July 31, 2014

Via Electronic Submission

US Pharmacopeial Convention
12601 Twinbrook Parkway
Rockville, Maryland 20852-1790

Re: Comments on Proposed General Chapter USP <800>
Hazardous Drugs – Handling in Healthcare Settings

On behalf of the Board of Directors and members of the International Academy of Compounding Pharmacists (IACP), I am pleased to submit the accompany series of comments to the proposed General Chapter USP <800> pertaining to Hazardous Drugs – Handling in Healthcare Settings.

Before beginning our detailed review of the draft standard, IACP wishes to again reiterate our position as outlined in a joint letter sent by six pharmacy organizations on July 10, 2014 to USP CEO Ronald T. Piervincenzi, Ph.D. That letter stated, in part:

We respectfully request that the chapter be numbered above <1000> in order to be classified as a general information chapter, imparting best practices. Although there are many best practices included in the proposed chapter, the impact on our members and their patients is too great at this time and compliance would be extremely difficult if not insurmountable to the vast majority of pharmacies and pharmacists.

Our members are currently held to regulations and guidelines from the Environmental Protection Agency (EPA) and the Occupational Safety and Health Administration (OSHA) which detail the handling of hazardous material, and although we appreciate the intent of the proposed chapter <800>, anything duplicative of currently enforceable rules can lead to confusion.

By placing this chapter above <1000>, our members will be afforded the opportunity to perform the appropriate analyses, including cost impacts and the impact upon the delivery of services to patients, and integrate best practices where appropriate. Given that no assessment of the financial impacts or the potential disruption to medication access has been conducted during the development of the proposed chapter <800>, we believe placing this chapter above <1000> to be the most prudent and appropriate course of action for USP. In addition, we recommend that a re-evaluation of implementation of the standards after a period of time occur, before consideration of renumbering the chapter.

IACP firmly believes that the renumbering of this chapter to above <1000> is critical to the ability of our members to assess and implement the key components of the standard while balancing the needs of patients and healthcare providers.
1. Introduction

1.2 Objective

*Lines 29-42.*

This includes but is not limited to receipt, storage, mixing, preparing, compounding, dispensing, administering, disposing and otherwise altering, counting, crushing or pouring HDs, and includes both sterile and nonsterile products and preparations.

*IACP Comment*

IACP is very concerned that the stated intent of this entire chapter so overly broad as to impose extensive burdens upon the entire health care and medication delivery system in the United States. Essentially, USP is proposing to significantly affect the day-to-day practice of all pharmacies, all wholesalers, all distributors, all hospitals, all clinics, all long-term care and assisted living facilities, and even veterinary practices without any assessment of whether or not the proposed standards will jeopardize patient access to medicines. Specifically, and which will be identified further in our comments, there are a number of manufactured prescription drugs containing ingredients deemed by NIOSH to be “hazardous” that are dispensed each and every day in pharmacies, administered by health-care staff, or self-administered by patients for which there is no scientific evidence of a true hazard but would still automatically require compliance with this chapter.

1.3 Overview

*Line 50*

*There is no acceptable level of personnel exposure to HDs.*

*IACP Comment*

This statement is unrealistic because it ignores existing and comparable approaches for minimizing and accommodating personnel exposure to other hazardous products. For example, the Nuclear Regulatory Commission (NRC) defines the processes by which personnel are to be monitored for exposure to radiation in oncology treatment centers and in nuclear pharmacies, how those risks are to be minimized, and establishes the guidelines for monitoring exposure.

Stating as a standard the unachievable expectation of “no acceptable level” will have the unintended consequence of pitting employees and personnel against employers, leading to litigation with the resultant increased cost to the overall health care system. Additionally, such a “black/white” mindset ignores the very real day-to-day exposure to so-called “hazardous” drugs such as hormones that individuals encounter from others, from the food chain, and in products used on a daily basis. It would be impossible, given this standard as written, to achieve such a perfect pharmacy vacuum of “no acceptable level of personnel exposure” when outside that bubble – in their homes, their communities, and society in general – personnel may be encountering the very same products and hazardous drugs.

This line is also contradicted by the clause and meaning within line 51 that reads that USP <800> is “intended to provide containment of HDs to as low a limit as reasonably achievable.” The phrase “no acceptable level” and “as low a limit as reasonably achievable” are two distinctly different levels. The former is an unacceptable statement; the latter is what should be the goal and objective.
Suggested Revision

The purpose of this chapter is to minimize personnel exposure to HDs.

