SPEAKING *of*...

High-Alert, High-Risk, and Hazardous Drugs

A Conversation with Patricia C. Kienle, RPh, MPA, FASHP

Patricia C. Kienle, RPh, MPA, FASHP
Director of Accreditation and Medication Safety
Cardinal Health Pharmacy Services

PP&P: **The terms high-alert, high-risk, and hazardous medications are sometimes used interchangeably. Is this a good idea?**

Patricia Kienle: Definitely not. Years ago, we often lumped everything together in the high-risk category. However, ISMP and other organizations suggested using the term "high alert" for drugs such as concentrated IV electrolytes, opiates and narcotics, insulin, and anticoagulants, and others as determined by the individual organization. Using the high-alert term for these types of medications sends a clear and more inclusive message throughout the whole medication use process, from receiving through administration.

When USP <797> became official, the term high risk suddenly took on new meaning. High-risk preparations as defined by <797> are essentially sterile preparations prepared from non-sterile ingredients.

Hazardous drugs are a completely different set of agents and are defined by the NIOSH alert. NIOSH, or the National Institute for Occupational Safety and Health, is part of the CDC. The agency's September 2004 alert titled "Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Healthcare Settings" outlines the process for determining what products are hazardous and how to manage those products. Furthermore, a list of suggested hazardous drugs is provided in Appendix A of the alert. While the bulk of these agents are chemotherapy drugs, there are others listed as well. In fact, a draft change to Appendix A was announced in April 2009, adding more recently approved drugs as well as removing one drug from the list.

It is important to recognize these three separate definitions and not use the terms interchangeably.

PP&P: **How is high risk defined?**

PK: In USP <797>'s revision bulletin there are three separate definitions for low, medium, and high risk. According to the bulletin, high risk "contains one of several non-sterile components," meaning that either the drug, the vial, or the container has been exposed to air worse than ISO Class 5, the classification of air in an IV hood. There are some additional issues that can cause a product to be categorized as high risk, such as compounding personnel who are improperly garbed or gloved, aqueous preparations that are stored for more than six hours before sterilization, or labeling or documentation from suppliers that was not verified. So while there are several different issues that can lead to defining a product as high risk, it is essentially those that are made from non-sterile drugs or components.

PP&P: **Does USP <797> also define hazardous drugs?**

PK: USP <797> addresses hazardous drugs, although in a different section from high-risk drugs since they are distinctly different issues. USP <797> generally follows the NIOSH definition, as it is intended to be compatible with the NIOSH alert.

PP&P: **In addition to identifying all the drugs that would fall into the high-risk category, what other identifying processes should pharmacy undertake?**

> **You need to know** where all the heparin is in your facility and how it is being handled.

PK: There are several steps that need to be taken. All sterile preparations that are being compounded need to be evaluated. While you may be familiar with practices in the pharmacy, it is crucial that you review what is happening on the nursing units and in the procedural areas, paying special attention to reviewing practices in the cath lab and interventional radiology. Pharmacy may not be aware of the large number of high-risk drugs, including heparin, being prepared in those areas. Keep in mind, the staff there do not think in the same terms as a pharmacist; do not simply ask whether IV heparin is being made because it is probably being used to flush catheters. You need to know where all the heparin is in your facility and how it is being handled. If you are distributing 10,000 unit vials of heparin to areas outside the pharmacy, it is highly likely that staff in those interventional areas are making some kind of mixture with it. These practices need to be brought under pharmacy control.

SPEAKING *of*...

Definitions

ISMP Definition of High-Alert Drugs
http://www.ismp.org/selfassessments/hospital/2004hospsm.pdf
Medications that have a high risk of causing serious injury or death to a patient if they are misused. Errors with these products are not necessarily more common but their results are more devastating. Examples of high-alert medications include heparin, warfarin, insulin, chemotherapy, concentrated electrolytes, opiate narcotics, neuromuscular blocking agents, thrombolytics, and adrenergic agonists. (A complete list can be found at www.ismp.org)

NIOSH Definition of Hazardous Drugs
http://www.cdc.gov/niosh/docs/2004-165/
Any drug identified by at least one of the following six criteria: carcinogenicity, teratogenicity or developmental toxicity, reproductive toxicity in humans, organ toxicity at low doses in humans or animals, genotoxicity, or new drugs that mimic existing hazardous drugs in structure or toxicity.

