COMMONWEALTH OF VIRGINIA
Board of Pharmacy

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Tentative Agenda of Ad Hoc Committee on Delivery of Prescription Drug Orders (HB1956), Guidelines for Counseling on Drug Disposal (HB2046), and Guidance for Complying with USP Chapter <800>

September 18, 2017

10:00AM

TOPIC	PAGES
Call to Order: Ellen Shinaberry, Chairman	
• Welcome & Introductions	
• Reading of Emergency Evacuation Script	
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.	
Agenda Items:	
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o Letters from Delegates Orrock, Peace, and Head	4-8
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o Excerpts from Minutes of May 2016 and June 2016 Board Meeting	18-20
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Adjourn	

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

HB 1956 Prescription drug order; requirements for shipping Schedule VI controlled substances.

another bill? go

Gordon C. Helsel, Jr. | all patrons ... notes | add to my profiles

Summary as introduced:

Delivery of prescription drug order; shipping Schedule VI controlled substances. Clarifies requirements related to delivery of prescription drug orders, including delivery of such orders by mail, common carrier, or delivery service, and requires the Board of Pharmacy to adopt regulations for the delivery of prescription orders by mail, common carrier, or delivery service.

Full text:

01/10/17 House: Prefiled and ordered printed; offered 01/11/17 17102125D **pdf | impact statement**

Status:

01/10/17 House: Prefiled and ordered printed; offered 01/11/17 17102125D
01/10/17 House: Referred to Committee on Health, Welfare and Institutions
01/17/17 House: Assigned HWI sub: Subcommittee #1
01/31/17 House: Subcommittee recommends laying on the table by voice vote
02/07/17 House: Left in Health, Welfare and Institutions

17102125D

HOUSE BILL NO. 1956

Offered January 11, 2017

Prefiled January 10, 2017

A BILL to amend and reenact § 54.1-3420.2 of the Code of Virginia, relating to delivery of prescription drug order; shipping Schedule VI controlled substances.

Patrons—Helsel and Peace

Referred to Committee on Health, Welfare and Institutions

Be it enacted by the General Assembly of Virginia:

1. That § 54.1-3420.2 of the Code of Virginia is amended and reenacted as follows:

§ 54.1-3420.2. Delivery of prescription drug order.

A. *Prescription drug orders may be delivered (i) directly to the patient or his legally authorized representative at the pharmacy; (ii) to the home of the patient, by hand delivery or by mail, common carrier, or delivery service; or (iii) to another delivery location, by hand delivery or by mail, common carrier, or delivery service, provided such delivery to such delivery location is authorized by federal law and regulations of the Board. The Board shall adopt regulations governing the delivery of prescription orders by mail, common carrier, or delivery service to a patient's home or to another delivery location, which shall include requirements related to access, accuracy, security, required records, storage, and accountability. Such regulations shall also include temperature control standards and shall require, for any drug requiring temperature control, a method approved by the United States Pharmacopeia by which the patient can detect temperature variances that could cause degradation of the drugs.*

B. Whenever any pharmacy permitted to operate in ~~this~~ *the* Commonwealth or nonresident pharmacy registered to conduct business in the Commonwealth delivers a prescription drug order *to a patient's home or another designated location* by mail, common carrier, or delivery service, ~~when the drug order is not personally hand delivered directly, to the patient or his agent at the person's residence or other designated location, the following conditions shall be required~~ *each shipment so delivered shall include the following*:

1. Written notice ~~shall be placed in each shipment~~ alerting the consumer that under certain circumstances chemical degradation of drugs may occur; and

2. Written notice ~~shall be placed in each shipment~~ providing a toll-free or local consumer access telephone number which is designed to respond to consumer questions pertaining to chemical degradation of drugs.

~~B. If a prescription~~ *C. Prescription* drug ~~order~~ *orders* for a Schedule VI controlled ~~substance is not personally hand delivered directly to the patient or the patient's agent, or if the prescription drug order is not delivered to the residence of the patient,~~ *substances shall only be delivered to a delivery location other than the patient's home if* the delivery location ~~shall hold~~ *holds* a current permit, license, or registration with the Board that authorizes the possession of controlled substances at that location. ~~The Board shall promulgate regulations related to the security, access, required records, accountability, storage, and accuracy of delivery of such drug delivery systems.~~ Schedule II through Schedule V controlled substances shall be delivered to an alternate delivery location only if such delivery is authorized by federal law and regulations of the Board.

~~C.~~ *D.* Prescription drug orders dispensed to a patient and delivered to a community services board or behavioral health authority facility licensed by the Department of Behavioral Health and Developmental Services upon the signed written request of the patient or the patient's legally authorized representative may be stored, retained, and repackaged at the facility on behalf of the patient for subsequent delivery or administration. The repackaging of a dispensed prescription drug order retained by a community services board or behavioral health authority facility for the purpose of assisting a client with self-administration pursuant to this subsection shall only be performed by a pharmacist, pharmacy technician, nurse, or other person who has successfully completed a Board-approved training program for repackaging of prescription drug orders as authorized by this subsection. The Board shall promulgate regulations relating to training, packaging, labeling, and recordkeeping for such repackaging.

~~D.~~ *E.* Prescription drug orders dispensed to a patient and delivered to a Virginia Department of Health or local health department clinic upon the signed written request of a patient, a patient's legally authorized representative, or a Virginia Department of Health district director or his designee may be stored and retained at the clinic on behalf of the patient for subsequent delivery or administration.

~~E.~~ *F.* Prescription drug orders dispensed to a patient and delivered to a program of all-inclusive care for the elderly (PACE) site licensed by the Department of Social Services pursuant to § 63.2-1701 and

overseen by the Department of Medical Assistance Services in accordance with § 32.1-330.3 upon the signed written request of the patient or the patient's legally authorized representative may be stored, retained, and repackaged at the site on behalf of the patient for subsequent delivery or administration. The repackaging of a dispensed prescription drug order retained by the PACE site for the purpose of assisting a client with self-administration pursuant to this subsection shall only be performed by a pharmacist, pharmacy technician, nurse, or other person who has successfully completed a Board-approved training program for repackaging of prescription drug orders as authorized by this subsection. The Board shall promulgate regulations relating to training, packaging, labeling, and recordkeeping for such repackaging.

COMMONWEALTH OF VIRGINIA
HOUSE OF DELEGATES
RICHMOND

ROBERT D. "BOBBY" ORROCK
POST OFFICE BOX 458
THORNBURG, VIRGINIA 22565

FIFTY-FOURTH DISTRICT

COMMITTEE ASSIGNMENTS:
HEALTH, WELFARE AND INSTITUTIONS (CHAIRMAN)
FINANCE
AGRICULTURE, CHESAPEAKE AND
NATURAL RESOURCES
RULES

February 17, 2017

The Honorable David Brown, Director
Virginia Department of Health Professions
9960 Mayland Drive
Richmond, VA 23233-1463

Dear Mr. Brown.

The Virginia Health, Welfare and Institutions Subcommittee voted to lay HB1956 on the table with a letter requesting the Virginia Board of Pharmacy to consider the issue related to any variances that may exist between mail-order and hand-delivered prescription medications.

I would appreciate your consideration of this and please inform me of any recommendations by November 2017.

Sincerely,

Robert D. (Bobby) Orrock, Sr.

RDO/rh

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COMMONWEALTH OF VIRGINIA
HOUSE OF DELEGATES
RICHMOND

CHRISTOPHER K. PEACE
POST OFFICE BOX 819
MECHANICSVILLE, VIRGINIA 23111

NINETY-SEVENTH DISTRICT

COMMITTEE ASSIGNMENTS:
GENERAL LAWS (VICE CHAIRMAN)
APPROPRIATIONS
HEALTH, WELFARE AND INSTITUTIONS

March 2, 2017

The Honorable David Brown, Director
Virginia Department of Health Professions
9960 Mayland Drive
Richmond, VA 23233-1463

RE: House Bill 1956 (Heisel): Delivery of prescription drugs orders

Dear Dr. Brown,

On Tuesday, January 31, 2016, the Virginia Health, Welfare and Institutions Subcommittee voted to lay HB1956 on the table with a letter. I understand that the Chair has sent a letter asking the Board of Pharmacy to consider and provide recommendations regarding variances that may exist between mail-order and hand-delivered prescription medications.

As a member of the subcommittee which heard the bill, I heard conflicting claims about federal regulations related to the transportation of prescription drugs, including how the federal standards impact transit from the manufacturer to the pharmacy to the consumer. This matter is particularly important as more and more medications are delivered via mail-order or common carrier, including high-cost specialty pharmaceuticals such as biosimilars and biologics. I am interested in understanding how and whether mail-order shipment requirements have kept pace with changing pharmaceutical products, and whether Virginia's patients are obtaining the information they need to make informed decisions about their mail-order medications, especially those for which temperature control is vital to maintaining the efficacy of the drug.

As such, I would like to request that, as the Board studies the issues as requested by the Chair, that the Board consider specific questions that I, and other members have, regarding this matter. Information related to the following questions will be of great help as we consider this issue going forward:

1. What states have implemented rules, regulations or guidance regarding the shipment of prescription drugs directly to the consumer by mail or common carrier?

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2. Of the states that do have some form of regulation to govern shipping, which states require some form of notice or instruction to the consumer related to temperature? Do any states require a method by which consumers can detect temperature variation?

3. Which states collect data related to problems with the shipping of prescription drugs, either for all licensed pharmacies that ship drugs by mail or common carrier, or for any health plan that is overseen or implemented by the state (i.e. a state employee health plan, Medicaid, plan, etc.?) What kinds of data are collected?

4. What federal regulations or guidelines exist related to temperature controls of mail order prescription drugs? Is this really covered by "track and trace" as was claimed by some?

5. What part of the shipping process do the federal regulations control? (i.e. the oversight and monitoring of medications between the manufacturer and the pharmacy or between the pharmacy and the consumer?)

6. Does the Commonwealth track current losses related to fraud, waste and spoilage of mail order prescription drugs and if so, what are the associated costs to the Commonwealth?

7. What is the approximate number of Virginians (covered by commercial plans) who are required to obtain medication via mail-order?

I appreciate the work the Board of Pharmacy does to protect the public and I thank you for your consideration of this request.

If you have any questions, please do not hesitate to contact me.

Sincerely,

Christopher K. Peace

CHRISTOPHER T. HEAD
POST OFFICE BOX 19130
ROANOKE, VIRGINIA 24019

SEVENTEENTH DISTRICT

COMMONWEALTH OF VIRGINIA
HOUSE OF DELEGATES
RICHMOND

COMMITTEE ASSIGNMENTS:
FINANCE
HEALTH, WELFARE AND INSTITUTIONS
MILITIA, POLICE AND PUBLIC SAFETY

May 22, 2017

The Honorable David Brown
Director
Virginia Department of Health Professions
9960 Mayland Drive
Richmond, VA 23233-1463

RE: House Bill 1956 (Helsel): Delivery of prescription drugs orders

Dear Dr. Brown,

I understand that the Chair of the Health, Welfare and Institutions Committee has sent a letter asking the Board of Pharmacy to consider and provide recommendations regarding variances that may exist between mail-order and hand-delivered prescription medications.

This came as a result of a motion I made to Table HB 1959 with a letter. During the subcommittee meeting that heard the bill, a number of concerning points were made. One speaker even indicated that if members are concerned about temperature excursions with certain drugs shipped from a pharmacy through mail order, there should be just as much concern over the shipment of drugs on the way to the pharmacy from a manufacturer or distributor. We need the Board's expertise to help clarify this and other questions. As such, I would like to request that, as the Board studies the issue as requested by the Chair, the Board consider a few specific questions which I have outlined below:

1. §54.1-3420.2 requires that all medications shipped by mail order include a written notice "alerting the consumer that under certain circumstances chemical degradation of drugs may occur." Is this notice specific to the drug(s) being shipped? What guidelines does the Board have in place for the content of these notices?

2. How does the Board track compliance with the law requiring this notice?

3. How does a consumer know if his or her medicine has been subjected to circumstances that can affect the drug's efficacy?

4. Conflicting information was presented to the subcommittee as to whether or not the federal government already has regulations or guidelines in place regarding temperature variations of drugs shipped by mail or common carrier. Are such regulations or guidelines in place, and do the guidelines cover all aspects of medication shipments,

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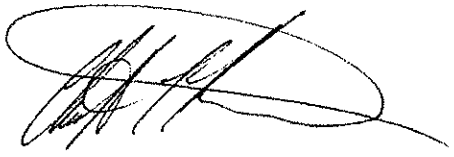
including transit from the manufacturer/wholesaler to the pharmacy, as well as shipment from the pharmacy to the consumer?

5. What is the current process used by pharmacies to determine whether the drugs received by the pharmacy have been exposed to conditions that could compromise the efficacy of the drug(s)? Does Virginia have guidelines specific to this shipping scenario, or do the manufacturers/wholesalers rely on federal regulations or guidelines when shipping to a pharmacy?

6. If there are no state or federal guidelines that cover shipment from the manufacturer/wholesaler to the pharmacy or pharmacy to consumer, is this something Virginia can address?

I appreciate your consideration of this request. If you have any questions, please do not hesitate to contact me.

Sincerely,



Christopher T. Head
Virginia House of Delegates

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September 6, 2017

By Email: caroline.juran@dhp.virginia.gov
Ms. Caroline Juran
Virginia Board of Pharmacy
9960 Mayland Drive
Richmond, VA 23233-1463

RE: House Bill 1956 / Ad-Hoc Study on Mail Order Delivery of Prescription Medications

Dear Ms. Juran,

I am writing on behalf of Temptime to provide comment on the ad-hoc committee's study related to the variances that exist between mail-order and hand-delivered prescription medications.

Temptime works to improve global public health and better patient outcomes by manufacturing temperature monitoring devices used in the shipment of medications. Temptime is one of many companies that manufacture a variety of temperature devices for this purpose.

Protecting Patients

Few issues are more important to public health than the proper storage and handling of medications. To properly maintain a medication's stability, many medications must be stored in a refrigerator or freezer. Excessive heat or cold—even a single exposure in some instances—can reduce a medication's potency and result in significant health risks to the patient.

Given the seriousness of temperature control as it relates to the efficacy of medication, it is critical that Virginia ensure that all medication, regardless of how it is delivered, is subject to the same temperature control standards and that patients, regardless of how they take receipt of their medications, have the information they need to ensure the medication's stability.

As more and more patients receive complex temperature sensitive medications by mail-order, the last mile of delivery (from the mail-order pharmacy to the patient) has generated greater attention. In 2015, the American Academy of Pediatrics, recognizing the importance of this issue, passed a resolution

advocating for improved safety of all mail-order medication.[1] The resolution advocated for, among other things, the use of visual temperature indicators on each box or vial of medication shipped in the mail. The Academy passed the resolution after a 2012 Yale University study related to the temperature of vaccines found that the temperature variances between refrigeration units placed vaccines at risk of reduced potency (and children at risk for ineffective protection) and that freeze indicators affixed to boxes of vaccines provided an early warning related to the risks of compromised medication.[2]

Additionally, in the last several years, separate classes of patients in California have filed two class actions alleging that, among other things, refrigerated specialty drugs (Enbrel) shipped to consumers are not being stored and maintained between a temperature of 36-46 degrees and that the shipper "has never provided or included a means by which Plaintiff or the Class could monitor or verify the temperature of the Enbrel or other Specialty Drugs after it left Caremark's pharmacy."[3]

As the use of complex drugs such as biologics and biosimilars continues to increase, it is critical that patients have access to information that indicates whether the medication has been subjected to conditions that cause degradation. Biosimilars and biologics are often both expensive and highly sensitive to temperature variances, and some patients indicate they have lost thousands of dollars in an effort to protect themselves from heat and freeze damaged medications.

Further, for those patients who are required to utilize mail-order services as part of a health plan's benefits, the issue is extremely important, as they may not have the resources to utilize a local brick and mortar pharmacy ("local pharmacy"). In these situations, the patient, who likely has no medical or chemical composition training, must "guess" whether his or her medication has been compromised.

Giving patients, at a minimum, a method by which to determine whether their medication may have been compromised by a temperature variance will create more uniformity between mail-order and local pharmacies and will help give patients the information they need to make informed decisions about their own health.

Variances: Mail-order and hand-delivered medication

Mail-order

Virginia code §54.1-3420.2 requires that drugs delivered by mail include a generic written notice "alerting the consumer that under certain circumstances chemical degradation of drugs may occur."

The consideration of temperature is important enough that Virginia law mandates this notice be provided to patients, yet the law does not require that the same patient who has received the notice (and, as a result, may be concerned whether his or her medication was left in the mailbox on a very hot or very cold

[1] Resolution #55 (15) – 2015 Annual Leadership Forum, American Academy of Pediatrics

[2] Angoff, R., Wood, J., Chernock, M. C., & Tipping, D. (2015). Visual Indicators on Vaccine Boxes as Early Warning Tools to Identify Potential Freeze Damage. *Infectious Diseases in Clinical Practice (Baltimore, Md.)*, *23*(4), 184–189.

[3] Boysen, Ryan. *CVS' Shoddy Shipping Ruined Arthritis Drug, Suit Says.* Law360. 3 February 2017.
Field, Emily. *Amgen, CVS Units Hit With Suit Over Arthritis Drug Shipping.* Law360. 20 October 2014.

day) have some means by which to determine whether the medication has been exposed to an extreme temperature event.

Virginia law also requires that medications delivered by mail include another written notice that provides "a toll-free or local consumer access telephone number which is designed to respond to consumer questions pertaining to chemical degradation of drugs." The law does not require that a physician or a pharmacist or an individual trained in chemical composition/degradation staff the consumer access telephone service, nor does the law require any sort of tracking related to the frequency or types of calls received by these services.

Consequently, the information a patient receives regarding chemical degradation could simply be "speculation" provided a telephone operator who can't visually inspect the medication or test it, and the operator, like the patient, can only make an educated guess as to whether the medication has been compromised.

Hand-delivery

In contrast to the handling of mail-order delivery medications, a local pharmacy that delivers medication by handing it directly to the patient is subject to a variety of very strict provisions related to the proper temperature control of drugs. These requirements provide patients with a level of confidence, knowing that the drugs have been in a monitored and controlled environment until the time they are handed to the patient.

The Virginia regulations covering pharmacies are very detailed in terms of the standards the pharmacy must meet, and so seriously does the Board take the issue, that the Regulation Committee recently recommended amendments to 18VAC110-20-150, which would require any pharmacy stocking cold temperature drugs to record the temperatures daily and to maintain the record for a period of two years.

It's difficult to imagine a local pharmacist filling a prescription for a temperature sensitive medication and then just walking away—leaving the drug on a counter, in a slot, or wherever room temperature drugs are stored while awaiting pickup for one, two, three or more days until the consumer arrives to get their medication.

Yet, this is exactly what happens daily with prescription drugs delivered through the mail. And, while most pharmacies take reasonable care in packaging the shipment of drugs, there are still days when the temperature is so high (or low) that the packaging may not be enough. This is further compounded if the patient is away for two or more days and cannot take immediate receipt of the medication, or if the system used for transport is not temperature controlled.

The Board's regulations for local pharmacies provide patients with confidence that, until the moment the medication is handed to the patient by the pharmacist, the medication has not been compromised in a way that could impact the medication's efficacy.

No similar protections exist in Virginia law for patients who receive their medications via mail-order and the goal of HB1956 was to give patients, at a minimum, the ability to determine whether the medication they receive by mail-order shipment may have been exposed to a heat or freeze event that could impact the efficacy of the drug, and subsequently, the patient's health.

