.	
Floors, walls and ceilings and other structures are smooth and easily cleanable	
Ceiling tiles are clean room grade and gasketed and sealed/clipped	
Air return vents are not blocked and are placed in a manner that allows adequate dilution of HEPA filtered air to prevent airborne contamination	

The control of air pressure, dust, humidity and temperature is adequate for the manufacturing, processing, storage or testing of drug products.	
Pressure gauges that monitor pressure differentials are calibrated.	
The facility is maintained in a clean and sanitary condition.	
The facility has written procedures that describe in sufficient detail the cleaning schedule, methods, equipment, and materials used in cleaning the facilities. Procedures are followed.	
The firm has an SOP for controlling rodents, birds, insects and other vermin. Pest control contracts specify which pesticides can be used. Procedures are followed and documented.	
The facility has a procedure for rotating cleaning solutions and documents in the cleaning record.	
Sporicidal agents are used. How often?	
The facility has validated the effectiveness of the cleaning solutions.	
All equipment has written procedures for use.	
Written procedures and schedules are established and followed for cleaning and maintenance of equipment and utensils used in the manufacture, processing, packing, or holding of a drug product.	
Surfaces that contact components, in-process materials, or drug products are not reactive, additive, or absorptive so as to alter the safety, identity, strength, quality or purity of the drug product.	
Ovens and autoclaves have been temperature mapped, the cycles have been validated, and are monitored with calibrated thermometers.	
Autoclaved cycles are verified with BI's.	
Depyrogenation cycles have been validated with ECVs and demonstrates a 3 log reduction in endotoxin units	
All equipment is validated for its intended use.	
Refrigerators, freezers and incubators are monitored with calibrated thermometers.	
Written SOPs for changing the filters and prefilters of all engineering controls are established and followed.	
Appropriate controls over computer or related systems assure the changes in master production and control records are made by authorized personnel only.	

Environmental Monitoring - 21CFR 211.113

Facility has an environmental monitoring program.	
Air quality is monitored regularly under operating conditions using volumetric air sampling to ensure the environment remains suitable for sterile compounding.	
Settling plates are used during compounding to monitor the quality of air during compounding processes and documented in the batch records.	
Non-viable particle counts occur during operations in areas most at risk to exposed product, containers and closures.	
Surface sampling is conducted after each batch prior to cleaning and documented on batch records.	
Surface sampling is routinely conducted in all classified spaces in those locations identified to be at highest risk of contamination.	
Surface sampling is conducted in critical areas that are in contact with products, containers or other components used in compounding.	
Media used in environmental and personnel monitoring has been shown to promote the growth of microorganisms and contains agents to neutralize cleaning solutions and disinfectants.	
Sampling data is collected and reviewed on a periodic basis as a means of evaluating the overall state of control of the compounding environment.	
Environmental Monitoring Data is trended to support the adequacy of clean room quality.	

Adverse changes in the environment are investigated and promptly remediated.	
Alert and action levels for CFU counts have been established in SOP's for the facility.	
Air pressure differentials are continuously monitored and demonstrate that a cascading pressure differential is maintained throughout the compounding area during production of sterile compounds. Alarms and deviations are documented, investigated, and remediated.	

