Consensus Statement on the Handling of Hazardous Drugs Per USP Chapter <800>

March 2017

The Hazardous Drug Consensus Group (HDCG) is a joint effort of the Accreditation Commission for Health Care / Pharmacy Compounding Accreditation Board (ACHC/PCAB) and the International Academy of Compounding Pharmacists (IACP). It consists of a number of experts from a wide range of backgrounds who have extensive experience in the handling of hazardous drugs. This group has been charged with the development off a Hazardous Drug Consensus Statement (HDCS).

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Table of Contents

Introduction

The 2016 publication of the following triad of new or revised documents concerning the handling of hazardous drugs (HDs) has placed this topic high on the agendas of healthcare providers who are in any way involved with these substances:

> USP <800> HAZARDOUS DRUGS—HANDLING IN HEALTHCARE SETTINGS (effective date July 1, 2018) (Source 1 as shown below, hereafter simply referred to as "<800>.")
>
> NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016 (Source 2 as described below.)
>
> OSHA technical document: "Controlling Occupational Exposure to Hazardous Drugs" (Source 3 as shown below.)

There is no doubt as to the potential adverse effects of such substances on the health of those exposed to them, and the reality that previous attempts to address this issue have either not met with resounding success or have not enjoyed adequate compliance. *

While it is a helpful document, <800> does not always provide adequate, unambiguous detail to entities as to how to fully comply with requirements.

Although <800>'s effective date of July 1, 2018, is a ways off, these issues have already led to unprecedented amounts of discussion and controversy. The almost inevitable outcome will be significant differences in the interpretation of many if not most components of the chapter - differences that will delay its effective and efficient implementation.

The Hazardous Drug Consensus Group (HDCG) is a joint effort of Accreditation Commission for Health Care / Pharmacy Compounding Accreditation Board (ACHC/PCAB) and the International Academy of Compounding Pharmacists (IACP). It consists of a number of experts from a wide range of backgrounds who have extensive experience in the handling of hazardous drugs. This group has been charged with the development off a Hazardous Drug Consensus Statement (HDCS) that will:

> Not simply rehash <800>, but create concise summaries of key topics concerning HDs based on all relevant sources listed below, and the knowledge and experiences of HDCG members.
>
> Provide concrete best practice recommendations (BPRs) when these sources described below do not provide adequate or concise guidance.
>
> Help the reader understand what is REQUIRED by <800> ("MUSTs") versus what is only SUGGESTED ("SHOULDs"). (Such items are always presented in caps.)
>
> Point out those aspects of <800> most likely to require the most significant changes and/or cost.
>
> Ask (and answer) some key questions that are likely on the minds of many.

Introduction, cont.

Use tables and graphics when helpful to simplify and summarize information.

In general use plain, to-the-point language whenever possible.

While July 1, 2018, may seem safely in the future, many <800> requirements, especially regarding facilities and equipment, might require significant time and resources. There are only a finite number of manufacturers of the equipment required for HD handling, or consultants to help clients prepare for <800>. One clear recommendation of the HDCG is to plan and act now, not later.

Topics have been arranged in a manner that only loosely follows that of <800> that we think will be more useful for the reader - although relevant sections of <800> are included in each section title. After a few introductory sections, we then proceed in rough chronological order as they would occur for the typical "entity."

Most sections of the HDCS will consist of the following sub-sections:

Good Reads - Recommended materials from the sources listed in the Hazardous Drug Library below. We do not imply you must read all listed materials, or that these sections reference all relevant materials listed in the Hazardous Drug Library, as in many cases there is overlap.

Discussion - Here we present concise but complete reviews of specific topics, drawing not only on <800> but other referenced sources. When appropriate, best practice recommendations (BPRs) based upon the experiences and expertise of HDCG members are also presented.

Questions and Answers - Sometimes the best way to summarize a topic is to pose and then answer a good question based upon the material. We attempt to cover all topics found in Source 4, described below, asked by actual practitioners of the USP in 2016, as well as some of our own that we think will be useful.

Attachments are provided at the end of the main body of the HDCS that have been referenced in the main text.

A copy of the recently published "USP <800> Preparation Checklist" is also included as Attachment J. This document, organized in a similar manner to the HDCS itself, can be used as a means of coming into compliance with <800>.

Tables of acronyms or definitions are not provided within the HDCS since so many of the primary and secondary sources described below contain such materials.

Not all topics and sub-topics concerning HDs or <800> are covered in this HDCS. Attention has been focused on those that, in the opinion and experience of the HDCS, are most in need of clarification or elaboration.

* - See Source 3, Section III.C and Section IV.D

Introduction, cont.

Questions and Answers

Q: When MUST I comply with <800>?

A: Although the chapter becomes "official" on July 1, 2018, some states, e.g. California and New Jersey, are already implementing "800-like" regulations. We strongly suggest, however, that you become as familiar with <800>'s requirements and what you will need to do to comply with them as soon as possible. Some requirements are not only easy; you are probably already meeting them. Others concerning facilities and equipment may require major changes that will require time and resources.

Q: Who is going to enforce <800>?

A: In theory, this is up to state boards of pharmacy. However, entities must realize that OSHA can enforce almost all aspects of <800> at this moment, since most of this chapter mirrors existing guidance such as is found in Source 3.

A Hazardous Drug Library

All entities involved with handling HDs are encouraged to obtain the following source documents on this topic, all of which are easily available via the Internet, and all but two of which are free.

Primary Sources - issued by federal regulatory bodies:

Source 1 - USP Chapter <800> Hazardous Drugs - Handling in Healthcare Settings.
Available most economically via purchase of USP's Compounding Compendium for $150 per year. This pdf document includes 74 other USP chapters of potential use to any compounding pharmacy, including <795> and <797>.
http://www.usp.org/store/products/usp-compounding-compendium

Source 2 - NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016.
This provides the "working list" of hazardous drugs by group that <800> is concerned with.
www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf

Source 3 - Controlling Occupational Exposure to Hazardous Drugs.
This free, excellent, well-organized, recently revised document is available at:
https://www.osha.gov/SLTC/hazardousdrugs/controlling_occex_hazardousdrugs.html

Source 4 - Frequently Asked Questions: <800> Hazardous Drugs—Handling in Healthcare Settings.
Some useful guidance for some commonly asked questions regarding HDs and <800> that were posed to the <800> Committee. Most of these questions will be addressed in appropriate sections of the HDCS.
http://www.usp.org/frequently-asked-questions/hazardous-drugs-handling-healthcare-settings

Secondary Sources - based upon review and analysis of primary sources:

Source 5 - Safe Handling of Hazardous Drugs: Reviewing Standards for Worker Protection, Pharmacy Practice News, October 23, 2016.
http://www.pharmacypracticenews.com/Review-Articles/Article/10-16/Safe-Handling-of-Hazardous-Drugs-Reviewing-Standards-for-Worker-Protection/38331/ses=ogst?enl=true

Source 6 - USP <800> Preparation Checklist.
This free document, allowing an entity to systematically assess its compliance with <800>, is available in the Compliance section of the Compounding Today website at:
http://compoundingtoday.com/Compliance/. From the landing page, under “Other Information Sources” click on “IJPC's USP <795>, <797> and <800> Gap Analysis Surveys.” Enter your email and information to receive a link to the Preparation Checklist.

Source 7 - 2016 Updated American Society of Clinical Oncology/Oncology Nursing Society Chemotherapy Administration Safety Standards, Including Standards for Pediatric Oncology. https://onf.ons.org/onf/44/1/2016-updated-american-society-clinical-oncologyoncology-nursing-society-chemotherapy

Source 8 - ASHP (American Society of Health-System Pharmacists) [2006]. Guidelines on Handling Hazardous Drugs. Am J of Health Syst Pharm 63:1172-1193.
https://www.ashp.org/doclibrary/bestpractices/prepgdlhazdrugs.aspx

A Hazardous Drug Library, cont.

Entity-Specific References

Entities MUST also have several documents / sets of documents readily accessible to workers:

List of Hazardous Drugs - see "Developing and Maintaining a List of Hazardous Drugs - <800> Section 2" below

Safety Data Sheets (SDSs) for at least all HDs on the List of Hazardous Drugs. These may be kept in electronic or hardcopy format as long as they are easy to access.

Standard Operating Procedures (SOPs) - see "Standard Operating Procedures - <800> Section 17" below.

Questions and Answers

Q: Do I need to get all the references?

A: You MUST at least obtain Sources 1 and 2. We strongly suggest that you obtain Sources 3 and 8, as they continue to include a lot of excellent information. "Entity-Specific References" will or have been developed by your entity.

Q: Do I have to read them all?

A: No. Our suggestion is to read this HDCS and refer to these other sources as needed. You will be creating and/or editing your "Entity-Specific References."

History, Background and Scope

Good Reads

The HDCS will not review the history of concerns over the effects of hazardous drugs on health care workers and previous actions taken to deal with them, as these topics are well covered elsewhere - see especially:

Source 3 - Sections II and III
Source 8 - Background

Discussion

Suffice it to say that:

These concerns are longstanding.
They are legitimate, being supported by sound science or sound extrapolation, representing reasonable actions that minimize HD exposure.
The effectiveness of such measures should be monitored, and acted upon as needed.

<800> states that it will apply to "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)."

The intent is for <800> to replace the very limited guidance concerning HDs found in USP <795> concerning nonsterile drugs and the more extensive guidance provided in <797> that nonetheless only applies to sterile products.

It is planned that the next version of USP <797> will only mention HDs in passing, referring to <800>.

<800> containment requirements apply to at least:

Any active pharmaceutical ingredient (API) appearing on the NIOSH List; that is, a substance that will be used to compound a final pharmaceutical product

Any antineoplastic (Group 1) drug requiring "manipulation" - such actions as dilution, reconstitution, mixing, transfer, and parenteral administration.

Note: HDs, including antineoplastics, NOT requiring manipulations other than counting or packaging, might not be required to comply with many aspects of <800>, although they still MUST be part of a risk assessment (as described below). Exceptions include when automated devices perform these actions, due to the potential for crushing should the machines malfunction. The entity's risk assessment will decide what if any additional precautions are needed in such a case.

History, Background and Scope, cont.

Questions and Answers

Q: What about dangerous substances NOT on the NIOSH List?

A: While <800> is only concerned with items on the NIOSH List or likely to be included in a future edition of this list (e.g. a new, closely related compound), a BPR is to evaluate other such dangerous substances and, at your discretion, add them to your own Hazardous Drug List, described below. A good example is fentanyl. It is not on the NIOSH List - but compounders certainly must be carefully protected from dermal or respiratory exposure to this potent drug. See the tragic result of unprotected exposure to this drug at: http://nypost.com/2014/06/16/family-sues-after-st-johns-pharmacy-student-dies-during-externship/

Program Management - <800> Section 4

Good Reads

Section 4 of Source 1

Discussion

<800> stipulates that each entity handling HDs MUST identify a "designated person" (DP) who, to paraphrase Section 4, is responsible for at least the following:

Creating and implementing procedures (typically in the form of SOPs) concerning HDs.

Performing a documented annual review of these SOPs (as per Section 17 of <800>).

Monitoring compliance with these SOPs and relevant rules and regulations.

Ensuring worker competency (which reasonably also entails coordinating worker training).

Ensuring "environmental control" of areas where HDs are found and handled, e.g. through environmental wipe sampling.

Overseeing facility monitoring, managing related documents, and acting on results, including incident reports concerning HDs (as may be inferred from Section 10 of <800>.

Section 4 appropriately points out that the DP MUST have a full understanding of the risks posed by HDs and their improper handling, and be capable of reporting breaches to management. This list of responsibilities is so significant that the DP must be given sufficient authority, time and resources to carry them out.

Questions and Answers

Q: How can the DP obtain the required training?

A: Several organizations are in the process of creating such training programs. Check the *Compounding Today* website for updates on this topic.

Q: Could a technician be the DP?

A: Certainly. However, as stated above, the DP must have the firm backing of management to be able to implement and enforce the provisions of <800>.

Risk Assessment and Exposure Control - <800> Sections 2, 3

Good Reads

Source 1 - Sections 2, 3
Source 3 - Sections III and IV

Discussion

<800> or other sources in our HD Library do not provide significant guidance on this very important topic of how to assess the risks to workers posed by how HDs are currently handled by an entity.

Yet such a risk assessment is one of the most important aspects of this entire topic in that most other actions taken by an entity regarding HDs should depend on the results of such an assessment.

As the readings listed above detail, attempts to reduce health care worker exposure to HDs beginning in 1986 have met with only limited success. Source 5 - Continuing Exposure describes recent studies that continue to show worker exposure to HDs.

Work areas, equipment, personal protective equipment (PPE) and workers themselves have been shown to contain measurable quantities of HDs. HDs can be found in the urine of workers - even those not intimately involved in their handling (Source 3 IV - Work Areas).

Part of this problem is due to limited compliance with existing handling recommendations; see Source 3 IV D.

Most studies of continued worker and workplace HD contamination have involved antineoplastics (NIOSH Group 1); little if any insight is available concerning other HD types, especially Group 3 drugs involving reproductive toxicity.

Based upon the anecdotal experiences of a number of members of the HDCG, it is highly likely that many nonsterile compounders handling Group 3 drugs are at best in partial compliance with existing guidance on this topic, much less what is present in <800>.

Consider the consequences of the following three statements - two direct quotes from Source 3 - III, and one fairly predictable based on the progress of science:

> "It is difficult to set safe levels of exposure to HDs on the basis of current scientific information…"
>
> "Therefore, it is essential to minimize exposure to all HDs."
>
> The sensitivity and scope of analytical methods used to detect HDs will surely continue to increase in coming years, pushing the "detectable" levels of these substances ever lower.

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

The term "as low as reasonably achievable" (ALARA), a concept mentioned briefly in Source 3, has a history of use regarding exposure to toxic chemicals and radiation, and should be kept in mind when evaluating HD exposure.

A BPR would be to reflect on the experiences of other industries forced to deal with various other occupational hazards, and adopt an approach in which HD risks are at least crudely quantified, and addressed in order of potential severity.

Below is a reasonable, serviceable outline of the steps involved in a risk assessment based upon precedent from other industries:

1. Create a list of hazardous drugs and substances

This is "the easy part," as it is simply the document resulting from "Developing and Maintaining a List of Hazardous Drugs - <800> Section 2" below.

Remember, however, to include other substances such as disinfectant / cleaning agents and strong acids and bases that pose an immediate or long-term health risk to workers.

Include the form of the drug, e.g. capsule, active pharmaceutical ingredient (API), sterile vials for reconstitution, bulk liquid, as risks may vary accordingly.

It might be perfectly acceptable to group similar agents if they are likely to pose similar risks. For instance, since all NIOSH Group 3 "reproductive risk" drugs used only for topical or oral preparations are likely to pose similar risks, an entity could be justified in simply considering them collectively.

2. Create a list of tasks involving potential exposure to these substances. For many entities this will include the following (many of which are discussed in detail in other sections of this document):

    a) Receipt and Storage
    b) Compounding
    c) Labeling and Packaging
    d) Transport / Dispensing
    e) Administering
    f) Patient Care Activities (handling body fluids)
    g) Disposal
    h) Deactivating and Cleaning
    i) Spill Handling

Table 1, “Examples of Potential Opportunities of Exposure Based on Activity in <800>,” offers some additional detail on some of these tasks.

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

3. Identify the routes of worker exposure for each of these tasks. The most obvious include:
   a) Injection
   b) Eye exposure
   c) Ingestion
   d) Inhalation
   e) Dermal exposure

4. Using a Severity Classification System matrix as shown below, complete an Assessment Matrix, also shown below, based upon the following factors:

   Impact: Would exposure have a high, medium or low effect on worker health?

   Probability: Based on existing conditions, is this exposure highly likely, moderately likely, or unlikely?

Severity Classification Matrix

Impact	Low	Medium	High
High	4	5	6	7	8
	3	4	5	6	7
Medium	2	3	4	5	6
	1	2	3	4	5
Low	0	1	2	3	4

Probability

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

Note: Attachments A, B and C accompanying the HDCS are Excel spreadsheets that may be used by the reader.

Assessment Matrix

Task	Exposure Route: Injection	Eye exposure	Ingestion	Inhalation	Dermal exposure	Total
Receipt & Storage	1	2	3	4	5	
Compounding	6	7	8	9	10	
Labeling and Packaging	11	12	13	14	15	
Transport / Dispensing	16	17	18	19	20	
Administering	21	22	23	24	25	
Deactivating and Cleaning	26	27	28	29	30	
Disposal	31	32	33	34	35	
Spill Handling	36	37	38	39	40	
Other:	41	42	43	44	45	

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

5. A Mitigations table is then created, as shown below, starting with those items with the highest Severity Scores and moving down. It is convenient to create a Cumulative % Total Severity column that displays the sum of the severity scores at a given point as a percentage of all severity scores. It may be unrealistic to address all Task / Exposure Routes with a score. The entity may elect to, for instance, immediately address those that add up to represent 50% of the total Severity Score.

Mitigations are classified as:

a) Engineering Controls
b) Handling
c) PPE
d) Deactivation / Cleaning
e) Other

A check can be placed in each Mitigation type upon which the entity decides to act.

Task / Exposure Route #	Severity Score	Cumulative % Total Severity	Mitigations				
			Engineering Controls	Handling	PPE	Deactivation / Cleaning	Other
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

6. The final step is to condense these mitigations into a set of action items as shown below.

#	Action Item Details	Assigned To	Target Date
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

This action plan will almost certainly require changes in SOPs, training, and auditing to ensure completion and compliance.

The HDCG strongly recommends that at least one actual, well-informed HD compounder be included in the risk assessment process.