Lines 52-53

HDs shall be compounded in proper engineering controls, as defined in this chapter.

IACP Comment
While USP 800 has tried to define “proper engineering controls,” the definitions and requirements for such controls listed in the following pages often contradict one another. This document should be revised to identify where discrepancies within those engineering controls exist, where new requirements may be unnecessary or redundant, and to recognize that the currently written definitions are flawed and incomplete and may require change.

Suggested Revision

HDs shall be compounded in settings with proper engineering controls as suggested in this chapter.

Lines 82-87

List of referenced documents from the American Society of Health-System Pharmacists and the Oncology Nursing Society

IACP Comment
IACP does not believe that a quasi-governmental standard setting body such as USP should reference documents or materials that are produced by non-profit professional associations unless USP has adequately vetted the process by which information was obtained, how it was reviewed, who was involved in the review process, and whether or not the materials were in any way influenced by individuals or corporations which had an economic interest in the setting of those guidelines or recommendations. Unlike OSHA and NIOSH, these organizations do not have a defined and open comment and review process whereby non-member associations and individuals may participate in their creation. In short, there is no means to assure that these documents are indeed, best practices but only recommendations from professional organizations with vested interests.

Suggested Revision

2. List of HDs

Lines 112-125

The National Institute for Occupational Safety and Health (NIOSH) maintains a list of antineoplastic and other HDs used in healthcare. The entity shall include all items on the current NIOSH list and may add others not on the NIOSH list. The entity’s list shall be reviewed at least annually and whenever a new agent or dosage form is used. If the information provided is deemed insufficient to make an informed decision, the drug should be considered hazardous until more information is available. Some dosage forms defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (e.g., coated tablets or
capsules—solid, intact medications that are administered to patients without modifying the formulation). Uncoated tablets may present a risk of exposure from dust by skin contact and/or inhalation when the tablets are counted. Any solid dosage form may pose a risk if altered, such as by crushing tablets or making solutions. The entity’s standard operating procedure (SOP) (see Appendix B) shall identify the risk mitigation strategies for items on the entity’s list of HDs.

**IACP Comment**

USP <800> proposes that all healthcare settings, including community and compounding pharmacies, must include all drugs included in the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2012. It appears, however, that USP did not review the preface to the list as NIOSH itself states in multiple places that there is uncertainty about the contents of the list as well. Indeed, NIOSH itself asserts in Appendix A under “General Approach to Handling Hazardous Drugs” that “no attempt has been made to perform drug risk assessments or propose exposure limits.”

IACP is seriously concerned about the inclusion of many non-antineoplastic drugs on the NIOSH list because of the potential for a drastic change in the provision of common medications to patients. We believe the list in and of itself to be of questionable reliability.

Perhaps the uncertainty about the accuracy of this list is no more in evidence than the inclusion of such commonly used medications as azathioprine, carbamazepine, clonazepam, all estrogen containing contraceptives and hormone replacement therapies, finasteride, megesterol, methyltestosterone, phenoxycbenzamine, raloxifene, tamoxifen, tetracycline, and zidovudine. Each and every one of these “hazardous drugs” are dispensed by pharmacists, administered by nurses or medication aides, or self-administered by patients each and every day. In order to comply with this list – and by extend USP <800>, every pharmacy in the United States would have to establish a hazardous drug risk mitigation SOP for dispensing a cycle of birth control pills.

While it does not appear that the USP Expert Committee reviewed the content of the list for appropriateness when developing this standard, it also appears that the Committee either unintentionally overlooked or intentionally ignored the caveats included within the document by NIOSH itself. The blanket adoption of the NIOSH list by USP as a legally enforceable standard was not what the list maker itself intended. Rather, and as stated repeatedly through the NIOSH introduction, this list was developed to provide guidance to health care facilities – not act as a mandate.

Complicating matters further is that NIOSH acknowledges, as does the literature, that there is little evidence that these drugs are actually hazardous to healthcare personnel.

In an article entitled *Understanding the New Proposed USP Chapter <800>* written by Luci A. Powers, MS, RPh and Eric S. Kastango, MBA, RPh, et al., states numerous times that there exists no reportable number of deaths or injuries resulting from the handling of hazardous drugs (HD) in the workplace. Although intended to argue the point of needed implementation, the following passage taken directly from the article in fact contradicts this point drastically:

> Since the first reported HD exposures, one of the roadblocks to achieving HD safety compliance has been the lack of documented evidence that HDs cause harm to health care workers. There is no clear, reportable number of deaths or injuries resulting from the handling of hazardous drugs (HD) in the workplace...so accurate counts remain elusive.