Control of Components, Containers and Closures

21CFR part211 Subpart E

Facility has a quality agreement with API suppliers to ensure all API's are manufactured in registered FDA facilities.	
Written procedures describe with sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures. Procedures are followed.	
Components and drug product containers and closures are handled and stored, at all times, in a manner to prevent contamination.	
Bagged or boxed components of drug product containers or closures are stored off the floor and suitably spaced to permit cleaning and inspection.	
Components, containers and closures are stored under quarantine until they have been sampled, tested or examined and released for use by the quality control unit. Each lot of components, containers and closures is appropriately identified as to its status (quarantined, approved, or rejected).	
Each component is tested for conformity to written specifications for identity, purity, strength and quality. Supplier analysis may be accepted provided that at least one specific identity test has been conducted by the firm and the firm has established the reliability of the supplier's analysis through validation of supplier's test results at appropriate intervals.	
Containers and closures are tested for conformity to written specifications. A certificate of testing from the supplier is acceptable if the reliability of the suppliers' test results is established and at least a visual identification is conducted by the firm.	
Each lot of component with potential for microbiological contamination are subjected to microbiological tests before use.	
Components, drug product containers and closures approved for use are rotated so that the oldest approved stock is used first. Deviations from this are temporary and appropriate.	
Drug product containers and closures are not reactive, additive, or adsorptive so as to alter the safety, identity, strength, quality or purity of the drug.	
Firm has written specifications, methods of testing if indicated, methods of cleaning, sterilizing and depyrogenating drug product containers and closures.	
Facility has a system in place to ensure final drug product containers, closures and stoppers are endotoxin free. Failures are investigated and documented.	
Written procedures include material transfer from less classified air to higher classified air and include procedures to sanitize materials prior to introduction into the clean room.	
Facility has appropriate sterile PPE.	
Materials for cleaning the PEC's are **sterile**.	
Filters used for sterilization have documentation that they are compatible with the product, are pharmaceutical grade, non-pyrogenic and capable of sterilizing the intended volume.	
Written procedures identify storage times beyond which materials must be reexamined before use.	
Release of retested material clearly identified for reuse.	

Production - 21CFR part 211 subpart F

There are written procedures for production and process controls to assure the drug products have the identity, strength, quality, and purity they purport to possess. Procedures are followed. Deviations are recorded and justified.	
Components removed from the original container to another are properly labeled.	
Weighing, measuring, or sub-dividing of components is supervised. Each container of component dispensed to manufacturing is examined by a second person.	
Each component added to the batch is verified by a second person unless added by automated equipment under 211.68.	
Actual and theoretical yields are determined at each production phase and are verified by a second person. If yields are calculated by automated equipment, verification is done by one person.	
Written procedures indicate how and who verifies that correct containers and packages are used for the finished product.	
In-process specifications have been established and followed for each production phase to ensure uniformity of drug product.	
Control procedures include disintegration time, adequacy of mixing, dissolution times and rates where appropriate.	
Quality control unit approves or rejects in- process materials that are tested during the production process after completion of significant phases of production.	
Time limits are established for the completion of each production phase; Deviations are justified and documented.	
Sterilization methods are validated.	
SOP's identify hold times for depyrogenated glassware, and the hold times have been validated.	
Integrity testing is conducted on all filters used to sterilize product and is documented on the batch record.	
Products prepared for lyophilization are maintained in ISO 5 laminar flow air throughout the production process from sterilization, filling, and transport to the lyophilizer.	
There are an adequate number of personnel to supervise the manufacture processing, packing, or holding of each drug product.	
All finished products are held in quarantine until QC has completed testing and releases the batch.	
A 100% inspection of finished sterile products for cracks, visible particles and significant defects is performed.	
Firm has written procedures that define the defects to be removed from the lot and actions to take if the number of critical defects exceeds the pre-determined level.	
Firm has a program for sampling and examination of inspected products that evaluates the effectiveness of inspection.	

Packaging and Labeling - 21 CFR part 211 subpart G

Written procedures describe the receipt, identification, storage, handling, examination and/or testing of labeling and packaging material. Procedures are followed.	
Written procedures describe control procedures employed for issuance of labeling. Procedures are followed.	
Written procedure specifies who is authorized to issue labels and strict control is exercised over labeling operations.	
Records are maintained for each shipment received of each different labeling material indicating receipt, examination/testing, and whether accepted or rejected.	
Labels and other labeling materials for each different drug product, strength, dosage form, or quantity of contents are stored separately and properly identified.	
Access to label storage area is limited to authorized personnel	
Obsolete and outdated labels, labeling and packaging materials are destroyed.	