Having access to temperature information will allow an informed conversation to take place between the patient, the patient's provider, and the pharmacy, and will give patients an important tool to protect their own health.

States

Virginia is not the first state to consider a requirement that mail-order shipments include a method by which the patient can determine whether the medication may have been subjected to a compromising heat or freeze event.

New Jersey's Board of Pharmacy recently finalized regulations that require all temperature sensitive medications shipped via mail-order to use adequate methods to ensure the temperature controlled conditions are maintained during delivery and requires the pharmacy to include instruction to the patient on how to detect temperature variance and how to report the variance (emphasis added):

> **New Jersey Administrative Code 13:39-5.11 Control and Monitoring of Temperature of Prescription Drugs and Chemicals**
> "2) A pharmacy that delivers a filled prescription drug or chemical to the patient, agent of the patient, or facility or healthcare provider providing care to the patient *by any method*, except when picked up directly from the pharmacy by the patient or his or her authorized agent, *shall*, in the professional judgment of the pharmacist, and in accordance with the pharmacy's policies and procedures as set forth in (d) below, use adequate methods to ensure temperature controlled conditions are maintained during facility storage, transportation, and delivery.
>
> i. To ensure that temperature control is maintained during delivery, the shipping processes may include the use of appropriate packaging material or devices according to information provided by the manufacturer, Chapter 1079 of USP, other learned treatises, or expert qualification analysis.
>
> ii. When packaging material or devices are used to maintain temperature control during delivery, *the contents of the package shall include instructions to the recipient how to easily detect improper storage or temperature variation, and instructions how to report the storage or temperature excursion to the pharmacy.*"

South Carolina recently began looking at the issue, as well. The Board of Health finalized regulations requiring that emergency medical services (EMS) responders control the temperature anywhere medications are stored to prevent drug adulteration, and to put in place requirements for the disposal of these medications in situations where a heat or freeze event occurred (emphasis added).

> **South Carolina Regulation 61-7 Section 601 Ambulance Design and Equipment**
> "5. Environmental Control and Medications: *The temperature in the patient compartment or anywhere medications are stored (QRVs, fire apparatus, rapid response vehicles, carry-in bags, and other) shall be monitored for temperature extremes to prevent drug adulteration.* Medications (excluding oxygen) and IV fluids will be removed and discarded if the temperatures reach or exceed one hundred (100) degrees Fahrenheit (thirty-eight (38) degrees Celsius). Medications and IV fluids shall also be removed and discarded if temperatures in the drug storage area drop below twenty (20) degrees Fahrenheit (negative seven (-7) degrees Celsius)."

Similarly, Iowa's Board of Pharmacy recently amended the Iowa Administrative Code (Chapter 11, Drugs in Emergency Medical Service Programs) to require that all Iowa Service Programs "...shall utilize a method

to provide continuous temperature control or monitoring, such as a temperature indicator, which at a minimum identifies when the drugs have been exposed to extreme temperatures. The service program shall regularly, but at least weekly, verify and document verification that the drugs have not been exposed to extreme temperatures."

Under Pennsylvania Code §27.18, prescription drugs that can deteriorate due to heat or cold, can be sent via mail-order "if it is shipped in a manner which would preserve the integrity of the drug, such as cold packs or other temperature control devices *and sensors that would alert the patient if the integrity of the drug was compromised.*"

In 2014, the Georgia Board of Pharmacy promulgated regulations mandating the inclusion of a temperature monitoring device in all temperature sensitive medications. The regulation was a result of legislation that successfully passed the Georgia General Assembly mandating the inclusion of a device in temperature sensitive medication sent by mail-order. Subsequently, legislation was passed changing "shall" to "may," and in February 2017 the Georgia Board of Pharmacy updated the regulations to reflect the code language.

In Washington State, SHB1765 was recently signed by the Governor. The legislation requires, among other things, that donated medications not equipped with a temperature indicator may only be released when the medication is accompanied by a donor form that attests that the donated medication has been stored in a manner and location that adheres to the condition established by the manufacturer and that the medication has not been adulterated.

Mail-order medication loss costs

Temptime is currently unaware of any mechanism by which to determine the numbers of patients in Virginia that receive medication by mail-order as compared to the numbers of patients that receive medication via hand-delivery. Our understanding is that this information is proprietary to the commercial health plans and mail-order pharmacies and it is not available publically. However, the anecdotal information we have collected indicates that waste related to temperature variance is likely high.

In 1997, a United States Pharmacopeia study found that about one quarter of packages delivered through the mail were exposed to "excessive heat which can diminish some medications' effectiveness. In the study, dummy packages with embedded temperature sensors were sent to 32 states. The study found that more than one in four mail-order prescription deliveries in the US were likely to be exposed to excessive heat during transit to the patient.[4]

In 2013, another study tested five packaging technologies commonly used by specialty pharmacies. The packages were subjected to real-world temperatures, and of the five systems tested, not one maintained the temperature range required for biologics. The study noted that the last mile of delivery is critical, given that medicines could be delayed or left exposed during this critical last stop in the cold chain.[5]

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[4] Okeke, C. C., Bailey, L. C., Medwick, T., and Grady, L. T., "Temperature Fluctuations During Mail Order Shipment of Pharmaceutical Articles Using Mean Kinetic Temperature Approach," Pharmacopeial Forum, 23(3) May-June 1997, page 4155-4182.

[5] Modality Solutions. The Cold, Hard Facts: What You Need To Know About Thermal Shipping Technologies. 2013.

In another attempt to obtain an accurate comparison between the numbers of patients receiving medication by mail-order or hand-delivery in Virginia, we reviewed the number of individuals enrolled in Virginia's state employee health plan.

In a presentation dated January 19, 2017, the Virginia Department of Human Resources Management reported that in 2016, 195,095 individuals were enrolled in Virginia's state employee health insurance plan. Of the total claims made in 2016, $273.1M was spent on medication claims[6].

The presentation goes on to note that of the claimed expenses, high cost specialty drugs such as Humira, Enbrel and Harvoni (all of which are temperature sensitive medications) were part of the "top ten" claim expenses. Additionally, the report notes that state employees filled five times more specialty prescriptions in 2016 than they did in 2012, and in 2016, the state spent 2.5 times more in costs of specialty drugs than in 2012.

Given the growing usage of complex medications by state employees, it is likely that a portion of these medications are delivered by mail-order. Temptime is continuing to work on obtaining detailed information related to the number of state employees receiving mail-order specialty drugs and we hope to provide this information to the committee by the hearing date.

Federal regulations

While the Food and Drug Administration, Drug Enforcement Agency and Centers for Medicare & Medicaid Services all have various rules related to prescription medications, none of these agencies have promulgated cold-chain rules related specifically to the last mile of delivery.

Under 21 CFR 205.50(c) the regulation governing state licensing of wholesale prescription drug distributors, the following is required for the storage of all prescription drugs:

> "(c) Storage. All prescription drugs shall be stored at appropriate temperatures and under appropriate conditions in accordance with requirements, if any, in the labeling of such drugs, or with requirements in the current edition of an official compendium, such as the United States Pharmacopeia/National Formulary (USP/NF).
>
> (1) If no storage requirements are established for a prescription drug, the drug may be held at "controlled" room temperature, as defined in an official compendium, to help ensure that its identity, strength, quality, and purity are not adversely affected."

Guidance for the last mile of delivery (pharmacy to patient) is provided by the United States Pharmacopeia (USP) and The National Formulary (USP-NF). The USP-NF guidance contains definitions, tests, and standards for chemical and biological drug substances. There are five general chapters that include information related to the temperature-sensitive supply chain.

- 1079: Good Storage and Shipping Practices
- 1083: Good Distribution Practices – Supply Chain Integrity

[6] http://hac.state.va.us/subcommittee/compensation_retirement/files/1-19-17/DHRM.pdf

- 1118: Monitoring Devices time, temperature and humidity
- 1077: Good Packaging Practices
- 1150: Pharmaceutical Stability

Specifically, USP-NF Chapter 1079 is intended to provide guidance on "good storage and distribution practices to ensure that medicine reaches the end user with quality intact." The end user is defined to include practitioners, patients and consumers.

The guidance provided by Chapter 1079 is clear that temperature control throughout the entire supply chain is critical, and notes that the guidance is intended to apply to all organizations and individuals involved in any aspect of the storage and distribution of a drug product, *including mail-order pharmacies.*

In a section devoted specifically to temperature monitoring, Chapter 1079 notes that:

> "when specific storage conditions are required and transportation qualification has not been performed, and in the absence of active or passive containers, environmental records or devices should be used to confirm that an acceptable range has been properly maintained during each stage in the supply chain."

Further, Chapter 1079 stresses the importance of temperature as it relates to medication stability, noting (emphasis added):

> *"Temperature is one of the most important conditions to control,* and requirements for each drug product should be based on stability data. Temperatures should be tracked using a monitoring systems.....*The monitoring devices should provide an alert mechanism if the preset ranges are breached...."*

Additionally, Chapter 1079 states that the following practices and controls are examples of appropriate measures that should be put in place to ensure environmental control along every step of the supply chain (emphasis added):

- "Temperature-monitoring equipment, a monitoring device, a temperature data logger, or other such device that is suitable for its intended purpose should be used.
- An appropriate number of temperature monitors or some other form of recordation or proof of temperature control. *Temperature monitor(s) should be used with every distribution process unless another process has been put in place to ensure specified temperature ranges.*
- Electronic temperature monitors should be calibrated to National Institute of Standards and Technology (NIST) or other suitable standard.
- Chemical temperature indicators may be used as appropriate.
- Predetermined temperature ranges should be set for all applicable areas, *as well as a plan of action in the event of an unacceptable excursion."*

The USP guidance is clear that temperature control is vital to the stability of medication throughout the entire supply chain, and whether medication is delivered via mail-order or by hand-delivery, the USP contemplates temperature monitors will be used at every step of the distribution process to ensure the end user has the information he or she needs to ensure the medication is safe to use.

Interestingly, we have heard some say that the implementation of Track & Trace as part of the Drug Supply Chain Security Act (DSCSA) is all that is needed to address temperature control in mail-order. We respectfully disagree.

Track & Trace is primarily designed for the purpose of limiting and preventing diversion of medication. There is no temperature control requirement related to Track & Trace, nor does the 2D barcode associated with Track & Trace measure temperature variances, or provide a method by which the patient can determine whether a temperature variance has occurred.

Shipment to pharmacies

Virginia law takes the issue of temperature control very seriously and outlines strict temperature control requirements for the wholesale distributors, manufacturers, warehouses and pharmacies that store and maintain prescription drugs.

So it remains puzzling that during the last mile of delivery, when the medication is most vulnerable, the law is virtually silent regarding the need for temperature control and/or a mechanism by which the patient can determine if degradation of the medication may have occurred.

Under Virginia Administrative Code 18VAC110-50-10 et seq. wholesale distributors, manufacturers and warehouses that receive, store and transport prescription drugs are required to provide, among other things, adequate temperature conditions. Additionally, these regulated entities, upon receipt of drugs, are required to review the integrity of the drugs, taking into account "the total facts and circumstances surrounding the transactions and the wholesale distributors, nonresident wholesale distributor or third-party logistics provider involved."

Additionally, if a prescription drug is stored before it is shipped to the pharmacy, under 18VAC110-50-50, the drug must be stored at appropriate temperatures and under appropriate conditions in accordance with the requirements of USP-NF or the drug's labeling instructions. Further, the regulation requires that temperature/humidity recordings or logs are utilized to ensure the proper storage of the medications.

So seriously does the Board take the issue of temperature control that, as already noted above, 18 VAC 110-20-10 et seq. imposes strict requirements on pharmacies storing or maintaining prescription drugs, including daily monitoring of refrigerator or freezer storage, as well as compliance with USP-NF.

It is only in the last mile of delivery that Virginia law is silent regarding temperature control mechanisms—and it is this situation that has left patients feeling unsafe, trying to guess whether the medication left on their front porch while they were at work, is safe to take or whether it has been exposed to a degrading heat or freeze event.

Conclusion

Virginia's patients need assurance that, regardless of the method in which they receive their medication, whether by mail-order or hand-delivery, the medication is safe and has been in a temperature controlled environment up until the moment the medication is received by the patient.

Giving patients, at a minimum, a method by which to determine whether their medication may have been compromised by a temperature variance will create more uniformity between mail-order and local

pharmacies and will help give patients the information they need to make informed decisions about their own health.

We ask the Board to consider a requirement that all mail-order medication shipped to Virginia patients include a method that easily allows the patient to determine if their medication has been subjected to a temperature variance.

Thank you for your time and consideration of this request. We look forward to working with you on this important matter.

Sincerely,

Michele Satterlund
McGuireWoods Consulting

cc: Jody Allen, Board of Pharmacy
Ryan Logan, Board of Pharmacy
Ellen Shinaberry, Board of Pharmacy
Sheila Elliott, Board of Pharmacy
Melvin Boone, Board of Pharmacy
Michael Thomas, McGuireWoods Consulting
Mike Rush, Temptime Corp.

decided it will not require practical experience in two practice settings. There was also some concern expressed with the availability of ASHP-accredited pharmacy technician training programs. Information from PTCB indicating an increase in the number of training programs was provided in the agenda packet.

MOTION:

The Committee voted unanimously to recommend to the full board that it adopt a legislative proposal requiring Pharmacy Technician Certification Board (PTCB) certification for initial pharmacy technician registration with a delayed effective date of July 1, 2018. (motion by Warriner, second by Boone)

- Consider 2017 Legislative Proposal for Requiring Temperature Monitoring Devices

At the March 2016 full board meeting, Michael Rush, Executive Director of Global Health Policy at Temptime Corporation requested the Board consider a legislative proposal requiring temperature sensitive medications shipped via mail to be accompanied with a device to monitor temperature during shipping. There was discussion regarding USP requirements which currently requires those shipping drugs to do so in an appropriate manner to ensure the drugs are stored at appropriate temperatures. Ms. Juran also stated that she was informed that the Georgia bill, HB132, referenced in the agenda packet was amended prior to Governor's signature and no longer requires shipments of drugs to include a temperature monitoring device.

MOTION:

The Committee voted unanimously to recommend to the full board that it take no action at this time on a legislative proposal requiring shipment of drugs to include a temperature monitoring device. (motion by Shinaberry, second by Boone)

- Consider 2017 Legislative Proposal for Addressing Compounding Best Practices

Ms. Juran highlighted certain best practices in Pew Charitable Trust's report summarizing Best Practices for State Oversight of Drug Compounding that it may wish to consider requiring in a legislative proposal. There was discussion regarding adverse event reporting for compounded drugs and ability for the Board to seize or quarantine a compounded product if there is a suspected cause for patient harm. Ms. Warriner expressed concern for the board possibly incurring costs associated with storing and possibly destroying seized drugs. She also concurred with the public comment provided that the board should not require adverse event reporting of compounded drugs without requiring adverse event reporting of all drugs. Ms. Shinaberry requested that Ms. Juran and Mr. Johnson comment on the best practice of inspecting sterile compounding pharmacies annually. Ms. Juran stated that current staffing levels would not allow sterile compounding pharmacies to be inspected annually if inspectors continue to inspect all non-compounding pharmacies every two years. She indicated they will continue to monitor inspection frequencies and may consider moving to a risk-based inspection schedule. The Board also discussed its current authority to embargo a drug product and its experience in requiring a recall through issuance of consent orders.

(motion by Saenz, second by Boone)

This issue was revisited later in the meeting, but no additional action was taken.

OTHER 2017 LEGISLATIVE PROPOSALS CONSIDERED:

- ADDRESSING COMPOUNDING BEST PRACTICES:

It was reported that the Regulation Committee reviewed The Pew Charitable Trusts' Best Practices for State Oversight of Drug Compounding. The Regulation Committee recommended no action on this subject. Much of the discussion at the full board meeting focused on the possible need to report adverse events to the board. There was not consensus on the subject. Some members did not want to require adverse event reporting solely from compounding pharmacists.

MOTION:

The Board voted unanimously to adopt a substitute motion to refer the matter back to the Regulation Committee for further review to determine if additional best practices in overseeing compounding should be required in law. (motion by Logan, second by Thornbury)

- REMOVING ONE PRESCRIPTION PER BLANK PROHIBITION:

The Regulation Committee reported that it reviewed the legislative proposal concerning the one prescription per blank prohibition and recommended to the Board that it take no action at this time based on concerns for patient safety which could result from difficulty in reading multiple prescriptions manually written on the same form. Ms. Elliott commented that the allowance could also preclude a patient from obtaining the best cost on individual drugs as it would prevent the patient from being able to present the individual prescriptions to different pharmacies. Ms. Warriner commented that chart orders containing multiple prescriptions is currently allowed in certain environments identified in law.

MOTION:

The Board voted unanimously, as recommended by the Regulation Committee, to take no action at this time regarding the draft legislative proposal to remove the prohibition of one prescription per blank in §54.1-3408.01.

- REQUIRING TEMPERATURE MONITORING DEVICES:

Ms. Shinaberry reported that the Regulation Committee reviewed the request from Michael Rush, Executive Director of Global Health Policy at Temptime Corporation to require temperature-sensitive drugs that are shipped via mail to be accompanied with a device to monitor temperature during shipping. The Regulation Committee recommended that the board take no action at this time.

MOTION:

The Board voted unanimously, as recommended by the Regulation Committee, to take no action at this time to require temperature-sensitive drugs that are shipped via mail to be accompanied with a device to monitor temperature during shipping.

NEW BUSINESS:

- CONSIDERATION FOR ACCEPTING INSPECTIONS OR DOCUMENTATION, IN LIEU OF FDA INSPECTION OF OUTSOURCING FACILITY FROM THE FOLLOWING:

- Bestech GMP Contracting, Inc.:

Matthew Bestercy, Owner and Principal Consultant for Bestech GMP Contacting, Inc. requested that the Board allow non-resident outsourcing facilities to be able to utilize their inspection report for initial licensure in lieu of the FDA inspection report. Virginia law requires an outsourcing facility needs to produce an FDA inspection report which is no older than one year from the date of applying for licensure. However, the FDA does not routinely perform annual inspections which will make it difficult for these facilities to obtain licensure in Virginia. Mr. Bestercy presented an overview of his company, the inspectors' qualifications, and the process to be used to inspect outsourcing facilities. His company would inspect in a manner similar to FDA and does a complete and thorough inspection. Mr. Bestercy agreed to map out their process, finalize inspection forms, and provide them to board staff prior to the September 7, 2016 board meeting for further consideration.

- Florida Department of Health:

The Florida Department of Health inspectors have received training from the FDA on how to inspect facilities operating under current Good Manufacturing Practices, and have been performing outsourcing facility inspections within Florida and in other states. Florida has not finalized their inspection report, so it was not available for review. The Board decided to table the discussion of whether it could accept a Florida inspection report from a nonresident outsourcing facility in lieu of an FDA inspection until the Florida inspection report was available for review.

- RESULTS FROM 2015 HEALTHCARE WORKFORCE SURVEYS:

Dr. Elizabeth Carter, Ph.D., Director, HWDC presented the Board with handouts that updated the Board with the results from the 2015 Healthcare Workforce Surveys for pharmacists and pharmacy technicians. Dr. Carter said that there has been an increase of female pharmacists from last year, it went up from 62%-63%. Also, diversity increased to 47%, the amount of PharmDs went up to 57% and there is

Add the following:

•⟨800⟩ HAZARDOUS DRUGS—HANDLING IN HEALTHCARE SETTINGS

(Chapter to become official July 1, 2018.)

