How to Perform a Hazardous Drug Risk Assessment in the Compounding Pharmacy

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There is a looming deadline on December 1, 2019 and that is the implementation of USP chapter <800>-Hazardous Drugs, Handling in Healthcare Settings. State Boards of Pharmacy (SBOP) are forming task forces and committees to determine if their state will fully implement the chapter or if they will only implement certain components of the chapters. And yet there are other states that are unsure what to do and may push the enforcement further down the timeline. Regardless of what your SBOP has determined regarding USP <800> enforcement, it is still wise to examine the risks associated with hazardous drug chemical handling in your entity. Mitigating risk may not be at the forefront of your mindset, but like the USP <800> deadline, the issue of chemical exposure risk is looming in all healthcare facilities that handle hazardous drugs (HDs).

A comprehensive risk assessment of every single hazardous drug (HD) on the NIOSH hazardous drug list is not absolutely required, yet you will need to review the list and identify those drugs and dosage forms that you handle in your pharmacy.[2] In the absence of the assessment of risk, you must implement all containment strategies defined in the chapter. Full implementation of the engineering controls necessary to maintain negative pressure can be an expensive endeavor with residual energy costs, so taking the time to perform a risk assessment may prove to be financially advantageous. What we will outline and explain in this paper is the process of risk assessment is relatively simple and the process will surely uncover truths about our current workflow habits.

The introduction section of the USP <800> chapter reveals the non-defined terminology of "occupational safety plan." There is not a clear-cut definition of "occupational safety plan" because it is a broad scope term. It can be summed up as "physical activities" and the risk of exposure from those activities. The physical activities defined in the chapter are a series of singular activities such as (but not limited to), unpacking, cleaning, and HD's, storing HDs, compounding and mixing HDs, manipulating dosage HD dosage forms, administering HDs, and cleaning up spills and handling waste. All the defined singular activities form a comprehensive workflow process and are worthy of dissection because each activity could reveal one or multiple risks of exposure. The term "risk" is important to conceptualize because it is "defined as the combination of the probability of occurrence of harm and the severity of that harm."[1] A compounding pharmacy must devise an occupational safety plan and to adequately do so requires a risk assessment.

Potential Benefits of Performing a Risk Assessment:

1. Set Quality Assurance Processes (ref. USP 797, 795, 1163)
2. Set Internal Standards (ex: PPE; workflow processes)
   Additional Resource Article: *Workflow Strategies to Minimize Exposure to Hazardous Drugs in the Compounding Pharmacy*
3. Decision making gets better. (learning curve; establish corp. policy and Standard Operating Procedures)
4. Regulatory Assurance (documentation makes them happy)
5. Reputation (Patients and Providers)
6. Competitive Advantage (use as a marketing tool)

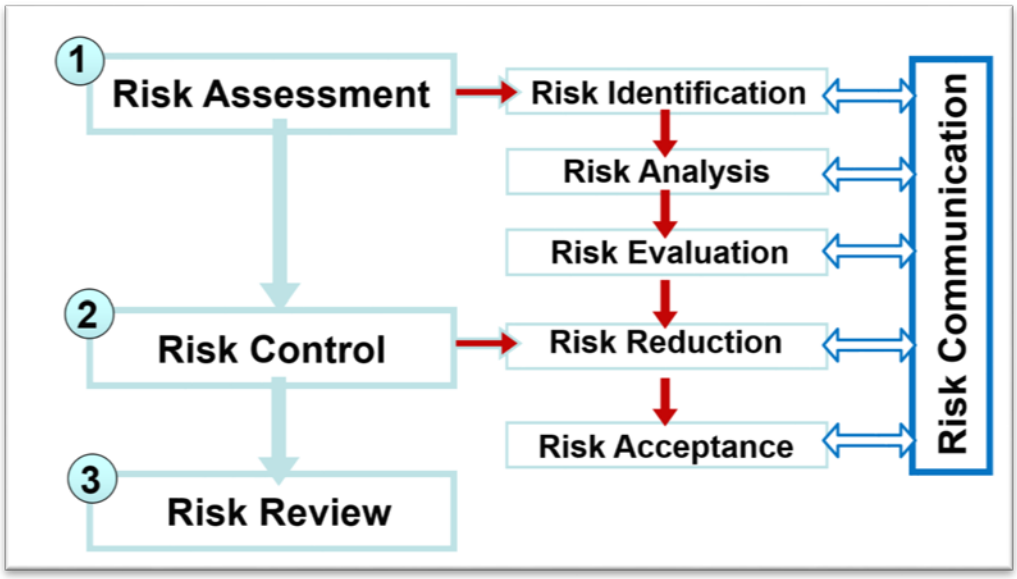
[1] Source: Guidance for Industry. Q9 Quality Risk Management. U.S. Department of Health and Human Services Food and Drug Administration. June 2006 ICH