Unlabeled drug filled product containers intended for future labeling are identified with drug name, strength, quantity and lot number.	
Written procedure specify how labels are issued, used, reconciled with production, returned when unused, and the specific steps for evaluation of any discrepancies.	
Written procedures call for the destruction of excess labeling on which lot and control #'s have been stamped or imprinted.	
100% Visual inspection is conducted for correct labeling during or after completion of finishing operations for hand applied labeling. Such examination is performed by one person and independently verified by a second person. Or use of electronic equipment to conduct 100% examination.	
Procedures are established and followed to assure that correct labels, labeling, and packaging materials are used.	
Procedures are designed to prevent mix-ups and cross-contamination by physical or spatial separation from operations on other products.	
Written procedures detail examination of packaging and labeling materials for suitability and correctness and is documented on the batch record.	
Drug labels include the statement "this is a compounded drug, the name, address and phone # of the facility.	
The label of the drugs contains the lot or batch #, the established name of the drug, dosage form and strength, quantity or volume, the date the drug was compounded, the expiration date, storage and handling instructions, NDC # (if available), the statements "not for resale" and " For Office Use Only," and a list of active and inactive ingredients identified by established name and the quantity or proportion of each ingredient and route of administration.	
The label or container contains the following: www.fda.gov/medwatch and 1-800-FDA-1088.	
Written procedures detail how equipment is to be checked immediately prior to use for removal of any labels, labeling, and packaging materials from prior print operations, and is documented on the batch record. Procedures are followed.	

Holding and Distribution
21CFR Part 211 Subpart H

Written procedures describing warehousing of drugs include quarantine of drug product before release by QC unit, storage under appropriate temperature, relative humidity, and light.	
Procedures for the warehousing of drugs are followed.	
Written procedures include FIFO of product distributed and a system whereby product can be recalled.	
The firm has conducted shipping studies to confirm that drug products can be shipped without negatively impacting the safety, identity, strength, quality and purity of the drug product.	

Laboratory –

21 CFR part 211 subpart I

Contract labs are FDA registered.	
Facility has qualified their contract labs.	
Laboratory specifications, standards, sampling plans and test procedures are approved by Quality Unit; deviations from written specifications are recorded and justified.	
All laboratory procedures are followed and documented contemporaneously.	
Laboratory controls include procedures designed to assure that components, containers, closures, drug products, and in-process materials, conform to appropriate standards of identity, strength, quality and purity.	
Instruments, apparatus, gauges, and recording devices are calibrated at suitable intervals in accordance with an established written program.	
Stability tests are derived from reliable, meaningful and specific tests methods and justify the assigned BUD of each drug product.	
There is a written program to assess the stability characteristics of each product. The program includes sample size and test interval, storage conditions, and testing the drug product in the same container closure system in which the product is distributed.	

Lyophilized products have stability data for both before and after reconstitution.	
Facility has approved finished product specifications for all CSPs.	
All batches of drug products have undergone appropriate laboratory testing to determine conformance to specifications.	
Procedures describe sampling and testing plans and include method of sampling and the number of units per batch to be tested.	
Acceptance criteria for sampling and testing conducted by the quality control unit are adequate to assure that batches of drug products meet appropriate specifications.	
Drug products failing to meet established specifications or any other relevant quality control criteria are rejected.	
Stability studies, microbial effectiveness testing on the preservative, container closure studies and sterility testing have been conducted to ensure the CSP continues to meet all specifications over the intended shelf life of the product.	
Sterility testing for all batches is conducted using a USP 71 test or a validated alternate test that is proven equivalent or superior to the USP<71> test. .	
Sterility tests for products requiring reconstitution are conducted using preservative free diluent.	
Method suitability has been conducted for all products.	
Endotoxin testing is conducted on all batches.	
Potency is conducted on all batches.	
Appropriate # of articles/volume is tested for sterility.	
The accuracy, sensitivity, specificity, and reproducibility of test methods are established and documented; failures are rejected.	
A reserve sample, representative of each lot or batch of drug product, is retained and stored under conditions consistent with product labeling and in the same container-closure system for 1 year past the BUD of the drug product.	