The HDCG also strongly recommends that entities seek consultative assistance should there be any uncertainty as to how to conduct and enact a risk assessment.

This risk assessment MUST be fully documented, and repeated at least annually. "Targeted" risk assessments should also be performed whenever significant changes in HDs handling, equipment, or procedures are introduced.

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

CASE STUDY: XYZ Pharmacy

XYZ Pharmacy is involved in sterile and nonsterile compounding, mostly of NIOSH Group 3 drugs. At the time of this risk assessment:

Many workers were allowed to receive shipments possibly containing HDs, and they did not wear any PPE.

Nonsterile compounding was always done within a C-PEC, but it was often not turned on. Appropriate PPE was also not always worn.

The pharmacy employed a driver who often delivered HDs; however, his vehicle did not contain a spill kit.

The pharmacy is not involved in administering any HDs.

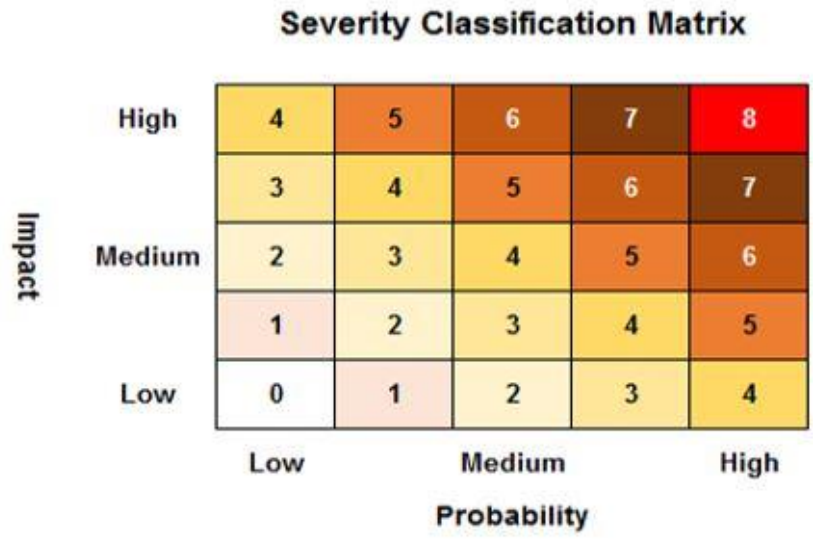
The C-PECs used for sterile and nonsterile compounding were treated only with isopropyl alcohol for routine and periodic "intense" cleaning. Workers who performed such cleaning only wore gloves. Reusable equipment such as mortars and pestles and spatulas were cleaned in a common sink with other equipment by workers not wearing gloves.

Disposable items used in compounding such as weigh boats were removed from the C-PEC and disposed of with "regular" trash.

Spills involving HDs used in nonsterile compounding occurred about once a week, but were usually simply "cleaned up" by workers without use of a spill kit and corresponding procedures.

XYZ Pharmacy conducted a risk assessment as follows:

a) The possibility of all forms of worker exposure was assessed for each step of the handling of HDs.



Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

b) This information was entered into an Assessment Matrix as shown:

Assessment Matrix

		Exposure Route					
		Injection	Eye exposure	Ingestion	Inhalation	Dermal exposure	Total
Task	Receipt & Storage	1 0	2 4	3 2	4 3	5 2	11
	Compounding	6 2	7 4	8 3	9 5	10 4	18
	Labeling and Packaging	11 1	12 1	13 1	14 2	15 2	7
	Transport / Dispensing	16 0	17 4	18 3	19 3	20 2	12
	Administering	21 0	22 0	23 0	24 0	25 0	0
	Deactivating and Cleaning	26 0	27 5	28 3	29 5	30 4	17
	Disposal	31 1	32 1	33 2	34 3	35 4	11
	Spill Handling	36 2	37 5	38 2	39 4	40 3	16
	Other:	41	42	43	44	45	

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

c) These exposures were entered into a Mitigations Table in order of the Severity Score assigned in the Assessment Matrix.

Mitigatitons Table

Task / Exposure Route #		Severity Score	Cumulative % Total Severity	Mitigations				
#	Description			Engineering Controls	Handling	PPE	Deactivation / Cleaning	Other
37	**Spill Handling - Eye exposure**	**5**	**5%**		**X**	**X**		
29	**Deactivating and Cleaning - Inhalation**	**5**	**11%**		**X**	**X**	**X**	
27	**Deactivating and Cleaning - Eye exposure**	**5**	**16%**		**X**	**X**	**X**	
9	**Compounding - Inhalation**	**5**	**22%**	**X**				
39	**Spill Handling - Inhalation**	**4**	**26%**		**X**			**X**
35	**Disposal - Dermal exposure**	**4**	**30%**		**X**			
30	**Deactivating and Cleaning - Dermal exposure**	**4**	**35%**		**X**	**X**	**X**	
17	**Transport / Dispensing - Eye exposure**	**4**	**39%**		**X**	**X**	**X**	
10	**Compounding - Dermal exposure**	**4**	**43%**	**X**				
7	**Compounding - Eye exposure**	**4**	**48%**	**X**				
2	Receipt & Storage - Eye exposure	4	52%					
40	Spill Handling - Dermal exposure	3	55%					
34	Disposal - Inhalation	3	59%					
28	Deactivating and Cleaning - Ingestion	3	62%					
19	Transport / Dispensing - Inhalation	3	65%					
18	Transport / Dispensing - Ingestion	3	68%					
8	Compounding - Ingestion	3	72%					
4	Receipt & Storage - Inhalation	3	75%					
38	Spill Handling - Ingestion	2	77%					
36	Spill Handling - Injection	2	79%					
33	Disposal - Ingestion	2	81%					
20	Transport / Dispensing - Dermal exposure	2	84%					
15	Labeling and Packaging - Dermal exposure	2	86%					
14	Labeling and Packaging - Inhalation	2	88%					
6	Compounding - Injection	2	90%					
5	Receipt & Storage - Dermal exposure	2	92%					
3	Receipt & Storage - Ingestion	2	95%					
32	Disposal - Eye exposure	1	96%					
31	Disposal - Injection	1	97%					
13	Labeling and Packaging - Ingestion	1	98%					
12	Labeling and Packaging - Eye exposure	1	99%					
11	Labeling and Packaging - Injection	1	100%					
45	Other: - Dermal exposure	0	100%					
44	Other: - Inhalation	0	100%					
43	Other: - Ingestion	0	100%					
42	Other: - Eye exposure	0	100%					
41	Other: - Injection	0	100%					
26	Deactivating and Cleaning - Injection	0	100%					
25	Administering - Dermal exposure	0	100%					
24	Administering - Inhalation	0	100%					
23	Administering - Ingestion	0	100%					
22	Administering - Eye exposure	0	100%					
21	Administering - Injection	0	100%					
16	Transport / Dispensing - Injection	0	100%					
1	Receipt & Storage - Injection	0	100%					

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

d) The pharmacy decided to immediately address the 10 items accounting for 50% of the total Severity Score.

Mitigatitons Table

Task / Exposure Route #		Severity Score	Cumulative % Total Severity	Mitigations				
#	Description			Engineering Controls	Handling	PPE	Deactivation / Cleaning	Other
37	Spill Handling - Eye exposure	5	5%		X	X		
29	Deactivating and Cleaning - Inhalation	5	11%		X	X	X	
27	Deactivating and Cleaning - Eye exposure	5	16%		X	X	X	
9	Compounding - Inhalation	5	22%	X				
39	Spill Handling - Inhalation	4	26%		X			X
35	Disposal - Dermal exposure	4	30%		X			
30	Deactivating and Cleaning - Dermal expos	4	35%		X	X	X	
17	Transport / Dispensing - Eye exposure	4	39%		X	X	X	
10	Compounding - Dermal exposure	4	43%	X				
7	Compounding - Eye exposure	4	48%	X				

e) An Action Plan including a description of the action, who was responsible for it, and a target date that would address these high-priority mitigations.

Action Plan

#	Action Item Details	Assigned To	Target Date
1	Inservice all employees on spill handling, including use of kits and PPE.	Mary	6/1/2017
2	Convert to peroxide followed by detergent for cleaning BSCs used in nonsterile and sterile compounding. Require full appropriate PPE for all deactivating and cleaning.	Fred	6/1/2017
3	Require full appropriate PPE for all deactivating and cleaning.	Fred	6/1/2017
4	Ensure that nonsterile BSC is turned on 24/7.	Mary	6/1/2017
5	Inservice all nonsterile compounders on proper PPE while compounding.	Mary	6/1/2017
6	Observationally monitor compliance with nonsterile compounding PPE.	Mary	6/1/2017
7	Inservice all compounders on requirement to place disposable items in sealable plastic bag before removing from BSC for disposal.	Mary	6/1/2017
8	Ensure that spill kits are available in delivery vehicles, and that drivers have been inserviced on their use.	Fred	6/1/2017

Risk Assessment and Exposure Control - <800> Sections 2, 3 cont.

Questions and Answers

Q: Would a risk assessment apply to patient treatment areas?

A: Certainly - if your entity is involved in this. An example might be an ambulatory infusion center (AIC) embedded in a home infusion pharmacy that administers chemotherapy.

Q: Could my risk assessment conclude that I do not need to follow any <800> requirements?

A: That is, in the opinion of the HDCG, "a stretch." The drugs appearing on the NIOSH List are there for a reason. While it is possible that an entity may find that some exposure risks are minimal, the risk assessment upon which such conclusions are based must be founded upon a conservative evaluation of its working environment.

Developing and Maintaining a List of Hazardous Drugs - <800> Section 2

Good Reads

The history and development of the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016 (Source 2), emerging from concerns over chemotherapy drugs in the 1980s, is well covered in:

Source 2 - Section II
Source 3 - Sections II and III

Discussion

Drugs have ended up on the NIOSH List based on possessing or being suspected of possessing, per animal or human data, one of more of the following traits:

a. Genotoxicity (mutagenicity) - ability to cause permanent changes to cellular genetic information, leading to mutations
b. Carcinogenicity - ability to cause cancer in living tissue
c. Teratogenicity / Developmental toxicity - ability to disturb the normal development of an embryo or fetus
d. Reproductive toxicity - ability to impair sexual function and fertility
e. Other "serious" low-dose organ toxicity
f. Structural or toxicity profiles of new drugs similar to those of substances already on the NIOSH List

Source 2 states that "drugs with safe-handling guidelines from the manufacturer are automatically put on the list because the manufacturer has determined their properties warrant special handling."

NIOSH has published this list every two years, beginning in 2010, and pledges to continue to do so. The NIOSH List places all hazardous drugs into one of three groups:

Group 1 - Antineoplastics

Group 2 - Non-Antineoplastics meeting one or more of the criteria described above.

Group 3 - Drugs "primarily" of reproductive risk to men and women trying to conceive, or women who are pregnant or breast-feeding

Note: There is some overlap, e.g. a drug in Group 1 may also pose reproductive risks such as those found in Group 3.

Developing and Maintaining a List of Hazardous Drugs - <800> Section 2 cont.

Note: Some drugs might not pose significant risk to some workers. For instance, a Group 3 drug might be unlikely to be of significant risk to a worker incapable of reproduction.

Any entity handling hazardous drugs MUST maintain a list of all such drugs that it stocks and works with.

<800> requires that this list MUST be reviewed and updated as needed at least annually. A BPR, however, is to scrutinize any new drug brought into the entity based on the following considerations:

It is already on the most current NIOSH List.

The Safety Data Sheet (SDS) for the drug contains "information of concern" in the following sections:

2. Hazard(s) identification
7. Handling and storage
8. Exposure controls / personal protection
14. Transport information

It is a new drug that is structurally similar to other drugs on the NIOSH List.

It is an investigational drug - since its toxicological profile is still relatively unknown, it should be considered hazardous unless ample evidence points otherwise.

The Warnings section of its drug package insert (DPI) contains language as to "Carcinogenesis, Mutagenesis, and Impairment of Fertility."

Questions and Answers

Q: So there is no "cut-and-dried" procedure for deciding if a drug NOT on the NIOSH List should be included in an entity's Hazardous Drug List?

A: No; the entity may use its discretion - but when in doubt, err on the side of caution, and add it to your list. See the tragic example described above concerning fentanyl.

Standard Operating Procedures - <800> Section 17

Good Reads

Review Attachment D.

Discussion

<800> Section 17 explicitly mentions a number of HD topics that MUST be covered by standard operating procedures (SOPs). Also occurring in other sections are six additional SOP topics. Attachment D organizes all of these topics into a reasonable order, dividing topics into two sections: those concerning Processes, and those of an Administrative and General nature. The Process topics are arranged in an approximate chronological order.

Questions and Answers

Q: MUST an entity create a separate set of SOPs concerning these topics?

A: No; existing documents can be edited to cover this material. However, a BPR is to create a "crosswalk" based on Attachment D. This document will help the DP ensure compliance with <800> as well as simplify worker training.

Training and Competency - <800> Sections 8, 9

Good Reads

Source 1 - Sections 8 and 9
Source 3 - Sections VII and VIII

Discussion

Training

Not surprisingly, the training of workers is a critical aspect of any entity's HD program.

Many members of the HDCS agree that many workers exposed to HDs, even if compliant with reasonable precautions, do not fully understand the risks associated with HDs and the rationale for many containment measures. Since understanding the "why" as well as the "how" is a key element in adult learning techniques, it is obvious that training concerning HD handling needs to include enough "theory" for workers to understand why containment measures are needed, and how they work. Such workers often detect new problems regarding HD handling as well as solutions to the challenge.

<800> requires the training of any workers who will come in contact with HDs prior to their exposure to these substances.

While not explicitly required, annual retraining, even if only on certain critical topics, is a definite BPR.

Training can and should be geared to the nature of potential exposure. For instance, those only involved in HD receipt or stocking need not be trained on the intricacies of HD compounding.

Be sure to include all workers, including contracted services, who may be exposed to HDs, e.g. janitorial staff or a courier service. Alternatively, such providers might be able to produce evidence of training by their organizations that will satisfy the entity's requirements.

Also remember to include all part time or per diem workers, students and volunteers.

Training MUST be documented. Minimally this should include a worker-signed and dated in-service record; a BPR is to include an outline of all topics covered by the training.

While not required, a written post-test is an excellent BPR, providing a verification of worker comprehension of presented information.

Below is a list of required or suggested training topics:

1. Entity's List of HDs
2. Reference materials and their use (HD List, SDSs, SOPs)
3. Risks associated with handling HDs
4. Relevant SOPs (Standard Operating Procedures)
5. PPE (Personal Protection Equipment)

Training and Competency - <800> Sections 8, 9 cont.

6. Use of engineering controls and other equipment
7. Exposure and spill management
8. HD waste disposal
9. Deactivation, Cleaning and Disinfection
10. Compounding techniques unique to HDs, e.g. negative pressure technique, or use of CSTDs for sterile compounding

<800> Section 8 requires that "Personnel of reproductive capability MUST confirm in writing that they understand the risks of handling HDs."

While details are not provided, a BPR is to ensure that such statements are explicit enough; entities should not "beat around the bush" or use only brief, vague statements. Attachment K is a sample of such a statement that may be of help to entities.

Another BPR precaution is to require all workers to sign such an acknowledgement statement.

Based upon Source 3 - Section VI.F., a definite BPR is to reassign pregnant or lactating females to work without exposure to HDs if at all possible.

Competency

Documented competency testing is required at least annually by <800>.

Ensure that this testing covers all functions that a given worker might perform, regardless of frequency. For instance, the ability to properly receive or stock HDs might apply even to workers typically involved only in compounding.

It is important to remember that competency assessment is not the same as "reinforcement training"; the worker MUST actually be observed performing the task by an evaluator capable of detecting incorrect procedures.

A BPR is to document competency assessment using a fairly detailed tool breaking down a given task, e.g. spill management, into a number of discrete elements.

Comments by the evaluator should be included as needed; the evaluator and worker should sign and date the document, which should be entered into the worker's human resource files.

A BPR is to consider improper techniques observed during competency assessment as due to overall improper training, not worker "error." This means that such issues, especially if seen with more than one worker, result in reinforcement training for all relevant workers.

Documented training and competency testing is also required by <800> for any "new HD or new equipment and prior to a new or significant change in process or SOP."

Process Validation

Although not required, some form of process validation, perhaps linked to competency evaluations, is a definite BPR.

Training and Competency - <800> Sections 8, 9 cont.

This would involve the use of some non-hazardous "marker" substance that is manipulated in place of the HD during compounding, spill control, etc. After the manipulation the extent of any contamination by the marker substance is evaluated.

Fluorescent chemicals (of which there are many) can be used for this purpose; an ultraviolet light is then used in a darkened room to detect undesired marker "contamination."

There is at least one commercially available product available for such validation, ChemoTest®, although it is geared to low- or medium-risk sterile compounding.

An equivalent process for nonsterile compounding can be easily developed using some inexpensive and highly fluorescent chemical such as cyanocobalamin (B12). This chemical is substituted for an ingredient in a HD-containing preparation. Care should be taken, however, to ensure that the work area is thoroughly cleaned and inspected using the ultraviolet light prior to validation testing to ensure that no other fluorescent residues are present.

Hazard Communication Program

<800> Section 8 briefly describes the need for a Hazard Communication Program (HCP) so as to meet OSHA requirements in this regard.

Becoming fully compliant with <800> and working through the "<800> Preparation Checklist" will likely fulfill these requirements.

However, a BDP is for the entity to nonetheless create a written HCP using, for instance, the excellent template to be found at https://www.osha.gov/dsg/hazcom/docs/State_of_Wisconsin_revised_Hazcom_Plan_2012.pdf.

Questions and Answers

Q: Where can such training be obtained?

