American Hospital Association

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July 31, 2014

United States Pharmacopeial (USP) Convention
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: USP Proposed General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings; Pharmacopeial Forum 40(3) [May–Jun. 2014].

To Whom It May Concern:

On behalf of our nearly 5,000 member hospitals, health systems and other health care organizations, and our 43,000 individual members, the American Hospital Association (AHA) appreciates the opportunity to comment on the United States Pharmacopeial (USP) Convention's proposed new general chapter *<800> Hazardous Drugs – Handling in Healthcare Setting*. According to USP, this chapter was created to identify the requirements for receipt, storage, mixing, preparing, compounding, dispensing and administration of hazardous drugs (HDs) so as to protect patients, health care personnel and the environment.

Protecting health care personnel from harm resulting from occupational exposures to environmental hazards, including HDs, is a priority for hospital and health systems. However, the significant compliance costs of the proposed chapter may force hospitals that prepare only a low volume of HDs, particularly small hospitals in rural areas, to limit the range of services they provide, reducing access to care in these communities. **The AHA urges USP to revise its proposals to allow for alternative approaches that keep health care personnel safe and minimize the need to make major renovations to the health care facility.**

The AHA believes that USP standards should be based on well-founded evidence. However, as discussed further below, many of the proposed requirements lack such evidence. For example, one fundamental gap in chapter <800> is that USP does not have, and therefore cannot take into account, the quantified acceptable exposure rates for HDs. Without the ability to consider acceptable exposure rates for HDs, the chapter cannot appropriately balance the cost of the proposed changes to engineering controls and other requirements with benefits to employee health and safety.

In addition, there is no scientific evidence or other documentation cited to support USP's decision to exclude from proposed chapter <800> the low-volume exemption contained within the current USP chapter <797> *Pharmaceutical Compounding – Sterile Preparations*. This

exemption permits facilities that prepare a low volume of HDs to place a biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI) in a non-negative pressure room. By eliminating this allowance, draft chapter <800> would require all HD compounding to be done in a separate area, designated for HD compounding, under negative pressure. However, positive pressure rooms are the standard in small rural facilities; implementing negative pressure rooms would be a costly new requirement for many small and rural health care facilities that compound only a low volume of HDs.

Furthermore, USP fails to acknowledge the significant compliance costs that the proposed rule would generate for hospitals, pharmacies, clinics or physician practices, and other compounding centers. For example, one of our member health systems estimates that each of its small hospitals would be required to spend at least $100,000 to come into compliance with the basic engineering control requirements for the standards. This amount includes $20,000 for a negative pressure barrier isolator and $80,000 for renovations, including establishing negative pressure rooms and venting. Compliance costs could easily be higher in older buildings where asbestos abatement would be required. In a hospital with its pharmacy located in the basement, as is often the case, the lack of access to venting would require that a chemotherapy compounding room be constructed away from the central pharmacy or that the entire pharmacy be moved. As a result, the AHA is concerned that small hospitals, particularly those located in rural communities, could close their programs, resulting in reduced access to care. Programs involving chemotherapy drugs (which are often used for purposes other than to treat cancer) would be at particular risk.

Instead, the AHA urges USP to revise its proposal to allow for the use of alternative approaches for hospitals and other health care providers that compound only a low volume of HDs, similar to the USP chapter <797> exemption, as long they use other methods to protect the health and safety of their personnel. For example, one approach could be to allow the use of closed-system drug-transfer devices (CSTDs)[1], such as PhaSeal, within either a positive or negative pressure barrier isolator.

Our detailed comments corresponding to specific line numbers within proposed chapter <800> follow.

- Lines 115-117: With regard to the list of HDs that health care providers would be required to maintain, this section states: "If the information provided is deemed insufficient to make an informed decision, the drug should be considered hazardous until more information is available." This is an ill-advised and overly broad approach for handling drugs marketed without an adequate risk profile because it inappropriately makes health care providers accountable for information that should be provided by drug manufacturers. Instead, regulators should require drug manufacturers to provide the appropriate information necessary to determine if a drug, in all its formulations, is

[1] A CSTD is a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system as well as the escape of hazardous drug or vapor concentrations outside the system.

hazardous. Health care providers should not be required to employ unnecessary engineering controls or other protective measures.

- Lines 220-221: The draft standard would prohibit HDs from being stored or unpacked in an area that is positive pressure relative to the surrounding areas. However, USP does not explain or otherwise provide evidence about the risk associated with using a positive pressure room for receiving and storing HDs. Specifically, meeting this requirement would involve extensive ventilation changes to potentially large receiving and storing rooms. Hospitals indicate that this would be virtually impossible to do without moving the shipping containers and cartons into the negative pressure buffer area, which could introduce dirty and possibly contaminated (due to broken glass vials) containers and corrugated cardboard into this area.

  Furthermore, while not explicitly discussed, this prohibition suggests that shipping cartons are contaminated at the manufacturing source or during distribution. Once again, this chapter demonstrates that regulators are not appropriately holding manufacturers and distributors of HDs responsible for releasing a clean, non-contaminated shipping carton into the supply chain. The contamination of shipping cartons within the supply chain could place numerous persons at risk.

- Lines 237-240: This section would require that, unless HDs already exist in their final unit dose or unit-of-use packaging, they must be stored separately from other inventory, in a manner to prevent contamination and personnel exposure. Implementing this requirement would involve extensive changes to hospital storage and ventilation systems, yet there is no evidence that co-storage of HDs with other drugs poses a risk or has resulted in harm. Therefore, we question whether this requirement is reasonable or necessary.

- Lines 243-246: This section would require a containment secondary engineering control (C-SEC) used for sterile preparations to have an exhaust located adjacent to the refrigerator's compressor and behind the refrigerator. This requirement would be unnecessary if the products stored in the refrigerator instead were required to be kept inside an overwrapped container, so as to contain any HD residue on the product.

- Lines 267-269: This section would require all containment primary engineering controls (C-PECs) to be externally vented. However, this should be unnecessary when using CSTDs.

- Lines 271-272: This section would require HD compounding activities to occur within a C-SEC whenever a C-PEC is required to be vented to the outside air through high efficiency particle air filtration. As noted above, we believe that the proposed requirement that C-PECs be externally vented should be unnecessary when using CSTDs.

- Lines 431-441: This paragraph suggests that certain commercially available CSTDs provide inadequate containment of HDs and inadequate protection against the introduction of contaminants. However, at the same time, in line 440, the proposed standard would require that these CSTDs be used by health care facilities. Therefore, we recommend that regulators require manufacturers of these products to demonstrate efficacy in containing HDs and protecting against contaminants.

- Lines 588-590: This section would require employers to maintain copies of safety data sheets in the workplace. We recommend that USP clarify that employers may satisfy this requirement by maintaining electronic documentation.

- Line 941-946: This section would require routine environmental wipe sampling. This type of sampling is not readily available in health care facilities, and this requirement is premature in that there are no definitive data related to environmental exposure or quantified acceptable exposure rates. Furthermore, the requirement to use CSTDs should obviate the need for this requirement. That is, if CSTDs are effective, then no environmental contamination would exist, with the exception of a spill or accidental environmental exposure.

If you have any questions, please feel free to contact me or Roslyne Schulman, director of policy, at (202) 626-2273 or rschulman@aha.org.

Sincerely,

/s/

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