Records and Reports
21CFR
Part 211 Subpart J

All records associated with a batch, including records of containers, closures and labeling are retained for at least 1 year after expiration of the batch. Records related to product distributed into the state of Florida are retained 4 years.	
Written records are maintained so that data can be used for evaluating, at least annually, the quality standards of each drug product. Procedures include a review of complaints, recalls, and investigations for each drug product, and include a representative number of batches, whether approved or rejected.	
Records of maintenance, cleaning, sanitizing, inspection and use of major equipment are kept and show the date, time, product, and lot number of each batch produced.	
Logs are signed or initialed and dated by persons performing and double checking the cleaning and maintenance of equipment. Entries are in chronological order.	
All components, containers, closures, and labeling are identified on batch records and traceable to the finished product.	
Master production and control records for each drug product are prepared and include batch size, name and strength of product, dosage form, name and weight of each ingredient, complete list of all components, statement of theoretical yield, % deviation from theoretical yield that requires an investigation, description of containers, closures and packaging materials, specimen of labels, complete manufacturing and control instructions, sampling and testing procedures, product specification, special notations and precautions to follow.	
Master production and control records are prepared, dated and signed with a full signature by one person and independently checked, dated and signed by a second person.	
Batch Production and Control records are accurate and complete.	
Batch records include documentation that each significant step was accomplished and includes date and time.	
Major equipment is identified on the batch record.	
The identity of each person performing, supervising, or checking each step is documented on the batch record.	
The firm has an SOP for product release. The production batch and control records, including those for packaging and labeling, are reviewed and approved by the quality unit to determine compliance before a batch is released or distributed.	

Complete records of any modification of an established method used in testing are maintained.	
Records of calibration for laboratory equipment and gauges area maintained.	
Distribution records contain the name, strength, description, dosage form, lot number, quantity of the drug product and the date shipped as well as the name and address of the consignee.	
Firm has written procedures for handling all complaints which include provisions for review by the quality control unit. Procedures are followed.	
A written record of each complaint is maintained in a file designated for drug product complaints. Records are maintained at the establishment where the drug product was manufactured, or if kept at another facility, are readily retrievable.	
Records of complaints include the name, strength and lot number of the drug as well as the name of the complainant, nature of the complaint and response to complaint.	
The firm maintains separate, complete and readily retrievable records of distribution into the state of Florida.	
The firm has SOPs for adverse event reporting to the FDA.	
Firm has record of adverse event reports submitted to FDA.	
ADEs are adequately reported to FDA. Reasons for not reporting an ADE are documented.	

Remarks:

21CFR210.1(b) “The failure to comply with any regulation set forth in this part and in parts 211 through 226 of this chapter in the manufacture, processing, packing, or holding of a drug shall render such drug to be adulterated under section 501(a)2(B) of the act and such drug, as well as the person who is responsible for the failure to comply, shall be subject to regulatory action”.

Virtual Inspection conducted by Senior Pharmacist,

I have read and have had this inspection report and the laws and regulations concerned herein explained and do affirm that the information given herein is true and correct to the best of my knowledge. I have received a copy of the Licensee Bill of Rights.

Investigator/Sr. Pharmacist Signature: Representative:

Date: Date:

California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833
Phone: (916) 518-3100 Fax: (916) 574-8618
www.pharmacy.ca.gov

Business, Consumer Services and Housing Agency
Department of Consumer Affairs
Gavin Newsom, Governor

INSPECTION REPORT

Pharmacy __ _ Hospital Pharmacy ____ Clinic ____ Exempt Hospital ____ Wholesaler ____ Hypodermic ___

Date: 6/15/2022 Inspector: Margaret Panella-Spangler

Firm: MEDISOURCERX Phone: (714) 455-1300

Address: 10525 HUMBOLT ST City: LOS ALAMITOS Zip: 90720

Ownership: CORPORATION

Permit #: OSF124 Permit Exp: 11/1/2022 DEA#: [redacted] DEA Exp: 1/31/2023

Date of Self Assessment Form: _____ Other Permit #: N/A Date of DEA Inventory: 3/31/2022