1. INTRODUCTION AND SCOPE

This chapter describes practice and quality standards for handling hazardous drugs (HDs) to promote patient safety, worker safety, and environmental protection. Handling HDs includes, but is not limited to, the receipt, storage, compounding, dispensing, administration, and disposal of sterile and nonsterile products and preparations.

This chapter applies to all healthcare personnel who handle HD preparations and all entities that store, prepare, transport, or administer HDs (e.g., pharmacies, hospitals and other healthcare institutions, patient treatment clinics, physicians' practice facilities, or veterinarians' offices). Personnel who may potentially be exposed to HDs include, but are not limited to: pharmacists, pharmacy technicians, nurses, physicians, physician assistants, home healthcare workers, veterinarians, and veterinary technicians.

Entities that handle HDs must incorporate the standards in this chapter into their occupational safety plan. The entity's health and safety management system must, at a minimum, include:

- A list of HDs
- Facility and engineering controls
- Competent personnel
- Safe work practices
- Proper use of appropriate Personal Protective Equipment (PPE)
- Policies for HD waste segregation and disposal

The chapter is organized into the following main sections:

1. Introduction and Scope
2. List of Hazardous Drugs
3. Types of Exposure
4. Responsibilities of Personnel Handling Hazardous Drugs
5. Facilities and Engineering Controls
6. Environmental Quality and Control
7. Personal Protective Equipment
8. Hazard Communication Program
9. Personnel Training
10. Receiving
11. Labeling, Packaging, Transport, and Disposal
12. Dispensing Final Dosage Forms
13. Compounding
14. Administering
15. Deactivating, Decontaminating, Cleaning, and Disinfecting
16. Spill Control
17. Documentation and Standard Operating Procedures
18. Medical Surveillance

Glossary

Appendices

Appendix 1: Acronyms

Appendix 2: Examples of Designs for Hazardous Drug Compounding Areas

Appendix 3: Types of Biological Safety Cabinets

References

2. LIST OF HAZARDOUS DRUGS

The National Institute for Occupational Safety and Health (NIOSH) maintains a list of antineoplastic and other HDs used in healthcare. An entity must maintain a list of HDs, which must include any items on the current NIOSH list that the entity handles. The entity's list must be reviewed at least every 12 months. Whenever a new agent or dosage form is used, it should be reviewed against the entity's list.

The NIOSH list of antineoplastic and other HDs provides the criteria used to identify HDs. These criteria must be used to identify HDs that enter the market after the most recent version of the NIOSH list, or that the entity handles as an investiga-

tional drug. If the information available on a drug is deemed insufficient to make an informed decision, consider the drug hazardous until more information is available.

Box 1: Containment Requirements

- Drugs on the NIOSH list that must follow the requirements in this chapter include:
  - Any HD API
  - Any antineoplastic requiring HD manipulation
- Drugs on the NIOSH list that do not have to follow all the containment requirements of this chapter if an assessment of risk is performed and implemented include:
  - Final dosage forms of compounded HD preparations and conventionally manufactured HD products, including antineoplastic dosage forms that do not require any further manipulation other than counting or repackaging (unless required by the manufacturer)
- For dosage forms of other HDs on the NIOSH list, the entity may perform an assessment of risk to determine alternative containment strategies and/work practices

Some dosage forms of drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (e.g., tablets or capsules—solid, intact medications that are administered to patients without modifying the formulation). However, dust from tablets and capsules may present a risk of exposure by skin contact and/or inhalation. An assessment of risk may be performed for these dosage forms to determine alternative containment strategies and/or work practices. If an assessment of risk is not performed, all HDs must be handled with all containment strategies defined in this chapter.

The assessment of risk must, at a minimum, consider the following:

- Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk only)
- Dosage form
- Risk of exposure
- Packaging
- Manipulation

If an assessment of risk approach is taken, the entity must document what alternative containment strategies and/or work practices are being employed for specific dosage forms to minimize occupational exposure. If used, the assessment of risk must be reviewed at least every 12 months and the review documented.

3. TYPES OF EXPOSURE

Routes of unintentional entry of HDs into the body include dermal and mucosal absorption, inhalation, injection, and ingestion (e.g., contaminated foodstuffs, spills, or mouth contact with contaminated hands). Containers of HDs have been shown to be contaminated upon receipt. Both clinical and nonclinical personnel may be exposed to HDs when they handle HDs or touch contaminated surfaces. *Table 1* lists examples of potential routes of exposure based on activity.

Table 1. Examples of Potential Opportunities of Exposure Based on Activity

Activity	Potential Opportunity of Exposure
Receipt	• Contacting HD residues present on drug containers, individual dosage units, outer containers, work surfaces, or floors
Dispensing	• Counting or repackaging tablets and capsules
Compounding and other manipulations	• Crushing or splitting tablets or opening capsules • Pouring oral or topical liquids from one container to another • Weighing or mixing components • Constituting or reconstituting powdered or lyophilized HDs • Withdrawing or diluting injectable HDs from parenteral containers • Expelling air or HDs from syringes • Contacting HD residue present on PPE or other garments • Deactivating, decontaminating, cleaning, and disinfecting areas contaminated with or suspected to be contaminated with HDs • Maintenance activities for potentially contaminated equipment and devices
Administration	• Generating aerosols during administration of HDs by various routes (e.g., injection, irrigation, oral, inhalation, or topical application) • Performing certain specialized procedures (e.g., intraoperative intraperitoneal injection or bladder instillation) • Priming an IV administration set
Patient-care activities	• Handling body fluids (e.g., urine, feces, sweat, or vomit) or body-fluid-contaminated clothing, dressings, linens, and other materials
Spills	• Spill generation, management, and disposal
Transport	• Moving HDs within a healthcare setting
Waste	• Collection and disposal of hazardous waste and trace contaminated waste

4. RESPONSIBILITIES OF PERSONNEL HANDLING HAZARDOUS DRUGS

Each entity must have a designated person who is qualified and trained to be responsible for developing and implementing appropriate procedures; overseeing entity compliance with this chapter and other applicable laws, regulations, and standards; ensuring competency of personnel; and ensuring environmental control of the storage and compounding areas. The designated person must thoroughly understand the rationale for risk-prevention policies, risks to themselves and others, risks of noncompliance that may compromise safety, and the responsibility to report potentially hazardous situations to the management team. The designated person must also be responsible for the oversight of monitoring the facility and maintaining reports of testing/sampling performed in facilities, and acting on the results.

All personnel who handle HDs are responsible for understanding the fundamental practices and precautions and for continually evaluating these procedures and the quality of final HDs to prevent harm to patients, minimize exposure to personnel, and minimize contamination of the work and patient-care environment.

Change to read:

5. FACILITIES AND ENGINEERING CONTROLS

HDs must be handled under conditions that promote patient safety, worker safety, and environmental protection. Signs designating the hazard must be prominently displayed before the entrance to the HD handling areas. Access to areas where HDs are handled must be restricted to authorized personnel to protect persons not involved in HD handling. HD handling areas must be located away from breakrooms and refreshment areas for personnel, patients, or visitors to reduce risk of exposure.

Designated areas must be available for:

- Receipt and unpacking
- Storage of HDs
- Nonsterile HD compounding (if performed by the entity)
- Sterile HD compounding (if performed by the entity)

Certain areas are required to have negative pressure from surrounding areas to contain HDs and minimize risk of exposure. Consideration should be given to uninterrupted power sources (UPS) for the ventilation systems to maintain negative pressure in the event of power loss.

5.1 Receipt

Antineoplastic HDs and all HD APIs 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.

5.2 Storage

HDs must be stored in a manner that prevents spillage or breakage if the container falls. Do not store HDs on the floor. In areas prone to specific types of natural disasters (e.g., earthquakes) the manner of storage must meet applicable safety precautions, such as secure shelves with raised front lips.

Antineoplastic HDs requiring manipulation other than counting or repackaging of final dosage forms and any HD API must be stored separately from non-HDs in a manner that prevents contamination and personnel exposure. These HDs must be stored in an externally ventilated, negative-pressure room with at least 12 air changes per hour (ACPH). Non-antineoplastic, reproductive risk only, and final dosage forms of antineoplastic HDs may be stored with other inventory if permitted by entity policy.

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.

Refrigerated antineoplastic HDs must be stored in a dedicated refrigerator in a negative pressure area with at least 12 ACPH [e.g., storage room, buffer room, or containment segregated compounding area (C-SCA)]. If a refrigerator is placed in a negative pressure buffer room, an exhaust located adjacent to the refrigerator's compressor and behind the refrigerator should be considered.

5.3 Compounding

Engineering controls are required to protect the preparation from cross-contamination and microbial contamination (if preparation is intended to be sterile) during all phases of the compounding process. Engineering controls for containment are divided into three categories representing primary, secondary, and supplementary levels of control. A containment primary engineering control (C-PEC) is a ventilated device designed to minimize worker and environmental HD exposure when directly handling HDs. The containment secondary engineering control (C-SEC) is the room in which the C-PEC is placed. Supplemen-

tal engineering controls [e.g., closed-system drug-transfer device (CSTD)] are adjunct controls to offer additional levels of protection. *Appendix 2* provides examples for designs of HD compounding areas.

Sterile and nonsterile HDs must be compounded within a C-PEC located in a C-SEC. The C-SEC used for sterile and nonsterile compounding must:

- Be externally vented •(ERR 1-Jun-2016)•
- Be physically separated (i.e., a different room from other preparation areas)
- Have an appropriate air exchange (e.g., ACPH)
- Have a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas

The C-PEC must operate continuously if it supplies some or all of the negative pressure in the C-SEC or if it is used for sterile compounding. If there is any loss of power to the C-PEC, or if repair or moving occurs, all activities occurring in the C-PEC must be suspended immediately. If necessary, protect the unit by covering it appropriately per the manufacturer's recommendations. Once the C-PEC can be powered on, decontaminate, clean, and disinfect (if used for sterile compounding) all surfaces and wait the manufacturer-specified recovery time before resuming compounding.

A sink must be available for hand washing. An eyewash station and/or other emergency or safety precautions that meet applicable laws and regulations must be readily available. Care must be taken to locate water sources and drains in areas where their presence will not interfere with required ISO classifications. Water sources and drains must be located at least 1 meter away from the C-PEC.

For entities that compound both nonsterile and sterile HDs, the respective C-PECs must be placed in separate rooms, unless those C-PECs used for nonsterile compounding are sufficiently effective that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they must be placed at least 1 meter apart and particle-generating activity must not be performed when sterile compounding is in process.

5.3.1 NONSTERILE COMPOUNDING

In addition to this chapter, nonsterile compounding must follow standards in *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩. A C-PEC is not required if manipulations are limited to handling of final dosage forms (e.g., counting or repackaging of tablets and capsules) that do not produce particles, aerosols, or gasses.

The C-PECs used for manipulation of nonsterile HDs must be either externally vented (preferred) or have redundant–HEPA filters in series. Nonsterile HD compounding must be performed in a C-PEC that provides personnel and environmental protection, such as a Class I Biological Safety Cabinet (BSC) or Containment Ventilated Enclosure (CVE). A Class II BSC or a compounding aseptic containment isolator (CACI) may also be used. For occasional nonsterile HD compounding, a C-PEC used for sterile compounding (e.g., Class II BSC or CACI) may be used but must be decontaminated, cleaned, and disinfected before resuming sterile compounding in that C-PEC. A C-PEC used only for nonsterile compounding does not require unidirectional airflow because the critical environment does not need to be ISO classified.

The C-PEC must be placed in a C-SEC that has at least 12 ACPH. *Table 2* summarizes the engineering controls required for nonsterile HD compounding.

Due to the difficulty of cleaning HD contamination, surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the nonsterile compounding area must be smooth, impervious, free from cracks and crevices, and non-shedding.

Table 2. Engineering Controls for Nonsterile HD Compounding

C-PEC	C-SEC Requirements
• Externally vented (preferred) or redundant–HEPA filtered in series • Examples: CVE, Class I or II BSC, CACI	• Externally vented • 12 ACPH • Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas

5.3.2 STERILE COMPOUNDING

In addition to this chapter, sterile compounding must follow standards in ⟨797⟩.

All C-PECs used for manipulation of sterile HDs must be externally vented. Sterile HD compounding must be performed in a C-PEC that provides an ISO Class 5 or better air quality, such as a Class II or III BSC or CACI. Class II BSC types A2, B1, or B2 are acceptable. For most known HDs, type A2 cabinets offer a simple and reliable integration with the ventilation and pressurization requirements of the C-SEC. Class II type B2 BSCs are typically reserved for use with volatile components. *Appendix 3* describes the different types of BSCs.

A laminar airflow workbench (LAFW) or compounding aseptic isolator (CAI) must not be used for the compounding of an antineoplastic HD. A BSC or CACI used for the preparation of HDs must not be used for the preparation of a non-HD unless the non-HD preparation is placed into a protective outer wrapper during removal from the C-PEC and is labeled to require PPE handling precautions.

The C-PEC must be located in a C-SEC, which may either be an ISO Class 7 buffer room with an ISO Class 7 ante-room (preferred) or an unclassified containment segregated compounding area (C-SCA). If the C-PEC is placed in a C-SCA, the beyond-use date (BUD) of all compounded sterile preparations (CSPs) prepared must be limited as described in ⟨797⟩ for CSPs

prepared in a segregated compounding area. *Table 3* summarizes the engineering controls required for 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 ACPH • Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas	As described in ⟨797⟩
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

ISO Class 7 buffer room with an ISO class 7 ante-room: The C-PEC is placed in an ISO Class 7 buffer room that has fixed walls, HEPA-filtered supply air, a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas and a minimum of 30 ACPH.

The buffer room must be externally vented. Because the room through which entry into the HD buffer room (e.g., ante-room or non-HD buffer room) plays an important role in terms of total contamination control, the following is required:

- Minimum of 30 ACPH of HEPA-filtered supply air
- Maintain a positive pressure of at least 0.02 inches of water column relative to all adjacent unclassified areas
- Maintain an air quality of ISO Class 7 or better

An ISO Class 7 ante-room with fixed walls is necessary to provide inward air migration of equal cleanliness classified air into the negative pressure buffer room to contain any airborne HD. A hand-washing sink must be placed in the ante-room at least 1 meter from the entrance to the HD buffer room to avoid contamination migration into the negative pressure HD buffer room.

Although not a recommended facility design, if the negative-pressure HD buffer room is entered though the positive-pressure non-HD buffer room, the following is also required:

- A line of demarcation must be defined within the negative-pressure buffer room for donning and doffing PPE
- A method to transport HDs, HD CSPs, and HD waste into and out of the negative pressure buffer room to minimize the spread of HD contamination. This may be accomplished by use of a pass-through chamber between the negative-pressure buffer area and adjacent space. The pass-through chamber must be included in the facility's certification to ensure that particles are not compromising the air quality of the negative-pressure buffer room. A refrigerator pass-through must not be used. Other methods of containment (such as sealed containers) may be used.

HD CSPs prepared in an ISO Class 7 buffer room with an ISO Class 7 ante-room may use the BUDs described in ⟨797⟩, based on the categories of CSP, sterility testing, and storage temperature.

Containment segregated compounding area (C-SCA): The C-PEC is placed in an unclassified C-SCA that has fixed walls, a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas, and a minimum of 12 ACPH. The C-SCA must be externally vented. A hand-washing sink must be placed at least 1 meter from C-PEC and may be either inside the C-SCA or directly outside the C-SCA.

Only low- and medium-risk HD CSPs may be prepared in a C-SCA. HD CSPs prepared in the C-SCA must not exceed the BUDs described in ⟨797⟩ for CSPs prepared in a segregated compounding area.

5.4 Containment Supplemental Engineering Controls

Containment supplemental engineering controls, such as CSTDs, provide adjunct controls to offer an additional level of protection during compounding or administration. Some CSTDs have been shown to limit the potential of generating aerosols during compounding. However, there is no certainty that all CSTDs will perform adequately. Until a published universal performance standard for evaluation of CSTD containment is available, users should carefully evaluate the performance claims associated with available CSTDs based on independent, peer-reviewed studies and demonstrated containment reduction.

A CSTD must not be used as a substitute for a C-PEC when compounding. CSTDs should be used when compounding HDs when the dosage form allows. CSTDs must be used when administering antineoplastic HDs when the dosage form allows. CSTDs known to be physically or chemically incompatible with a specific HD must not be used for that HD.

6. ENVIRONMENTAL QUALITY AND CONTROL

Environmental wipe sampling for HD surface residue should be performed routinely (e.g., initially as a benchmark and at least every 6 months, or more often as needed, to verify containment). Surface wipe sampling should include:

- Interior of the C-PEC and equipment contained in it

- Pass-through chambers
- Surfaces in staging or work areas near the C-PEC
- Areas adjacent to C-PECs (e.g., floors directly under C-PEC, staging, and dispensing area)
- Areas immediately outside the HD buffer room or the C-SCA
- Patient administration areas

There are currently no studies demonstrating the effectiveness of a specific number or size of wipe samples in determining levels of HD contamination. Wipe sampling kits should be verified before use to ensure the method and reagent used have been tested to recover a specific percentage of known marker drugs from various surface types found in the sampled area. There are currently no certifying agencies for vendors of wipe sample kits.

There is currently no standard for acceptable limits for HD surface contamination. Common marker HDs that can be assayed include cyclophosphamide, ifosfamide, methotrexate, fluorouracil, and platinum-containing drugs. An example of measurable contamination would be cyclophosphamide levels >1.00 ng/cm², which were shown in some studies to result in uptake of the drug in exposed workers. If any measurable contamination is found, the designated person must identify, document, and contain the cause of contamination. Such action may include reevaluating work practices, re-training personnel, performing thorough deactivation, decontamination, cleaning, and improving engineering controls. Repeat the wipe sampling to validate that the deactivation/decontamination and cleaning steps have been effective.

7. PERSONAL PROTECTIVE EQUIPMENT

Personal Protective Equipment (PPE) provides worker protection to reduce exposure to HD aerosols and residues. Additional PPE may be required to handle the HDs outside of a C-PEC, such as treating a patient or cleaning a spill. The NIOSH list of antineoplastic and other HDs provides general guidance on PPE for possible scenarios that may be encountered in healthcare settings. Disposable PPE must not be re-used. Reusable PPE must be decontaminated and cleaned after use.

Gowns, head, hair, shoe covers, and two pairs of chemotherapy gloves are required for compounding sterile and nonsterile HDs. Two pairs of chemotherapy gloves are required for administering antineoplastic HDs. Gowns shown to resist permeability by HDs are required when administering injectable antineoplastic HDs. For all other activities, the entity's SOP must describe the appropriate PPE to be worn based on its occupational safety plan and assessment of risk (if used). The entity must develop SOPs for PPE based on the risk of exposure (see *Types of Exposure*) and activities performed.

Appropriate PPE must be worn when handling HDs including during:

- Receipt
- Storage
- Transport
- Compounding (sterile and nonsterile)
- Administration
- Deactivation/decontamination, cleaning, and disinfecting
- Spill control
- Waste disposal

7.1 Gloves

When chemotherapy gloves are required, they must meet American Society for Testing and Materials (ASTM) standard D6978 (or its successor). Chemotherapy gloves should be worn for handling all HDs including non-antineoplastics and for reproductive risk only HDs. Chemotherapy gloves must be powder-free because powder can contaminate the work area and can adsorb and retain HDs. Gloves must be inspected for physical defects before use. Do not use gloves with pin holes or weak spots.