2 Source: Kienle, P. *The Chapter <800> Answer Book*, Bethesda, MD: ASHP: 2017.

Stakeholders

Each person in the pharmacy has a different perspective on the matter of risk and under the umbrella of "risk management" each of those persons are considered "stakeholders." The Pharmacist in Charge (PIC) and the business owners have obvious reputable and equitable stakes, but what about the technicians? Technicians are actively opening chemical containers, scooping, weighing, and manipulating active chemicals that have occupational exposure limits (OELs). Many years ago, after speaking at a conference education session on *Quality and Safety in the Compounding Lab*, a young lady in her late twenties approached me and asked, "Do you think the reason why I have had three miscarriages is because I work in a compounding pharmacy?" That young lady's story should not be interpreted as an incrimination on the industry, but instead should be considered as a potential hazard in the absence of a thorough risk assessment and implementation of mitigation strategies such as consistent training on good lab practices and active monitoring of personnel proficiency. The take away here is every employee at the pharmacy has a perspective and stake that should be considered during the risk assessment process and it is almost a guarantee that soliciting those perspectives will reveal valuable information.

Risk Assessment- The Process



Step 1: *Risk Identification*

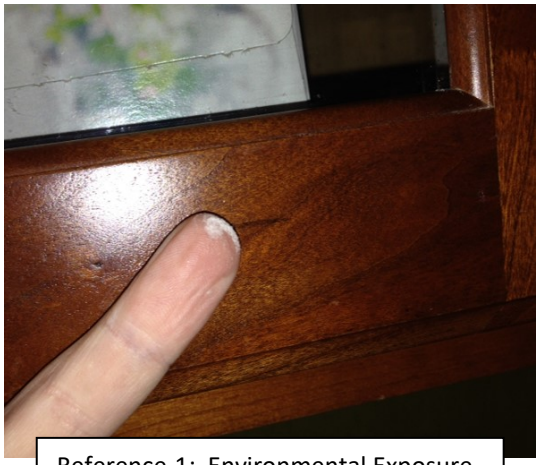
A compounding pharmacy, which is qualified as an "entity" in the USP chapter "must maintain a list of HDs, which must include any items on the current NIOSH list that the entity handles." This identification process can be easily achieved by printing off the NIOSH hazardous drug list and highlighting those HDs on hand and posting in the compounding room, or alongside the other important "readily available" documents, and safety data sheets (SDS).

Recently during a site visit we discovered the SDS three ring binder to be readily available, but completely empty, meaning no hard copies of the SDS sheets were available. After inquiring of the lab manager, she boldly proclaimed the SDS documents were digital and therefore "readily available" and the technicians knew how to access them. To validate her claim, I challenged a technician to produce an SDS. The technician proceeded to walk over to the bright yellow SDS

three ring binder to discover it was void of content. The lab manager reminded the technician that she was told the documents were digital. We completely agree that removing as much paper from a compounding room is a good idea, but the main point here is, consistency is key with training, even if it seems repetitive. To further validate this point, consider that in instances of severe weather or a power outage that may disrupt internet service, SDS paper copies should be available.