The article goes on to state; “to date there is no conclusive proof of the link between HD exposure and cancer in health care workers...” In addition, the studies referenced by the article (http://www.cdc.gov/niosh/topics/antineoplastic/pubs.html), primarily deal only with antineoplastic drugs,
begging the question as to the accuracy of lumping all hazardous drugs into one category. Even the “NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2012” admits that there is a severe lack of published data as to how to define a hazardous drug, and in turn recommends that each organization create its own list of drugs considered to be hazardous, and that “this document presents guidance for making such a facility-specific list.” It goes on to say “compliance requires practice-specific assessments for drugs used at any one time by a facility.”

Additionally, the 2012 NIOSH list is currently under revision. Many of the drugs being added to the list for the forthcoming 2014 update are also commonly used medications in community, acute and post-acute treatment centers. These include: abacavir, abiraterone, apomorphine, deferiprone, dexmetotomindine, ezogabine, fluconazole, misoprostol, nevirapine, spironolactone, topiramate, ulipristal, and warfarin. These non-chemotherapeutic medications have not been demonstrated to be hazardous to personnel – yet, USP is unwittingly consigning them to the level of HDs solely because of their inclusion on a “recommended” list.

Suggested Revision
Replace lines 112-117 with the following:

The entity shall develop a list of hazardous drugs based upon practice-specific assessments of drugs used at any one time within its facility. The entity shall establish a process for an assessment of new drugs as they are used and when appropriate include them on the list of hazardous drugs. Entities are encouraged to use reference sources including the NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings when developing their list of hazardous drugs.

Remove lines 118 to 123.

Retain lines 124-125.

The entity’s standard operating procedure (SOP) (see Appendix B) shall identify the risk mitigation strategies for items on the entity’s list of HDs.

4. Responsibilities of Personnel Handling HDs

Lines 170-177

Each entity shall have a compounding supervisor who is the designated individual responsible for developing and implementing appropriate procedures; overseeing facility compliance with this chapter and other applicable laws, regulations, and standards; ensuring competency of personnel; and assuring environmental control of the compounding areas. The compounding supervisor shall also be responsible for the continuous monitoring of the facility and compounded sterile preparations (CSPs), including reports of all testing from all contractors and laboratories on facilities, CSPs, and/or their components.

IACP Comment
Although throughout the draft standard references are made to administration of HDs, this section appears to be solely focused on the establishment of an individual responsible for the oversight of compounding activities. There are no provisions here for the creation of an individual within an entity with responsibilities outside of those personnel engaged in compounding. For example, in institutional facilities where patient administration occurs, an individual outside of the pharmacy and/or compounding location should be designated and hold corresponding responsibilities for the assurance that all HD administration occurs in compliance with established laws, regulations and standards. Yet, that is not
specified in this draft. In institutional faculties where storage and handling of HDs occurs, including disposal and spill management, outside of the areas where compounding activities occur, an individual within the facility other than the pharmacy department should be designated and hold corresponding responsibilities for the assurance that all HD storage and handling occurs in compliance with established laws, regulations and standards. That is not specified in this draft. In healthcare delivery models where in-home administration of potential HDs occurs (e.g., home infusion services), an individual outside of the pharmacy and/or compounding location should be designated and hold corresponding responsibilities for the assurance that all HD administration, disposal, and spill management occurs in compliance with established laws, regulations and standards.

As written, this portion of the standard leaves a significant gap in accountability or appears to be an attempt to hold the compounding supervisor solely responsible for the handling of all HDs within a facility even if that individual has neither the authority nor the ability to assure compliance with laws, regulations and standards in departments other than the pharmacy.

What specifically is USP attempting to accomplish with this section that fails to include such significant and obvious instances where HD handling, storage and administration require unique expertise far greater than just that of the poorly outlined “compounding supervisor”? Aside from identifying an individual responsible for management of the compounding of HDs, it appears that USP has neglected to carry forward the other components of its own standard to assure that all health care entities are capable of compliance and will establish the necessary individual responsible for compliance with the standard.

**Suggested Revision**

IACP believes this entire section needs to be revised to specify the individuals within an entity who are engaged in various aspects of HD management as outlined in Section 3, lines 136-167. No single person, including a “compounding supervisor” has the ability to comply with this section.