USP <797> Definition of High-Risk CSPs
http://www.usp.org/products/797Guidebook/
CSPs compounded under any of the following conditions are either contaminated or at a high risk to become contaminated:

1. Non-sterile ingredients, including manufactured products not intended for sterile routes of administration (e.g., oral), are incorporated or a non-sterile device is employed before terminal sterilization

2. Any of the following are exposed to air quality worse than ISO Class 5 for more than one hour:
   - Sterile contents of commercially manufactured products
   - CSPs that lack effective antimicrobial preservatives
   - Sterile surfaces of devices and containers for the preparation, transfer, sterilization, and packaging of CSPs

3. Compounding personnel are improperly garbed and gloved

4. Non-sterile water-containing preparations are stored for more than six hours before being sterilized

5. It is assumed, and not verified by examination of labeling and documentation from suppliers or by direct determination, that the chemical purity and content strength of ingredients meet their original or compendial specifications in unopened or in opened packages of bulk ingredients

The United States Pharmacopeial Convention. Revision Bulletin <797> Pharmaceutical Compounding–Sterile Preparations. 2008. pages 10-11.

The next step is to determine which current practices are appropriate, with the goal of eliminating or at least minimizing any preparation that occurs outside of pharmacy. Standardize solutions and purchase commercially available products when possible, and when that is not an option, any compounding should be done in the pharmacy. Finally, anything that is still prepared on the floor must meet the immediate use category in <797>.

Also, pay particular attention to hazardous drugs. With any drug we prepare, the goal is to protect the patient; but with hazardous drugs, we also need to protect the employees preparing the drug. The NIOSH alert provides excellent information on employee protection.

> Anything that is still prepared on the floor **must meet the immediate use category in <797>.**

***PP&P*: Is there a current, definitive list of hazardous drugs?**

PK: Appendix A in the NIOSH alert contains a list of hazardous drugs. In addition, the April 2009 draft update contains suggested changes to that list. However, Appendix A is not intended to be the only list used, rather it should be an organization's starting point. You then need to review products that are new to the market and analyze how they are used in your organization. Every organization should create a list of hazardous drugs that reflects its own practices. Many organizations assess new formulary agents—such as biologics—to determine if they should be handled as hazardous agents.

***PP&P*: Are all hazardous drugs covered under USP <797>?**

PK: USP <797> deals with sterile, parenteral agents only. While most hazardous drugs are parenteral, there are a number of hazardous drugs, such as finasteride, procarbazine, and podophyllum resin that are not. Therefore an assessment of hazardous drugs must include all dosage forms, not just parenterals.

***PP&P*: What steps would you recommend pharmacists take when conducting a formulary assessment?**

PK: Begin with an understanding of the distinction between high-alert, high-risk, and hazardous drugs as each of these items must be properly identified on the formulary. It may be easiest to identify the high-alert drugs first, as this is generally a relatively short list, including the agents previously mentioned: concentrated electrolytes, opiates, narcotics, insulin, and anticoagulants. Next, take a look from a USP <797> perspective at any high-risk drugs that are being prepared. Hazardous drugs also need to be identified starting with the list in the NIOSH alert and adding or deleting other agents as appropriate. Finally, go through the formulary and note those agents that have these special precautions. Make sure that all personnel, including purchasing and receiving staff, are aware of the special handling requirements, particularly those for the hazardous drugs. It is important that these staff members understand that they are dealing with hazardous drugs.

***PP&P*: How can purchasing and receiving staff be properly trained to handle**

> Too often **non-formulary items and patients' own medications slip** under the radar and are not properly addressed.

products that require special precautions?

PK: Start with an in-service and then document their competency in knowing what to look for. We cannot expect purchasing and receiving staff to understand specific drug issues, but they can identify products marked as hazardous. Your suppliers should all employ a method for identifying hazardous drugs, and the receiving and shipping personnel need to be able to recognize the particular color or warning signs on the packaging, know what the signs mean, and take the necessary special precautions.

***PP&P*: How should non-formulary items that enter the hospital be managed?**

PK: That is a very good point: Too often non-formulary items and patients' own medications slip under the radar and are not properly addressed. These are two important areas for pharmacy to manage. Start with an assessment to determine if any non-formulary agents or patients' own medications fall into any of these three categories. Pharmacy must identify these agents to ensure the staff members administering these products are able to identify their risks and follow the same precautions that would be in place for formulary items.

It is crucial to establish good policies and procedures in advance so that you are not simply reacting to challenges as they come up. The more practical your policies and procedures are, the more likely your staff will follow them consistently for every identified agent. ■

Patricia C. Kienle, RPh, MPA, FASHP, an employee of Cardinal Health since 1999, currently serves as the director of accreditation and medication safety. She is the recipient of an MPA in health service administration from Marywood College in Scranton, Pennsylvania, a BS in pharmacy from Philadelphia College of Pharmacy and Science, and has completed an executive fellowship in patient safety from Virginia Commonwealth University. Patricia is also an adjunct associate professor at Wilkes University in Wilkes-Barre, Pennsylvania.