Step 2: *Risk Analysis*

This is an important step because we now get into the workflow process and examine the series of singular HD handling activities as defined in the USP <800> chapter. The *Appendix 1 Hazardous Drug Worksheet* is a simple and useful tool that sequentially walks through the HD handling processes and is provided at the end of this article. The worksheet was developed by an industry collaboration called the Hazardous Drug Consensus group and can be downloaded by clicking this link at *Compounding Today.*



Reference-1: Environmental Exposure

One of the HD workflow processes that is undoubtedly the physical activity with greatest exposure risk occurs during the compounding workflow. Inspection of the lab area during the risk analysis step should be scrutinized. This will require some literal hands to reveal some truths on how clean or how dirty your lab really is. This inspection is even more effective with a UV flashlight that can be purchased for less than $15.00. One approach we commonly engage in is wiping a finger (it's probably better accomplished wearing gloves) or shining the UV flashlight over the top of door jambs, behind hoods, and on shelving where dry chemicals are stored. Eight out of ten labs we visit will reveal a similar result to the Reference-1 picture revealing environmental exposure.

No matter how many times you think you have reinforced good behavior, or reprimanded unacceptable behavior, this simple qualitative test is effective. Now the risk analysis step incurs a couple of risk questions such as, "*why is powder residue present on surfaces outside the containment primary engineering controls (C-PEC)?*" With each risk discovery, a follow-up question of "*What are the potential harms?*" should be strongly considered. In the above Reference-1 picture scenario, the environmental contamination is present due to inconsistent safe workflow habits and an absence of good lab practices. The potential harm is environmental contamination, which is a good indication of personnel exposure and a leading cause of cross contamination with other formulations.

Step 3: *Risk Evaluation*

Risk evaluation compares the identification and analysis against the "risk criteria." The risk criteria are a set of industry standards and/or defined quantitative benchmarks. The problem with performing a comprehensive risk evaluation is that there are no established risk criteria or

acceptable levels of environmental exposure in the compounding industry. Depending on what SDS is referenced, there may or may not be a defined OEL in "Section 11. Toxicological Information" which may or may not reveal a guideline of daily exposure limits.

With the absence of true benchmarks, we would advise to start your own by performing a Gap analysis. A Gap analysis is a simple tool that evaluates the current state versus a desired future state. Using another example from a client site visit, we discovered that the container used to dispense anticipatory stock of progesterone capsules contained a distinctive powder residue as evident in Reference-2 picture. Again you should interject the risk analysis question of "why" this occurred. The potential risks are inhalation and dermal exposure during dispensing, which may be occurring outside of a negative pressure room. The mitigation is a corrective action that defines a thorough de-dusting of capsules prior to removing from the C-PEC which is written in the pharmacy's *Standard Operating Procedures* (SOP).

Reference-2: powder residue

It is recommended that the current state risk discoveries be photographed as benchmarks and compared against future results. After implementing new SOPs as part of a "risk control" solution, the quarterly, bi-annual, or annual observations will be compared against the benchmarks and prove important during the risk evaluation step.

Risk Control: Reduce the Risk

Risk control is to fix the problems discovered during risk assessment by reducing the risks to an acceptable level. We have determined the effectiveness of visual observation of the HD processes as a qualitative assessment method. Process mapping brings a visual component to the gap analysis and can also be used as an SOP supplement and employee training tool. An example of a process map defining the HD receiving process can be found in Appendix-3.

The Apendix-3 process map could hypothetically portray a current state with chemical parcels being delivered via USP or FedEx through the front door, received by the front retail staff, and the outer shipping box opened in that general space. Receiving and opening a damaged chemical container in a general area outside the negative pressure room could result in an environmental and personnel exposure, so we consider that path to be the wrong model. The corrective future state for receiving HD's essentially reroutes the receiving process by mapping the chemical parcel to a controlled area of "neutral or negative pressure" per USP <800> guidelines. The process map is solid visual personnel training supplement to the written SOP process. To reinforce an earlier point, all future processes of handling HD's from to receiving, all the way through dispensing, really need to be examined, observed, and possibly rewritten and retrained.