**5. Facility Design and Engineering Controls**

**5.1 General Guidance**

**Lines 207-213**

*Signs designating the hazard shall be prominently displayed before entry into the HD area.*

*Separate designated areas shall be available for (see Appendix D):*

- Unpacking HDs
- Nonsterile HD compounding (if performed by the entity)
- Sterile HD compounding (if performed by the entity)

*Designated HD handling areas shall be segregated from non-HD areas."

**5.2 Storage of HDs – General Observations**

**Lines 220-223**

*HDs shall not be stored, unpacked, compounded, or otherwise manipulated in an area that is positive pressure relative to the surrounding areas. A laminar air flow workbench (LAFW) or compounding aseptic isolator (CAI) shall not be used for the compounding of an HD.*
IACP Comments

This would require that all areas with HD's (sterile or non sterile) would have to be in a negative pressure room for unpacking, storage and dispensing unless in unit of use packaging. What about physical limitations/capital expense involved in making the receiving area negative pressure? Will manufacturers/outside vendors/purchasing groups separate HD's from non HD's and label accordingly? What happens if the items are mixed? What is potential for cross contamination within the totes? Cleaning guidelines for totes containing HD's? Most hospital pharmacies have USP <797> compliant clean rooms for sterile processing. However most do not have negative pressure rooms for receiving areas. What will the impact/limitations for retail settings be for dispensing/handling HD's will be implemented. Will all medications on the NIOSH list be included such as those listed above which are commonly used in pharmacy settings that are non-antineoplastics?

Suggested Revisions

This section needs further exploration as the currently written standard fails to outline how storage requirements and receipt of materials from outside suppliers may not be handled in a manner consistent with USP <800> placing undue burden upon the compounding section of the entity.

Lines 237-240

Unless the HDs already exist in their final unit dose or unit-of-use packaging, HDs shall be stored separately from other inventory in a manner to prevent contamination and personnel exposure, which includes storage in a negative pressure room with at least 12 air changes per hour (ACHPH).

Lines 237-240

Refrigerated HDs shall bored in a dedicated refrigerator in the HD storage room, buffer room, or containment segregated compounding area (C-SCA). In a containment secondary engineering control (C-SEC) used for sterile preparations, an exhaust located adjacent to the refrigerator’s compressor and behind the refrigerator should be considered.

Lines 250-252

Storage of sterile and nonsterile HDs may be intermingled. HD storage in sterile compounding buffer area shall be limited to those used for sterile compounding (see chapter (797)).

IACP Comment

As the standard is currently written, it could be interpreted that there are meant to be 9 (nine) total separate, designated areas for drugs and drug handling.

1. (Line 210) Unpacking of HDs.
2. (Lines 237-240, Lines 250-251) Storing non-refrigerated HDs (sterile and non-sterile) in a negative pressure room
3. (Line 242) Storing of refrigerated HDs (sterile and non-sterile) in a negative pressure HD storage room
4. (Lines 216-217, Lines 237-238) Storing of non-HDs
5. (Line 242) Storing of refrigerated non-HDs (possibly two separate refrigerators required for refrigerated sterile vs. non-sterile non-HDs)
6. (Line 211) Nonsterile HD compounding  
7. (Line 212) Sterile HD compounding  
8. (Line 211) Nonsterile Non-HD compounding  
9. (Line 212) Sterile Non-HD compounding

With the understanding that HDs should be treated appropriately, and safely, we must consider the environments in which HDs are used. Many pharmacies which provide compounding services or which receive and dispense drugs deemed to be hazardous have neither the space nor the means necessary for the renovations required to meet the proposed standard in its current form. Additionally, many institutional facilities including hospitals and long-term care facilities, physician offices, outpatient clinics, oncology clinics, and veterinary offices do not have the space nor the ability to execute the necessary establishment of these areas to satisfy the proposed standard.

Has USP conducted any economic impact assessments on the cost to implement this section of the standard? If so, from whom and in what manner was that assessment conducted? If not, has there been any determination of the effect of this standard and its potential nine separate areas for unpacking, storing, handling, etc. on whether an entity may choose to discontinue providing HDs despite medical necessity because of undue cost burden?

IACP believes that all pharmacies’ share a responsibility in promoting the safe handling of drugs, however this requirement puts a heavy financial burden on our members to create handling areas that may be overkill for the safe handling practice that this standard is trying to embody.

**Suggested Revision**

IACP believes this entire section needs to be revised to specify specifically whether these different areas may be combined or be in the same physical location as well as address the cost burden associated with the implementation of this standard’s requirement.

**Lines 229-230**

For occasional nonsterile HD compounding...