A: In theory the entity's DP can create and deliver such training. However, several organizations are in the process of creating such training programs. Check the *Compounding Today* website, http://compoundingtoday.com/index.cfm, for updates on this topic.

Facilities and Equipment - <800> Section 5.3, 5.4

Good Reads

Source 1 - Sections 5.3 and 5.4

Discussion

Understanding the details of how to comply with <800> primary and secondary engineering controls can be challenging under the best of circumstances for the excellent reason that there are many variables and requirements to consider.

Attachment E is provided to organize all information as conveniently as possible, and should be referenced during this discussion.

C-PECs

Containment primary engineering controls (C-PECs) are devices that use negative air pressure at the face opening to avoid exposing workers and the environment to HDs while compounding.

Examples include Biological Safety Cabinets (BSCs), Containment Ventilated Enclosures (CVEs) and Compounding Aseptic Containment Isolators (CACIs).

CVEs and CACIs are devices in which compounders use built-in gloves to access HDs that are appealing alternatives for use in low-volume nonsterile and sterile compounding, respectively.

C-PECs MUST, in the case of sterile compounding, be externally vented; this is preferred but not REQUIRED for nonsterile compounding.

If a C-PEC used in nonsterile compounding is NOT vented, exhaust air MUST go through "redundant" HEPA filtration so as to remove as much particulate matter as possible. Manufacturers should be expected to provide documentation as to whether their equipment in fact meets <800> requirements in this regard.

A Class I BSC is recommended for compounding nonsterile HDs. Such units provide negative pressure to protect the user from contamination, but do not purport to protect the preparation from microbial contamination.

A Class II Type A2 BSC is appropriate for almost all instances of sterile HD compounding. Type B2 BSCs are advisable if volatile HDs are frequently compounded. Both provide at least ISO Class 5 air.

"Unusual" situations will be discussed below.

C-PECS MUST be certified by an appropriate vendor at least annually for nonsterile compounding, and every six months for sterile compounding.

Facilities and Equipment - <800> Section 5.3, 5.4 cont.

C-SECs

Containment secondary engineering controls (C-SECs) are separate rooms within which C-PECs MUST be located.

C-SECs MUST:

1. Be fixed wall
2. Feature smooth, impervious surfaces, walls, ceilings, floors, countertops and shelving that is free of cracks and crevices to avoid accumulations of residues, and facilitate their easy cleaning should this occur
3. Be at a negative pressure with regard to the area from which it is entered of 0.01 - 0.03 inches of water
4. Feature 12 or more air changes per hour (ACPHs) for nonsterile compounding, and 30 or more for sterile compounding
5. Be externally vented to the outside environment

C-SECs used for sterile compounding are of two kinds:

1. Ante and buffer room arrangements with strict air quality standards as defined in USP <797>. Since the buffer room MUST be at a negative pressure to the ante room, the ante room MUST contain at least ISO Class 7 air. The ante room MUST be at a 0.02 or greater inches of water positive pressure to the area from which it is entered.
2. Containment-segregated compounding areas (C-SCAs) without defined air quality standards. C-SCAs are in effect nonsterile C-SECs used to house C-PECs with the expectation of shorter beyond-use dates as defined in USP <797> due to the lower air quality in the room. They MUST therefore feature a negative pressure with regard to adjacent areas of 0.01 - 0.03 inches of water and 12 or more ACPH, and should similarly be made of smooth, easily cleaned surfaces. In effect, C-SCAs are the same as C-SECs used for nonsterile compounding.

C-SECS MUST be certified by an appropriate vendor at least annually for nonsterile compounding, and every six months for sterile compounding.

Concerning sinks placed in C-SECs:

A sink MUST be available for handwashing and other cleaning activities

For nonsterile facilities and C-SCAs, the sink MUST be at least 1 meter from the C-PEC.

For sterile facilities, the sink MUST be located in the ante room at least 1 meter from the entrance to the buffer room.

For C-SCAs, the sink may be placed at least 1 meter away from the C-PEC within the C-SCA, or immediately outside of the entrance to the C-SCA.

Facilities and Equipment - <800> Section 5.3, 5.4 cont.

> While not stipulated, a BPR is to separate the nearest edges of a sink from the nearest edge of the C-PEC and entrance, as applicable, by 1 meter

The pressure between the C-SEC buffer room and ante room MUST, as per <797>, be measured and recorded at least daily. While a similar requirement for the measurement of pressure between a C-SEC used in nonsterile HD compounding and adjacent areas is not actually stipulated in <800>, it is certainly a BPR.

An eyewash station (and/or other "emergency precautions" as required by local regulations) MUST be "readily available;" logical locations include near sinks and in "close proximity" to sterile and nonsterile BSCs. Eyewash units that attach to faucets are a convenient option to consider.

Refrigerators should only be placed in C-SECs when needed to house HDs requiring refrigeration - for all practical purposes, antineoplastic HDs used in sterile compounding. See "Receipt and Storage - <800> Sections 5.1, 5.2, 10" below for more information on this topic. If possible, they should be placed near the external exhaust vent.

By inference, doors into C-SECs should also be "rigid," e.g. not hanging plastic strips or similar arrangements.

The amount of equipment, shelving and supplies in the C-SEC should be kept at a minimum so as to reduce the surface area that might collect HD residues. When feasible, removable, cleanable covers should be placed over equipment - e.g. keyboard covers.

Closed cabinets and drawers should not be used in C-SECs, as the goal is to circulate and exhaust potentially contaminated air, not allow it to stagnate in closed areas.

Pass-through windows are an appealing option in both sterile and nonsterile C-SECs in that the movement of ingredients and finished products might be accomplished without the need for workers to enter and exit C-SECs.

> While such a "window" is possible connecting a C-SEC buffer room to adjacent areas, a double-doored "box" with sealed doors that cannot both be opened at the same time is at least a BPR so as to prevent unclassified air from being drawn into the C-SEC when the window is opened. An even better option is to pump at least ISO Class 7 air into this chamber so that when either door it opened, Class 7 air is pushed into the respective rooms. is needed in which at least ISO Class 7 was pushed out of this device into both the C-SEC buffer room and adjacent area. While possible, this is a challenging design feature.
>
> A window connecting a C-SEC used for nonsterile and adjacent areas must include a sealed door, but need not be a “box” as described above for sterile.

A BPR is for the floors and walls of all C-SECs to be of uniform color, and completely without texture. Variegated surfaces can conceal stains and spills; even slight texture increases the difficulty of deactivation, cleaning and disinfection. Another BPR is for flooring to be “coved” up the walls of the C-SEC to simplify cleaning.

Facilities and Equipment - <800> Section 5.3, 5.4 cont.

Layouts

Attachment F shows several common C-SEC and C-PEC configurations:

1. Simple Nonsterile C-SEC and C-PEC Arrangement
2. Simple Sterile C-SEC and C-PEC Arrangement
3. High Risk Sterile C-SEC and C-PEC Arrangement

This scenario provides for a suitable way to conduct pre-sterilization procedures such as weighing and combining ingredients within, as per USP <797> requirements, an ISO Class 8 or better air. Use of a Type I or II BSC within the buffer room will fulfill this requirement if actual sterile compounding is not occurring at the same time.

4. Preferred Hazardous and Non-Hazardous Sterile C-SEC and C-PEC Arrangement
5. Non-Preferred Hazardous and Non-Hazardous Sterile C-SEC and C-PEC Arrangement

This arrangement, appearing in Appendix 2 of <800>, is not ideal in that (a) care must be taken not to contaminate the non-HD buffer room while moving HD ingredients and finished products through it (b) in general, it is not desirable to use one buffer room as a means of accessing another.

Additionally: (a) a line of demarcation must be drawn near the entrance into the negative pressure C-SEC for the donning of PPE (b) HD ingredients, products, and wastes must be carefully transported in and out of the negative pressure C-SEC and through the non-HD buffer room so as to minimize contamination.

This arrangement is presumably presented since it might be the only realistic option for some sterile compounders due to space limitations, allowing a sterile C-SEC to be created within what was once a non-HD buffer room.

6. Sterile C-PEC within a C-SCA
7. Sterile and Nonsterile C-PECs within a C-SCA

As noted earlier, products prepared in both (6) and (7) will have restricted beyond-use dates due to the unclassified air within the room.

8. "Oncology Clinic" Layout - this scenario appears in <800> Appendix 2
9. Sterile and Nonsterile Hazardous Drug Arrangement

Now for a few caveats:

> A C-PEC used for sterile HD compounding may be used for "occasional" nonsterile HD compounding, but since it must undergo thorough cleaning and disinfection afterward, this is not a practical solution for most pharmacies.

Facilities and Equipment - <800> Section 5.3, 5.4 cont.

A C-PEC used for sterile HD compounding MAY be used for non-HD sterile compounding, but since it MUST be thoroughly deactivated, cleaned and disinfected first so as to prevent cross-contamination, the ingredients and final product MUST be protected from exposure during movement in and out of the C-SEC, and proper PPE use is challenging, this is not a practical solution for most pharmacies. In the event that this must be done, a BPR is for the pharmacy to perform a risk assessment as to whether these final products, although made from non-hazardous ingredients, should in fact be treated as HDs.

Although <800> allows the negative pressure in a C-SEC used for nonsterile compounding to be obtained via the C-PEC, since (a) the C-PEC MUST have the capability to in fact accomplish this (b) the C-PEC MUST be externally vented (c) it MUST remain on 24 / 7 (d) it is difficult to in fact obtain the required ACPH and negative pressure range, this is not a practical solution for most pharmacies.

Although <800> allows for separate C-PECs devoted to sterile and nonsterile HD compounding to be placed in the same C-SEC, the nonsterile C-PEC MUST be "sufficiently effective" so as allow the buffer room to maintain at least ISO Class 7 air. It is a BPR to avoid this arrangement if possible in that:

(a) It is impractical to routinely monitor the success of maintaining ISO Class 7 air

(b) Additional nonsterile ingredients and materials are being introduced into the buffer room. If used, nonviable and viable particle counting activities required every six months should be performed while both sterile and nonsterile compounding is being performed to evaluate this "worst case" scenario.

There are many other PEC and SEC scenarios that pharmacies may feel compelled to create based upon preparation volume, limited space, immovable barriers such as weight-bearing walls, and the inability to externally exhaust air, and of course expense.

Some scenarios might be <u>better</u> than those shown on the attachment - for instance, the addition of a separate, negative pressure room for pre-sterilization and/or product storage (including a refrigerator).

Entities should exercise considerable caution before embarking on any design not very similar if not identical to those shown on the attachment, and try to avoid "non-preferred" designs if possible.

Based on the expense often involved in creating or reconfiguring these facilities, serious consideration should be given to obtaining the recommendations of a competent, independent consultant – that is, someone not associated with the vendor performing the work or selling the equipment.

"Modular" designs built using premade components have many merits, including the ability to fit into small or unusually configured spaces, known qualities such as airflow and materials suitability, and usually the ability to be moved or modified in the future. They may, however, be costlier than traditional "dry wall" construction.

The competence of vendors engaged to construct these facilities should also be carefully "vetted"; many sterile and nonsterile C-SECs continue to be built that violate obvious provisions of USP <795>, <797> and <800>. Ensure that contract language provides for redress should the facility be later revealed to be non-compliant with one or more of these chapters.

Facilities and Equipment - <800> Section 5.3, 5.4 cont.

Entities should also consult any state board of pharmacy requirements concerning hazardous drug handling to ensure that additional, more restrictive measures have not been implemented.

Questions and Answers

Q: What exactly is meant by "external" venting?

A: The air from C-PECs and C-SECs requiring such venting MUST exhaust their air outside of the building. There are no exceptions to this requirement. An entity should consult with their local building codes, however, to ensure that their plans to not violate local regulations.

Q: Why MUST C-PECs used for sterile compounding be externally vented, but for ones used in nonsterile compounding this is only a "SHOULD?"

A: There is concern that many antineoplastic HDs are volatile enough that significant amounts of them might not be captured by HEPA filtration.

Q: Why is "redundant" HEPA filtration required for C-PECS that recirculate air?

A: The hope is to remove particulate not captured by a single filter, or to guard against possible leaks in one unit.

Q: So I need to use an externally vented BSC even if I only compound a few antineoplastic drugs a year?

A: Correct. No "wiggle room" here as is the case in the current version of <797>.

Q: MUST I perform pre-sterilization tasks such as weighing out ingredients within a BSC?

A: No "wiggle room" here, either; a BSC must be used.

Q: May I turn my C-PEC used for nonsterile HD compounding off when not in use?

A: You cannot turn it off if relying on it to provide some or all of the negative pressure in your C-SEC. If this is not the case, if you turn the unit off, it should have been treated with a deactivating agent and cleaned first, and you need to know manufacturer recommendations for how long the unit must run when turned back on before it is fully functional.

Q: May I turn my C-PEC used for sterile HD compounding off when not in use?

A: No. In the event of an unavoidable event such as a power failure or required repairs, this C-PEC must be given a thorough treatment with a deactivating agent, cleaned, and disinfected.

Facilities and Equipment - <800> Section 5.3, 5.4 cont.

Questions and Answers

Q: May I turn my C-SEC used for HD compounding off when not in use?

A: No; for sterile and nonsterile compounding, it MUST remain on 24/7.

Q: MUST my nonsterile C-SEC have a door?

A: While not explicitly forbidden, it is difficult to imagine how a negative pressure differential range of between 0.01 - 0.03 inches of water could be maintained between the C-SEC and the area outside of it. A BPR would be to have a door, if for no other reason than to contain contaminated air in the event of a power failure.

Q: Why is there a negative pressure range for C-SECs?

A: The minimum value is to ensure that the pressure is adequate to constantly pull air into the room. The maximum value is to ensure that air velocity is not so high as to possibly blow about HDs, especially APIs.

Q: Is there any minimum size limit for a C-SEC?

A: No, this is determined by the ability of at least one worker and a C-PEC to fit in the area. Obviously below a "critical point," workflow and worker safety will be compromised. Also, be sure that your state board of pharmacy does not have a minimum size requirement.

Q: Do we need to have a safety shower?

A: While this is based on local regulations and your "mix" of HDs and other hazardous substances, the answer is "probably not" unless you handle caustic substances such as strong acids and/or bases. Your risk assessment can be used to evaluate this issue.

Q: What if constraints such as landlord / owner permission prevent me from taking measures such as external venting, or I simply do not have the space to create needed facilities?

A: This is unfortunate, but unavoidable. One of the reasons that USP provided over two years to implement <800> was to give entities as much time as possible to comply.

Personal Protective Equipment - <800> Section 7

Good Reads

Source 1 - Section 7
Source 2 - Table 5
Source 3 - Section V.C.3.

Discussion

Although a lengthy section of <800> is devoted to the topic of personal protective equipment (PPE) to be used in the handling of HDs, how to implement this guidance raises many questions.

Table 5 found in Source 2, the NIOSH List of Hazardous Drugs, is referenced in <800> and in many ways provides more useful information.

Section V.C.3 of Source 3 provides the best discussion of PPE of any source in the Hazardous Drug Library.

The problem is, even a careful synthesis of the information in these sources leaves many unanswered questions.

Attachment G provides in a systematic manner a description of required or recommended PPE based upon the aforementioned sources or, when they are silent, the experience and expertise of HDCG members.

Appropriate PPE, shown on the horizontal axis, is described for each step in the handling of HDs, shown on the vertical axis.

When required by one of the Primary Sources, these sources are listed. When seen as best practice recommendations based on HDCG consensus, "BPR" appears.

Footnotes provide important details in many cases.

PPE should not leave areas where HDs are being handled. Reusable items such as eye and respiratory protection should be treated with a deactivating agent and cleaned after each use, and before being removed from areas where HDs are handled.

Entities MUST ensure that gloves in fact meet the criteria shown in Footnote 2 of Attachment G. Any reputable vendor will be able to verify the suitability of their products in this regard.

Disposable gowns MUST be impermeable, closing in the back, and have cuffs that tighten about the worker's wrists. Manufacturers MUST be able to verify that their products meet <800> requirements.

Eye / face and respiratory protection is a complex topic in that full-face respirators, while cumbersome and costly, preclude the need for additional eye / face protection, and also provide all protection given by fit-tested NIOSH-certified N95 masks.

All disposable PPE should be treated as "trace" contaminated waste (see below) unless known to have been significantly contaminated with a HD, in which case it should be treated as "bulk" contaminated waste.

Personal Protective Equipment - <800> Section 7 cont.

Questions and Answers

Q: Why are double chemo gloves required for so many tasks?

A: It is basically to ensure worker protection should the outer pair fail due to puncture, etc.

Receipt and Storage - <800> Sections 5.1, 5.2, 10

Good Reads

Source 1 - Section 10
Attachment H

Discussion

Refer to Attachment R&S for this discussion.

Receipt

While antineoplastic (NIOSH Group 1) and active pharmaceutical ingredient (API) HDs are preferably unpacked in a negative pressure area, this is challenging to most entities, and is not required.

More important is the proper handling of shipments that might contain exposed HDs resulting from broken containers. While it is expected that all HDs arrive in sealed containers, e.g. plastic bags, the implications should a shipment not be so sealed are limited as long as it is undamaged.

Nonetheless, entities should lodge a complaint with any supplier when shipments containing HDs arrive unsealed, as this is an <800> requirement.

Any shipment container that appears to be or is damaged should be refused by workers upon delivery.

If the entity does not succeed in declining the delivery, the item should be (a) transported to a C-PEC if possible (b) placed in a sealed container - a plastic bin or large re-sealable plastic bag (c) labeled as "hazardous" (d) quarantined in a negative pressure area (presumably where other HDs are stored) while the supplier is contacted so as to arrange for its return.