Risk Review: The Case for Establishing a Medical Surveillance Program

Establishing a Medical Surveillance program in your facility is a "should" and not a "must" in the USP <800> chapter. While it is a recommendation and not a requirement, your organization may have specific policies you are required to follow. Medical surveillance's purpose is to minimize adverse effects for personnel exposed to HDs. To determine if a worker has been exposed or is exhibiting symptoms associated with exposure, one must do an assessment of the worker, including physical assessment and documentation of symptoms, physical findings, and laboratory studies to determine if there is deviation from expected norms.[1,2] Consistent medical screening is a great risk management strategy and one that could prevent long term repercussions to years of hazardous drug chemical exposures. One question often asked is: "Should all employees have to sign forms acknowledging the risks of handling HDs?" This has been a requirement since Chapter <797> was updated and is required by <800>. Personnel of reproductive capability must confirm in writing that they understand the risks. Whether or not an employee is required to share information about their personal health has not been established, yet we would encourage personnel to refer to their employee health policies or risk management department for further guidance.

Even though USP <800> does not require a pharmacy establish a medical surveillance program, there are consistencies between the chapter language and the parameters of a medical surveillance program. Elements of a medical surveillance program for workers exposed to hazardous drugs should include the following:

- Establishes hazardous communication to personnel (required by USP <800> under Section 8)
- Evaluates engineering controls (required by USP <800> under Section 5)
- Identifies hazardous drug exposure process (evaluated during risk assessment)
- Availability of Personal Protective Equipment (PPE) and appropriate use of PPE
- Reproductive and general health questionnaire (completed at time of hire and periodically thereafter)
- History of drug handling (estimate of prior and current exposure, including dates of duty assignment)
- Plan to provide initial baseline clinical evaluation, including appropriately targeted medical history, physical examination, and laboratory testing for workers identified as being potentially exposed to hazardous drugs.
- A follow-up for workers who have shown health changes suggesting toxicity or who have experienced an acute exposure

Summary

Even though the risk assessment has been defined in a process map showing a linear progress through risk identification, risk analysis, and risk evaluation, understand that your actual process may not be as linear. We can't stress enough that taking pictures of the current state is a beneficial first step towards documenting and implementing mitigation strategies for risk control. One of the steps not defined under risk control on the process map is called "risk acceptance." Risk

acceptance comes after implementing well designed engineering controls, training employees, and writing SOPs and is an understanding that there is no level of perfection. Unfortunately risk is present wherever healthcare facilities handle HDs. However, an entity handling HDs should continuously strive for process improvement to minimize personnel and environmental exposures to HDs.

Author:
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Appendix-1: Hazardous Drug Worksheet

Hazardous Drug Risk Assessment Worksheet

Drug Name:

Chemical Form:

SDS Attached: Yes____ No____

Antineoplastic:_____ Carcinogen:_____ Reproductive Risk:_____

		Exposure Route					
		Injection	Eye exposure	Ingestion	Inhalation	Dermal exposure	Notes: PPE Recommend.; Containment; Process
Task	Receipt						
	Storage						
	Compounding						
	Labeling and Packaging						
	Transport / Dispensing						
	Administering						
	Deactivating and Cleaning						
	Disposal						
	Spill Handling						
	Other:						

Appendix-2: Example of a Hazardous Drug Worksheet

Hazardous Drug Risk Assessment Worksheet

Drug Name: Progesterone Date Performed: 18March2017

Chemical Form: Powder

SDS Attached: Yes ✓ No ___

Antineoplastic: ___ Carcinogen: ✓ Reproductive Risk: ✓

		Exposure Route					
		Injection	Eye exposure	Ingestion	Inhalation	Dermal exposure	Notes: PPE Recommend.; Containment; Process
Task	Receipt		✓		✓	✓	Follow Appendix# - Process Map: Receiving Hazardous Drugs
	Storage						Follow Appendix# - Process Map: Receiving Hazardous Drugs
	Compounding		✓	✓	✓	✓	Reference Yesterday's Presentation on Safe Workflow Handling
	Labeling and Packaging				✓	✓	
	Transport / Dispensing						
	Administering						
	Deactivating and Cleaning		✓	✓	✓	✓	
	Disposal		✓	✓	✓	✓	Reference SOP- Workflow Doc# - Disposing of HD's
	Spill Handling		✓	✓	✓	✓	Reference SOP- Workflow Doc# - HD Chemical Spill Clean Up Procedures
	Other:						

Appendix-3: Process Map for Receiving Hazardous Drugs