When used for sterile compounding, the outer chemotherapy gloves must be sterile. Chemotherapy gloves should be changed every 30 minutes unless otherwise recommended by the manufacturer's documentation and must be changed when torn, punctured, or contaminated. Hands must be washed with soap and water after removing gloves.

7.2 Gowns

When gowns are required, they must be disposable and shown to resist permeability by HDs. Gowns must be selected based on the HDs handled. Disposable gowns made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of uncoated materials. Gowns must close in the back (i.e., no open front), be long sleeved, and have closed cuffs that are elastic or knit. Gowns must not have seams or closures that could allow HDs to pass through.

Cloth laboratory coats, surgical scrubs, isolation gowns, or other absorbent materials are not appropriate protective outerwear when handling HDs because they permit the permeation of HDs and can hold spilled drugs against the skin, thereby increasing exposure. Clothing may also retain HD residue from contact, and may transfer to other healthcare workers or various surfaces. Washing of non-disposable clothing contaminated with HD residue should only be done according to facility pol-

icy as drug residue may be transferred to other clothing. Potentially contaminated clothing must not be taken home under any circumstances.

Gowns must be changed per the manufacturer's information for permeation of the gown. If no permeation information is available for the gowns used, change them every 2–3 hours or immediately after a spill or splash. Gowns worn in HD handling areas must not be worn to other areas in order to avoid spreading HD contamination and exposing other healthcare workers.

7.3 Head, Hair, Shoe, and Sleeve Covers

Head and hair covers (including beard and moustache, if applicable), shoe covers, and sleeve covers provide protection from contact with HD residue. When compounding HDs, a second pair of shoe covers must be donned before entering the C-SEC and doffed when exiting the C-SEC. Shoe covers worn in HD handling areas must not be worn to other areas to avoid spreading HD contamination and exposing other healthcare workers.

Disposable sleeve covers may be used to protect areas of the arm that may come in contact with HDs. Disposable sleeve covers made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of uncoated materials.

7.4 Eye and Face Protection

Many HDs are irritating to the eyes and mucous membranes. Appropriate eye and face protection must be worn when there is a risk for spills or splashes of HDs or HD waste materials when working outside of a C-PEC (e.g., administration in the surgical suite, working at or above eye level, or cleaning a spill). A full-facepiece respirator provides eye and face protection. Goggles must be used when eye protection is needed. Eye glasses alone or safety glasses with side shields do not protect the eyes adequately from splashes. Face shields in combination with goggles provide a full range of protection against splashes to the face and eyes. Face shields alone do not provide full eye and face protection.

7.5 Respiratory Protection

Personnel who are unpacking HDs that are not contained in plastic should wear an elastomeric half-mask with a multi-gas cartridge and P100-filter until assessment of the packaging integrity can be made to ensure no breakage or spillage occurred during transport. If the type of drug can be better defined, a more targeted cartridge can be used.

Surgical masks do not provide respiratory protection from drug exposure and must not be used when respiratory protection from HD exposure is required. A surgical N95 respirator provides the respiratory protection of an N95 respirator, and like a surgical mask, provides a barrier to splashes, droplets, and sprays around the nose and mouth.

For most activities requiring respiratory protection, a fit-tested NIOSH-certified N95 or more protective respirator is sufficient to protect against airborne particles. However, N95 respirators offer no protection against gases and vapors and little protection against direct liquid splashes (see the Centers for Disease Control and Prevention's (CDC's) Respirator Trusted-Source Information).

Fit test the respirator and train workers to use respiratory protection. Follow all requirements in the Occupational Safety and Health Administration (OSHA) respiratory protection standard (29 CFR 1910.134). An appropriate full-facepiece, chemical cartridge-type respirator or powered air-purifying respirator (PAPR) should be worn when there is a risk of respiratory exposure to HDs, including when:

- Attending to HD spills larger than what can be contained with a spill kit
- Deactivating, decontaminating, and cleaning underneath the work surface of a C-PEC
- There is a known or suspected airborne exposure to powders or vapors

7.6 Disposal of Used Personal Protective Equipment

Consider all PPE worn when handling HDs to be contaminated with, at minimum, trace quantities of HDs. PPE must be placed in an appropriate waste container and further disposed of per local, state, and federal regulations. PPE worn during compounding should be disposed of in the proper waste container before leaving the C-SEC. Chemotherapy gloves and sleeve covers (if used) worn during compounding must be carefully removed and discarded immediately into a waste container approved for trace contaminated waste inside the C-PEC or contained in a sealable bag for discarding outside the C-PEC.

8. HAZARD COMMUNICATION PROGRAM

Entities are required to establish policies and procedures that ensure worker safety during all aspects of HD handling. The entity must develop SOPs to ensure effective training regarding proper labeling, transport, storage, and disposal of the HDs and use of Safety Data Sheets (SDS), based on the Globally Harmonized System of Classification and Labeling of Chemicals (GHS).

Elements of the hazard communication program plan must include:

- A written plan that describes how the standard will be implemented
- All containers of hazardous chemicals must be labeled, tagged, or marked with the identity of the material and appropriate hazard warnings
- Entities must have an SDS for each hazardous chemical they use (29 CFR 1910.1200)
- Entities must ensure that the SDSs for each hazardous chemical used are readily accessible to personnel during each work shift and when they are in their work areas
- Personnel who may be exposed to hazardous chemicals when working must be provided information and training before the initial assignment to work with a hazardous chemical, and also whenever the hazard changes
- Personnel of reproductive capability must confirm in writing that they understand the risks of handling HDs

9. PERSONNEL TRAINING

All personnel who handle HDs must be trained based on their job functions (e.g., in the receipt, storage, compounding, repackaging, dispensing, administrating, and disposing of HDs). Training must occur before the employee independently handles HDs. The effectiveness of training for HD handling competencies must be demonstrated by each employee. Personnel competency must be reassessed at least every 12 months. Personnel must be trained prior to the introduction of a new HD or new equipment and prior to a new or significant change in process or SOP. All training and competency assessment must be documented.

The training must include at least the following:

- Overview of entity's list of HDs and their risks
- Review of the entity's SOPs related to handling of HDs
- Proper use of PPE
- Proper use of equipment and devices (e.g., engineering controls)
- Response to known or suspected HD exposure
- Spill management
- Proper disposal of HDs and trace-contaminated materials

10. RECEIVING

The entity must establish SOPs for receiving HDs. HDs should be received from the supplier in impervious plastic to segregate them from other drugs and to allow for safety in the receiving and internal transfer process. HDs must be delivered to the HD storage area immediately after unpacking.

PPE, including chemotherapy gloves, must be worn when unpacking HDs (see *Personal Protective Equipment*). A spill kit must be accessible in the receiving area.

The entity must enforce policies that include a tiered approach, starting with visual examination of the shipping container for signs of damage or breakage (e.g., visible stains from leakage, sounds of broken glass). *Table 4* summarizes the steps for receiving and handling of damaged shipping containers.

Table 4. Summary of Requirements for Receiving and Handling Damaged HD Shipping Containers

If the shipping container appears damaged	• Seal container without opening and contact the supplier • If the unopened package is to be returned to the supplier, enclose the package in an impervious container and label the outer container "Hazardous" • If the supplier declines return, dispose of as hazardous waste
If a damaged shipping container must be opened	• Seal the container in plastic or an impervious container • Transport it to a C-PEC and place on a plastic-backed preparation mat • Open the package and remove undamaged items • Wipe the outside of the undamaged items with a disposable wipe • Enclose the damaged item(s) in an impervious container and label the outer container "Hazardous" • If the supplier declines return, dispose of as hazardous waste • Deactivate, decontaminate, and clean the C-PEC (see *Deactivating, Decontaminating, Cleaning, and Disinfecting*) and discard the mat and cleaning disposables as hazardous waste

When opening damaged shipping containers, they should preferably be transported to a C-PEC designated for nonsterile compounding. If a C-PEC designated for sterile compounding is the only one available, it must be disinfected after the decontamination, deactivation, and cleaning step before returning to any sterile compounding activity.

Damaged packages or shipping cartons must be considered spills that must be reported to the designated person and managed according to the entity's SOPs. Segregate HDs waiting to be returned to the supplier in a designated negative pressure area. Clean-up must comply with established SOPs.

11. LABELING, PACKAGING, TRANSPORT AND DISPOSAL

The entity must establish SOPs for the labeling, packaging, transport, and disposal of HDs. The SOPs must address prevention of accidental exposures or spills, personnel training on response to exposure, and use of a spill kit. Examples of special

exposure-reducing strategies include small-bore connectors (such as Luer Lock) and syringes, syringe caps, CSTDs, the capping of container ports, sealed impervious plastic bags, impact-resistant and/or water-tight containers, and cautionary labeling.

11.1 Labeling

HDs identified by the entity as requiring special HD handling precautions must be clearly labeled at all times during their transport. Personnel must ensure that the labeling processes for compounded preparations do not introduce contamination into the non-HD handling areas.

11.2 Packaging

Personnel must select and use packaging containers and materials that will maintain physical integrity, stability, and sterility (if needed) of the HDs during transport. Packaging materials must protect the HD from damage, leakage, contamination, and degradation, while protecting healthcare workers who transport HDs. The entity must have written SOPs to describe appropriate shipping containers and insulating materials, based on information from product specifications, vendors, and mode of transport.

11.3 Transport

HDs that need to be transported must be labeled, stored, and handled in accordance with applicable federal, state, and local regulations. HDs must be transported in containers that minimize the risk of breakage or leakage. Pneumatic tubes must not be used to transport any liquid HDs or any antineoplastic HDs because of the potential for breakage and contamination.

When shipping HDs to locations outside the entity, the entity must consult the Transport Information on the SDS. The entity must ensure that labels and accessory labeling for the HDs include storage instructions, disposal instructions, and HD category information in a format that is consistent with the carrier's policies.

11.4 Disposal

All personnel who perform routine custodial waste removal and cleaning activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment to prevent HD contamination. Disposal of all HD waste, including, but not limited to, unused HDs and trace-contaminated PPE and other materials, must comply with all applicable federal, state, and local regulations.

12. DISPENSING FINAL DOSAGE FORMS

HDs that do not require any further manipulation, other than counting or repackaging of final dosage forms, may be prepared for dispensing without any further requirements for containment unless required by the manufacturer or if visual indicators of HD exposure hazards are present (e.g., HD dust or leakage).

Counting or repackaging of HDs must be done carefully. Clean equipment should be dedicated for use with HDs and should be decontaminated after every use. Tablet and capsule forms of antineoplastic HDs must not be placed in automated counting or packaging machines, which subject them to stress and may create powdered contaminants.

13. COMPOUNDING

Entities and personnel involved in compounding HDs must be compliant with the appropriate USP standards for compounding including ⟨795⟩ and ⟨797⟩. Compounding must be done in proper engineering controls as described in *Compounding*. When compounding HD preparations in a C-PEC, a plastic-backed preparation mat should be placed on the work surface of the C-PEC. The mat should be changed immediately if a spill occurs and regularly during use, and should be discarded at the end of the daily compounding activity. Disposable or clean equipment for compounding (such as mortars and pestles, and spatulas) must be dedicated for use with HDs.

Bulk containers of liquid and API HD must be handled carefully to avoid spills. If used, APIs or other powdered HDs must be handled in a C-PEC to protect against occupational exposure, especially during particle-generating activities (such as crushing tablets, opening capsules, and weighing powder).

14. ADMINISTERING

HDs must be administered safely using protective medical devices and techniques. Examples of protective medical devices include needleless and closed systems. Examples of protective techniques include spiking or priming of IV tubing with a non-HD solution in a C-PEC and crushing tablets in a plastic pouch.

Appropriate PPE must be worn when administering HDs. After use, PPE must be removed and disposed of in a waste container approved for trace-contaminated HD waste at the site of drug administration. Equipment (such as tubing and needles) and packaging materials must be disposed of properly, such as in HD waste containers, after administration.

CSTDs must be used for administration of antineoplastic HDs when the dosage form allows. Techniques and ancillary devices that minimize the risk posed by open systems must be used when administering HDs through certain routes. Administration into certain organs or body cavities (e.g., the bladder, eye, peritoneal cavity, or chest cavity) often requires equipment for which locking connections may not be readily available or possible.

Healthcare personnel should avoid manipulating HDs such as crushing tablets or opening capsules if possible. Liquid formulations are preferred if solid oral dosage forms are not appropriate for the patient. If HD dosage forms do require manipulation such as crushing tablet(s) or opening capsule(s) for a single dose, personnel must don appropriate PPE and use a plastic pouch to contain any dust or particles generated.

15. DEACTIVATING, DECONTAMINATING, CLEANING, AND DISINFECTING

All areas where HDs are handled and all reusable equipment and devices must be deactivated, decontaminated, and cleaned. Additionally, sterile compounding areas and devices must be subsequently disinfected.

The entity must establish written procedures for decontamination, deactivation, and cleaning, and for sterile compounding areas disinfection. Additionally, cleaning of nonsterile compounding areas must comply with ⟨795⟩ and cleaning of sterile compounding areas must comply with ⟨797⟩. Written procedures for cleaning must include procedures, agents used, dilutions (if used), frequency, and documentation requirements.

All personnel who perform deactivation, decontamination, cleaning, and disinfection activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment from contamination. All personnel performing these activities must wear appropriate PPE resistant to the cleaning agents used, including two pairs of chemotherapy gloves and impermeable disposable gowns (see *Personal Protective Equipment*). Additionally, eye protection and face shields must be used if splashing is likely. If warranted by the activity, respiratory protection must be used.

The deactivating, decontaminating, cleaning, and disinfecting agents selected must be appropriate for the type of HD contaminant(s), location, and surface materials. The products used must be compatible with the surface material. Consult manufacturer or supplier information for compatibility with cleaning agents used. Agents used for deactivation, decontamination, and cleaning should be applied through the use of wipes wetted with appropriate solution and not delivered by a spray bottle to avoid spreading HD residue. All disposable materials must be discarded to meet EPA regulations and the entity's policies. Perform cleaning in areas that are sufficiently ventilated. *Table 5* summarizes the purpose and example agents for each step.

Table 5. Cleaning Steps

Cleaning Step	Purpose	Example Agents
Deactivation	Render compound inert or inactive	As listed in the HD labeling or other agents which may incorporate Environmental Protection Agency (EPA)-registered oxidizers (e.g., peroxide formulations, sodium hypochlorite, etc.)
Decontamination	Remove HD residue	Materials that have been validated to be effective for HD decontamination, or through other materials proven to be effective through testing, which may include alcohol, water, peroxide, or sodium hypochlorite
Cleaning	Remove organic and inorganic material	Germicidal detergent
Disinfection (for sterile manipulations)	Destroy microorganisms	EPA-registered disinfectant and/or sterile alcohol as appropriate for use

15.1 Deactivation

Deactivation renders a compound inert or inactive. Residue from deactivation must be removed by decontaminating the surface.

There is no one proven method for deactivating all compounds. The ultimate goal should be complete surface decontamination. Products that have known deactivation properties (EPA-registered oxidizing agents that are appropriate for the intended use) should be used when possible. Care should be taken when selecting materials for deactivation due to potential adverse effects (hazardous byproducts, respiratory effects, and caustic damage to surfaces). Damage to surfaces is exhibited by corrosion to stainless steel surfaces caused by sodium hypochlorite if left untreated. To prevent corrosion, sodium hypochlorite must be neutralized with sodium thiosulfate or by following with an agent to remove the sodium hypochlorite (e.g., sterile alcohol, sterile water, germicidal detergent, or sporicidal agent).

15.2 Decontamination

Decontamination occurs by inactivating, neutralizing, or physically removing HD residue from non-disposable surfaces and transferring it to absorbent, disposable materials (e.g., wipes, pads, or towels) appropriate to the area being cleaned. When choosing among various products available for decontaminating HDs, consideration should be given to surface compatibility and facility requirements. It is imperative to adhere to manufacturer's use instructions. Because of the growing number of assays available for HDs, additional surface wipe sampling is now possible and should be done to document the effectiveness of any agent used for decontamination of HD residue from work surfaces (see *Environmental Quality and Control*).

The amount of HD contamination introduced into the C-PEC may be reduced by wiping down HD containers. The solution used for wiping HD packaging must not alter the product label. The work surface of the C-PEC must be decontaminated between compounding of different HDs. The C-PEC must be decontaminated at least daily (when used), any time a spill occurs, before and after certification, any time voluntary interruption occurs, and if the ventilation tool is moved.

C-PECs may have areas under the work tray where contamination can build up. These areas must be deactivated, decontaminated, and cleaned at least monthly to reduce the contamination level in the C-PEC. Accessing this area may be difficult. Deactivate, decontaminate, and clean as much as possible of the C-PEC surfaces before accessing the area under the work tray. When deactivating, decontaminating, and cleaning the area under the work tray of a C-PEC, the containment airflows are compromised by opening the cabinets. To provide protection to the worker performing this task, respiratory protection may be required.

15.3 Cleaning

Cleaning is a process that results in the removal of contaminants (e.g., soil, microbial contamination, HD residue) from objects and surfaces using water, detergents, surfactants, solvents, and/or other chemicals. Cleaning agents used on compounding equipment should not introduce microbial contamination. No cleaning step may be performed when compounding activities are occurring.

15.4 Disinfection

Disinfection is a process of inhibiting or destroying microorganisms. Before disinfection can be adequately performed, surfaces must be cleaned. Disinfection must be done for areas intended to be sterile, including the sterile compounding areas.

16. SPILL CONTROL

All personnel who may be required to clean up a spill of HDs must receive proper training in spill management and the use of PPE and NIOSH-certified respirators (see *Personal Protective Equipment*). Spills must be contained and cleaned immediately only by qualified personnel with appropriate PPE. Qualified personnel must be available at all times while HDs are being handled. Signs must be available for restricting access to the spill area. Spill kits containing all of the materials needed to clean HD spills must be readily available in all areas where HDs are routinely handled. If HDs are being prepared or administered in a non-routine healthcare area, a spill kit and respirator must be available. All spill materials must be disposed of as hazardous waste.

The circumstances and management of spills must be documented. Personnel who are potentially exposed during the spill or spill clean up or who have direct skin or eye contact with HDs require immediate evaluation. Non-employees exposed to an HD spill should follow entity policy, which may include reporting to the designated emergency service for initial evaluation and completion of an incident report or exposure form.

SOPs must be developed to prevent spills and to direct the clean up of HD spills. SOPs must address the size and scope of the spill and specify who is responsible for spill management and the type of PPE required. The management of the spill (e.g., decontamination, deactivation, and cleaning) may be dependent on the size and type of spill. The SOP must address the location of spill kits and clean-up materials as well as the capacity of the spill kit. Written procedures should address use of appropriate full-facepiece, chemical cartridge-type respirators if the capacity of the spill kit is exceeded or if there is known or suspected airborne exposure to vapors or gases.

17. DOCUMENTATION AND STANDARD OPERATING PROCEDURES

The entity must maintain SOPs for the safe handling of HDs for all situations in which these HDs are used throughout a facility. The SOPs must be reviewed at least every 12 months by the designated person, and the review must be documented. Revisions in forms or records must be made as needed and communicated to all personnel handling HDs.

The SOPs for handling of HDs should include:

- Hazard communication program
- Occupational safety program
- Designation of HD areas

- Receipt
- Storage
- Compounding
- Use and maintenance of proper engineering controls (e.g., C-PECs, C-SECs, and CSTDs)
- Hand hygiene and use of PPE based on activity (e.g., receipt, transport, compounding, administration, spill, and disposal)
- Deactivation, decontamination, cleaning, and disinfection
- Dispensing
- Transport
- Administering
- Environmental monitoring (e.g., wipe sampling)
- Disposal
- Spill control
- Medical surveillance

Personnel who transport, compound, or administer HDs must document their training according to OSHA standards (see OSHA Standard 1910.120 Hazardous Waste Operations and Emergency Response) and other applicable laws and regulations.

18. MEDICAL SURVEILLANCE

Medical surveillance is part of a comprehensive exposure control program complementing engineering controls, safe work processes, and use of PPE. Healthcare workers who handle HDs as a regular part of their job assignment should be enrolled in a medical surveillance program. The general purpose of surveillance is to minimize adverse health effects in personnel potentially exposed to HDs. Medical surveillance programs involve assessment and documentation of symptom complaints, physical findings, and laboratory values (such as a blood count) to determine whether there is a deviation from the expected norms.

Medical surveillance can also be viewed as a secondary prevention tool that may provide a means of early detection if a health problem develops. Tracking personnel through medical surveillance allows the comparison of health variables over time in individual workers, which may facilitate early detection of a change in a laboratory value or health condition. Medical surveillance programs also look for trends in populations of workers. Examining grouped data compared with data from unexposed workers may reveal a small alteration or increase in the frequency of a health effect that would be obscured if individual workers' results alone were considered.

Medical surveillance evaluates the protection afforded by engineering controls, other administrative controls, safe work processes, PPE, and worker education about the hazards of the materials they work with in the course of their duties. The data-gathering elements of a medical surveillance program are used to establish a baseline of workers' health and then to monitor their future health for any changes that may result from exposure to HDs.

Elements of a medical surveillance program should be consistent with the entity's Human Resource policies and should include:

- Development of an organized approach to identify workers who are potentially exposed to HDs on the basis of their job duties
- Use of an entity-based or contracted employee health service to perform the medical surveillance while protecting the confidentiality of the employees' personal medical information
- Initial baseline assessment (pre-placement) of a worker's health status and medical history. Data elements collected include a medical (including reproductive) history and work history to assess exposure to HDs, physical examination, and laboratory testing. Methods used to assess exposure history include a review of:
  - — Records of HDs handled, with quantities and dosage forms
  - — Estimated number of HDs handled per week
  - — Estimates of hours spent handling HDs per week and/or per month
  - — Performance of a physical assessment and laboratory studies linked to target organs of commonly used HDs, such as a baseline complete blood count. Biological monitoring to determine blood or urine levels of specific HDs is not currently recommended in surveillance protocols, but may have a role in the follow-up of acute spills with a specific agent.
- Medical records of surveillance should be maintained according to OSHA regulation concerning access to employee exposure and medical records
- Monitoring workers' health prospectively through periodic surveillance using the elements of data gathering described above (updated health and exposure history, physical assessment, and laboratory measures, if appropriate)
- Monitoring of the data to identify prevention failure leading to health effects; this monitoring may occur in collaboration with the employee health service
- Development of a follow-up plan for workers who have shown health changes suggesting toxicity or who have experienced an acute exposure. This follow-up should include evaluation of current engineering and administrative controls and equipment to ensure that all systems are appropriately and accurately implemented (see *Follow-Up Plan*)
- Completion of an exit examination when a worker's employment at the entity ends, to document the information on the employee's medical, reproductive, and exposure histories. Examination and laboratory evaluation should be guided by the individual's history of exposures and follow the outline of the periodic evaluation

18.1 Follow-Up Plan

The occurrence of exposure-related health changes should prompt immediate re-evaluation of primary preventive measures (e.g., administrative and engineering controls, PPE, and others). In this manner, medical surveillance acts as a check on the effectiveness of controls already in use.

The entity should take the following actions:

- Perform a post-exposure examination tailored to the type of exposure (e.g., spills or needle sticks from syringes containing HDs). An assessment of the extent of exposure should be conducted and included in a confidential database and in an incident report. The physical examination should focus on the involved area as well as other organ systems commonly affected (i.e., the skin and mucous membranes for direct contact or inhalation, the pulmonary system for aerosolized HDs). Treatment and laboratory studies will follow as indicated and be guided by emergency protocols
- Compare performance of controls with recommended standards; conduct environmental sampling when analytical methods are available
- Verify and document that all engineering controls are in proper operating condition
- Verify and document that the worker complied with existing policies. Review policies for the use of PPE and employee compliance with PPE use and policies. Review availability of appropriate PPE (see *Personal Protective Equipment*)
- Develop and document a plan of action that will prevent additional exposure of workers
- Ensure confidential, two-way communication between the worker and the employee health unit(s) regarding notification, discussions about a change in health condition, or detection of an adverse health effect
- Provide and document a follow-up medical survey to demonstrate that the plan implemented is effective
- Ensure that any exposed worker receives confidential notification of any adverse health effect. Offer alternative duty or temporary reassignment
- Provide ongoing medical surveillance of all workers at risk for exposure to HDs to determine whether the plan implemented is effective

GLOSSARY

Active pharmaceutical ingredient (API): Any substance or mixture of substances intended to be used in the compounding of a drug preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans and animals or affecting the structure and function of the body.

Alternative duty: Performance of other tasks that do not include the direct handling of HDs.

Ante-room: An ISO Class 7 or cleaner room where personnel hand hygiene, garbing procedures, and other activities that generate high particulate levels are performed. The ante-room is the transition room between the unclassified area of the facility and the buffer room.

Assessment of risk: Evaluation of risk to determine alternative containment strategies and/or work practices.

Beyond-use date (BUD): The date or time beyond which a compounded preparation cannot not be used and must be discarded (see ⟨795⟩ and ⟨797⟩). The date or time is determined from the date or time when the preparation was compounded.

Biological safety cabinet (BSC): A ventilated cabinet often used for preparation of hazardous drugs. These cabinets are divided into three general classes (Class I, Class II, and Class III). Class II BSCs are further divided into types (Type A1, Type A2, Type B1, and Type B2). See *Appendix 3* for details.

Buffer room: A type of C-SEC under negative pressure that meets ISO Class 7 or better air quality where the C-PEC that generates and maintains an ISO Class 5 environment is physically located. Activities that occur in this area are limited to the preparation and staging of components and supplies used when compounding HDs.

Chemotherapy glove: A medical glove that meets the ASTM Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs (D6978) or its successor.

Classified space: An area that maintains an air cleanliness classification based on the International Organization for Standardization (ISO).

Cleaning: The process of removing soil (e.g., organic and inorganic material) from objects and surfaces, normally accomplished by manually or mechanically using water with detergents or enzymatic products.

Closed-system drug-transfer device (CSTD): A drug-transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of HD or vapor concentrations outside the system.

Compounded preparation: A nonsterile or sterile drug or nutrient preparation that is compounded in a licensed pharmacy or other healthcare-related facility in response to or anticipation of a prescription or a medication order from a licensed prescriber.

Compounding aseptic containment isolator (CACI): A specific type of CAI that is designed for the compounding of sterile HDs. The CACI is designed to provide worker protection from exposure to undesirable levels of airborne drugs throughout the compounding and material transfer processes and to provide an aseptic environment with unidirectional airflow for compounding sterile preparations.

Compounding aseptic isolator (CAI): An isolator specifically designed for compounding sterile, non-hazardous pharmaceutical ingredients or preparations. The CAI is designed to maintain an aseptic compounding environment throughout the compounding and material transfer processes.
Compounding personnel: Individuals who participate in the compounding process.
Containment primary engineering control (C-PEC): A ventilated device designed and operated to minimize worker and environmental exposures to HDs by controlling emissions of airborne contaminants through the following:
- The full or partial enclosure of a potential contaminant source
- The use of airflow capture velocities to trap and remove airborne contaminants near their point of generation
- The use of air pressure relationships that define the direction of airflow into the cabinet
- The use of HEPA filtration on all potentially contaminated exhaust streams

Containment secondary engineering control (C-SEC): The room with fixed walls in which the C-PEC is placed. It incorporates specific design and operational parameters required to contain the potential hazard within the compounding room.
Containment segregated compounding area (C-SCA): A type of C-SEC with nominal requirements for airflow and room pressurization as they pertain to HD compounding.
Containment ventilated enclosure (CVE): A full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through HEPA filtration and prevent their release into the work environment.
Deactivation: Treatment of an HD contaminant on surfaces with a chemical, heat, ultraviolet light, or another agent to transform the HD into a less hazardous agent.
Decontamination: Inactivation, neutralization, or removal of HD contaminants on surfaces, usually by chemical means.
Doff: To remove PPE.
Don: To put on PPE.
Disinfection: The process of inhibiting or destroying microorganisms.
Engineering control: Primary, secondary, and supplemental devices designed to eliminate or reduce worker exposure to HDs.
EPA-registered disinfectant: Antimicrobial products registered with the Environmental Protection Agency (EPA) for healthcare use against pathogens specified in the product labeling.
Externally vented: Exhausted to the outside
Final dosage form: Any form of a medication that requires no further manipulation before administration.
Globally Harmonized System of Classification and Labeling of Chemicals (GHS): A system for standardizing and harmonizing the classification and labeling of chemicals.
Goggles: Tight-fitting eye protection that completely covers the eyes, eye sockets, and facial area that immediately surrounds the eyes. Goggles provide protection from impact, dust, and splashes. Some goggles fit over corrective lenses.
Hazardous drug (HD): Any drug identified by at least one of the following criteria:
- Carcinogenicity, teratogenicity, or developmental toxicity
- Reproductive toxicity in humans
- Organ toxicity at low dose in humans or animals
- Genotoxicity or new drugs that mimic existing HDs in structure or toxicity

High-efficiency particulate air (HEPA) filtration: An extended-medium, dry-type filter in a rigid frame, having a minimum particle collection efficiency of 99.97% for particles with a mass median diameter of 0.3 µm when tested at a rated airflow in accordance with MIL STD 282 using IEST Recommended Standard RP-CC001.5.
Negative-pressure room: A room that is maintained at a lower pressure than the adjacent areas; therefore the net flow of air is into the room.
Pass-through: 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.
Personal protective equipment (PPE): Items such as gloves, gowns, respirators, goggles, faceshields, and others that protect individual workers from hazardous physical or chemical exposures.
Positive-pressure room: A room that is maintained at a higher pressure than the adjacent areas; therefore, the net flow of air is out of the room.
Repackaging: The act of removing a product from its original primary container and placing it into another primary container, usually of smaller size.
Safety data sheet (SDS): An informational document that provides written or printed material concerning a hazardous chemical. The SDS is prepared in accordance with the HCS [previously known as a Material Safety Data Sheet (MSDS)].
Spill kit: A container of supplies, warning signage, and related materials used to contain the spill of an HD.
Standard operating procedure (SOP): Written procedures describing operations, testing, sampling, interpretation of results, and corrective actions that relate to the operations that are taking place.
Supplemental engineering control: An adjunct control (e.g., CSTD) that may be used concurrently with primary and secondary engineering controls. Supplemental engineering controls offer additional levels of protection and may facilitate enhanced occupational protection, especially when handling HDs outside of primary and secondary engineering controls (e.g., during administering).

Unclassified space: A space not required to meet any air cleanliness classification based on the International Organization for Standardization (ISO).

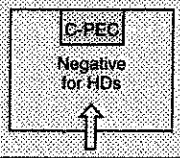
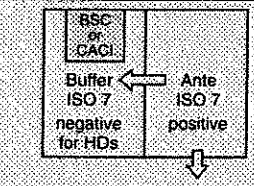
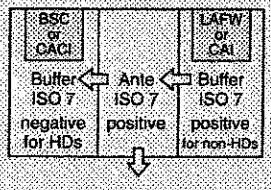
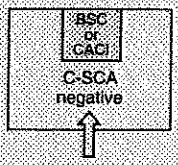
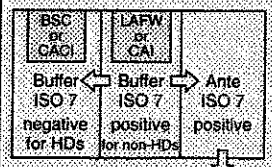
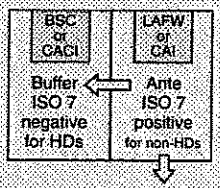
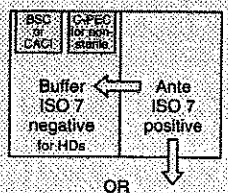
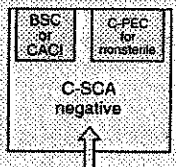
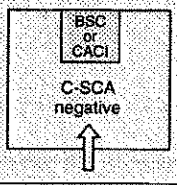
Change to read:

APPENDICES

Appendix 1: Acronyms

ACPH	Air changes per hour
API	Active pharmaceutical ingredient
ASTM	American Society for Testing and Materials
BSC	Biological safety cabinet
BUD	Beyond-use date
CACI	Compounding aseptic containment isolator
CAI	Compounding aseptic isolator
CDC	Centers for Disease Control and Prevention
C-PEC	Containment primary engineering control
C-SCA	Containment segregated compounding area
C-SEC	Containment secondary engineering control
CSP	Compounded sterile preparation
CSTD	Closed-system drug-transfer device
CVE	Containment ventilated enclosure
EPA	Environmental Protection Agency
GHS	Globally Harmonized System of Classification and Labeling of Chemicals
HCS	Hazard Communication Standard
HD	Hazardous drug
HEPA	High-efficiency particulate air
IV	Intravenous
LAFW	Laminar airflow workbench
NIOSH	National Institute for Occupational Safety and Health
ONS	Oncology Nursing Society
OSHA	Occupational Safety and Health Administration
PAPR	Powered air-purified respirator
PPE	Personal protective equipment
SDS	Safety Data Sheet
SOP	Standard operating procedure
ULPA	Ultra-low particulate air
UPS	Uninterrupted power source

Appendix 2: Examples of Designs for Hazardous Drug Compounding Areas[a]

Use	Optimal Primary and Secondary Control	Minimum ACPH	Limitations Primary and Secondary Control	Minimum ACPH	Notes for limitations
Nonsterile HD compounding		12			
Sterile HD compounding	 OR 	30	 OR  **This design is not recommended** OR  Typically used in oncology clinic settings.	12 30 30	Maximum BUD as described in <797> for segregated compounding area. If this design is in place, measures must be taken to avoid contamination of the positive-pressure buffer room. Maximum BUD as described in <797>.
Both sterile HD and nonsterile HD compounding	A separate room for sterile and nonsterile compounding is recommended		 OR  OR 	30 12 12	For rooms used for both sterile and nonsterile compounding, particle-generating activity must not be performed when sterile compounding is in process. C-PECs must be at least 1 meter apart. Maximum BUD as described in <797> for segregated compounding area. Maximum BUD as described in <797> for segregated compounding area.

[a] The arrows indicate direction of airflow.

Appendix 3: Types of Biological Safety Cabinets

Class I: A BSC that protects personnel and the environment but does not protect the product/preparation. A minimum velocity of 75 linear feet/minute of unfiltered room air is drawn through the front opening and across the work surface, providing personnel protection. The air is then passed through a HEPA/ULPA (ultra-low particulate air) filter, either into the room or to the outside in the exhaust plenum, providing environmental protection.

Class II: Class II (Types A1, A2, B1, and B2) BSCs are partial barrier systems that rely on the movement of air to provide personnel, environmental, and product/preparation protection. Personnel and product/preparation protection are provided by the combination of inward and downward airflow captured by the front grille of the cabinet. Side-to-side cross-contamination of products/preparations is minimized by the internal downward flow of HEPA/ULPA filtered air moving toward the work surface and then drawn into the front and rear intake grilles. Environmental protection is provided when the cabinet exhaust air is passed through a HEPA/ULPA filter.

Type A1 (formerly, Type A): These Class II BSCs maintain a minimum inflow velocity of 75 feet/minute; have HEPA-filtered, down-flow air that is a portion of the mixed down-flow and inflow air from a common plenum; may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy; and may have positive-pressure contaminated ducts and plenums that are not surrounded by negative-pressure plenums. Type A1 BSCs are not suitable for use with volatile toxic chemicals and volatile •radionuclides.• (ERR 1-Oct-2016)

Type A2 (formerly, Type B3): These Class II BSCs maintain a minimum inflow velocity of 100 feet/minute; have HEPA-filtered, down-flow air that is a portion of the mixed down-flow and inflow air from a common exhaust plenum; may exhaust HEPA-filtered air back into the laboratory or to the environment through an exhaust canopy; and have all contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for minute quantities of volatile toxic chemicals and trace amounts of •radionuclides,• (ERR 1-Oct-2016) they must be exhausted through properly functioning exhaust canopies.

Type B1: These Class II BSCs maintain a minimum inflow velocity of 100 feet/minute; have HEPA-filtered, down-flow air composed largely of uncontaminated, recirculated inflow air; exhaust most of the contaminated down-flow air through a dedicated duct exhausted to the atmosphere after passing it through a HEPA filter; and have all contaminated ducts and plenums under negative pressure or surrounded by negative-pressure ducts and plenums. If these cabinets are used for work involving minute quantities of volatile toxic chemicals and trace amounts of •radionuclides,• (ERR 1-Oct-2016) the work must be done in the directly exhausted portion of the cabinet.

Type B2 (total exhaust): These Class II BSCs maintain a minimum inflow velocity of 100 feet/minute; have HEPA-filtered, down-flow air drawn from the laboratory or the outside; exhaust all inflow and down-flow air to the atmosphere after filtration through a HEPA filter without recirculation inside the cabinet or return to the laboratory; and have all contaminated ducts and plenums under negative pressure or surrounded by directly exhausted negative-pressure ducts and plenums. These cabinets may be used with volatile toxic chemicals and •radionuclides.• (ERR 1-Oct-2016)

Class III: The Class III BSC is designed for work with highly infectious microbiological agents and other hazardous operations. It provides maximum protection for the environment and the worker. It is a gas-tight enclosure with a viewing window that is secured with locks and/or requires the use of tools to open. Both supply and exhaust air are HEPA/ULPA filtered. Exhaust air must pass through two HEPA/ULPA filters in series before discharge to the outdoors.

Change to read:

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● (Official 1-Jul-2018)

FAQs: <800> Hazardous Drugs—Handling in Healthcare Settings

Last updated: August 18, 2017

The following are responses provided by members of the USP Compounding Expert Committee. Responses have been provided for informational purposes only, and should not be construed as an official interpretation of USP text or relied on to demonstrate compliance with USP standards or requirements.

General

1. What is a hazardous drug?

A hazardous drug is any drug identified as hazardous or potentially hazardous by the National Institute for Occupational Safety and Health (NIOSH) on the basis of at least one of the following six criteria: carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity in humans, organ toxicity at low doses in humans or animals, genotoxicity, and new drugs that mimic existing hazardous drugs in structure or toxicity. NIOSH maintains a list of antineoplastic and other hazardous drugs used in healthcare settings.

2. What is the purpose of this chapter?

The purpose of the chapter is to describe practice and quality standards for handling hazardous drugs in healthcare settings and help promote patient safety, worker safety, and environmental protection. The chapter defines processes intended to minimize the exposure to hazardous drugs in healthcare settings. The chapter was developed by the USP Compounding Expert Committee with the assistance of the USP Compounding with Hazardous Drugs Expert Panel and government liaisons from the U.S. Food and Drug Administration (FDA) and the U.S. Centers for Disease Control and Prevention (CDC) including NIOSH. The chapter was published for the first time for public comment in March 2014. Based on the public comments received, the chapter was revised and proposed for another round of public comments in December 2014. The chapter was revised again and published in the USP-NF in February 2016.

3. Why was the chapter developed?

The public health need for developing <800> was based on published reports of adverse effects in healthcare personnel from occupational exposure to hazardous drugs.[1] General Chapter <800> was developed based on existing guidance documents published by the National Institute for Occupational Safety and Health (NIOSH), American Society of Health-System Pharmacists (ASHP), and the Oncology Nursing Society (ONS). ASHP published a Technical Assistance Bulletin in 1986 and NIOSH published an alert on preventing occupational exposure in 2004. There was a known risk of hazardous drug exposure in healthcare settings from published medical reports, but there was no enforceable standard to minimize the potential risk of exposure.

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4. Who enforces the chapter?

The enforcement of USP standards depends on local, state, and federal regulatory agencies. Accrediting bodies like The Joint Commission survey for compliance with USP compounding standards. The CMS State Operations Manual, which is used by surveyors to ensure that all of the Conditions of Participation are being met, includes references to USP standards. Additionally, many state pharmacy practice acts have included references to USP compounding standards. Each professional licensing board also has the ability to enforce the regulations of that state, which may include USP compounding standards.

5. Who does the chapter apply to?

Chapter <800> was written to protect all workers, patients and the general public who may be accessing facilities where hazardous drugs (HDs) are prepared. This includes but is not limited to pharmacists, technicians, nurses, physicians, physician assistants, home healthcare workers, veterinarians, and veterinary technicians. If any workers come in contact with HDs, they must receive HD training, and be assessed for an understanding of the training. All personnel who handle HDs are responsible for understanding the fundamental practices and precautions and for continually evaluating these procedures and the quality of final HDs to prevent harm to patients, minimize exposure to personnel, and minimize contamination of the work and patient-care environment.

6. What settings does the chapter apply to?

The chapter applies to all healthcare personnel who handle HD preparations and all entities that store, prepare, transport, or administer HDs (e.g., pharmacies, hospitals and other healthcare institutions, patient treatment clinics, physicians' practice facilities, or veterinarians' offices).

7. Does the chapter apply to administration of HDs?

Yes, the chapter applies to administration of HDs. If non-antineoplastic or reproductive risk HD dosage forms do require manipulation such as crushing tablet(s) or opening capsule(s) for a single dose, alternative containment strategies and work practices as defined in the assessment of risk must be used (e.g. appropriate personnel protective equipment (PPE), use a plastic pouch to contain any dust or particles generated). If antineoplastic HD dosage forms require manipulation, the requirements of Chapter <800> must be followed.

8. What is the status of the General Chapter <800> and when will General Chapter <800> become official?

General Chapter <800> was published on February 1, 2016 in the First Supplement to USP 39–NF 34. The USP Compounding Expert Committee approved a delayed official implementation date of July 1, 2018 to allow entities additional time to implement the standard. With the delayed official date, entities have more than two years to implement this new standard.

9. Will there be updates or changes to the chapter?

The final version of the chapter was published on February 1, 2016. An erratum was published on May 26, 2016 to remove the requirement that the Containment Secondary Engineering Control (C-SEC) be externally vented through high-efficiency particulate air (HEPA) filtration. This revision does not remove the requirement that the C-SEC be externally vented.

10. How can I obtain a copy of General Chapter <800>?

General Chapter <800> was published on February 1, 2016 in the First Supplement to USP 39–NF 34. You may purchase the chapter through a subscription to the USP Compounding Compendium (http://www.usp.org/store/products-services/usp-compounding-compendium) or USP-NF (http://www.usp.org/store/products-services/usp-nf).

11. Have there been any documented/published studies involving harm related to handling of HDs?

Yes, there are several studies demonstrating risks associated with handling HDs. Some of references are included in the References section of the chapter.

Assessment of Risk

12. Can repackaging containers of commercially available HD oral liquids into prescription containers or unit-dose packages be considered under an assessment of risk?

Yes, final dosage forms of commercially available HD oral liquids that do not require any further manipulation other than pouring and repackaging may be considered under an assessment of risk.

13. Can I do an assessment of risk for an entire group of HDs (i.e. Group 1, Group 2, or Group 3) instead of listing each individual HD?

No. The assessment of risk must list each drug and dosage form individually. Dosage forms of drugs within the same group might not have the same risk of exposure. For example, priming an intravenous line may have more risk of exposure than dispensing tablets without further manipulation. HDs appear on the NIOSH list based on different characterizes, such as specific reproductive risks. The facility may have the same information for several drugs or dosage forms, but the facility's list needs to be specific to the drug and dosage form.

Personnel

14. Where does the designated person obtain training? How much training does the designated person need?

Any training should begin with reading the chapter in it is entirety. All of the requirements for HD handling are defined in the chapter and the chapter provides many references to other source documents. If additional training is required, many professional organizations conduct training and continuing education programs on the subject. The chapter does not specify a minimum number of training hours. The designated person must have a thorough understanding of the standards to be able to develop and implement appropriate procedures; oversee entity compliance with the chapter and other applicable laws, regulations, and standards; ensure competency of personnel; and ensure environmental control of the storage and compounding areas.

Facilities and Engineering Controls

15. Are there requirement for posting signs that HDs are being handled in the facility?

Signs are not required to be posted at the entrance of facilities. However, signs designating the hazard must be prominently displayed before the entrance to the HD handling areas. Additionally, signs must be available for restricting access to areas where HD spills occur.

16. Can sterile and nonsterile HDs be stored together?

See Section 5.2 of the Chapter for guidance on storage. 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. Antineoplastic HDs requiring manipulation other than counting or repackaging of final dosage forms and any HD active pharmaceutical ingredient (API) must be stored separately from non-HDs in a manner that prevents contamination and personnel exposure. These HDs must be stored in an externally ventilated, negative-pressure room with at least 12 air changes per hour (ACPH). Non-antineoplastic, reproductive risk only, and final dosage forms of antineoplastic HDs may be stored with other inventory if permitted by entity policy. Refrigerated antineoplastic HDs must be stored in a dedicated refrigerator in a negative pressure area with at least 12 ACPH [e.g., storage room, buffer room, or containment segregated compounding area (C-SCA)].

17. Can refrigerated non-antineoplastic HDs be stored with antineoplastic HDs?

Yes, a refrigerator must be dedicated to HD storage and located in a negative pressure room with at least 12 ACPH. Refrigerated antineoplastic HDs must be stored in this dedicated refrigerator. HD APIs requiring refrigeration must also be stored according to the Chapter. Other HDs may be stored in this dedicated refrigerator or may be stored with other inventory if an assessment of risk has been performed and implemented.

18. Where should the sink be located?

Care must be taken to locate water sources and drains in areas where their presence will not interfere with required ISO classifications. Water sources and drains must be located at least 1 meter away from the Containment Primary Engineering Control (C-PEC). Within an ISO classified area, a hand-washing sink must be placed in the ante-room at least 1 meter from the entrance to the HD buffer room to avoid contamination migration into the negative pressure HD buffer room. Within an unclassified C-SCA, a hand-washing sink must be placed at least 1 meter from C-PEC and may be either inside the C-SCA or directly outside the C-SCA.

19. Is the C-PEC used for sterile compounding required to be exhausted to the outside or can the C-PEC be recirculated into the negative pressure C-SEC which is exhausted to the outside of the building?

The Chapter requires that all C-PECs used for manipulation of sterile HDs must be externally vented. Sterile HD compounding must be performed in a C-PEC that provides an ISO Class 5 or better air quality, such as a Class II or III biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI). Class II BSC types A2, B1, or B2 are acceptable. C-PECs used for pre-sterilization procedures such as weighing and mixing must be either externally vented (preferred) or have redundant –HEPA filters in series and must provide personnel and environmental protection, such as a Class I BSC or Containment Ventilated Enclosure (CVE). A Class II BSC or a CACI may also be used.

20. Can non-HDs and HDs be compounded in C-PECs located in the same C-SEC?

Separate rooms (C-SECs) are required for sterile, nonsterile, HD and non-HD compounding with two exceptions:
(1) Per section 5.3 Compounding, for entities that compound both nonsterile and sterile HDs, the respective C- PECs must be placed in separate rooms, unless those C-PECs used for nonsterile compounding are sufficiently effective that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they must be placed at least 1 meter apart and particle-generating activity must not be performed when sterile compounding is in process; and
(2) Per section 5.3.2 Sterile Compounding, a BSC or CACI used for the preparation of HDs must not be used for the preparation of a non-HD unless the non-HD preparation is placed into a protective outer wrapper during removal from the C-PEC and is labeled to require PPE handling precautions.

21. Can a Laminar Airflow Workbench (LAFW) or compounding aseptic isolator (CAI) be used for compounding a non-antineoplastic HD?

Section 5.3.2 specifies that a LAFW cannot be used for compounding an antineoplastic HD. However, for handling non-antineoplastic and reproductive risk HDs, each facility may conduct an assessment of risk and implement strategies different than those required in the chapter. A LAFW does not provide any protection for the worker from the HD. A LAFW or CAI may be used for non-antineoplastic HDs, however, alternative containment strategies and/or work practices must be determined during the assessment of risk.

22. Can a BSC or CACI used for compounding HDs be used for compounding non-HDs?

If a non-HD is prepared in a C-PEC where HDs have been prepared, then the non-HD should be handled and labeled as an HD. The non-HD preparation should be placed into a protective outer wrapper during removal from the C-PEC and should be labeled to require PPE handling precautions. All associated materials and wrappers should be discarded as HD waste because the preparation and associated materials have potentially been contaminated by exposure to HDs.

23. Can the negative pressure to the C-SEC be reduced or turned off when the room is not in use?

No, the C-SEC must maintain a negative pressure of 0.01 to 0.03 inches of water column relative to all adjacent areas at all times.

24. Can the ACPH in the C-SEC be set below the minimum requirement when the C-SEC is not in use?

No, the C-SEC must have an appropriate air exchange (e.g., 12 or 30 ACPH) at all times.

25. May a CACI, isolator, robotic device, or similar device be used to compound a sterile HD outside of a C-SEC?

No. A CACI, isolator, robotic device, or similar device may act as the C-PEC if it meets the containment requirements of the chapter as well as the requirements listed in <797>. However, the device must be placed in C-SEC meeting all of the requirements in the chapter.

26. Can the C-PEC be used to create 100% of the external venting for the C-SEC?

Yes, if that C-PEC can function appropriately as the sole source of exhaust from a room. Most direct-connected (no canopy connection) C-PECs do not integrate well into rooms where they are the only exhaust from that room. Fluctuation in building HVAC systems will impact direct connected devices but not canopy connected devices to the same extent.

27. Are closed-system drug-transfer devices (CSTDs) required for compounding HDs?

No, the Chapter does not require a CSTD for compounding HDs, although it is recommended. However, the Chapter does require that CSTDs be used when administering antineoplastic HDs when the dosage form allows.

28. Is there an evaluation tool one can use for evaluating the performance of the different CSTDs available?

NIOSH created a draft performance standard protocol for the containment-type CSTDs. This proposed protocol was published in the Federal Register on September 8, 2015. Five CSTDs were tested by NIOSH and two showed test substance concentration levels below the limit of detection meaning that only 2 of the 5 CSTDs evaluated prevented escape of vapors of the test substance. The protocol has not been released in final form.

29. How can a CSTD be chemically incompatible with a HD?

Depending on the chemical composition of the drug being compounded and the composition of the CSTD device, chemical incompatibilities may exist. In March 2015, FDA warned against the use of bendamustine with CSTDs, syringes, and adapters containing polycarbonate or acrylonitrile-butadiene-styrene (ABS). The component in bendamustine (N, N-dimethylacetamide (DMA)) dissolved the ABS or polycarbonate on contact.

30. What is meant by "fixed walls"?

Fixed walls are solid hard wall modular or 'stick-build' construction. According to the Chapter, fixed walls are required to prevent the egress of HD contamination from the C-SEC (either a C-SCA or HD buffer room) as well as ingress of contamination into the ISO Class 7 HD buffer room.

31. Are pressure gauges required to monitor the pressure differential between the C-SEC and the adjacent areas?

The entity must be compliant with the appropriate USP standards for compounding including <795> and/or <797> and in accordance with applicable federal, state, and local regulations. Presence of a pressure gauge and at least daily monitoring is currently required for sterile compounding per USP <797>. However, pressure monitoring is not addressed in nonsterile compounding per USP <795>, so

entities should follow applicable federal, state, and local regulations. Presence of a pressure gauge and at least daily monitoring of negative pressure storage areas and nonsterile compounding areas helps ensure pressure requirements are continually maintained in these areas.

Environmental Quality And Control

32. Is environmental wipe sampling required?

No. The chapter recommends but does not require the performance of environmental wipe sampling. Some common marker HDs that can be assayed include cyclophosphamide, ifosfamide, methotrexate, fluorouracil, and platinum-containing drugs. If no wipe sampling kit is available for the specific HDs used by the entity, the performance of environmental wipe sampling would not be appropriate.

33. Why is environmental wipe sampling recommended when there is currently no standard for acceptable limits on HD surface contamination?

Environmental wipe sampling for HD surface residue should be performed to verify containment. Contamination in any amount indicates a lack of containment. Wipe sampling kits need to be evaluated to ensure they are appropriate for HDs used by the entity. If contamination is found, the chapter states that the designated person must identify, document, and contain the cause of contamination. Such action may include reevaluating work practices, re-training personnel, performing thorough deactivation, decontamination, cleaning, and improving engineering controls. Repeat the wipe sampling to validate that the deactivation/decontamination and cleaning steps have been effective.

34. Does every area where HDs are handled require environmental sampling?

The chapter recommends, but does not require, the performance of environmental "wipe sampling." The term "sampling" indicates that a portion, or sample, of the entire population be tested.

35. What are the acceptable limits for HD surface contamination?

There is currently no standard for acceptable limits for HD surface contamination. Contamination in any amount indicates a lack of containment and must be addressed.

Personal Protective Equipment (PPE)

36. Are the PPE and Engineering Controls specified in Table 5 of the current NIOSH list required?

<800> requires entities to maintain a list of HDs that include any items on the current NIOSH list that the entity handles. However, the list of PPE and engineering controls in Table 5 of the 2016 NIOSH list is a recommendation and may be use to guide the development of the entity's policy. Section 7 of <800> states that "gowns, head, hair, shoe covers, and two pairs of chemotherapy gloves are required for compounding sterile and nonsterile HDs. Two pairs of chemotherapy gloves are required for administering antineoplastic HDs. Gowns shown to resist permeability by HDs are required when administering injectable antineoplastic HDs. For all other activities, the entity's SOP must describe the appropriate PPE to be worn based on its occupational safety plan and assessment of risk (if used). The entity must develop SOPs for PPE based on the risk of exposure and activities performed."

37. What PPE is required for administering HDs?

For administering all antineoplastic HDs, two pairs of chemotherapy gloves tested to ASTM D6978 standard must be worn. For administering injectable antineoplastic HDs, gowns shown to resist permeability by HDs must be worn in addition to two pairs of chemotherapy gloves. For administering other HDs, the entity must establish policies describing the PPE required. Table 5 of the NIOSH List provides additional recommendations for PPE based on the HD formulation and activity.

38. Are compounders required to remove all PPE when leaving the compounding area?

Yes, all PPE would need to be removed when leaving the HD compounding area. The goal is to contain all hazardous contamination within the negative pressure room.

39. Can gowns be re-worn during the same day if a compounder leaves the HD compounding area?

Disposable PPE must not be re-used. Consider all PPE worn when handling HDs to be contaminated with, at minimum, trace quantities of HDs. PPE must be placed in an appropriate waste container and further disposed of per local, state, and federal regulations. PPE worn during compounding should be disposed of in the proper waste container before leaving the C-SEC.

40. What documentation is required to show that a gown will resist permeability by HDs?

Gowns used for HD handling must be shown to resist permeability by HDs which can be determined by testing against ASTM F739-12. Manufacturers of gowns used for handling HDs should provide results of ASTM F739-12 testing. The gown manufacturer should be able to provide permeability data for commonly used HDs.

Compounding

41. Is an entity required to have two sets of equipment, one set for compounding HDs and another second set for compounding non-HDs?

General Chapter <800> states that "disposable or clean equipment for compounding (such as mortars and pestles, and spatulas) must be dedicated for use with HDs." This refers to equipment (or parts of equipment) that comes in direct contact with HDs. Equipment that does not come in direct contact with HDs may be shared between HD and non-HD compounding areas provided it is deactivated, decontaminated and cleaned before it is removed from the HD area. Equipment used in HD compounding must be operated in the C-SEC unless it is operated as a closed system (e.g. certain mixers, terminal sterilization using an autoclave or convection oven).

42. During nonsterile compounding with HD APIs, are all steps of the compounding process required to be performed in the C-PEC?

General Chapter <800> states that "bulk containers of liquid and API HD must be handled carefully to avoid spills. If used, APIs or other powdered HDs must be handled in a C-PEC to protect against occupational exposure, especially during particle-generating activities (such as crushing tablets, opening capsules, and weighing powder)." It is recognized that under some circumstances, it is not possible to perform all steps of the compounding process in the C-PEC (e.g. due to equipment size or function). It is important for the safety of personnel that powdered HDs be weighed and mixed to the wet stage or made into capsules in the C-PEC. Once nonvolatile, non-antineoplastic, powdered HDs are wet, an assessment of risk may be performed to determine alternative containment strategies and/or work practices. The NIOSH list of antineoplastic and other HDs provides general guidance on PPE for possible scenarios that may be encountered in healthcare settings including instances where a C-PEC cannot be used.

43. Where should HD APIs be handled prior to sterilization when compounding sterile HDs?

In addition to <800>, sterile compounding must follow standards in <797> which states that presterilization procedures for high-risk level CSPs, such as weighing and mixing, shall be completed in no worse than an ISO Class 8 environment. Per <800>, presterilization procedures for high-risk level HD CSPs can occur in the HD ISO Class 7 negative pressure buffer room if the C-PEC used for the nonsterile presterilization procedures is sufficiently effective that the room can continuously maintain ISO 7 classification. If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they must be placed at least 1 meter apart and particle-generating activity must not be performed when sterile compounding is in process. Alternatively, an ISO Class 8 or better negative pressure room could be used. An ISO Class 7 negative pressure room would be necessary if it leads directly into the HD ISO 7 negative pressure buffer room.

44. Does the chapter apply if the HD is dissolved in a liquid dosage form and does not become an aerosol or gas?

HDs that do not require any further manipulation, other than counting or repackaging of final dosage forms, may be prepared for dispensing without any further requirements for containment unless required by the manufacturer or if visual indicators of HD exposure hazards are present (e.g., HD dust or leakage). Consideration must be given to the aerolization of HDs in liquid formulations.

45. If the HD is a liquid dosage form, may it be compounded in a positive pressure non-HD cleanroom?

No, HD CSPs must be filtered in a BSC or CACI located in an ISO 7 room with negative pressure of 0.01 to 0.03 inches of water and 30 ACPH.

46. Can an assessment of risk be performed on concentrated solutions of HDs (i.e. hormone concentrates)?

No, concentrated solutions of HDs (i.e. hormone concentrates) is an HD API that is further manipulated into a final dosage form and is subject to the containment requirements in <800>. General Chapter <800> defines an API as "any substance or mixture of substances intended to be used in the compounding of a drug preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans and animals or affecting the structure and function of the body.

47. What kind of materials may be used for the cabinets and counters in the nonsterile compounding room?

The chapter states that cabinets in the nonsterile compounding area must be smooth, impervious, free from cracks and crevices, and non-shedding but does not limit or define the specific materials that may be used.

Hazard Communication Program

48. Do personnel of reproductive capability include both male and females?

Yes, the chapter applies to anyone capable of reproduction.

Receiving

49. What PPE is required for receiving HDs?

At least one pair of chemotherapy gloves tested to ASTM D6978 standard must be worn when unpacking HDs (see section 10. Receiving). The entity's policies must address if any additional PPE is required. Table 5 of the 2016 NIOSH List of Antineoplastics and Other Hazardous Drugs in Healthcare Settings provides additional recommendations for PPE and engineering controls based the formulation of HD and the activity. The entity's policy should address situations where HDs are received in intact containers and where HDs are received in containers that may be damaged.

50. Are suppliers required to ship HDs in impervious plastic?

No, the chapter recommends that suppliers ship HDs in impervious plastic to segregate them from other drugs and allow for safety in the receiving and internal transfer process.

51. Does the HD return waiting area have to be separate from the regular HD storage area?

No, a separate area is not required. HDs waiting to be returned to the supplier must be segregated in a designated negative pressure area. The regular HD storage area may be designated for this purpose.

52. What container materials are considered impervious?

The type of impervious packaging will vary with the situation and type of HD. Impervious packaging may be "soft" or "firm". HDs must be transported in containers that minimize the risk of breakage or leakage.

53. What is the tiered approach for receiving HDs?

The tiers will be defined by the entity's SOPs based on considerations such as the facility design and types of HDs being handled.

Labeling, Packaging, Transport And Disposal

54. What must be on the label for HDs?

HDs identified by the entity as requiring special HD handling precautions must be clearly labeled at all times during their transport. Labeling must be compliant with the appropriate USP standards for compounding including <795> and/or <797> and in accordance with applicable federal, state, and local regulations.

55. What kind of packaging containers can be used for packaging HDs?

The chapter states that packaging containers and materials must be selected to maintain physical integrity, stability, and sterility (if needed) of the HDs during transport. Packaging materials must protect the HD from damage, leakage, contamination, and degradation, while protecting healthcare workers who transport HDs. The entity must have written SOPs to describe appropriate shipping containers and insulating materials, based on information from product specifications, vendors, and mode of transport. Other sources of information may include the chemical or formula and the SDS. In addition, there are multiple chapters in the USP Compounding Compendium that describes packaging.

56. Can HDs be transported in pneumatic tubes, robots, or patient carts?

Each facility must conduct an assessment of risk and develop SOPs accordingly. HDs must be transported in containers that minimize the risk of breakage or leakage. Pneumatic tubes must not be used to transport any liquid HDs or any antineoplastic HDs because of the potential for breakage and contamination.

57. Are personnel involved in waste removal and cleaning required to don PPE?

Yes, personnel must wear appropriate PPE based on their assigned tasks.

Medical Surveillance

58. What if the employee wants to keep their medical records private from the employer?

Medical surveillance is recommended but not required by the chapter. The entity may choose to use a contracted employee health service to perform the medical surveillance while protecting the confidentiality of the employees' personal medical information.

59. What "health variables" should be followed over time for individual workers?

The chapter recommends an initial baseline assessment (pre-placement) of a worker's health status, medical history and collection of data elements including a medical (including reproductive) history and work history to assess exposure to HDs, physical examination, and laboratory testing. Methods used to assess exposure history include a review of:

- Records of HDs handled, with quantities & dosage forms
- Estimated number of HDs handled per week
- Estimates of hours spent handling HDs per week and/or per month
- Performance of a physical assessment and laboratory studies linked to target organs of commonly used HDs such as a baseline complete blood count.

60. In a medical surveillance program, how does an employer obtain data from the unexposed workers for comparison to the exposed workers?

The chapter recommends an initial baseline assessment (pre-placement) of a worker's health status, medical history and collection of data elements including a medical (including reproductive) history and work history to assess exposure to HDs, physical examination, and laboratory testing. Methods used to assess exposure history include a review of:

- Records of HDs handled, with quantities & dosage forms
- Estimated number of HDs handled per week
- Estimates of hours spent handling HDs per week and/or per month
- Performance of a physical assessment and laboratory studies linked to target organs of commonly used HDs such as a baseline complete blood count.

April 24, 2017

Ms. Caroline D. Juran, Executive Director Virginia Board of Pharmacy
9960 Mayland Drive, Suite 300
Henrico, VA 23233-1463

RE: Non-compliance of CETA CAG-002-2006 guide to the ISO 14644-1:2015(E) Standard

Dear Ms. Juran,

My name is Hank Rahe and I am the technology director for Containment Technologies Group, Inc. (CTG). My responsibilities at CTG include reviewing standards, rules and regulations both state and federal. Certifications performed in compliance with your state's rules and regulations, as well as, USP <797> is critical. However, CTG has identified a conflict between your state's rules, USP <797> and the ISO 14644-1:2015(E) standard-classification of air particulate concentration certification.

Specifically, your rules and regulations as well as USP <797> are in direct conflict with the Controlled Environment Testing Association (CETA), CETA CAG-002-2006 guide, to certify CAI/CACI's. The Guide's testing conditions not acceptable to the ISO 14644-1:2015;(
E) standard- classification of air particulate concentration certification.

Attached is a copy of the NABP letter, a letter to United States Pharmacopeia concerning non-compliance of the CETA Guide and the specifics of the non-compliance of the CETA Guide to the ISO standard.

The CETA Guide's failure to comply with the testing conditions (see attached details) of the ISO Standard negates any certification using the CETA guide. All pharmacies that employ CAI/CACI's as their Primary Engineering Control devices (PEC) and are certified to the CETA Guide are out of compliance with ISO 14644-1:.2015(E) classification of air cleanliness by particle concentration required by your board's rules as well as USP <797>.

Non- compliance is a very serious problem and many pharmacies are not aware of the issue. Informing sterile compounding pharmacies through communications and your inspector's visits that any reports stating "certified to the CETA guide CAG-002-2006" is non-compliant will allow them to contact their certification company for correct testing procedures to those described in the ISO standard.

As part of our goal of patient safety awareness we will be sending out this information to pharmacy directors across the county. This letter is intended to prepare your board for questions you may receive.

Please let me know if you need additional information

Sincerely,

Hank Rahe, BSIM, MSE
Director Technology CTG
hrahe@mic4.com
317 713-8203

Attachments:

March 31, 2017

Carmen A. Catizone, Executive Director NABP
1600 Feehanville Drive
Mount Prospect, IL 60056

RE: Non-compliance of CETA guide to ISO Standards

Dear Ms. Catizone,

I am writing to seek your help in communicating with members of your association.

On August 26, 2016 you were copied on a letter (attached) to Dr. Sun, United States Pharmacopeia concerning the noncompliance of the Controlled Environment Testing Association CETA CAG-002-2006 to ISO 14644-1: 2015(E). The testing conditions required by the ISO Standard are not followed by the CETA guide.

I understand how my letter could be overlooked thus the follow up.

CETA guide failure to comply with the testing conditions (see attached details) of the ISO Standard negates any certification using the CETA guide. All pharmacies that employ CAI/CACI's as their Primary Engineering Control devices (PEC) and are certified to the CETA guide are out of compliance with ISO 14644-1:.2015(E). All state boards of pharmacy, USP <797>, USP <800> and FDA guidance require this ISO Standard for classification of air cleanliness by particle concentration. As you are also aware, pharmacy boards and federal agencies, such as the FDA, depend upon the certification as part of their inspection process.

Communications will be going out to state pharmacy boards presidents, USP, federal agencies and individual pharmacy directors making them aware of the problem of being certified to the CETA guide. This is likely to create questions and concerns that will reach your association members.

I look forward to working with you and NABP to communicate this important information. Let me know if you have any questions.

Sincerely,

Hank Rahe , Director Technology CTG
hrahe@mic4.com
317 713-8203

CC: NABP Executive Committee

Attachments:

August 23, 2016

United States Pharmacopeia
Dr. Jeanne Sun, Scientific Liaison to the Compounding Expert Committee
12601 Twinbrook Parkway
Rockville, MD 20852-1790

RE: ISO 14644-1:2015 (E)

Dear Dr. Sun,

As you may be aware that the International Standards Organization has issued a second addition of ISO 14644-1:2015(E) in December 2015.

ISO 14644-1: 2015(E) Classification of air cleanliness by particle concentration is sited in both USP <797>, and USP <800> as a requirement for levels of air cleanliness. The language of ISO 14644-1: 2015 (E) addresses the required test conditions "occupancy states" for testing cleanliness levels by particle concentrations to comply with the ISO standard. The USP standards are inconsistent with the language of the ISO standards and causes confusion, when comparing the required testing conditions.

The ISO 14644-1:2015 (E) require occupancy states [1] during testing be "as built, at rest, and operational" while USP <797> and USP <800> use the term "dynamic conditions". Though the terms dynamic conditions and operational would seem to mean the same thing dynamic conditions cannot be cross referenced with ISO 14644-1:2015(E). For consistency USP should change the wording in USP <797> and USP <800> to properly identify the state in which the standard air cleanliness particle concentration is to be measured.

Also, USP <797> currently references the Controlled Environment Testing Association (CETA) as an example (per Susan deMars your chief legal counsel) of testing and certification of Compounding Aseptic Isolators (CAI) and Containment Compounding Aseptic Isolator (CACI). A number of state pharmacy boards have wrongly interrupted this to mean the CETA guide is the required testing standard for USP <797>, while USP sites it only as an example of testing and certification. USP should clarify that the CETA reference is an example to state pharmacy boards.

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In addition, the CETA guide has compliance issues with the ISO 14644-1:2015(E) standard in that the CETA guide CAG-002-2006 requires "particle elevation" [2] for tests 2.06, 2.07and 2.09 which conflicts with ISO 14644-1:2015(E) requirements for an operational state while performing testing. The CETA guide also has additional conflicting testing requirements such as only testing for vertical airflow (2.08) and stating in the overview of the document that it is not intended to set specific acceptance criteria and yet follows with a series of subjective test acceptance criteria.

In summary I am requesting USP to align the wording for levels of air cleanliness with the ISO standard 14644-1: 2015(E) and inform your customers, the state pharmacy boards, that the CETA referenced in the current USP <797> is only an example.

Thank you for your attention to this important matter and I look forward to the changes.

Sincerely,

Hank Rahe, BSIM, MSE
Director Technology CTG
317 713-8203
hrahe@mic4.com

CC: Ms. Susan deMars, Chief Legal Counsel USP
Mr. Dan King, Frost, Brown, Todd LLC
Ms. Carmen Catizone, Executive Director NABP
Mr. Dale Atkinson, Atkinson & Atkinson LLC legal Counsel NABP
Executive Directors all state Boards of Pharmacy
Legal Counsels all state Boards of Pharmacy

1. ISO 14644-1:2015 (E): Cleanrooms and associated controlled environment – Pat 1: Classification of air cleanliness by particle concentration, p3 3.3 Occupancy states; Ch -1223 Vernier, Geneva Switzerland
2. CETA Compounding Isolator Testing Guide CETA CAG-002-2006 Revised December 8, 2008. P3 glossary of terms- particle elevation, Controlled Environment Testing Association,1500 Sunday Drive, Suite 102, Raleigh, NC 27607

Specific wording ISO 14644-1(E); 2015

ISO 14644-1:2015 (E): Cleanrooms and associated controlled environment – Pat 1: Classification of air cleanliness by particle concentration, p3 3.3 Occupancy states; Ch -1223 Vernier, Geneva Switzerland

The language of ISO 14644-1: 2015 (E) addresses the required test conditions "occupancy states" for testing cleanliness levels by particle concentrations to comply with the ISO standard. The required occupancy states [1] are as built, at rest, and operational.

Specific wording CETA CAG-002-006

CETA Compounding Isolator Testing Guide CETA CAG-002-2006 Revised December 8, 2008. P3 glossary of terms- particle elevation, Controlled Environment Testing Association,1500 Sunday Drive, Suite 102, Raleigh, NC 276

CETA guide CAG-002-2006 requires **"particle elevation"** for testing and has additional conflicting testing requirements such as **only testing for vertical airflow** and stating in the overview of **the document that it is not intended to set specific acceptance criteria.**

1. The CETA guides are not standards and contain tests to not meet ISO standard 14644-1:2015(E). **Each of these tests require an adjustment to background particle levels (particulate elevation) that do not represent operational conditions.** The specific tests that create the barrier for the MIC contained in CETA-CAG-002-2006:
   a. 2.06 Particle Containment Integrity and Enclosure Leak Test -Procedure 2- "If the count is too low, elevate the background levels"
      1. Increasing particle counts above operational levels overcomes the capabilities of the MIC which has been validated challenge levels of 400,000 particles of 0.5 micron (ISO class 9). Documentation informs customer of the limit

   b. 2.07 Recovery Time Determination Test - Procedure 6- "fill the chamber with particulate"
      1. Elevates background inside the MIC to levels exceeding ISO Class 9 (1,000,000) exceeding any operational condition under which compounding would occur.

   c. 2.09 Preparation ingress and Egress Test- Procedure "If the count is too low elevate the background levels"
      1. Elevates background particulates in the anti-chamber (airlock) to a level exceeding ISO class 9. This exceeds any operation condition in a pharmacy compounding area.

   d. 2.08 Airflow Smoke Test- Specifics "Airflow in the Direct Compounding Area is **downward**
      1. This does not allow for horizontal airflow such as the MIC's unidirectional airflow and would fail the MIC based on the wording in the standard.

   e. General Responsibility Section "The engineering and design concept employed are up to the individual manufacturer's discretion.

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TO: EXECUTIVE OFFICERS – STATE BOARDS OF PHARMACY

FROM: Carmen A. Catizone, Executive Director/Secretary

DATE: August 30, 2017

RE: United States Pharmacopeia (USP) Questions

NABP received a number of requests regarding USP General Chapter <800> Hazardous Drugs – Handling in Healthcare (Chapter <800>) and whether there is a conflict with Controlled Environment Testing Association (CETA) Certification for and USP Standards concerning air cleanliness.

Concerning USP Chapter <800>, NABP is aware of requests to states by entities potentially impacted by USP Chapter <800> regarding the adoption and enforcement of USP Chapter <800>. Additionally, states are being asked to delay implementation of Chapter <800> or adopt standards that are less stringent. The attached document from USP answers questions regarding USP's rationale for Chapter <800> and the planned implementation date. USP indicated to NABP that it is not considering further revisions to the Chapter or delaying the implementation date of July 2018.

The second issue concerns a series of letters to states from Containment Technologies Group (CTG) citing a conflict between CETA Certification of primary engineering control devices and USP Standards. The attached document from USP addresses this issue.

If you require additional information or have any questions, please feel free to contact me at ExecOffice@nabp.pharmacy.

Attachment

cc: NABP Executive Committee

USP U.S. Pharmacopeial Convention
Global Expertise
Trusted Standards
Improved Health

Question: Why should states adopt General Chapter <800> *Hazardous Drugs – Handling in Healthcare Settings*?

Answer: General Chapter <800> *Hazardous Drugs – Handling in Healthcare Setting* is a new standard which becomes official on July 1, 2018. The purpose of <800> is to ensure preparation quality and protect patients, healthcare workers, facility employees, and the public who either handle hazardous drugs or are in proximity to environments where hazardous drugs are handled. The chapter defines processes for quality requirements intended to minimize and mitigate risks of exposure in handling, distribution, and administration of hazardous drugs. General Chapter <800> is an important part of the quality framework and is essential in ensuring a quality environment to protect the practitioner and the patient from exposure to hazardous drugs.

The public health need for developing <800> was based on published reports of adverse effects in healthcare personnel from occupational exposure to hazardous drugs.[1] General Chapter <800> was developed based on existing guidance documents published by the National Institute for Occupational Safety and Health (NIOSH), American Society of Health-System Pharmacists (ASHP), and the Oncology Nursing Society (ONS). ASHP published a Technical Assistance Bulletin in 1986 and NIOSH published an alert on preventing occupational exposure in 2004. There was a known risk of hazardous drug exposure in healthcare settings from published medical reports, but there was no enforceable standard to minimize the risk of exposure. In 2010, the Compounding Expert Committee began development of a chapter based on this public health need. In 2011, an Expert Panel was formed to gain additional expertise in handling hazardous drugs which included experts practicing in healthcare settings, medical schools, research organizations, as well as federal agencies. The chapter was proposed for public comment twice and each time, the Compounding Expert Committee reviewed all of the public comments and made changes to the chapter based on these comments.

One of the most significant changes to General Chapter <800>, after its initial proposal for public comment, is the allowance for an assessment of risk. The chapter distinguishes between bulk drug substances and antineoplastic dosage forms requiring manipulation which must meet all of the containment requirements and other dosage forms which may qualify for an assessment of risk. Under an assessment of risk, the entity may determine alternative containment strategies and work practices for handling the hazardous drug. The intent of this change is to

[1] Sessink PJ, Bos RP. Drugs hazardous to healthcare workers. Evaluation of methods for monitoring occupational exposure to cytostatic drugs. Drug Saf. April 1999; 20(4): 347-59. Venitt S, Crofton-Sleigh C, Hunt J, Speechley V, Briggs K. Lancet, Monitoring exposure of nursing and pharmacy personnel to cytotoxic drugs: urinary mutation assays and urinary platinum as markers of absorption. Jan 1984;1(8368): 74-7. (See also https://www.cdc.gov/niosh/topics/antineoplastic/default.html).

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offer more flexibility to healthcare practitioners in handling certain dosage form which has less potential for exposure while still requiring adequate protection to personnel handling certain antineoplastic drugs and bulk ingredients.

General Chapter <800> should be adopted by regulatory bodies to ensure preparation quality and to protect patients, healthcare practitioners, and the public who either handle hazardous drugs or are in proximity to environments where hazardous drugs are handled.

Question: General Chapter <797> *Pharmaceutical Compounding – Sterile Preparations* references both ISO 14644-1 and CAG-002-2006–section 2.09. Is there a conflict between these two guidance documents?

Answer: ISO 14644-1 is an international standard for classification of air cleanliness by particle concentration that is used across all industries concerned with clean environments. USP General Chapter <797> references this international standard to define the ISO classification of particulate matter in the primary and secondary engineering control. The chapter additionally requires certification of engineering controls following procedures "such as those outlined in *Certification Guide for Sterile Compounding Facilities* (CAG-003-2006)." The Compounding Expert Committee included the CETA CAG-003-2006[2] certification procedures as an example because it is the only reference guide that the committee is aware of that consolidates industry standards for the specific needs of the compounding industry. CETA CAG-003-2006 also references ISO 14644-1 for particle count classification.

USP <797> further references CAG-002-2006 *section 2.09* as sample procedures for placing Compounding Aseptic Isolators (CAI) and Compounding Aseptic Containment Isolators (CACI) outside of an ISO Class 7 buffer area. CAG-002-2006 section 2.09 is specifically referenced because it defines tests that prove whether a CAI or CACI can be placed outside of an ISO classified room. The test procedures in CAG-002-2006 are more robust than ISO 14644-1 because the tests increase the background particulate count. Section 2.09 increases background levels to prove that particulate contamination from the room is not dragged into the CAI or CACI when materials are transferred into or removed from the isolator. The procedures in ISO 14644-1 are not relevant to CAG-002-2006 section 2.09, and thus specific test procedures outlined in ISO 14644-1 are not referenced in these sections. Consequently, there is no conflict between CAG-002-2006 section 2.09 and ISO 14644-1.

[2] Controlled Environment Testing Association (CETA), www.CETAinternational.org.

Sept 7, 2017

Dear Members of the Virginia Board of Pharmacy Ad Hoc Committee:

We appreciate the opportunity to provide written comment regarding the committee's discussion of USP 800 implementation. It goes without saying that implementation of USP 800 standards in all settings that use hazardous substances is a huge undertaking! Over the past year there has been, and continues to be, more and more discussion about this implementation, its challenges and validities. We appreciate the Board considering all facets of this major change to practice sites across the state. At this point in time, we are not sure what items are on the agenda for the committee to discuss, but we were hoping to bring up the following concerns.

- **Decreased patient access to medications** – Many of our colleagues are expressing concern that they will not be able to continue to provide medications that contain hazardous substances because they cannot afford the required facility changes. As an example, approximately 50% of our business will be considered Hazardous once USP 800 goes into effect. Across the state that adds up to a lot of patients looking for a place to fill a lot of prescriptions.
- **Expenses cannot be absorbed in the normal course of business** – Compliance with USP 800 will drive prices up, potentially causing patients to abandon needed therapies. As an example, our remodel pricing is being quoted at over $400,000 and we're one small pharmacy. We cannot imagine what the larger hospitals and clinics are facing.
- **Employee and patient safety is always a top priority** – We already comply with NIOSH/OSHA guidelines to ensure our employees are not unduly exposed to hazardous substances. Additionally, there have been questions raised as to the science behind the USP guidelines and whether they would actually lead to reduced exposure and/or improved worker safety.
- **The status of adoption of USP 800 by other states is changing** – Some states are only partially implementing USP 800 or pushing the compliance date back to allow more time for pharmacies to make the necessary changes or further determine if these standards are necessary. See the attached NASPA USP 800 state chart.
- **Vendors may experience shortages and delays** – Because all facilities across the country need to be compliant on the same day, we are already hearing of shortages of supplies and delays in services related to USP 800 compliance.
- **Inspections standards not yet published** – There are different interpretations out there for meeting USP 800 standards. Before we can invest this much money we really need to know the Board's inspection standards as they relate to USP 800.

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Leesburg, VA 20175
(703) 779-3301

We appreciate the committee's consideration of our concerns and plan to be present at the meeting on September 18th to assist in any way we can.

Thank you,

Cheri Garvin, RPh, Jay Gill, PharmD, and Alexander Pytlarz, PharmD

State	USP 800 Adopted	Notes
Alabama	No	Proposing regulations to require compliance with all current requirements of USP.
Alaska	No	No discussions, so far. BOP plans to make changes to compounding regulations in the near future. USP 800 may be discussed at the time. No specific timeframe given as to when regulation changes will be made.
Arizona	Yes	Requires that pharmacies follow USP compendium; therefore, USP 800 is automatically adopted by reference.
Arkansas	No	Will be discussed at September BOP mtg.
California	Yes	
Colorado	No	
Connecticut	Yes	
Delaware	No	Request made by one state department to have added to agenda for August BOP meeting.
District of Columbia		
Florida	No	
Georgia	No	Under review. No timetable for action.
Hawaii	No	No plans at this time to adopt.
Idaho	No	Group of national pharmacy associations (APhA, NCPA, NACDS) asked BOP not to act until 2021. BOP indicated it has no plans to pursue addt'l rule changes related to USP 800 in the near future.
Illinois	No	BOP was asked for 5-year stay.
Indiana	No	It will be discussed in the coming months.
Iowa	Yes	
Kansas	No	BOP just recently acquired legislative authority to regulate compounding. BOP is currently in the process of promulgating rules and regulations with USP 795 & 797. Will take up USP 800 in early 2018.

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Kentucky	No	BOP is assembling a task force to review. Believes there will be some form of USP 800 coming soon.
Louisiana	No	USP 800 is on the BOP's Aug. 25 meeting agenda for discussion. The board's general operating position is that all of the USP chapters numbered below 1000 are enforceable standards, and pharmacies are expected to comply with those standards, even though they may not be included formally in regulations (USP 795, 797 were adopted).
Maine	No	Will be discussed; but no plans for rulemaking at this time.
Maryland	No	Currently proposing legislation for compliance with all USP standards.
Massachusetts	Yes	State law requires all pharmacies to adhere to USP; therefore, it's adopted by reference. BOP in process of drafting addt'l hazardous compounding regs. Pharmacies need to comply with USP 800 by July 1, 2018 deadline.
Michigan	No	
Minnesota	No (though, it's enforceable in Minnesota; see notes)	BOP has not officially adopted USP 800 in Minnesota Rules Chapter 6800; however, the BOP considers USP to be enforceable even though it has not formally adopted.
Mississippi	No	BOP is discussing.
Missouri	No	BOP is watching. No discussion planned.
Montana	No	Will eventually adopt into pharmacy rules, but waiting to see what other states are doing.
Nebraska	No	BOP is discussing.
Nevada	No	Board discussed at its July meeting and directed staff to start the rulemaking process for changes for USB 800 by scheduling a workshop with the board. First workshop will be at the board's September meeting.
New Hampshire	No	No discussions planned at this time.

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New Jersey	No	BOP is revising some regulations. There will be reference to USP 800, though it's not clear if the board will adopt it in total. More information may be available in the fall.
New Mexico	Yes	USP is the official compendium for New Mexico; therefore, USP 800 is automatically adopted by reference.
New York	No	Not planned for discussion at next board meeting. May be discussed sometime.
North Carolina	Yes	By reference.
North Dakota	No	Informal discussions have taken place. BOP exec indicated there hasn't been time to officially to discuss at BOP mtgs.
Ohio	No	BOP was asked to delay by national associations (APhA, NCPA, NACDS).
Oklahoma	No	Task force reviewing. Possibly in 2018 may propose through rulemaking.
Oregon	No	BOP is having issue in deciding whether USP 800 is OSHA, pharmacy, or both. There will be further discussion. May be several months before anything is finalized. Compounding rules are scheduled for rewriting in the fall.
Pennsylvania	No	Has not finalized regulations regarding sterile compounding.
Rhode Island	Yes	Will be referenced in upcoming regulation updates.
South Carolina	No	No immediate plans to discuss.
South Dakota	Yes	Inspectors are becoming educated to the standards and helping with IV room rebuilds, etc., in order to be compliant.
Tennessee	Yes	Any facility that compounds sterile products shall comply with applicable USP standards.
Texas	No	BOP formed a task force to make recommendations. Report is scheduled for August 1 BOP mtg.
Utah	No	Compounding task force is reviewing the standard.
Vermont	No	

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Virginia	Yes	Inspectors are getting educated on the standards and will be helping to educate pharmacists on the requirements.
Washington	Yes	By reference. Must follow USP standards. PQAC instructed staff to begin work on the intersection and coordination of USP 800 with the state's labor & industry laws on hazardous materials. Commission is considering a complete rewrite of all rules, which will be discussed Sept. 13-15 and will include how to include USP 800.
West Virginia	Yes	Board inspector said they won't be enforced until 2021.
Wisconsin	No	
Wyoming	No	National pharmacy associations (APhA, NCPA, NACDS) asked BOP to delay rulemaking.

Virginia Board of Pharmacy

COMPLIANCE WITH USP STANDARDS FOR COMPOUNDING

§54.1-3410.2 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 published as an official standard in February 2016 with a delayed implementation date of July 1, 2018. The Board expects those performing sterile and non-sterile compounding to comply with USP Chapter 800 as of July 1, 2018.

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.

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

   A subscription to the current version of "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. ~~The latest edition, USP 36- NF 31, published on November 1, 2012 becomes official May 1, 2013.~~

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, 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.

12. 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.

13. 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.

14. 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.

15. 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?

Yes, sterility tests for autoclaved CSPs are not required unless they are prepared in batches of more than 25 units. The board would expect to see that biological indicators are used with each autoclave batch and that the cycle time and temperature were recorded on a log or printer tape directly from the autoclave.

16. 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.

17. 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.

18. 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.

19. 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.

20. 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

21. 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.

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.

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.

37. May a prescriber or patient obtain a 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://secure01.virginiainteractive.org/dhp/cgi-bin/search_publicdb.cgi by searching the business name and choosing the occupation of "non-resident pharmacy".

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. 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.

41. 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

42. What drugs MUST comply with all USP Chapter <800> containment requirements?

Drugs on the NIOSH list that 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.

43. What drugs do NOT have to comply with all the USP Chapter <800> containment requirements?

Drugs on the NIOSH list that do not have to follow all the containment requirements of this chapter if an assessment of risk is performed and implemented include:

- Final dosage forms of compounded HD preparations and conventionally manufactured HD products, including antineoplastic dosage forms, that do not require any further manipulation other than counting or repackaging (unless required by the manufacturer)

44. How should a pharmacist determine how to comply with 800?

Pharmacists should ask themselves the following questions, at a minimum:

- What drugs do I receive, store, dispense that are deemed hazardous pursuant to the NIOSH list?
- 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.?

45. 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 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.

46. 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

47. 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.

48. What minimal questions and/or information will an inspector for the Board of Pharmacy be asking during an inspection? Note: Enforcement of Chapter <800> will not begin until after the July 1, 2018 effective date of the chapter.

- Does the pharmacy perform sterile or non-sterile compounding?
- Does the pharmacy stock HDs? The list of HDs the pharmacy stocks must be provided for inspector review.
- Are all HDs 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 for all situations in which the HDs are used throughout the facility.

49. 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 ACPH • Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas • Fixed walls

50. 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 ACPH • Negative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas	As described in (797)
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

51. 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.

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 ACTS OF ASSEMBLY -- 2017 SESSION

CHAPTER 114

An Act to require the Board of Pharmacy to develop guidelines for the provision of counseling and information regarding disposal of unused drugs.

[H 2046]

Approved February 21, 2017

Be it enacted by the General Assembly of Virginia:

1. *§ 1. That the Board of Pharmacy shall develop guidelines for the provision of counseling and information regarding proper disposal of unused dispensed drugs, including information about pharmacy drug disposal programs in which the pharmacy participates pursuant to § 54.1-3411.2, by pharmacists to patients for whom a prescription is dispensed.*

VaAware (http://vaaware.com/)

Addiction, prevention & recovery resources

MENU

Disposal

Drug Take-Back Programs are the safest method for disposing of prescription drugs because they are organized and closely monitored by local, state, and federal government agencies. These agencies ensure and oversee the proper disposal of the drugs in accordance with federal law. Check with your pharmacist and local law enforcement agency for more information about drug-take back days and locations. Here are two drug disposal locator tools:

AwareRx (https://nabp.pharmacy/initiatives/awarxe/drug-disposal-locator/)

DEA Diversion (http://www.deadiversion.usdoj.gov/drug_disposal/takeback/)

Certain Local Pharmacies are authorized to collect drugs for destruction, and the Board of Pharmacy maintains a list (http://www.dhp.virginia.gov/Pharmacy/destructionsites.asp) of those authorized collectors, and the DEA has a locator (https://www.deadiversion.usdoj.gov/pubdispsearch/spring/main?execution=e1s1) of public disposal locations.

Home Disposal has risks of diversion and environmental contamination, but when completed correctly is a viable option if a take back program is not available.

- **Step 1–** Remove medications from their original containers. If the medication is solid, crush it or add water to dissolve it and then mix the medication with an undesirable substance, such as kitty litter or coffee grounds. This makes the mixture unattractive to children and pets and unrecognizable to potential abusers who may go through your trash.
- **Step 2–** Place the mixture in a container with a lid or in a sealable baggie to prevent the medication from leaking, and throw it into the trash.
- **Step 3-** When discarding the original containers, scratch out or remove identifiers on the bottle and/or packaging. Remember: DO NOT dispose of medications in the toilet or sink, unless specifically instructed to on the label. DO NOT give medicine to friends or family. This is not only potentially illegal, but a drug that works for you could be dangerous for someone else.

For more information, check out the FDA's Disposal of Unused Medicines: What You Should Know (http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/SafeDisposalofMedicir

A note on **Environmental Contamination**- Many people believe that flushing or simply throwing away drugs is the best way to dispose of medications; however, if not disposed of properly, the drugs can contaminate the ground and waterways. Wastewater treatment plants are not designed to remove or process many compounds found in medications. Instead, when flushed or put in a landfill, the drugs are discharged into our surface and ground water. Pharmaceutical contaminants in water have been shown to cause serious harm to fish and wildlife living in and near rivers and lakes. Humans can also be exposed to these chemicals when they drink water drawn from contaminated bodies of water or eat wild game or fish.

Learn More

- The Virginia Board of Pharmacy offers a comprehensive list of authorized collectors (http://www.dhp.virginia.gov/Pharmacy/destructionsites.asp) of drugs for safe destruction.
- The AwareRX Pharmacy (http://www.awarerx.pharmacy/) offers a wealth of resources on the proper use, storage and disposal of prescription drugs.
- Additionally, the U.S. Food and Drug Administration details best practices (http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm101653.htm) for safe disposal of unused medications.
- Learn more about proper storage of prescription drugs on the homepage of Safeguard My Meds (http://www.safeguardmymeds.org/how-to-safeguard-your-prescription-meds/).
- The National Council on Patient Information and Education's "Tips on Safe Storage and Disposal of Your Prescription Medicines" give specific recommendations for the safe storage and disposal of prescription drugs. Click through the document below to learn more.

(http://vaaware.com/storage/disposal/)

Useful Links

- Governor's Task Force On Prescription Drug And Heroin Abuse (https://www.dhp.virginia.gov/taskforce/)
- CDC Information on Opioids (http://www.cdc.gov/drugoverdose/index.html)
- US HHS's Law Enforcement Responses to Opioids (http://www.hhs.gov/opioids/law-enforcement-resources/index.html)

Resources

- Facts (http://vaaware.com/storage/facts/)
- Storage (http://vaaware.com/storage/storage/)
- Disposal (http://vaaware.com/storage/disposal/)
- Drug Takeback Information (http://vaaware.com/storage/drug-takeback-information/)
- Where to Seek Treatment (http://drugfreeva.org/)

News Feed

- A New Direction on Drugs (http://A%20New%20Direction%20on%20Drugs)
- Public wants more government action against opioid abuse (http://Public%20wants%20more%20government%20action%20against%20opioid%20abuse)
- Many addicts going without meds that curb opioid abuse
- Authorities in Va. debate how to treat addictions (http://www.richmond.com/news/article_8fb88c61-f117-569a-9614-32681f5277da.html)
- Addicted to a Treatment for Addiction (http://www.nytimes.com/2016/05/29/opinion/sunday/addicted-to-a-treatment-for-addiction.html?_r=0)
- Long-Acting Opioid Treatment Could Be Available In A Month (http://www.npr.org/sections/health-shots/2016/05/27/479755813/long-acting-opioid-treatment-could-be-available-in-a-month)
- House Passes Bills to Combat Opioid Abuse in U.S. (http://www.wsj.com/articles/house-passes-bills-to-combat-opioid-abuse-in-u-s-1463090994)

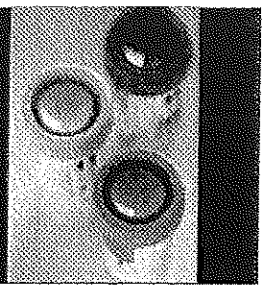
VaAware | Addiction, prevention & recovery resources

(http://vaaware.com)

Email us at info@vaaware.com (mailto:matt.treacy@dhp.virginia.gov)

Tips on Safe Storage and Disposal of Your Prescription Medicines

National Council on Patient Information and Education



Where do you keep your medicines? Are they in different places—with some in the medicine cabinet, some in the kitchen, and some in the bedroom or elsewhere? As a parent, grandparent, or family member, it's important that you organize and keep track of your medicines.

After all, you will want to know where a particular medicine is when you or someone else needs to find it. And you will want to keep your medicines secure so that a child, or a teenager, or even a stranger, does not get into them. That way, you can help prevent an accidental injury, as well as do your part to stop the possible abuse of prescription medicines.

The first step in getting organized is to take a look at all the medicines you have. You should try to do this type of inventory every six months, or at least once a year.

Start by checking the expiration date on the bottle—you don't want to take any chances with a medicine that no longer works the way it's supposed to. Also, look for medicines that are discolored, dried out, crumbling, or show other signs that they are past their prime. Check the expiration date for eye drops and eardrops, too. They may no longer be effective and, worse, could be a breeding ground for bacteria or fungus.

In addition, look for leftover prescription medicines from a previous illness or condition. You will want to discard these since you should never try to treat yourself (or anyone else) with a prescription medicine. Your symptoms might seem similar to what you had before, but the cause could be different or the medicine may not be the right one this time around.

Proper Disposal of Prescription Medicines

Federal Guidelines encourage consumers to:

- Take unused, unneeded, or expired prescription drugs out of their original containers and throw them in the trash.
- Mixing prescription drugs with an undesirable substance, such as used coffee grounds or kitty litter, and putting them in impermeable, non-descript containers, such as empty cans or sealable bags, will further ensure the drugs are not diverted.
- Flush prescription medications down the toilet only if the label or accompanying patient information specifically instructs doing so.
- Take advantage of community pharmaceutical take-back programs or community solid waste programs. Where these programs exist, they are a good way to dispose of unused pharmaceuticals.

Find a cool, dry area

Now that you've identified the medicines you want to keep, the next step is to find a safe place to keep them.

You'll want to store your medicine in an area that is convenient, but is also cool and dry – since heat and humidity can damage medicines. That's why a bathroom is not a good place to keep your medicines unless you are able to keep the room well ventilated. (However, the bathroom medicine chest is an ideal place to keep items such as bandages, tweezers, gauze, cotton balls, scissors, and other products that aren't affected by heat or humidity.)

Lock up your medicines

If there are children around, you might want to find an area where you can lock up your medicines. A cabinet or a drawer with a lock on it would work.

It's also an excellent idea to lock up any controlled substances that have been prescribed for you. These include medicines such as hydromorphone (Dilaudid®), oxycodone (OxyContin® and Percocet®), hydrocodone (Vicodin®), and alprazolam (Xanax®).*

The theft and abuse of prescription medicines is a serious problem. You play a big role in keeping these powerful medicines out of the hands of those who shouldn't have them. Since it is dangerous, as well as illegal, for anyone but you to use a controlled substance prescribed for you, a locked storage area can help keep a stranger or someone else from gaining access to them.

Be smart...and safe

Here are some other suggestions that can help you be smarter about storing and using your medicines.

- Keep your medicines separate from those of your spouse or other family members (for instance, on a different shelf or at least on a separate side of a shelf). This will make it less likely that you take the wrong ones by mistake.
- You may find it helpful to have a countertop or tabletop near where you keep your medicine so you can open the bottle with it resting on the flat surface. In case you drop your pill, it will land on the tabletop and not be lost down the drain or on the floor. (But be sure not to leave your medicine bottles out on the counter afterwards.)
- Good lighting near where you store your medicines will help you make sure you are taking the right medicine. Never take medicines in the dark.
- Keep the medicine in the bottle it came in. The amber color protects the medicine from light. You will also have the information right there about what the medicine is and how often to take it. The label will also have the phone number of the pharmacy so you can call when it is time for a refill.
- Never mix different medicines in the same bottle. You might end up taking the wrong one by mistake. It is also possible that some of one medicine could rub off on another and affect how well it works.
- Keep the lids on your pill bottles tightly closed. A cap can't be childproof if it's not fastened correctly.
- If there is cotton in the pill bottle when you first open it, remove the cotton and throw it away. The cotton can absorb moisture and affect the medicine that is inside.

*Dilaudid is a registered trademark of Abbott Laboratories. OxyContin is a registered trademark of Purdue Pharma, L.P. Percocet is a registered trademark of Endo Pharmaceuticals. Vicodin is a registered trademark of Abbott Laboratories. Xanax is a registered trademark of Pfizer Inc.

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The NCPIE Coalition-working together to promote safe medicine use

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