If an apparently undamaged shipment container, when opened, reveals an exposed HD, the entity should (a) transport the container to a C-PEC if possible (b) treat the exposed HD as a "spill" (c) enclose it in a sealed container (d) label the container as "hazardous" (e) quarantine the item in a negative pressure area and contact the supplier to arrange for its return.

In the remarkable event that a supplier does not provide for the item's return, dispose of the item as "bulk" hazardous waste. A BPR is to insist on a full refund, a credit for disposal costs, and file a complaint with various regulatory agencies.

If an item is to be returned, ensure that it is done so in a sealed container, e.g. double re-sealable plastic bags. Large items can be placed in individually sealed "garbage bags."

<800> contains provisions in the event that a damaged shipping container "must" be opened - namely that this is performed in a C-PEC. A BPR is to avoid this if at all possible; quarantine the container and compel the supplier to deal with the issue as described above.

Receipt and Storage - <800> Sections 5.1, 5.2, 10 cont.

Should an exposed HD nonetheless be encountered, it MUST be handled as a "spill," as described elsewhere.

As numerous studies have shown significant residues on HD containers (see Source 8 - Ventilation Controls and Source 3 - V.B.3), a prudent BPR is to routinely wipe the outsides of all received HDs, including those such as manufactured products that will not be further manipulated, with a disposable towel soaked with an oxidizing agent, e.g. hydrogen peroxide or dilute bleach solution. These wipes should be disposed of as "trace" HD waste as described elsewhere.

Unless a spill is encountered, only a single pair of "chemo" gloves need be worn by workers receiving and unpackaging HDs.

Storage

<800>'s injunctions regarding HD storage may be largely summed up in the following sentence: All HDs that are active pharmaceutical ingredients (APIs), injectable antineoplastics, or antineoplastics that will be crushed or otherwise "manipulated" other than simple counting and packaging, MUST be stored in a separate, negative pressure, externally vented room with at least 12 ACPH.

For many nonsterile compounders, the C-SEC might be the only practical place for HD storage.

For sterile compounders, the C-SEC buffer room might be the only practical choice for HD storage.

Source 4's response to Question 12 requires all areas where HDs are "handled" to be labeled as "Hazardous Drugs - Restricted Access" or similar language to this effect.

HDs should not be stored on the floor, and reasonable care should be taken to prevent breakage should a container fall off a shelf through, e.g., use of "lipped" shelving.

Shelving should be smooth, impervious and easily cleaned. A BPR is to treat all contents of a nonsterile HD storage area with a deactivating agent followed by a cleaning agent on at least a quarterly basis.

Another BPR is to avoid the use of laminated wood. While the exterior of such products is impervious to liquids, all too often the highly porous particleboard underneath such coating is exposed via seams, holes or cracks, all of which can retain HD residues.

If storage containers are used, they too should be impervious and easily cleaned, e.g. made of smooth plastic. Cardboard of any kind should be avoided if at all possible.

As mentioned previously, refrigerators should only be placed in C-SECs in order to house HDs requiring storage at controlled cold temperatures. In effect, this means some antineoplastic HDs used for sterile compounding. It is acceptable, however, to place other HDs requiring refrigeration in the same unit should the case arise. Keep in mind that completed HD-containing products are not required to be placed in a negative pressure environment. Attempt to place a refrigerator near an air exhaust duct if possible. A BPR is to obtain a "solid state," "coil-less" refrigerator that has a far lower surface area.

While "entities" such as nursing stations, nursing homes and outpatient clinics might only be

Receipt and Storage - <800> Sections 5.1, 5.2, 10 cont.

receiving "finished" HD products that are thereby largely exempt from <800> requirements, a

BPR is for such entities to consider worst-case scenarios such as spills and exposure events in their risk assessment, and handle such products carefully. This might include storage precautions similar to those applied to pharmacies.

Questions and Answers

Q: Why aren't suppliers and manufacturers of HDs required to seal such drugs in plastic, or at least clearly mark them as HDs?

A: Good question. They should be. There are mixed reports coming in to members of the HDCG regarding compliance. All entities should let such suppliers and manufacturers know that this is their expectation, and that they will preferentially purchase from those that do comply with these requirements.

Q: Why are suppliers and manufacturers allowed to ship HDs with external trace contamination?

A: Another good question. Again, entities should urge their suppliers and manufacturers to not only ensure that products arrive without such contamination, but are willing to document this fact.

Compounding - <800> Section 13

Good Reads

Source 8 - Work Practices (although only concerned with sterile compounding)
Source 3 - Section V.E.1

Discussion

Very little space is devoted to this important topic in <800> or for that matter any of the documents in our HD Library. There is nothing unique, per se, about compounding techniques involving this diverse group of drugs; the common theme involves minimizing the generation or spread of HD contamination during this process.

Another goal should be to perform as many manipulations of HDs as possible within a C-PEC and C-SEC by properly garbed workers so as to avoid potential exposure at the time of administration. An example would be the preparation of a final dose of an oral antineoplastic in the pharmacy so as to avoid the need for patent care workers to split tablets or open capsules.

Although <800> allows the counting and packaging of HDs to be largely exempted from restrictions, a BPR is to whenever possible use prepackaged "unit dose" forms of these drugs when available.

Another BPR that is also an <800> "SHOULD" is to use a deactivating agent and clean equipment such as counting trays and spatulas after each use when dealing with HDs of any kind, especially NIOSH Group 1 antineoplastics.

Below is a list of BPRs based upon these goals:

Avoid movements in and out of the C-PEC even more than would be done during other types of sterile or nonsterile compounding so as to reduce the likelihood of spreading HD contamination.

To this end, assemble and introduce into the C-PEC all needed supplies, equipment, ingredients and containers prior to compounding.

While <800> has this as a "SHOULD," a BPR is to create a separate set of reusable equipment for compounding HDs. When this is not possible, such equipment MUST be treated with a deactivating agent and cleaned after each use in HD compounding.

Avoid rapid movements during compounding due to the likelihood of thereby causing spills or air turbulence that could spread contamination outside of the C-PEC.

Retain all used containers, supplies and other waste within the C-PEC, placing them in a waste container built into the C-PEC, or into a re-sealable plastic bag kept within the work area during the preparation.

Conduct actual compounding upon a disposable "plastic-backed preparation mat" placed on the C-PEC work surface. (These mats MUST be sterile in the case of sterile compounding.)

Compounding - <800> Section 13 cont.

When applicable for sterile preparations, tubing should be attached and "primed" prior to the introduction of HDs into the main vehicle container.

Closed-system drug-transfer devices (CSTDs) such as ChemoLock®, Equashield® and ONGUARD® are with good reason SUGGESTED for use by <800> when compounding sterile HDs if the container allows their use, based on evidence that they reduce the amount and extent of HD contamination of the environment. In the case of NIOSH Group 1 HDs, they MUST be used, if the container allows their use.

As the answer to Question 19 of Source 4 describes, however, some CSTDs appear to be more effective than others; entities should request manufacturer information in this regard before selecting a product.

Always use negative pressure technique when extracting a liquid from a closed container if a CSTD cannot be used.

Luer-lock fitting should be used whenever possible for all syringes, needles and tubings.

Wipe up or contain even minor spills immediately should they occur.

Set up the preparation for checking in a manner that will not require the pharmacist to reach into or touch anything within the C-PEC.

Wipe down finished containers and, if applicable, tubing, with an oxidizing agent, e.g. hydrogen peroxide or a dilute bleach solution, followed by a "dry wipe" so as to remove HD residues or byproducts. A final wipe of critical sites such as injection ports that have been used to inject HDs into the final product with a SIPA-impregnated pad prior to capping or transport is in order.

Collect and dispose of all remaining waste in either the built-in waste container or into a plastic bag that is then sealed and disposed of in a larger trace hazardous waste container.

Small sharps / hazardous waste containers may be kept in C-PECs as appropriate, but treated with a deactivating agent and cleaned prior to removal and disposal.

Deactivate and clean (and, for sterile compounding, disinfect) the interior of the C-PEC after each compounding activity.

Assuming your risk assessment supports it, the simple counting and packaging of manufactured dosage forms such as capsules or tablets does not require any special handling other than use of one pair of "chemo" gloves, the use of dedicated counting trays and spatulas, and the use of a deactivating agent and cleaning after their use.

If the volume of such counting and packaging is significant, the pharmacy should consider the use of a C-PEC for these activities.

Questions and Answers

Q: What about a finished dosage form that is a liquid?

A: Based on your risk assessment, it may be acceptable to handle such a product as one would capsules or tablets. However, the greater risk of spills and volatilization involved in a liquid should be seriously considered.

Labeling, Packaging, Transport and Dispensing - <800> Sections 11, 12

Good Reads

Source 1 - Sections 11 and 12

Discussion

The labeling of final preparations containing HDs can be challenging for at least the following reasons:

Labeling immediately after preparation is a widely recognized standard of good practice.

Keeping labels as close as possible to the product to which they are to be applied is a widely recognized best practice.

Paper-based labels are liable to absorb water-based HD solutions and retain airborne HD powders.

Directly applying water-based deactivating, cleaning or disinfecting agents to paper-based labels could blur or fade printing.

Labels for sterile products should not be brought into the C-PEC.

There is no obvious universal solution as to how to navigate these challenges. Each entity must include this issue in its risk assessment and develop a solution that balances the exposure of labels to HDs against the chance of applying labels to the wrong product.

Labeling HD Final Preparations for Use in Controlled Settings

While no source found in our Hazardous Drug Library specifically requires or even recommends it, many state boards of pharmacy require that a finished HD product to be directly administered to a patient (versus dispensed) bear some form of warning label to ensure its proper handling and disposal by workers. Surely this should at least apply to antineoplastic or other HDs posing immediate danger to the handler. The exact text and use of such labels would be an entity or state specific decision.

Labeling HD Final Preparations to be Dispensed

There is similarly very little "official" guidance concerning the use of precautionary labels in the case of final HD preparations dispensed to consumers. The desire to inform the consumer must be balanced against the alarm that use of a word like "hazardous" might cause if used on a hormone replacement product, for example.

It should also be kept in mind that the primary reason a substance is placed on the NIOSH List is due to its potential effect on health care workers following prolonged exposure - a concern that does not necessarily extend to the patient. This is especially true of many NIOSH Group 2 and 3 drugs.

Labeling, Packaging, Transport and Dispensing - <800> Sections 11, 12 cont.

While a number of the manufactured forms of drugs on the NIOSH List include "black box" warnings, these cautions do not always correspond with why the drug is considered hazardous.

A prudent BPR is for a pharmacy to ensure that patient verbal and written information emphasizes the need for special handling on a case-by-case basis.

Packaging and Transport

The reader is asked to refer to Attachment I for this discussion.

There is a "great divide" on the topic of packaging and transport that separates NIOSH Group 1 HDs from NIOSH Group 2 and 3 drugs.

Group 2 and 3 drugs can essentially be handled as would any non-HD preparation. A BPR would be to place it in a re-sealable plastic bag that will contain leakage, and could be used for product disposal.

Additional labeling might not only not required, but might be alarming, as described above, to the outpatient user of such products.

Concerning NIOSH Group 1 drugs, whether transported within an institution, e.g. a hospital or within an outpatient clinic, or via a courier, driver or other worker, the following recommendations apply:

> Use "reasonable" packaging and protection that will prevent product damage and spillage.
>
> Place the product in a re-sealable bag that is labeled along the lines of "Hazardous Drug: Dispose of Properly."
>
> For transport within an institution, <800> prohibits the use of pneumatic tube systems for the transport of "liquid HDs or any antineoplastic HDs" to avoid the chance of breakage and difficult-to-treat contamination.
>
> A BPR for, e.g. home infusion pharmacies using couriers or drivers, would be to box any NIOSH Group 1 product as if it were being shipped via common carrier.

For NIOSH Group 1 drug products transported via common or premium carriers such as USPS, UPS or FedEx, the situation is complicated to some extent by Department of Transportation (DOT) regulations. (Although the USPS is technically exempt from DOT, similar internal requirements govern hazardous transport.)

Section 14 of Safety Data Sheets (SDSs) contains "Transport Information," most importantly if the drug is or is not "regulated" regarding transport by DOT. If it <u>is</u> regulated, the drug is subject to Hazardous Materials (HazMat) Transportation restrictions if it is to be shipped to the end user. If it is <u>not</u> regulated, it may at the discretion of the pharmacy be transported as would any other finished product.

A review of Section 14 of the SDSs for 20 common NIOSH Group 1 drugs conducted by a HDCG member found them all classified as "hazardous," "toxic" or "poisonous." (Uniform language is unfortunately not always used.) A similar search of 20 common Group 2 and Group 3 drugs found none to be so classified. Instead, then, of referring to SDSs every time a product is shipped, a

Labeling, Packaging, Transport and Dispensing - <800> Sections 11, 12 cont.

reasonable BPR would be to is to treat all antineoplastic (NIOSH Group 1) HDs as "regulated" and all other HDs as not.

Section 14 of SDSs will also contain a "UN number." NIOSH Group 1 HDs all bear the UN number 2811. This section also gives the drug's "Packaging Group." All Group 1 HDs are Packing Group "III," meaning that there are very few restrictions on how they may be shipped - especially for the quantities that any pharmacy involved in compounding NIOSH Group 1 drugs would be involved in.

These classifications dictate how NIOSH Group 1 drugs may be shipped. Fortunately, the quantities of such drugs typically shipped via ground or air are usually small enough to be "exempt" from further restrictions.

Attachment I describes these provisions:

1. The total volume of HD per container may not exceed 1 liter for air transport, and 4 liters for ground transport.
2. Containers used for these shipments MUST meet "Packaging Group III" standards. The supplier of boxes or other containers used for HD shipments should be able to rapidly confirm whether products do or do not meet these requirements.
3. The pharmacy is well advised to discuss required labeling and packaging requirements with its common or premium carrier of choice.
4. Those responsible for packaging HD products for "exempt" shipment MUST receive training on this topic.

Questions and Answers

Q: I'm still confused about the shipping requirements for HDs for the common carrier we use. What should I do?

A: Discuss this matter with the customer representative of your common carrier. As with HD waste disposal, there is enough regional variation that a single answer is simply not possible. When in doubt, use common sense.

Administering - <800> Sections 14, 5.4

Good Reads

Source 7
Source 8 - Appendix G

Discussion

Based on the likelihood that the typical reader of the HDCS will have little if any involvement in administering HDs, the abbreviated coverage of this topic in <800>, and the existence of Source 8's highly useful Appendix G, as well as Source 7, little discussion will be devoted to this topic here.

Closed-system drug-transfer devices (CSTDs) such as ChemoLock® Equashield® and ONGUARD® are with good reason a MUST when administering antineoplastic HDs - if the container allows their use - based upon evidence that they reduce the amount and extent of HD contamination of the environment.

Questions and Answers

Q: Are there constraints as to where <800> will apply regarding administration?

A: Not in theory. If you are an entity that "administers" HDs to patients, you are under <800>'s jurisdiction.

Deactivating, Decontaminating, Cleaning and Disinfecting - <800> Section 15

Good Reads

Source 1 - Section 15

Discussion

While definitions of these four terms are presented in Section 15 and the Definitions section of <800>, the important issues to keep in mind on this topic are as follows:

There is some overlap in some of these terms, as well as differing definitions available from various valid sources.

For our purposes, we shall use the terms "deactivation," meaning the rendering the HD chemically inert, and "cleaning," meaning the physical removal of an HD from a surface.

"Disinfection" is of course a critical process for sterile compounding and a desirable one even for nonsterile compounding.

While chemical deactivation of HDs is the ideal goal, as <800> states, there is no single agent capable of accomplishing this for the very chemically diverse set of drugs found on the NIOSH List.

Oxidizing agents such as sodium hypochlorite, sodium dichloroisocyanurate (NaDCC), hydrogen peroxide or hydrogen peroxide / peracetic acid combinations, however, appear as close to "universal deactivators" as any readily available, easily used and affordable substances. These agents also have the added advantage of being highly effective disinfectants.

Contrary to common opinion, not only does isopropyl alcohol (IPA) not deactivate most HDs, its rapid evaporation might actually spread HD contamination. Since it is also not a particularly effective detergent, its use in nonsterile HD cleaning is not recommended.

A dilute sodium hypochlorite solution created using simple household bleach is inexpensive and easy to create. However, there is danger involved in creating such dilute solutions, and they rapidly degrade. Additionally, unless deactivated with sodium thiosulfate or removed using water, isopropyl alcohol or a detergent solution, they corrode stainless steel such as is often found in C-PECs and carts used in sterile compounding. Bleach solutions may be acidified so as to extend their expiration dates.

There are commercially available sodium dichloroisocyanurate (NaDCC) products that will deactivate many HDs, not degrade surfaces, and act as an effective disinfectant.

Household nonsterile 3% hydrogen peroxide solution is an inexpensive but very effective oxidizing and disinfecting agent.

Since there are commercially available sterile hydrogen peroxide / peracetic acid combinations that deactivate many HDs and act as effective disinfectants, they are a reasonable one-step process for the sterile compounder.

Although they do not clean (physically remove) HD residues, and are not practical for daily use,

Deactivating, Decontaminating, Cleaning and Disinfecting - <800> Section 15 cont.

commercially available peroxide "foggers" offer another deactivation option for nonsterile and sterile compounders. They should be seen as supplemental to the immediate use of a liquid oxidizing solution on surfaces. These products produce oxidizing vapors that penetrate everywhere that air penetrates, presumably deactivating many HD residues in areas that are extremely difficult if not impossible to reach otherwise.

In many cases an entity handling HDs will need to rely heavily on the physical removal (cleaning) while also attempting to deactivate many such substances.