Hours M-F: 0730-1600 Hours Saturday closed Hours Sunday: closed

PIC _____ _____ Administrator _____

RPH Consultant _____ _____

Staff RPH Name:	License #:	Staff Name:	License #:
PALLAVI D BADKAR	RPH75987	EMMA R SHEEHAN	TCH149972
VENUS FIROUZEHEE	RPH76758	RONNIE L PENROSE	TCH8714
		ROSEMARIE J TAUTUA	TCH77376
		TERRY PASKE	MANAGER

Inspector Remarks:

Medisource Outsourcing renewal inspection
Conducted on June 15, 2022
Completed by Inspectors Lyle Matthews and Peg Panella-Spangler
Assisted by Pallavi Badkar, Director of Operations, Terry Paske, Quality Manager, Venus Firouzehee, Production Manager
DEA registration, Narcotic inventory: DEA registration [redacted] -no controlled substances on hand, inventory provided during inspection

A partial Inspection was completed on 6/15/2022. Several documents were reviewed by Inspector Panella-Spangler prior to the in person inspection. Once the facility is back in production, Inspector Matthews will revisit to observe smoke studies, production, labeling and packaging and other documents as required to complete the inspection.

Since last renewal there have been no other state inspection(s) or executed recalls or ADEs/ADRs submitted (FDA SRP). The FDA provided an Establishment Inspection Report (EIR) pursuant to the FDA inspection in 2020 which produced a form 483 with seven inspectional observations on the firm's 503(B) outsourcing operations.

Annual outsourcing renewal inspection. Firm is licensed in California, Utah and Arizona. Firm produces two commercial products and one clinical trial drug in the following container closure types:

INSPECTION REPORT

- Glutathione 200 mg/mL in 30 mL amber vials, 120 days BUD assigned, 5 batches were released in 2021, 4 batches in 2022, since the last inspection
- Methylcobalamin 1 mg/mL in 30 mL amber vials, 270 days BUD assigned, 4 batches were released in 2022, since last inspection
- Methylcobalamin 5mg/ml in 30 ml amber vials, 60 day BUD with a stability currently in progress, no lots have been released for sale at the time of inspection
- Clinical trial drug in syringes, Aviptadil Acetate 0.1mg/ml in a 12 ml syringe. Drug stock is segregated and production occurs on different business days from 503B operations. Over 60 dispositions of the investigational drug were released since last inspection

Glutathione and methylcobalamin 1mg/ml have been shipped to California customers in the last 12 months. Several products are under R&D including but not limited to Thiamine 100 mg/Pyridoxine 100 mg injection, Ascorbic acid 500 mg/mL, Lidocaine 40 mg/mL, and Calcium gluconate 10%.

Follow-up to last year's inspection:
Per inspection remark, the visual inspection defect kit was updated. Promised date was September 2021. A deviation was created. This was provided with the pre-inspection documents.

Quality: Subpart B
Personnel and organization: New quality manager 2021, new production pharmacist 2022. Very small staff and some staff members have reporting to quality and production, blurring distinct units for each.
Policies and Procedures: Viewed during inspection
Personnel training and PPE: Facility dedicated scrubs. Single use disposable sterile coveralls with booties, hoods, sleeves, and goggles. Firm has re-usable sterile gowns, booties, hoods, and goggles as back-up.
Vendor qualifications: viewed vendor chart; quality agreements are in place. Critical vendors will be requalified annually. Other vendors to be requalified biannually. Chart provided at inspection was not updated or several vendor qualifications were out of date.
Validations and qualifications: New IOPQ provided for equipment
CAPAs, deviations, and customer complaints: Provided, several selected for review and reviewed during inspection.
ADRS: none reported since last inspection
Essential Copies / Drug Shortages:

Facilities: Subpart C
Layout: Small facility in a office business park. Floor plan was provided. Approximately 5000 square feet with a clean room suite of approximately 1000 square feet.
Inspectional walk-through:
Critical Utilities: Monthly routine maintenance by Air West; invoices viewed. Process gases included compressed air (crimping) and nitrogen (not in use). Both are delivered from purchased tanks. COA for compressed air viewed.
Certifications were conducted by TSS Inc. in November 2021
ISO 8 areas - Gown room, Prep room, SC ante room, SC room, Hallway: All areas had dynamic testing and met specifications for non-viable particles, air flow, pressurization and HEPA filter leak tests.
ISO 7 areas - Fill room 1 and Fill room 2. Each fill room has one ISO 5 laminar airflow workbench. All areas had

INSPECTION REPORT

dynamic testing and met specifications for non-viable particles, air flow, pressurization and HEPA filter leak tests.
ISO 5 workbenches; As above
Compounding space and aseptic area cleaning: cleaning logs provided. Cleaning/disinfecting agents include TX650 TexQ, Spor-Klenz, and 70% IP A; all sterile.

- Daily (TX650 and IP A) - only in areas where personnel have entered
- Weekly (Spor-Klenz and IP A) - in all ISO classified areas and sterilization room
- Monthly (TX650, Spor-Klenz, and IP A) - in all ISO classified areas and sterilization room

Equipment: Subpart D
Calibration and Equipment Maintenance: Master list provided during inspection and viewed
IQ, OQ, PQ: Provided for new equipment: Calibration document for new thermometer, IOPQ for new refrigerator, IOPQ for pH meter, all provided during inspection
Sterilizing Filter selection & compatibility: in batch record
Equipment cleaning log: Concerns it only takes 2 minutes to clean an incubator, January 2022 log

Control of Components and Drug Product Containers and Closures: Subpart E
Identification and inventory: There are dedicated areas for released and quarantined goods. Color coded hold (yellow), release (green), and quarantine (orange) stickers are used.
Storage conditions: Glutathione and Methylcobalamin finished goods are stored under refrigeration and protected from light.
Quarantine and release: Done by Quality
Component/ API testing: Annually for APL Every two years for components and excipients. Glutathione bulk API has had the COA from the vendor confirmed. Methylcobalamin bulk API has been tested for ID, assay, bioburden, and endotoxin. Firm is awaiting finalized results for the remaining COA tests for Methylcobalamin from ARL and Element labs.
Container Closure Suitability and Integrity: viewed for Methylcobalamin 1 mg/rnl (vacuum decay) at least at the beginning and at the end of the study period

Production and Process Controls: Subpart F
Master & Batch records: reviewed sample batches for the two products and investigational drug product: Batch records are not drug specific per CFR 211.188

- Components, bill of materials, equipment identification, personnel identification was not provided with pre inspection batch records
- Production processing steps with verification steps: Not in order and possible to switch out pages
- Specification sheet & laboratory COAs / raw materials: Not for all
- Production environmental monitoring and personnel monitoring sampling
    - Continuous non-viable particulate monitoring & volumetric viable air sampling during batch production in ISO-5
- Post-production evaluation – inspection, labeling, sampling: Deferred during inspection
- Processing start / end times noted
- In-Process controls – bubble point testing of filter, pH check, weight check, bioburden before filtration and

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end of hold time

- Limits of production time / hold time of intermediates – reviewed

Method Suitability and Container Closure Integrity: In the process of a very large investigation into their vials
Yields: Noted on the batch record
Remarks:

1. Per CFR 211.186, the Master Production records are not compliant making the batch records non-compliant. Please review the CFR and ensure new master production records and the batch records are compliant. Current draft is not adequate.