**IACP Comment**

No definition of “occasional” is provided. We are concerned that such vagueness creates a new “lower floor” that will vary between entities – some having a more stringent definition (hourly) vs. others (weekly). Without a definition, entities may define it based upon their own economic needs rather than a defined and consistent standard.

**Suggested Revision**

Provide a clear definition of what constitutes “occasional” or reword the sentence in its entirety to provide specificity.

**Lines 237-240**

Unless the HDs already exist in their final unit dose or unit-of-use packaging, HDs shall be stored separately from other inventory in a manner to prevent contamination and personnel exposure, which includes storage in a negative pressure room with at least 12 air changes per hour (ACPH).
IACP Comment

Many non-sterile compounds such as those containing estrogens or progesterone do not pose a significant threat of volatilization. Should finished compounded preparations such as semi-solid dosage forms and solid dosage forms which may contain an HD be packaged in additional overwraps? Does USP intend that those completed preparations be stored in a negative pressure environment prior to delivery either to the patient, the patient’s agent or to an individual within a facility who will be responsible for administration? In those instances where a compounded HD is dispensed from the pharmacy and is sent to a hospital medication room prior to administration, what storage requirements would be necessary? Does this standard not also imply that such non-compounding area storage locations be also negative pressure and contain the appropriate air handling systems? This is not addressed.

Additionally, we would like to comment on another section with 237-240 requiring the storage room for HDs to be externally ventilated. It may not be possible for certain compounding businesses to meet the requirement in its current form for a number of reasons. To begin, this requirement may be impossible to put into practice for many compounding locations that don’t have ownership of place of business.

Even if ownership of space is met, externally ventilating a room can cost approximately $1500 per every ten feet of ductwork required. This does not account for the cost of the blower on the roof – another $2000 nor the electricity to continuously run the blower (required by the proposed standard- line 422).

It should be noted that this estimate per 10’ of ductwork is only for those labs that have a straight shot to the external environment. For labs where ductwork may need to make a 90-degree angle, additional charges will need to be taken into account for each turn.

In addition, this estimate does not take into account the cost of additional HVAC systems to create the make-up air necessary to meet the 12 ACPH required by the proposed USP 800 standard. Because the standard requires that this system pull continuously, we must consider the amount by which each lab’s energy bill will increase in order to heat and cool this make-up air. Without knowledge of the size of each storage room, a typical HVAC system pulling at 100lpm (which should give a 10’ x 10’ room at least 12 ACHPH) costs approximately $5000 USD per year to run (of course costs will raise and lower slightly due to a change in kWh per location).

These costs are estimates to meet the requirement on lines 237-240 that all HD storage areas should be externally ventilated. External venting of Containment Primary and Secondary Engineering Controls are evaluated below in our comments.

Suggested Revisions

Again, the draft standard states its objective as minimizing personnel exposure to HDs throughout an entity; however, the written standards appear solely to be for the handling of HDs within the compounding and/or pharmacy environment. There is a significant running disconnect between the stated objectives, the written standards, and the practicality of implementing those standards in a meaningful way throughout a healthcare facility. IACP recommends a complete review of the intent of this section.

IACP requests that USP examine the costs associated with the implementation of these standards for external venting and determine the impact on access to medications, the ability of existing facilities and entities to comply with this standard.
5. Facility Design and Engineering Controls

5.1 General Guidance

Lines 227-228

When asepsis is not required, a Class I BSC, CVE, or an isolator intended for containment applications may be sufficient. A Class II BSC may be used if it is dedicated for nonsterile preparations.

5.3 Engineering Controls

5.3.1 Background

Lines 256-258

Within this chapter, engineering controls are divided into three categories representing primary, secondary, and supplementary levels of control (see Appendix A and Appendix C for more details). C-PECs provide the environment at the point of use and are integrated into the C-SEC (i.e. room). The C-SEC supports the C-PEC. Supplemental engineering controls are adjunct controls [e.g., closed-system drug-transfer device (CSTD)] used in conjunction with primary and secondary control strategies.

Lines 263-266

HDs that require alteration shall be manipulated (mixed, diluted, compounded, and others) in a C-PEC in an area that is physically separated from other preparation areas, that is under negative pressure, and has at least 12 ACPH. Additional criteria are listed below.

5.3.2 Containment Primary Engineering Controls

Lines 268-269

All C-PECs shall be externally vented and place in a restricted access segregated room with has a minimum negative pressure of 0.01 inches of water column.

IACP Comments

While we recognize and agree with USP’s attempt to create a safer environment for pharmacists and technicians working with HDs, we feel that the current standard creates unrealistic expectations for working environments. First and foremost, it should be understood that a total exhaust hood (an externally ventilated hood), is not possible for a majority of pharmacies that work with HDs. As previously stated, many small compounding businesses have neither the space nor the means necessary for the renovations required to meet the proposed standard in its current form.

Similar to the requirement for external venting of HD storage areas, external venting of all C-PEC’s may not be attainable for all compounding pharmacies. For example, not all pharmacies have ownership of their physical place of business. This may force pharmacies to close unnecessarily due to a C-PEC requirement that cannot be physically met. Furthermore, this regulation puts an unrealistic monetary
requirement upon pharmacies dealing with HDs that may be able to externally vent their C-PEC, but may not be able to fiscally afford to do so.

For example, in order to externally ventilate a 4’ hood at 100 lcfm for a typical workweek, the pharmacy will be required to pay not only for the hood, but for its installation, ductwork, bends in ductwork, blower requirements, make-up HVAC air, and electricity costs associated with heating and cooling that make-up air. These costs are explained above, but can be estimated at approximately: $5,000 per hood, $1,500 per 10’ of straight ductwork, $2,000 per required blower, and $5,000 - $7,000 per hood for heating and cooling costs associated with make-up air. These estimates are per hood, and do not include bends in ductwork, make-up HVAC, and electricity costs associated with running the blower.

Please note, these costs should be multiplied for the number of hoods the pharmacy requires.

IACP believes that the requirement of externally ventilating the C-PEC is unnecessary. If other C-PEC solutions did not exist in today’s marketplace, we would gladly support the installation of total exhaust (externally ventilated) hoods. With recognition that these externally ventilated/total exhaust hoods exist for certain applications, we feel that this is unnecessary for the provision of compounding services and the protection of personnel from HD exposure at this time.

If the USP feels that a single pass through HEPA/ULPA filtration is not appropriate, then dual-pass designs should be considered as an alternative to total exhaust hoods. These hoods push contaminated air through two stages of HEPA/ULPA filtration before venting back into the room. Ductless hoods with this design have been tested and certified by third parties as appropriate for use with HDs, APIs, etc. In addition, ductless designs are typically cheaper than the total exhaust hood alone and only cost approximately $200 per year in energy cost to run.

Because of their design, HEPA/ULPA filters simply filter to a standard. These standards are 0.3 microns or larger with a 99.997% efficiency for HEPA and 0.12 microns or larger with a 99.95% efficiency for ULPA filters.

**Suggested Revisions**

Since ductless variations exist that push contaminated air through a two-stage HEPA/ULPA filtration process, we believe that these hoods should be accepted as C-PECs without the requirement of external exhaust.

### 5.3.3 Containment Secondary Engineering Controls

**Lines 271-272**

> HD compounding activities must occur within a C-SEC where any C-PEC shall be vented to the outside air through high efficiency particle air (HEPA) filtration.

**IACP Comment**

Requiring that a C-PEC run through HEPA filtration before being exhausted is more than likely more harmful to the user in its current state. HEPA filtration will capture 99.97% of all HD, API, non-HD, etc. powders that are larger than 0.3 microns in size.
Suggested Revision

If the standard is hoping to externally vent all evaporated vapors, then carbon filtration should be considered in conjunction with dual-pass HEPA/ULPA filtration in ductless designs as appropriate.

5.4 Nonsterile HD Compounding

5.4.1 C-PEC for Nonsterile HD Compounding

Lines 281-282

Nonsterile HD compounding shall be performed in a C-PEC that provides personnel and environmental protection, such as a Class I BSC or CVE.

Lines 284-285

The C-PEC used for nonsterile compounding shall be externally vented.

IACP Comment

IACP Comment

It should be noted that throughout the standard, a Class I BSC is deemed appropriate for use. By definition, Class I BSC air is “passed through a HEPA/ULPA filter either into the room or to the outside in the exhaust plenum, providing environmental protection” (Appendix C: Types of Biological Safety Cabinets. USP 800 proposed chapter. 2014.)

Therefore, according to the standard, non-sterile hazardous drug compounding can be done in a non-externally ventilated area.

Suggested Revision

Requirements for external venting for compounding of non-sterile HDs should be eliminated from the proposed standard.

6. Personal Protective Equipment

6.5 Respiratory Protection

Lines 552-554

Personnel unpacking HDs that are not contained in plastic should wear an elastomeric half-mask with a multi-gas cartridge and P100-filter. If the type of drug can be better defined, then a more targeted cartridge could be used.

IACP Comments

It should be known that Class I BSC cabinets exist for the unpacking of HDs and bulk HDs that are not contained in plastic, but rather small, medium, or bulk containers. These cabinets utilize specially blended carbon specific to the user’s compounding (during liquid handling) and a dual HEPA/ULPA filtration method for ensuring containment of HD powders. These cabinets offer better airflow patterns overall, and safer HEPA/ULPA and carbon filtration than the elastomeric half-masks proposed.
Suggested Revisions
While not all pharmacies have access (or possibly the space) for such a device, we would like to propose that this type of device be included in lines (552-554) as appropriate measures of personal protection while unpacking HDs and bulk HDs that are not contained in plastic.

9. Receiving

Lines 644-648

HDs should be received from the supplier sealed in impervious plastic to segregate them from other drugs, to allow for safety in the receiving and internal transfer process, and should be immediately delivered to the C-SEC. HDs shall only be stored in areas with the ventilation controls described in this chapter.

IACP Comments

The C-SEC as defined earlier in the chapter is not necessarily the same space as the HD externally vented storage room. Lines (644-648) should note that delivery to either location is appropriate, should the standard continue to require a separate externally ventilated storage room for HDs.

12. Compounding HD Dosage Forms

Lines 750-781

Compounding personnel are responsible for ensuring that HDs are accurately identified, measured, diluted, and mixed and are appropriately sterilized (when appropriate), packaged, sealed, labeled, stored, dispensed, and distributed. These performance responsibilities include maintaining clean conditions and providing labeling and supplementary instructions for the proper administration of HDs.

Work practices for compounding nonsterile HD dosage forms shall include:

- Using requirements listed in chapter (795)
- Avoiding use of active pharmaceutical ingredients (APIs) if a suitable manufactured product is available and appropriate for use, e.g., using an injection rather than a bulk powder
- Manipulation of any HDs (such as crushing tablets or opening capsules) shall be performed carefully, within a C-PEC using appropriate PPE. Clean equipment (such as mortars and pestles, spatulas, and others) shall be dedicated for use with HDs. Crushing tablets or opening caps should be avoided if possible; liquid formulations should be used if oral solids are not appropriate for the patient.
- Handling bulk containers of liquid HDs carefully to avoid spills. These containers shall be dispensed and maintained in sealable, impervious plastic bags or other suitable containers to contain any inadvertent contamination.
- Ensuring that processes for labeling the compound do not introduce contamination into non-HD areas.
- Dispensing in the final dose and form whenever possible.

Work practices for compounding sterile HD dosage forms shall include:

- Using requirements listed in chapter (797).
- Avoiding the use of APIs if a suitable manufactured product is available and appropriate for use, e.g., using an injection rather than a bulk powder.
 Appropriately preparing materials used in compounding before introduction into the Class II BSC or the pa-through of a CACI (see chapter (797) for details).

- Ensuring that processes for labeling the compound do not introduce contamination into non-HD areas.

The compounding areas shall be properly cleaned after compounding activities.

IACP Comments

We believe that underlined sections above places an unnecessary restriction on the compounding pharmacist in regards to the use of APIs to force them to use manufactured, and liquid formulations. Requiring pharmacists to use pre-manufactured drugs or liquid formulations would appear to be both unnecessary and an added cost to the purchaser of ingredients. Additionally, existing federal law through the Drug Quality and Security Act provides a pathway for specifying those APIs which should not be used in compounding by physicians or pharmacists; the inclusion of this language in a USP chapter restricts the professional decision making of the professional.

14. Cleaning: Deactivation, Decontamination, Cleaning and Disinfection

Lines 814-824

Personnel performing cleaning activities (including compounding, direct care, environmental services, laundry, waste handling, and others) shall be protected from inadvertent exposure to HDs.

IACP Comment

While this section speaks to those individuals performing cleaning activities separate from the HD compounding function, we believe that the requirement for two pairs of ASTM chemotherapy gloves for all aspects of cleaning seems excessive and inconsistent with the existing guidelines and standards within health-systems. For example, as written, it would be assumed that such housekeeping staff involved in such typical cleaning activities as toilet scrubbing, linen removal and laundering would also be required to be appropriately protected with double-gloving even though no actual exposure to an HD would exist. Merely the treatment of a patient with an HD could be interpreted to mandate gloving, gowning, and even face masks although there is no evidence that the metabolites of an HD are of risk to personnel.

Does the USP Expert Committee truly envision this kind of activity in an anticoagulation clinic where patients who are currently on warfarin – a planned addition to the NIOSH HD list in 2014 – are regularly tested for their INRs? Because, in order to be compliant with this standard, all individuals who may become exposed to the blood of an HD treated patient could be at risk.

17. Environmental Quality and Control

Lines 941-946

To ensure containment of HDs, environmental wipe sampling to detect uncontained HDs should be performed routinely (e.g., initially as a benchmark and at least every 6 months, or often as needed, to verify containment). This sampling should include surface wipe sampling of the working area of C-PEC; countertops where finished preparations are placed; areas adjacent to BSCs and CACIs, including the floor directly under the working area; and patient administration areas.
IACP Comments

It appears that this practice should be suggested rather than required as it can create an added cost to the pharmacy owner. Additionally, and again, the chapter is moot on the sampling and containment of HDs outside the compounding area despite its intent to be all-inclusive. For example, in an outpatient oncology center, should all treatment rooms be tested and sampled? Similarly, should all areas where HDs are stored after delivery from the pharmacy be similarly tested? Who is responsible for that compliance and what, if any, influence or authority does the “compounding supervisor” defined above have in that area?

Suggested Revision

We suggest substitute language which emphasizes the development of SOPs rather than proscriptive mandates.

To ensure containment of HDs, environmental wipe sampling to detect uncontained HDs should be performed routinely (e.g., initially as a benchmark and at least every 6 months, or often as needed, to verify containment). The method of sampling and the areas to be sampled shall be specified in the entity’s SOPs.

19. Medical Surveillance

Lines 970-973

The goal of medical surveillance is to minimize adverse health effects in workers exposed to HDs. A medical surveillance program involves collecting and interpreting data to detect changes in the health status of working populations potentially exposed to hazardous substances.

Lines 977-978

Employers shall ensure that healthcare workers who are exposed to HDs are routinely monitored as part of a medical surveillance program.

IACP Comments

Upon initial read, the standard doesn’t seem to give clear instruction as to what the required medical surveillance practice is, nor what it should appear to be. We believe that the Expert Committee should define and/or provide specific references to the development and implementation of a medical surveillance program and what is considered to be acceptable or non-acceptable in terms of the structure, process, evaluation, and implementation as well as the individual or corporation ultimately accountable for the program. Additionally, there are specific personnel and human resource issues which may arise in order to comply with a mandatory exit physical that may conflict with HIPAA. It does not appear that this has been considered by the Expert Committee. IACP is also concerned with the significant additional cost burden that a medical surveillance program may have on a compounding pharmacy that must institute such a program with mandatory physicals when that pharmacy may not currently provide health or medical insurance coverage for its employees.

We have additional questions about this entire section and its implementation. There is concern that the overall program for employee monitoring needs additional detail. The references provided in the draft standard give some guidance, but not as much definition as needed. It will be important to know what is required and how much latitude the facility will have to define the program. Chemotherapy programs
have consistently used certain products as "markers" - will these be identified in the future by USP or would that be left to the individual facility. What specifically does “handling” by an employee constitute and how will past hours spent handling be measured and documented as well as differentiated from potential exposure to HDs at other facilities and in environments external to the entity’s?

The IACP membership, comprised of more than 2,200 pharmacists and pharmacy technicians engaged in the specialty practice of prescription drug compounding, provided many questions and observations to our Academy that indicate a deep concern about the economic impact – both in capital investment as well as in extensive staff training and SOP revisions – which the proposed general chapter <800> would require. We believe as a professional association that while well intended, this chapter may have significant impact on the ability of many compounding pharmacies to provide services to their patient and provider communities. Given that representatives of USP specifically stated that no assessment of cost or impact was conducted prior to the publication of this draft chapter, IACP believes that further study is absolutely required.

Again, IACP strongly encourages USP to renumber this chapter to above <1000> so that it may serve as a guideline which the profession of pharmacy may implement and, given the lessons learned with the implementation of USP <797>, provide time to identify inconsistencies, unreasonable and unworkable standards, and make the necessary corrections and adjustments in order to facilitate the achievement of the overall objective of protecting personnel from the consequences of HD exposure.

IACP thanks you for your consideration of our comments and we look forward to additional dialogue with USP as it balances these and others recommendations during the review process for general chapter <800>.

Sincerely,

[Signature]

David G. Miller, R.Ph.
Executive Vice President & CEO

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