This emphasizes the importance of using an effective detergent, and the physical removal of it and any HD-containing residues, as a second step in cleanup.

Through something resembling an "80/20 Rule" exercise, entities should attempt to ensure that their deactivation protocols in fact result in the destruction of that small number of drugs that constitute the majority of their compounding activity.

Drug-specific information on an effective deactivating agent is often difficult to obtain, although safety data sheets and Internet searches can be of some help.

Equipment, work areas and reusable utensils should be treated with a deactivating agent and cleaned after each use. This policy should apply to counting trays and other items used in the dispensing even of manufactured dosage forms of HDs such as antineoplastic capsules.

C-PECs MUST be treated with a deactivating agent and cleaned at least daily when in use, and after spills.

C-PECs such as a Class II Type A2 BSC with removable work areas MUST be dissembled, treated with a deactivating agent and cleaned and, if used in sterile compounding, disinfected at least monthly.

Liquid agents should be applied directly or via towels versus by spraying, which might disperse HD residues. For sterile compounding, towels pre-saturated with SIPA are available for disinfection tasks.

Entities handling only a small number of HDs are advised to research the effect of selected deactivating agents on these drugs.

Ultimately, the effectiveness of deactivation and physical cleaning will rely on environmental surface sampling or ultraviolet light validation (to be discussed later).

Questions and Answers

Q: How often do I need to deactivate / clean?

A: This is up to the entity to decide based upon a risk analysis and, in the case of sterile compounding, the requirements of <797>. A BPR is to perform this on any C-PEC work surface between products, especially if changing between NIOSH groups of HDs. As stated above, dissembled BSCs MUST be treated with a deactivating agent and cleaned at least monthly. A BPR is that all areas involved in the receipt and compounding of HDs should be treated with a deactivating agent and cleaned every day of use. Regarding storage areas, a BDP is to perform this at least quarterly.

Disposal - <800> Sections 7.6, 11.4

Good Reads

Source 1 - Sections 7.6 and 11.4

Discussion

As little specific guidance on HD disposal is provided by the sources in our Hazardous Drug Library, most of what follows should be considered BPRs.

We need to remember that hazardous DRUGS as defined by NIOSH have little relationship to hazardous waste as defined by the EPA's Resource Conservation and Recovery Act (RCRA)*.

Complicating the picture is the existence of many local and state rules and regulations regarding all manner of waste.

Specifically, your state may require you to register as a hazardous waste generator, including California, Delaware, Florida, Maine, Massachusetts, Maryland, Minnesota, New Hampshire, New Jersey, Ohio, Rhode Island and Vermont.

Finally, entities involved in administering HDs may have to deal with sharps and biohazardous waste, further complicating the picture.

While an entity may attempt to master this complex issue on its own, a definite BPR is to obtain assistance from a medical supply provider or a vendor specializing in hazardous waste disposal.

For our purposes, all materials containing or presumably contaminated by NIOSH-Group 1 HD should be grouped as follows: **

"Trace" waste:

1. Containers and tubings with less than 3% by weight of the HD remaining in them, including disposable plastic-backed mats
2. All disposable utensils and supplies involved in compounding HD preparations or cleaning areas where these products are compounded or stored
3. PPE used in the compounding, cleaning or administration of HDs unless significantly contaminated

"Bulk" waste:

1. Containers and tubings with more than 3% by weight of the HD remaining in them
2. Significantly contaminated utensils, supplies and PPE used in compounding, cleaning, administration or other handling activities involving HDs
3. Materials used in cleaning HD spills.

Disposal - <800> Sections 7.6, 11.4 cont.

As one HDCG member has advised, "If it's pourable, it's bulk."

When in doubt, treat an item as "bulk" waste.

While the cost of disposing of bulk wastes is significantly higher than trace waste, small facilities may nonetheless find it easier to simply "overclassify" and treat everything as bulk waste.

** Although some RCRA P-Listed drugs also appear on NIOSH's Group 1 list.*

*** This is a significant point! RCRA apparently only covers "chemotherapy" drugs - NIOSH Group 1.*

Questions and Answers

Q: How long can I use a trace or bulk waste container?

A: There is no clear guidance here, but a BDP is to use containers that will be full at least every month, requiring their movement to a hazardous waste disposal area awaiting pickup.

Spills and Exposure Events - <800> Section 16

Good Reads

Source 3 - Section V.H.
Source 8 - Spill Management, Appendix I and Appendix J

Discussion

The best coverage of this topic in any of the sources listed in the HD Library is found in Section V.H. of Source 3, which in turn frequently references the 2006 version of ASHP's Guidelines on Handling Hazardous Drugs (Source 8). The following discussion will largely recap and amplify upon this material.

First, an entity MUST define what it considers a spill. While not surprisingly there is no absolute definition possible, three simple criteria are of use here. Consider the event a "spill" if:

1. The event happens outside of a C-PEC and cannot be easily contained with materials readily at hand to a worker already wearing PPE.
2. The event cannot be easily contained with materials readily at hand to a worker already wearing PPE regardless of location.
3. The size of the spill and the toxicity of the spilled substance.

Exposure Events

Note that a "spill" and an "exposure event" are often not the same thing; a minute amount of a caustic HD splashing into the eye might not involve a "spill." And even a large spill can and hopefully often is handled without any worker exposure to the HD.

The immediate treatment of a significant exposure event should take priority over essentially all spill events in that worker injury, possibly severe, may result unless treated. Exposure events should result in:

1. Removal of PPE, if applicable
2. Use of eye wash stations or sinks, depending on the site of exposure
3. The washing of exposed skin should
4. The notification of management
5. Medical attention should be sought at the discretion of management
6. The creation of an incident report

Spills and Exposure Events - <800> Section 16 cont.

Spill Handling

"Notification" is the first step. Without leaving the area of the spill so as to prevent the inadvertent exposure of other workers, the first worker to discover the spill notifies management and other workers that a spill has happened.

"Emergency containment," if easily performed, is appropriate for large spills likely to rapidly spread. This might entail simply placing readily available paper towels on top of a spill.

Either the discovering worker, or another worker authorized to manage spills, obtains an appropriate spill kit.

Not all spills are created equal, and spill size is not the only criterion. A broken vial of a caustic chemotherapy drug or strong acid is not the same as a hormone replacement cream. Entities may well wish to have more than one kind of kit available; more on this below.

The PPE contained in the spill kit is donned, including a respirator as described below if appropriate.

Contain the spill using absorbent materials in the kit, beginning from the least contaminated areas and moving toward the most contaminated.

Treat glass fragments or other sharps with great caution, hopefully using a scoop provided in the kit.

Dispose of all materials in the bag provided by the kit.

Deactivate the area, if possible, using an oxidizing agent such as peroxide or a dilute bleach solution as discussed in another section, followed by cleaning with a detergent and water.

Remove and dispose of PPE as trace hazardous waste or, if overtly contaminated, bulk hazardous waste.

Wash hands with water and detergent.

Treat with a deactivating agent and clean reusable PPE such as a respirator if relevant.

The need for further deactivation or cleaning actions should be evaluated, e.g. if the spill reached the HEPA filter of a C-PEC.

Management should evaluate those involved in spill cleanup as to the need for medical intervention or monitoring.

An incident report MUST be created that will become part of the entity's performance improvement database.

A worker's involvement in an HD spill or exposure event should be noted in their human resource record, as well as information as to any medical interventions made.

Spill Kits

A wide variety of spill kits containing all items stipulated by ASHP 2006 and other sources are readily available commercially.

Spills and Exposure Events - <800> Section 16 cont.

As noted above, an entity should also obtain "specialty" spill kits based upon the use of other toxic substances, e.g. strong acids or bases.

Care should be taken that purchased spill kits in fact contain all recommended contents, and that these contents are appropriate for the entity. For instance, enclosed PPE may not fit some or all workers. "Home grown" kits, if properly assembled, can be superior. Each entity needs to evaluate its options in this regard.

The following contents list is derived almost entirely from what is found in Source 8 as well as most commercially available kits:

1. Personal Protective Equipment
    a. two pairs of gloves, one of which is "heavy duty" to minimize sharps injury
    b. disposable gown
    c. disposable shoe covers
    d. a "face shield" of some kind
2. One or more signs for placement near the spill
3. Plastic-backed absorbent pads
4. Disposable toweling
5. Two or more sealable bags for disposal of the spill and PPE labeled appropriately
6. Scoop for glass fragments and other sharps
7. Container for such sharps

* <800>'s language on the topic of respiratory and eye protection when handling spills can be distilled down to the following BPR. When handling hazardous drug spills, use either:

1. A full-face, chemical cartridge-type respirator or
2. An N95 respirator plus goggles (usually provided in spill kits)

Most available kits are able to at least handle a one liter spill volume as per Source 8's convenient "rule of thumb."

A BPR is for an entity to have additional absorbent materials available at the same location as spill kits should it wish to prepare for a "worst case scenario" of spills larger than this.

Another BPR is to ensure that the gloves contained in the chemo kit are large enough to be used by all workers who may use the kit, and place additional gloves with the kit should this not be the case.

While it is variously stated that spill kits should be placed in "all areas where an HD spill may occur / are routinely handled," realistically this translates for most entities into the following:

1. Within the C-SEC
2. Where HDs are received

Spills and Exposure Events - <800> Section 16 cont.

3. Where HDs are stored
4. Where HDs are prepared for transport
5. Where HDS are administered

More important than the quantity of kits is:

That they are rapidly (e.g. within 30 seconds) obtainable

That all workers know where they are

A BPR is to, when practical, place such kits near eye wash stations or fire extinguishers - other items that all workers should at all times know the location of.

Another BPR is to link an inspection of spill kits for presence and completeness to some periodic event such as the inspection of inventory for expired goods or routine facility cleaning.

Training and competency

<800> and other sources stipulate that at least one worker trained and competent in the use of an HD spill kit MUST be available whenever the entity is in operation.

BPRs regarding this topic include:

Simply requiring all workers who compound or administer HDs to undergo annual training and competency, as no entity will be open without at least one such worker present.

Alternatively, requiring all pharmacists to undergo such training, since a pharmacy may not open without a pharmacist's presence.

Linking this requirement to other mandatory training and competency, e.g. observed sterile competency assessment.

Including an actual "return demonstration" handling of a mock spill by the worker (although not explicitly required by any source listed in the HD Library). A single kit plus supplementary PPE, absorbent material and bags can be used for multiple competency assessments to avoid the consumption of multiple, costly spill kits.

Questions and Answers

Q: How many spill kits do I need?

A: There is no simple answer to this question. One must consider how rapidly a kit could be brought to a site where it is needed.

Environmental Monitoring - <800> Section 6

Good Reads

Source 1 - Section 6

Discussion

Although described in <800> as a "SHOULD" versus a "MUST," some form of environmental wipe sampling (EWS) in the opinion of the HDCS is STRONGLY recommended.

An entity cannot assess its success in controlling environmental contamination if it cannot in some way measure the extent of such contamination. A sampling program can not only detect shortcomings, it could reveal "overkill" in which the entity is wasting time and resources treating contamination that does not exist.

Source 3 - Section 4 lists numerous studies that have detected significant amounts of HD contamination in the workplace.

The intent here is to measure the success of the containment and handling processes implemented by the entity in limiting the amount of HD contamination that can, in fact, be detected in various areas.

While still a "work in progress," entities in conjunction with external analytical labs can in all likelihood obtain meaningful, reasonably quantitative results from an EWS program.

Since the actual HDs handled by entities, the abilities of analytical labs to quantitatively analyze submitted samples, and the costs of such tests vary widely, a customized EWS should be developed in cooperation with the analytical lab.

When feasible, the most commonly handled HDs should be tested for, with the results extrapolated to all HDs.

If more than one HD is tested for, strive for "chemical diversity" so as to determine if deactivating agents are in fact working against a variety of handled HDs.

Although the most common EWS program will entail wiping suitable "swabs" or similar supplies over a defined surface area in certain defined locations, experiments involving leaving collection materials in certain areas for prolonged periods before "harvesting" are also underway.

<800> suggests several locations for EWS, which has inspired the following modified list:

1. Work surfaces within C-PECs and C-SECS
2. Floors of C-SECs
3. Shelving and the tops of C-PECs and other equipment within the C-SEC when applicable
4. Pass-through windows if applicable
5. Areas immediately adjacent to C-SECs
6. Sinks used to clean HD-contaminated utensils and equipment

Environmental Monitoring - <800> Section 6 cont.

7. Packaging, shipment and dispensing areas
8. HD administration areas, when applicable

It is important to keep in mind that the goal of EWS is not zero detectable HDs per se, but a realistic, quantitative assessment of the success of containment strategies. Should negative results emerge from the first round of EWS, for instance, the entity should be concerned that there is some flaw in the process, or that different areas should be tested.

Thus, EWS should be performed before periodic cleaning, using large total sampling areas, and targeting the areas most likely to contain measurable amounts of HD. If minimal HD residues are found under such "worst case" conditions, it is quite likely that average conditions are in fact better.

No suggested EWS frequency is mentioned in any sources within our HD library. So as to establish a baseline, and document the success of improved containment and cleaning strategies implemented after the receipt of initial results, the HDCG suggests testing every three months for at least two cycles, dropping to every six months or year based on acceptable results.

<800> correctly states that "acceptable" exposure limits for all but a handful of HDs are purely speculative. However, several concepts should be kept in mind:

1. Statistical process control techniques such as control charts may assist in evaluating whether tested HD levels are in fact changing in a "significant" manner.
2. A set of precisely defined EWS areas should be used consistently so as to increase the chance that actual changes in HD contamination are correctly measured, and can be compared historically.
3. However, sampling a few previously unsampled areas may have merit as a way of validating the results from other locations as well as potentially detecting previously unknown "hot spots."

Ultraviolet Light Testing

The fact that many chemicals used in compounding, including multiple HDs, are fluorescent under ultraviolet light can serve as the basis for an excellent, low cost, non-quantitative evaluation of facility and equipment contamination.

This process simply involves purchasing an inexpensive ultraviolet unit (readily available on the Internet), turning off overhead lighting, and examining the same areas that would be involved in an EWS program.

While not quantitative, UV testing is in some ways qualitatively superior to EWS in that contamination hiding in crevices, equipment, and difficult-to-reach areas can be easily seen and clearly identified.

If significant contamination is thus detected, a thorough, targeted deactivation and cleaning campaign can be launched, followed by a repeat UV examination.

Environmental Monitoring - <800> Section 6 cont.

Quick UV scans of the compounding environment before routine cleaning might assist workers in locating areas to target; a follow-up scan after the cleaning will validate the success of these efforts.

Continued problems may require adjustments in the deactivation and cleaning process, and agents used for these activities.

Questions and Answers

Q: Do we have to do environmental testing for all of the HDs we handle?

A: First, EWS is a "SHOULD" versus a "MUST." But no, there is no reason to test for ALL HDs. Focus on a few HDs that are (a) very commonly compounded and (b) inexpensive to test for, based on conversations with your analytical lab. If results come back good (or bad) for these HDs, it is reasonable to extrapolate for all the HDs you handle.

Medical Surveillance - <800> Section 18

Good Reads

Source 1 - Section 18
Source 3 - Section VI

Discussion

While a "SHOULD" versus a "MUST" in <800>, the HDCG strongly recommends that entities implement a medical surveillance program (MSP). An MSP might not only detect significant health outcomes due to exposure to HDs but also provide some degree of protection from unwarranted worker litigation. An MSP that continues to yield "negative" results may also reassure workers and management as to the effectiveness of HD handling practices in place.

Such a program entails the medical monitoring of workers handling HDs so as to detect adverse health effects possibly due to this exposure, in many cases hopefully in time for corrective actions to be taken.

In a broad sense an MSP is the ultimate measure of the success of all measures taken to minimize worker exposure to HDs.

Source 3 - Section VI offers a parallel and often clearer review of this topic than what is found in <800>. What follows is a paraphrasing of the information from these two sources:

1. Identify workers who are potentially exposed to HDs. A reasonable BPR would be to review the Assessment Matrix developed as part of the entity's risk assessment, and focus on those workers involved in the activities with the highest total.
2. Identify a "health service," contracted or in-house, to be used to collect actual data. Nearby occupational health clinics might be willing to work with an entity in this regard.
3. A "baseline" database is established consisting of the gathering of:
    a) A medical history with emphasis on reproductive and cancer and current status, and prior exposures to HDs.
    b) Information as to the types of HDs the worker is currently or will be exposed to and the frequency and intensity of such exposure. (Ideally a "baseline" database is obtained from workers prior to employment.)
    c) Physical examination information focusing on such "targeted organ systems" such as skin, mucous membranes and the lymphatic system.
    d) Laboratory data, e.g. a complete blood count with differential, as relevant.
    e) The same or similar information is gathered "periodically." A BPR would be to repeat this screening annually.

Medical Surveillance - <800> Section 18 cont.

f) A "follow-up plan" that would be launched if results of concern are discovered. This might include a more thorough "post-exposure examination" of the worker, leading to treatment if needed. Issues that might be investigated as root causes of results of concern are:

Functioning of engineering controls

Compliance with PPE requirements

Comparing worker results with those of others involved in similar tasks and/or with "control" workers not involved in these tasks may be of help.

4. Findings from this investigation are implemented, and their success monitored. Means of monitoring success might include:
   a) Environmental sampling
   b) More frequent and/or elaborate medical surveillance

5. An "exit examination," presumably similar or identical to the "baseline" and ongoing monitoring, it conducted whenever a worker leaves employment with the entity.

Known overt exposure should, aside from immediate medical attention, also result in a heightened monitoring program for an acceptable period of time.

The entity should follow OSHA guidelines as to the maintenance of MSP records in a confidential manner. The MSP should provide for the confidentiality of worker records while at the same time alerting the entity of results of concern that should be addressed.

Questions and Answers

Q: What if an employee does not want to participate in an MSP?

A: Employees should be encouraged, but not required, to participate. An entity may want to ask employees wishing to "opt out" to sign a document to this effect. However, it should be easy to design an MSP that protects employee privacy while still allowing the discovery of potentially significant health issues that may be due to HD handling.

Notices

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Attachment A

Assessment Matrix

Task	Exposure Route: Injection	Eye exposure	Ingestion	Inhalation	Dermal exposure	Total
Receipt & Storage	1	2	3	4	5	
Compounding	6	7	8	9	10	
Labeling and Packaging	11	12	13	14	15	
Transport / Dispensing	16	17	18	19	20	
Administering	21	22	23	24	25	
Deactivating and Cleaning	26	27	28	29	30	
Disposal	31	32	33	34	35	
Spill Handling	36	37	38	39	40	
Other:	41	42	43	44	45	

Attachment B

Task / Exposure Route #	Severity Score	Cumulative % Total Severity	Mitigations				
			Engineering Controls	Handling	PPE	Deactivation / Cleaning	Other
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							

Attachment C

#	Action Item Details	Assigned To	Target Date
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

Attachment D

Topic	800 Section(s)	Type
Process		
1. Receipt	5.1, 10	Required
2. Storage	5.2	Required
3. Hand hygiene and PPE	7	Required
4. Compounding	5.3, 13	Required
5. Labeling	11.1	Inferred
6. Packaging	11.2	Inferred
7. Transport	11.3	Required
8. Dispensing	12	Required
9. Administration	14	Required
10. Deactivation / Decontamination / Cleaning / Disinfection	15	Required
11. Spill control	10, 16	Required
12. Disposal	11.4	Required
Administrative and General		
1. List of HDs	2	Inferred
2. Engineering controls	5	Required
3. Safe work practices	-	Required
4. Exposure prevention / reduction	-	Inferred
5. Environmental monitoring	6	Required
6. Safe work practices	-	Inferred
7. Training and competency	8, 9	Inferred

Attachment E

C-PECs and C-SECs

Containment primary engineering controls (C-PECs)

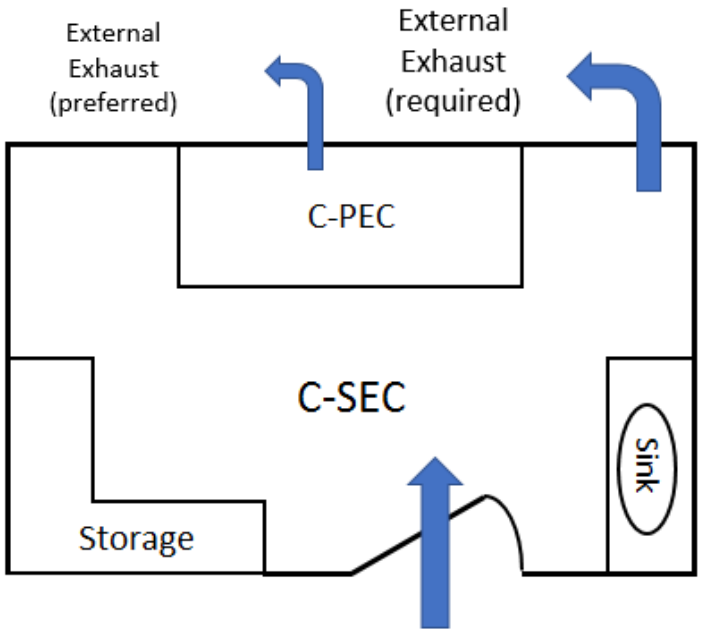
	Nonsterile	Sterile
Conformation	-	-
Venting	External preferred: redundant HEPA filtration if not	External required
Pressure	-	-
Air Exchanges	-	-
Filtration	Redundant HEPA filtration unless externally vented	-
Air Class	-	≤ ISO 5
Examples	Class I Biological Safety Cabinet (BSC), Containment Ventilated Enclosure (CVE), or any C-PEC suitable for sterile compounding	Class II or III Biological Safety Cabinet (BSC), Compounding Aseptic Containment Isolator (CACI)*
Sink	-	-
		* Class II type A2 BSCs are typical

Containment secondary engineering controls (C-SECs)

	Nonsterile	Sterile		
		Containment Segregated Compounding Area (C-SCA)	Ante Room +	Buffer Room
Conformation	Fixed wall; smooth, impervious, crack / crevice free		Fixed wall; smooth, impervious, crack / crevice free; comply with USP 797 requirements*	
Venting	External required			External required
Pressure	Negative 0.01 - 0.03 " water with respect to adjacent areas		≥ 0.02 " water with respect to adjacent unclassified areas*	Negative 0.01 - 0.03 " water with respect to adjacent areas
Air Exchanges	≥ 12 air exchanges per hour (ACPH)		≥ 30 air exchanges per hour (ACPH)	≥ 30 air exchanges per hour (ACPH)
Filtration	-	-	-	
Air Class	-	-	≤ ISO 7	≤ ISO 7
Examples	-	-	-	
Sink	≥ 1 meter from C-PEC	≥ 1 meter from C-PEC (may be outside of C-SCA)	≥ 1 meter from buffer room entrance	
			*If ante room is accessed by HD and non-HD buffer rooms, the non-HD buffer room must have a positive pressure towards it.	

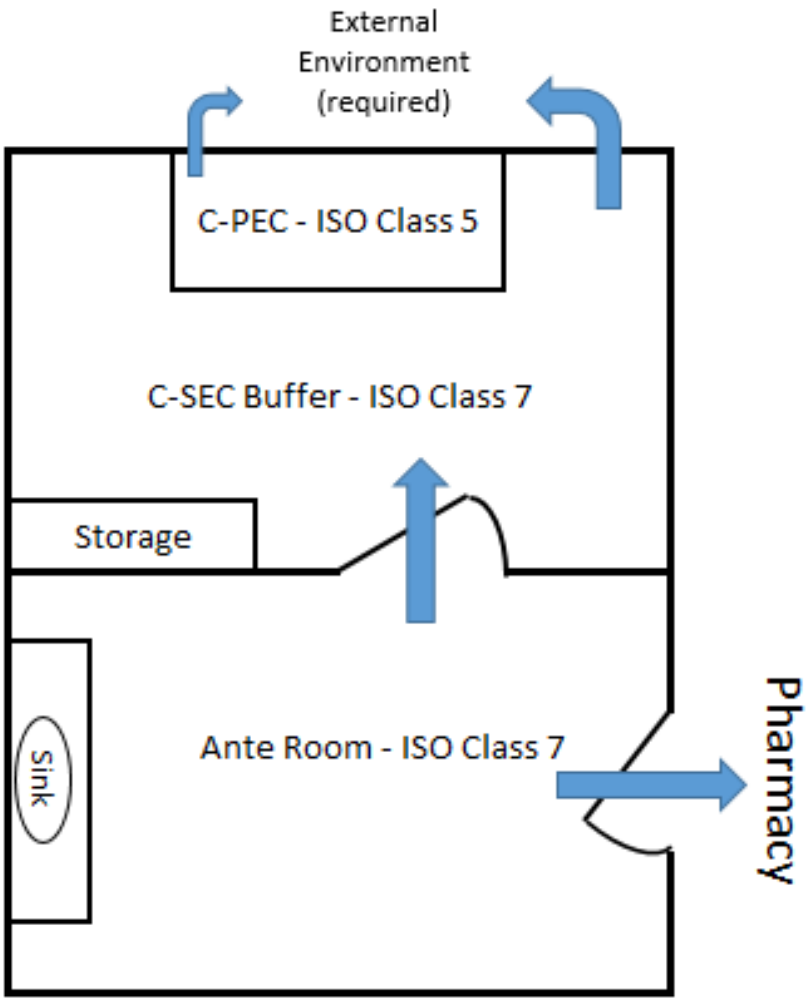
Attachment F– Pg. 1

1. Simple Nonsterile C-SEC and C-PEC Arrangement



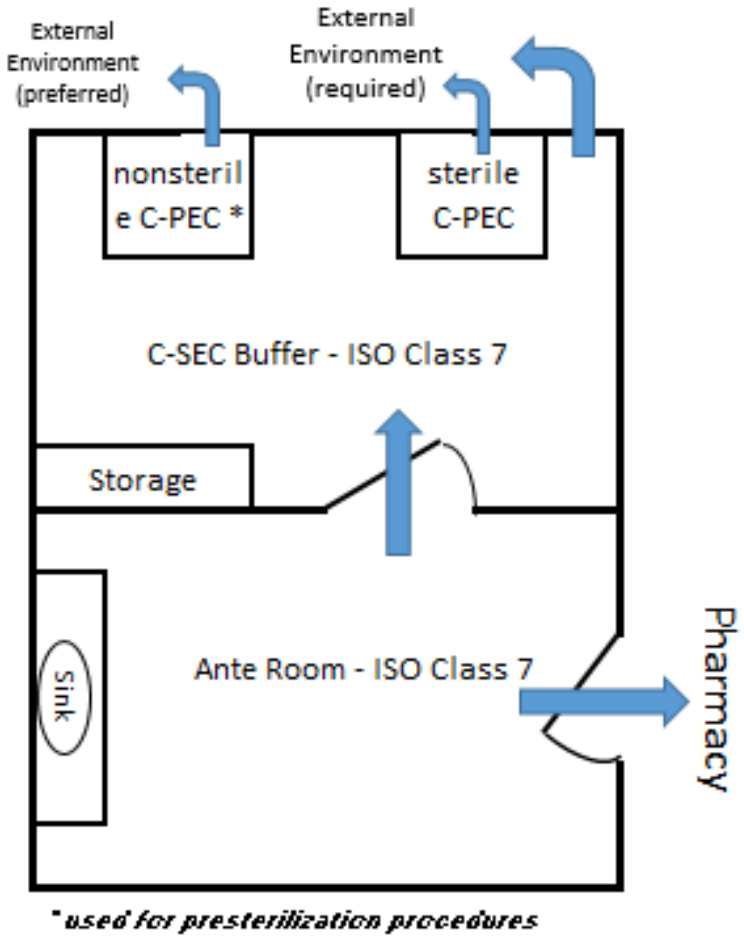
Attachment F – Pg. 2

2. Simple Sterile C-SEC and C-PEC Arrangement



Attachment F – Pg. 3

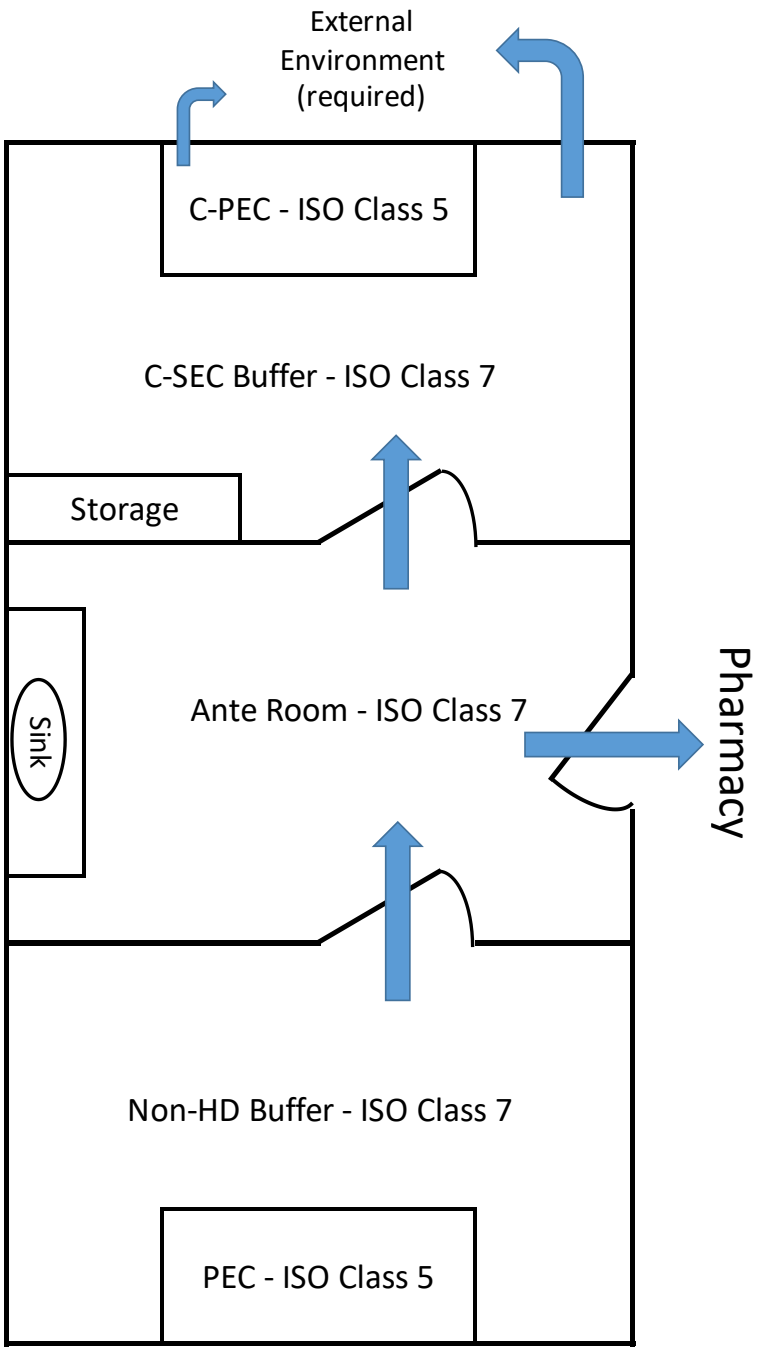
3. High Risk Sterile C-SEC and C-PEC Arrangement



"used" for presterilization procedures

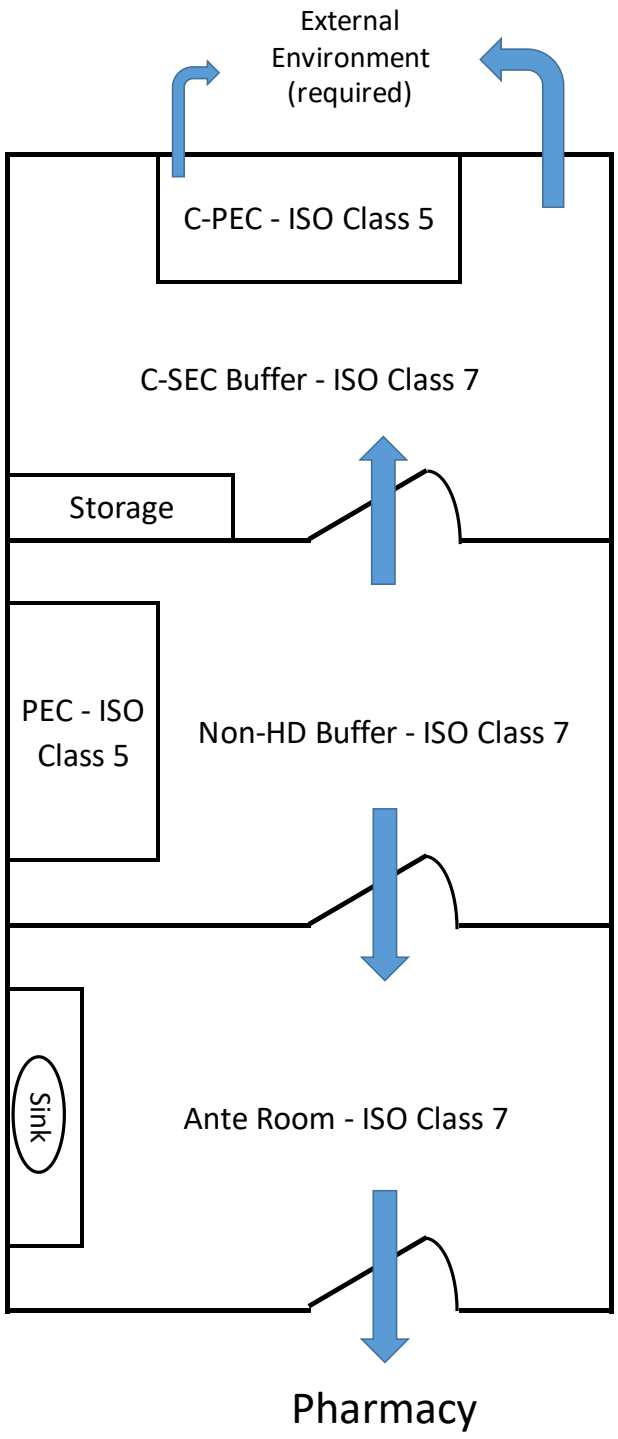
Attachment F– Pg. 4

4. Preferred Hazardous and Non-Hazardous Sterile C-SEC and C-PEC Arrangement



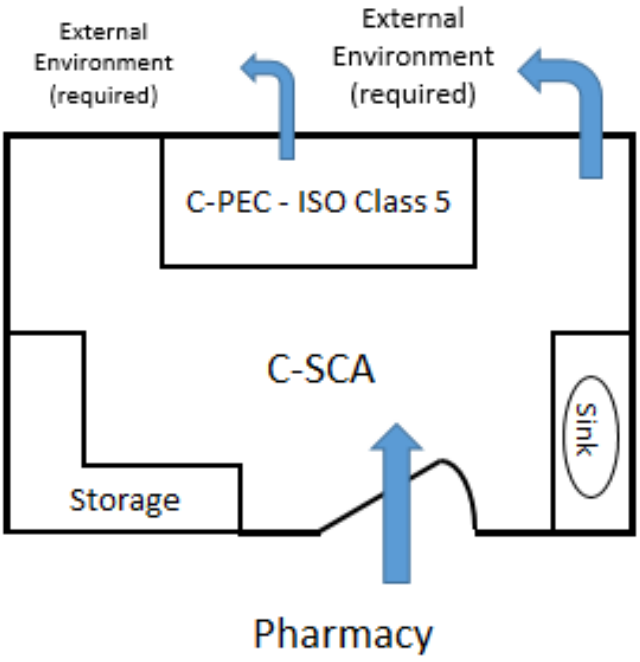
Attachment F – Pg. 5

5. Non-Preferred Hazardous and Non-Hazardous Sterile C-SEC and C-PEC Arrangement



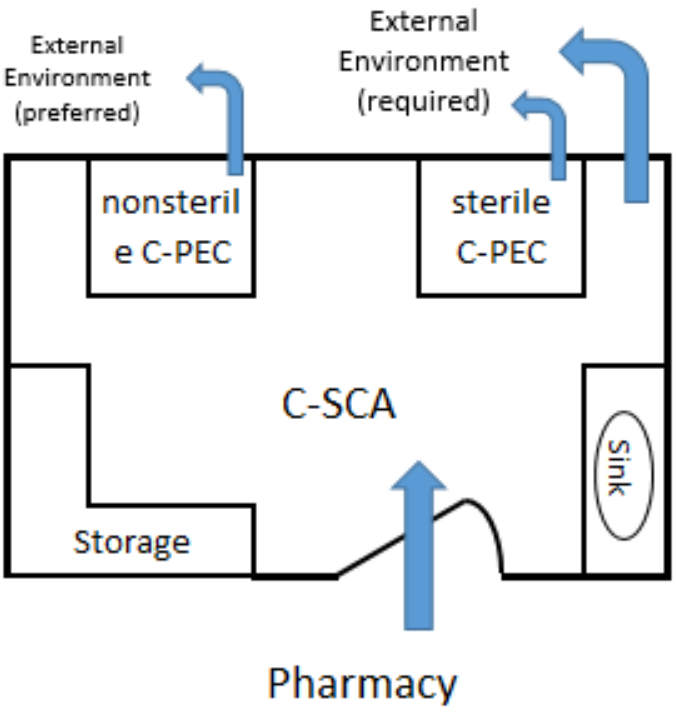
Attachment F – Pg. 6

6. Sterile C-PEC within a C-SCA



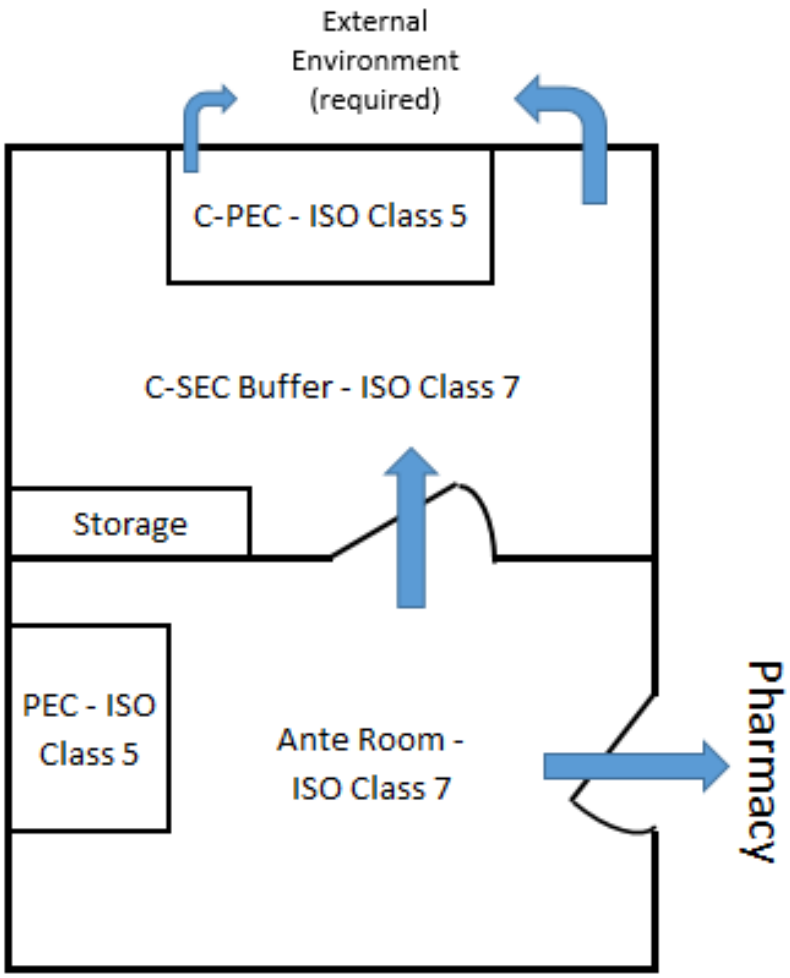
Attachment F – Pg. 7

7. Sterile and Nonsterile C-PECs within a C-SCA



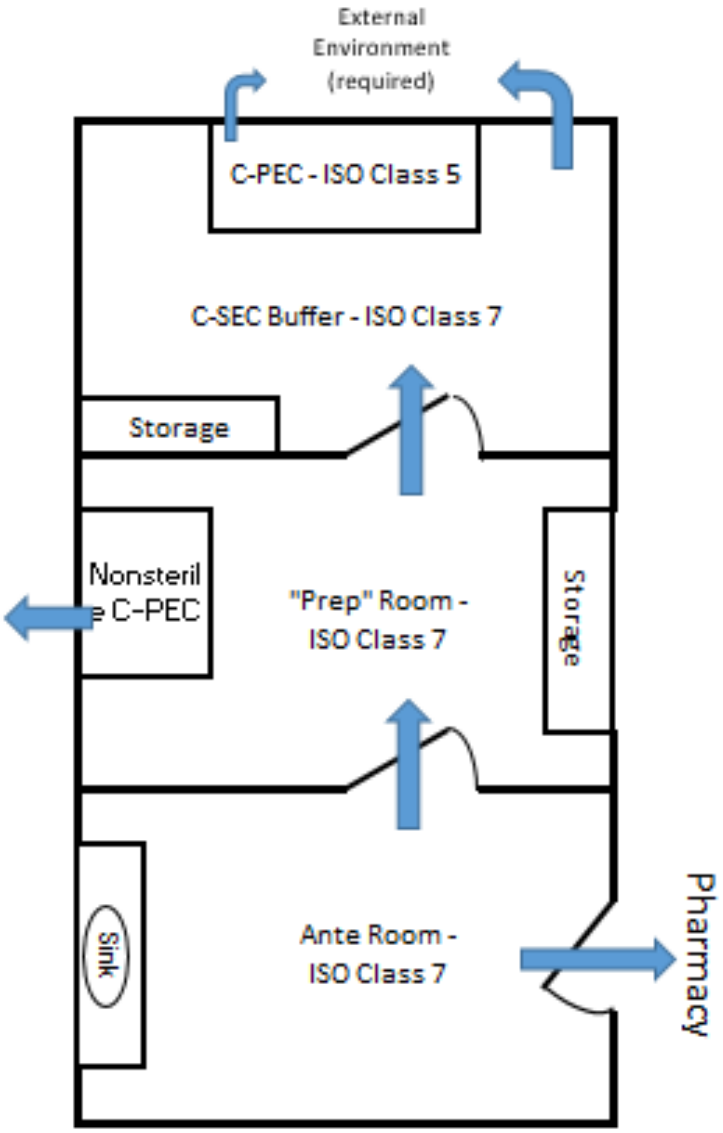
Attachment F – Pg. 8

8. "Oncology Clinic" Arrangement



Attachment F – Pg. 9

9. Sterile and Nonsterile Hazardous Drug Arrangement



Attachment G

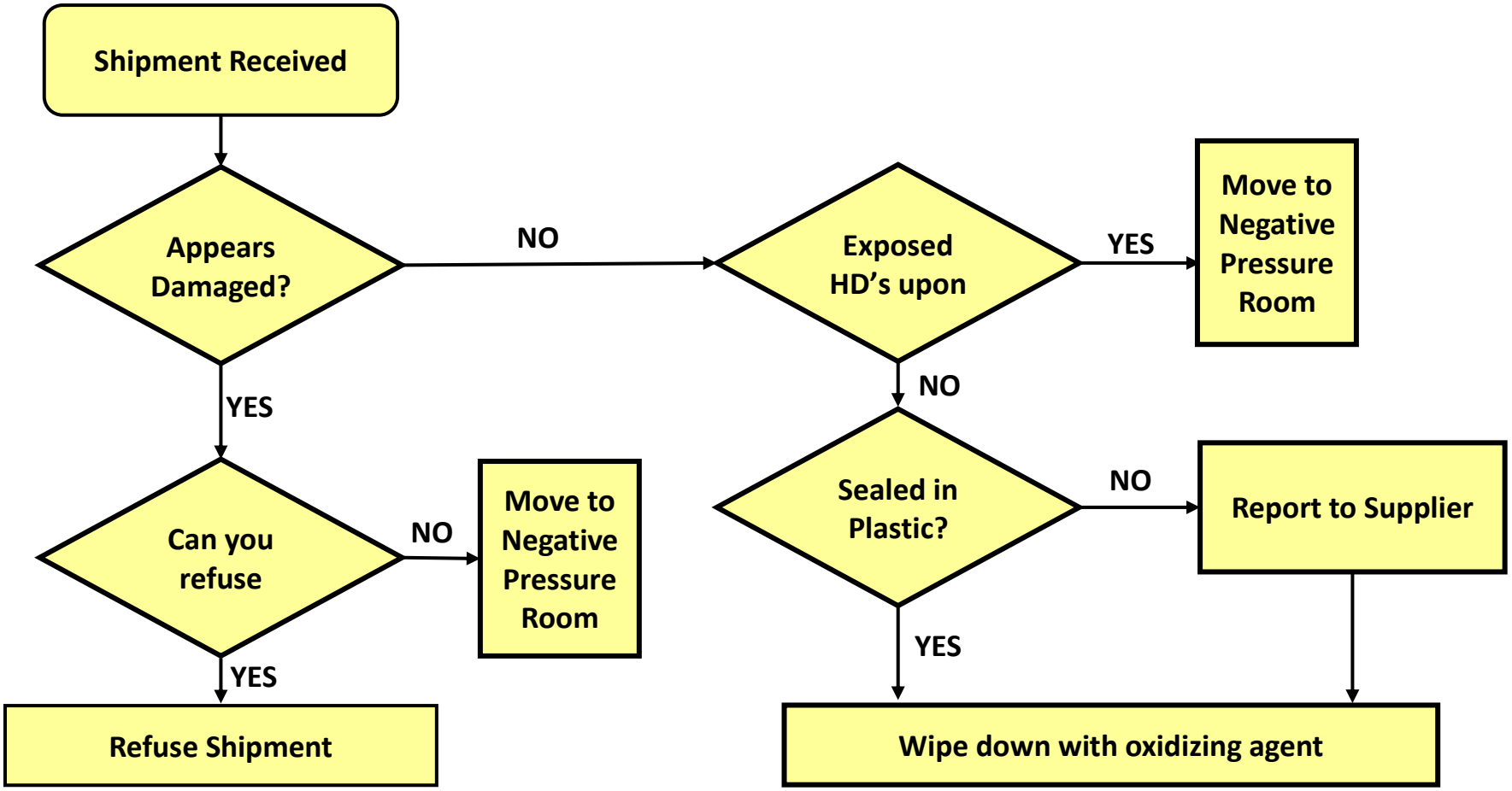
Personal Protective Equipment

Activity	Gloves	Gowns	Sleeve Covers	Head / Hair Cover	Shoe covers	Eye / Face [12]	Respiratory Protection
Receipt & Storage							
General	1 pair [2]						
Not in plastic	1 pair [2]	BPR					N95
Suspected breakage	1 pair [2]	BPR					N95 - BPR
Compounding [8]							
Nonsterile	2 pair [2]	Yes [7]	Optional [4]	Yes [5]	2 pair [11]		
Sterile	2 pair [2, 3]	Yes [7]	Optional [4]	Yes [5]	2 pair [11]		
Administration	2 pair [2, 6]	13				Yes [1]	

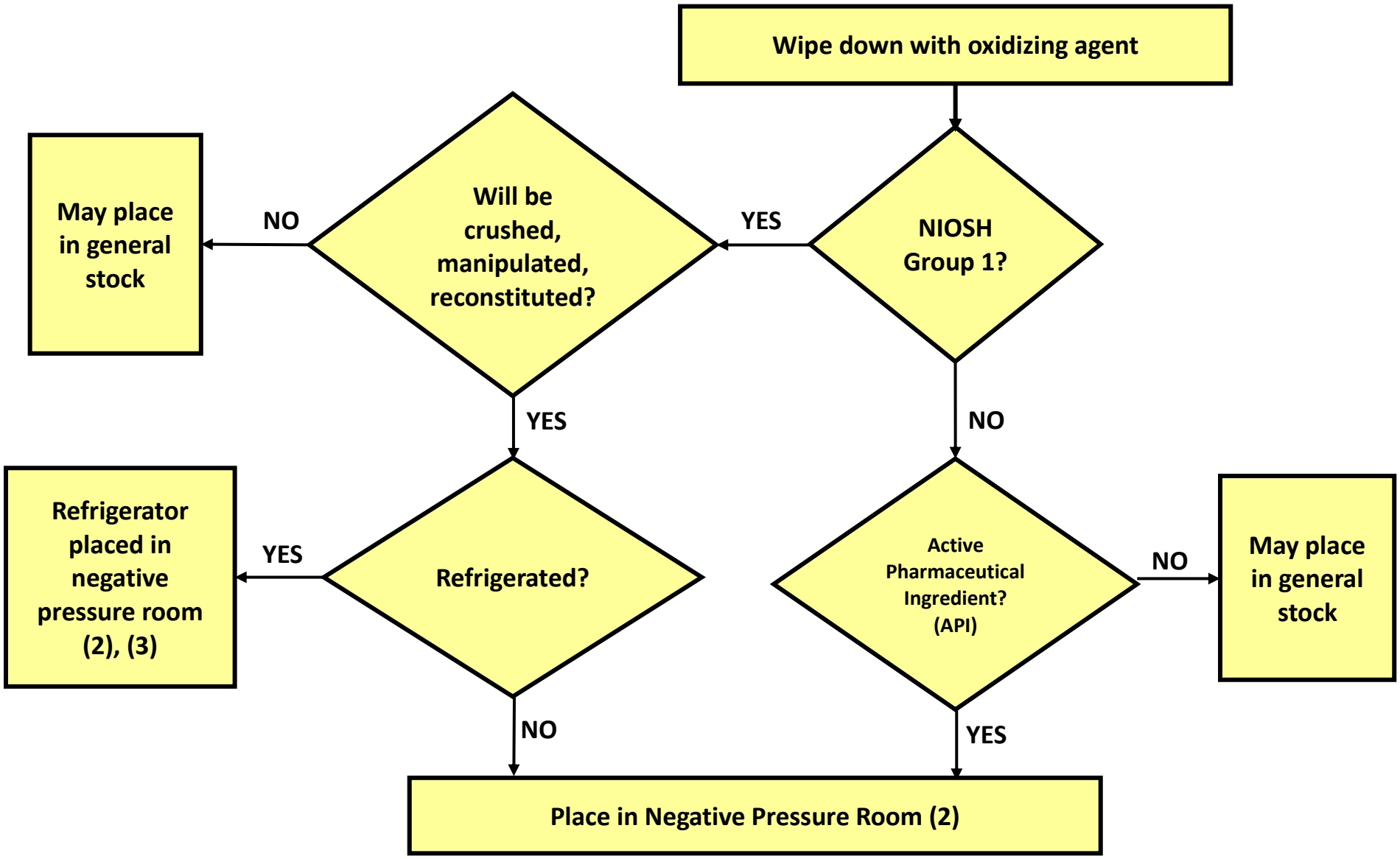
Activity	Gloves	Gowns	Sleeve Covers	Head / Hair Cover	Shoe covers	Eye / Face [12]	Respiratory Protection
Deactivation / Decontamination / Cleaning / Disinfection							
General	2 pair [2]	Yes [7]		BPR	BPR	1, 9	FFR - BPR [12]
Underneath C-PEC work surface	2 pair [2]	Yes [7]		BPR	BPR	1, 9	FFR - BPR [12]
Above eye level	2 pair [2]	Yes [7]		BPR	BPR	Yes [1]	FFR - BPR [12]
Spills							
General	BPR	BPR			BPR	Yes [1]	N95
Spill too large for kit	BPR	BPR			BPR	Yes [1]	FFR
Other suspected exposure to powder, vapor	BPR	BPR			BPR	Yes [1]	N95
Disposal	BPR	BPR					

Attachment H -Pg. 1

HD Reciept and Storage Flowchart



Cont. on next slide


Wipe down with oxidizing agent
NIOSH Group 1?
YES
Will be crushed, manipulated, reconstituted?
NO
May place in general stock
NO
YES
Refrigerated?
YES
Refrigerator placed in negative pressure room (2), (3)
NO
Active Pharmaceutical Ingredient? (API)
NO
May place in general stock
YES
Place in Negative Pressure Room (2)

Attachment H – Pg. 2

HD Receipt and Storage

1 - Essentially all antineoplastic injections
2 - Externally ventilated, negative pressure room with ≥ 12 ACPH. A C-SEC may be used, but avoid storage of nonsterile items in a C-SEC used for sterile compounding to avoid additional entrances and departures.
3 - If the room is a C-SEC, attempt to place refrigerator coils near air-intake vent, or use a "solid state" refrigerator

Examples	Storage Location
Any active pharmaceutical ingredient (API)	Externally ventilated negative pressure room with ≥ 12 ACPH
NIOSH Group 1 manufactured product to be crushed or used in compounding	
NIOSH Group 1 manufactured product requiring refrigeration	Externally ventilated negative pressure room with ≥ 12 ACPH or C-SEC
NIOSH Group 1 manufactured product simply to be counted and packaged	Regular stock

Attachment I

NIOSH Group Shipping Categories

NIOSH Group 1			NIOSH Group 2, 3
Internal transport / use, e.g. inpatient or outpatient clinic	**Ground transport: courier, driver, employee**	**Common or premium carrier (e.g. USPS, UPS, FedEx)**	Use reasonable packaging and protection as would for any non-HD drug product
Use reasonable packaging and protection as would for non-HD other drug product	Use reasonable packaging and protection as would for non-HD other drug product	Ground limit: 4 liters total in box	BPR: place in a re-sealable bag that can be used for its final disposal
However, place in re-sealable bag that can also be used for final disposal	However, place in re-sealable bag that can also be used for final disposal	Air limit: 1 liter total in box	Special labeling not required
Bag must be labeled, e.g. "Hazardous Drug: Dispose of Properly"	Bag must be labeled, e.g. "Hazardous Drug: Dispose of Properly"	Must use "Packaging Group III" qualified containers	
Do NOT use pneumatic tube for transport	BPR is to package as if for common carrier transport	Bag must be labeled, e.g. "Hazardous Drug: Dispose of Properly"	
		Label container "E" for "Exempt"	

Attachment J

USP <800> Preparation Checklist

This checklist is a successor to the USP <800> Gap Analysis posted on the* Compounding Today *website approximately one year ago. It includes new information and recommendations as to how best to comply with USP <800> by July 1, 2018.

It should be seen as an accessory to the Hazardous Drug Consensus Statement, which will be available free of charge on* Compounding Today *in the near future. This document will provide in-depth interpretations of USP <800> as well as best practice recommendations provided by a group of seasoned and diverse experts.

Preliminary Work

Criteria	Current Status	Plan	Assigned To	Target Date
Assemble a Hazardous Drug Library consisting of at least:				
Source 1 - USP Chapter <800> Hazardous Drugs - Handling in Healthcare Settings - available most economically via purchase of USP's Compounding Compendium for $150 per year. http://www.usp.org/store/products/usp-compounding-compendium.				
Source 2 - NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016 www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf				
Source 3 - Controlling Occupational Exposure to Hazardous Drugs - https://www.osha.gov/SLTC/hazardousdrugs/controlling_occex_hazardousdrugs.html				
Source 4 - ASHP (American Society of Health-System Pharmacists) [2006]. Guidelines on handling hazardous drugs. Am J of Health Syst Pharm 63:1172-1193. https://www.ashp.org/-/media/assets/policy-guidelines/docs/guidelines-handling-hazardous-drugs.ashx?la=en				

Program Management - USP <800> Section 4

Create a job description for the Designated Person (DP) required to manage all aspects of hazardous drug handling that includes at least the following elements:

Creating and implementing procedures (typically in the form of SOPs) concerning HDs				
Performing a documented annual review of these SOPs (as per Section 17 of USP <800>)				
Monitoring compliance with these SOPs and relevant rules and regulations				
Ensuring worker competency (which reasonably also entails coordinating worker training)				
Ensuring "environmental control" of areas where HDs are found and handled, e.g. through environmental wipe sampling				
Overseeing facility monitoring, managing related documents, and acting on results, including incident reports concerning HDs (as may be inferred from Section 10 of USP <800>				
Identify an individual to become DP.				
Ensure that the DP has or obtains sufficient training, time and resources to fulfill his/her duties.				
Ensure that all workers understand the importance of the DP role, and are ready to support it.				

Developing and Maintaining a List of Hazardous Drugs - USP <800> Section 2

Create a hazardous drug and substance list:

Identify all drugs stocked or likely to be stocked that appear on the NIOSH List 2016 (Source 2 above)				
Add additional hazardous or dangerous substances, e.g. strong acids or bases, toxic cleaning agents, etc., as desired.				
Make this list available to all workers with potential exposure to HDs				
Conduct a documented in-service with all workers as to the location and nature of this list.				
Ensure that this list will be reviewed and edited as needed at least annually.				
Ensure that new HDs introduced to the workplace will be added to this list, and workers notified.				

Risk Assessment and Exposure Control - USP <800> Sections 2, 3

Create a Risk Assessment Matrix (Attachment A) in which a number from 1 to 4 as read from the Severity Classification Matrix is assigned to each type and exposure route to items on the HD List in the Assessment Matrix.				
Create a mitigations table (Attachment B), starting with items that have the highest score from the assessment matrix, where potential mitigations are identified.				
Condense these potential mitigations in an action item list (Attachment C).				
Implement these actions, modifying changes in standard operating procedures (SOPs) as needed.				
Ensure that the risk assessment will be reviewed at least annually, and whenever there are significant changes in process, facilities or equipment, or based upon undesirable environmental sampling or medical surveillance results.				

Standard Operating Procedures - USP <800> Section 17

Ensure that SOPs exist that cover the following topics with regard to HDs. (These may be stand-alone documents, or incorporated into existing ones.) (References to relevant sections of USP <800> are provided in parentheses when applicable.)

Process

Receipt (5.1, 10)				
Storage (5.2)				
Hand hygiene and PPE (7)				
Compounding (5.3, 13)				
Labeling (11.1)				
Packaging (11.2)				
Transport (11.3)				
Dispensing (12)				
Administration (14)				
Deactivation / Decontamination / Cleaning / Disinfection (15)				
Spill control (10, 16)				
Disposal (11.4)				

Administrative and General

List of HDs (2)				
Engineering controls (5)				
Safe work practices (-)				
Exposure prevention / reduction (-)				
Environmental monitoring (6)				
Safe work practices (-)				
Training and competency (8, 9)				

Training and Competency - USP Sections 8, 9

Identify all workers, including part time, per diem, and contracted, who are exposed to HDs (see the list of tasks on Attachment A).
Develop a training program including at least the following topics:

Entity's List of HDs				
Reference materials and their use (HD List, SDSs, SOPs)				
Risks associated with handling HDs				
Relevant SOPs				
Personal protective equipment (PPE)				
Use of engineering controls and other equipment				
Exposure and spill management				
HD waste disposal				
Deactivation, cleaning and disinfection				
Compounding techniques unique to HDs, e.g. negative pressure technique, or use of CSTDs for sterile compounding				
Deliver and document this training.				
Ensure that this training will be delivered to any new workers.				
Decide if reinforcement training will be provided periodically.				
Develop a competency testing process for all workers exposed to HDs based on the Tasks on Attachment A.				
Decide if process validation using some fluorescent "marker" substance will be included in some aspects of competency testing such as compounding, deactivation and cleaning, and spill management.				
Observe and document competencies.				
Ensure that similar competency testing will be performed at least annually.				
Create a Hazard Communication Program (HCP) so as to meet OSHA requirements in this regard. A template may be found at: https://www.osha.gov/dsg/hazcom/docs/State_of_Wisconsin_revised_Hazcom_Plan_2012.pdf.				

Facilities and Equipment - USP Section 5.3, 5.4

C-PECs

Containment primary engineering controls (C-PECs) used for sterile compounding of HDs are externally vented.					
Containment primary engineering controls (C-PECs) used for nonsterile compounding of HDs are either externally vented or use "redundant" HEPA filters.					
C-PECs are certified annually if used for nonsterile compounding and every six months if used for sterile compounding.					

C-SECs

Containment secondary engineering controls (C-SECs) used for nonsterile HD compounding:

Are fixed wall					
Feature smooth, impervious walls and ceilings					
Feature a sink for hand washing located at least 1 meter from the C-PEC					
Are at a negative pressure of 0.01 - 0.03 inches of water with regard to the area from which it is entered					
Feature 12 or more air changes per hour (ACPH)					
Are externally vented to the outside environment					

Containment secondary engineering controls (C-SECs) used for sterile HD compounding of the buffer room and ante room configuration:

Are fixed wall					
Feature smooth, impervious walls and ceilings					
Feature a sink for hand washing in the ante room that is located at least 1 meter from the entrance to the buffer room					
Are at a negative pressure of 0.01 - 0.03 inches of water with regard to the ante room					

Feature 30 or more ACPH					
Feature a buffer room externally vented to the outside environment					
Feature an ante room with at least ISO Class 7 air with a positive pressure with respect the area from which it is entered of at least 0.02 inches of water					
Containment secondary engineering controls (C-SECs) used for sterile HD compounding of the containment segregated compounding area (C-SCA) configuration meet the same requirements as listed above for C-SECs used for nonsterile HD compounding.					
C-SECs are certified annually if used for nonsterile compounding and every six months if used for sterile compounding.					

Other equipment:

An eye wash station is "readily available" within a nonsterile C-SEC or C-SCA, in the ante room of a sterile C-SEC, and other locations of potential HD exposure.					
Antineoplastic HDs requiring refrigeration are placed in a negative pressure room, either a separate room or a C-SEC.					
Shelving and supplies are kept at a minimum with C-SECs to reduce the total surface area upon which HDs might collect.					

Personal Protective Equipment - USP <800> Section 7

Review Attachment G for compliance with required or recommended personal protective equipment (PPE).
Create a customized version of this diagram based on your actual practice, and ensure its use in conjunction with an SOP on this topic.

Review the following requirements and recommendations regarding PPE:

PPE should not leave the areas where HDs are handled.				
Reusable equipment such as eye and respiratory protection should be treated with a deactivating agent and cleaned after each use, and before being removed from areas where HDs are handled.				
Treat all disposable PPE as "trace" contaminated waste unless known to have been significantly contaminated with an HD, in which case it should be treated as "bulk" contaminated waste.				

Receipt and Storage - USP <800> Sections 5.1, 5.2, 10

Receipt

Develop and implement processes concerning the following topics:				
The refusal of obviously damaged shipment containers suspected of containing HDs				
How to handle HD shipments that arrive apparently or actually damaged that cannot be refused, or undamaged shipments that, upon opening, contain exposed HDs, including (a) transport to a C-PEC if possible (b) containment in, e.g., a sealable plastic bag (c) labeling as "hazardous" (d) quarantine until arrangements are made for their disposal as "bulk" hazardous waste, or their return				

The wiping of all received HD containers with an oxidizing agent such as dilute sodium hypochlorite or hydrogen peroxide so as to remove any residues on the container				

Storage

All HDs that are active pharmaceutical ingredients (APIs) or antineoplastics (NIOSH Group 1) that will be crushed or in some other way "manipulated" are stored in a negative pressure, externally vented room with at least 12 ACPH.				
For nonsterile compounders, this might often be the C-SEC; for sterile compounders, it might often be the C-SEC buffer room.				
The storage area should feature smooth, impervious walls and ceilings similar to a C-SEC if it is a different room.				
Antineoplastic (NIOSH Group 1) HDs requiring refrigeration must be placed in a negative pressure environment. If this is a C-SEC buffer room, place the refrigerator close to an air exhaust duct if possible.				
HDs such as capsules or tablets that will only be counted and packaged need not be stored under special conditions.				
Shelving should be smooth, impervious, easily cleaned, and "lipped" if possible to reduce the chance of HD containers falling and breaking.				
HDs should not be stored on the floor.				

Compounding - USP Section 13

Review compliance with the following best practice recommendations concerning HD compounding:

Assemble and introduce into the C-PEC all needed supplies, equipment, ingredients and containers prior to compounding.				
Use closed-system drug-transfer devices (CSTDs) whenever the HD container allows their use.				
Use negative pressure technique when extracting a liquid from a closed container if a CSTD cannot be used.				

Conduct actual compounding upon a disposable "plastic-backed preparation mat" placed on the C-PEC work surface.				
Use a separate set of utensils dedicated to HD compounding whenever possible and applicable.				
Retain all used containers, supplies and other waste within the C-PEC, placing them in a waste container built into the C-PEC, or into a resalable plastic bag kept within the work area during the preparation.				
When applicable for sterile preparations, tubing should be attached and "primed" prior to the introduction of HDs into the main vehicle container.				
Wipe down finished containers and, if applicable, tubing, with an oxidizing agent, e.g. hydrogen peroxide, followed by a "dry wipe" so as to remove HD residues or byproducts.				
Collect and dispose of all remaining waste in either the built-in waste container or into a plastic bag that is then sealed and disposed of in a larger trace hazardous waste container.				
Deactivate and clean (and, for sterile compounding, disinfect) the interior of the C-PEC after each compounding activity.				

Labeling, Packaging, Transport and Dispensing - USP Sections 11, 12

Ensure that HD final product labeling complies with state board of pharmacy requirements.				

Ensure that antineoplastic (NIOSH Group 1) HDs shipped via common or premium carrier, e.g. FedEx, UPS, USPS, comply with the following requirements:

The amount of HD transported by ground does not exceed 4 liters per box.				
The amount of HD transported by air does not exceed 1 liter per box.				
Containers comply with "Packaging Group III" requirements as verified with the vendor providing containers used in shipment.				

Review compliance with the following best practice recommendations concerning HD labeling, packaging, transport and dispensing of antineoplastic (NIOSH Group 1) HDs:

Use "reasonable" packaging and protection that will prevent product damage and spillage.				
Place the product in a re-sealable bag that is labeled along the lines of "Hazardous Drug: Dispose of Properly."				
Do not use a pneumatic tube system for the in-house transport of "liquid HDs or any antineoplastic HDs."				

Administering - USP Sections 14, 5.4

If involved in HD administration:

Obtain Appendix G of Source 4 and review current practices for compliance with this document.				
Ensure that closed-system drug-transfer devices (CSTDs) are used whenever the container allows when administering antineoplastic (NIOSH Group 1) drugs.				

Deactivating, Decontaminating, Cleaning and Disinfecting - USP <800> Section 15

Review compliance with the following best practice recommendations concerning deactivation, cleaning and disinfection:

On at least a daily basis, equipment used in HD compounding, including C-PECs, scales, etc., are routinely treated with a decontaminating oxidizing agent such as sodium hypochlorite or hydrogen peroxide followed by cleaning with a detergent solution.				

In the case of sterile compounding, this is followed by the use of a disinfectant (unless the product used for decontamination or cleaning also serves this function).				
Liquid decontaminating, cleaning and disinfecting agents are not sprayed onto objects, thereby avoiding the potential spread of HD contaminants.				
Reusable utensils involved in HD compounding or handling are similarly decontaminated and cleaned after each use.				

Disposal - USP Sections 7.6, 11.4				
Consider obtaining a consult with the vendor who provides your hazardous and biohazardous disposal containers to ensure compliance with all current local, state and federal rules and regulations regarding HD disposal.				
Ensure that the following items are treated as "trace" hazardous waste:				
Containers and tubings with less than 3% by weight of the HD still remaining in them				
All disposable utensils and supplies involved in compounding HD preparations or cleaning areas where these products are compounded or stored				
PPE used in the compounding, cleaning or administration of HDs unless significantly contaminated				
Ensure that the following items are treated as "bulk" hazardous waste:				
Containers and tubings with more than 3% by weight of the HD remaining in them				
Significantly contaminated utensils, supplies and PPE used in compounding, cleaning, administration or other handling activities involving HDs				
Materials used in cleaning HD spills				

Spills and Exposure Events - USP Section 16					
At least one spill kit, either assembled by the entity or purchased commercially, is "readily available" to the area or areas where HDs are received, stored, compounded, prepared for shipment, and disposed of.					
Kits are periodically, e.g. monthly while performing expired drug checks or facility cleaning, inspected to ensure they are present and have not been used.					
There is a list of workers authorized to use HD spill kits that will ensure that at least one such person is present at all times the entity is occupied.					
At least annually, all such workers are given a documented in-service on kit location and use.					
At least annually, document that all workers know the location of spill kits, the definition of a spill, and who is authorized to manage a spill should it occur.					
At least annually, document that all workers know the definition of an "exposure event," such as the splash of caustic substances to eyes or skin, and how they should be handled.					

Environmental Monitoring - USP Section 6					
Should the entity decide to conduct environmental wipe sampling as suggested but not required by USP <800>, contact an analytical lab or vendor to discuss such a program.					
The entity should consider the periodic examination of all areas where HDs are stored, compounded and disposed of, and reusable utensils and equipment cleaned, with an ultraviolet light with overhead lighting turned off so as to detect fluorescence indicative of potential HD contamination.					

Medical Surveillance - USP Section 18					
Should the entity decide to conduct a medical surveillance program for workers exposed to HDs as suggested but not required by USP <800>, contact an occupational health clinic or similar resource to discuss such a program.					

Attachment K

Hazardous Drug Acknowledgement Statement

I understand that working with hazardous drugs in a pharmacy setting might cause health issues such as rashes, infertility, miscarriage, birth defects, and possibly cancer.

I understand that the accidental exposure to some of these drugs might additionally cause irritation or damage to skin, eyes, or other exposed body parts.

I understand that the pharmacy will follow reasonable policies and procedures in order to minimize my exposure to these drugs in accordance with commonly available information and guidance by such entities as the FDA and OSHA.

I understand that the pharmacy will also provide for safety measures such as spill kits and eye wash stations to help limit my exposure to, or limit the results of, accidental exposure to such drugs.

I also understand that these policies and procedures will be routinely reviewed and revised as needed in light of new information.

I have been provided with training concerning hazardous drugs, and have passed a test verifying my understanding of key information concerning them.

I understand that similar training will be repeated at least annually.

_____ _____

Printed Employee Name Date

_____ _____

Employee Signature Date