Packaging and Labeling Control: Subpart G
Acceptance of packaging and labeling materials:
Control of labels: Documented in the batch record
Line clearance: Deferred until production visualized
Visual inspection of product postproduction: Noted in the batch record, AQL done twice, before and after labeling. Per ICH and ANSI respectively.
Examination of finished labeled product: Noted in the batch record

Holding and Distribution: Subpart H
Warehousing procedures: No changes
Distribution procedures: Noted new SOP for packaging and distribution of product. SOP allows for hand delivery of product due to an "emergency" situation.

1. Pack-out procedures: Described in detail in new SOP #: PKC-003 MOCA #: M21-DOC-036 Revision #: 03 Effective: 12/20/2021

Laboratory Controls: Subpart I
Stability studies: All completed by independent laboratories (Eagle Analytical/ARL/Focus)
Release testing: Provided with batch record: specs include appearance, potency<1225>, sterility via Scan RDI, endotoxin <85>, pH<791>, sub-visible particles/particulates <788>/<789>, visual inspection<790/1790>, and preservative content
Testing Samples: Noted in batch record.
Reserve samples: 10 samples kept per batch; noted in batch record.
Equipment & facility: EM and PPM incubated in house and read in house: Samples sent out for ID when growth occurs
Environmental Sampling: new SOP effective 7/21/2021 SOP#: PPC-002 MOCA #: M21-DOC-004 Revision #: 05
ISO 5 Areas Daily and weekly except for personnel

- Personnel sampling include R/L fingertips, R/L sleeve, gown, hood at the end of each batch for aseptic operator for ISO 5 after production
- Non-viable particle counts - one-minute samples taken continuously in during production,
- Viable air sampling done passively during production Settling plate in ISO 5 - max of 4 hours; on left and right side of hood

ISO 7 Areas Daily and weekly except for personnel

INSPECTION REPORT

- Viable air sampling once during production in ISO 7
- At the beginning of each batch fill in ISO 7 (pumps, crimper, cart)
- Non-viable air sampling during production

ISO 8 Areas in the hallway and gowning area have Weekly monitoring
ISO 8 Areas in the building are monitored monthly
Media control: Commercial media used; growth promotion performed on each lot. Incubation at two temperatures (1) 30 to 35 deg C for NLT 72 hours followed by (2) 20 to 25 deg C for 5 to 7 days; first and second reading of plates.

Records and Reports: Subpart J
Batch records: Not drug product and batch size specific and could have data changed out
Usage and cleaning logs: See under facility and equipment
Annual product reviews: Provided for glutathione dated 6/25/2021.

Discussion:

1. [redacted]
2. [redacted]

The CA State Board of Pharmacy grants its inspectors the authority to inspect per CFR 210 and 211 for compliance with current Good Manufacturing Practices [BPC 4129.2(b)]

BPC 4129.1 (e) An outsourcing facility licensed pursuant to this section shall provide the board with all of the following:

1. [redacted]
2. [redacted]
3. [redacted]
4. [redacted]

***Notification of recalls, ADRs, and complaints to the Board's email address: compounding.report@dca.ca.gov**

Please send all remark and observation responses to Peg Panella-Spangler: peg.panella-spangler@dca.ca.gov no later than June 30, 2022

The deviations and observed non-compliances referenced in this report are not intended to be an all-inclusive list of deviations and non-compliances that may exist at your firm. Your firm is responsible for investigating and determining the causes of any deviations and observed non-compliances and for

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Department of Consumer Affairs
Gavin Newsom, Governor

INSPECTION REPORT

preventing their recurrence or the occurrence of any other non-compliances and deviations.

Licensee Remarks:

I have reviewed, discussed,understand and received a copy of this form .

Pharmacist (sign) _____

Pharmacist (print) _____

Inspector (sign) _____

Owner(sign) _____

Inspector (print) _____

Owner(print) _____

Additional information (for example - corrective plan of action, Quality Assurance outcomes, factors in mitigation, etc.) you want to submit for consideration may be sent on the attached form to my attention at the above address no later than 14 calendar days from the date above. Please include a copy of this form with any information that you submit.

Within 14 calendar days from the above date, please submit to me at the above address the following: