

**A Gap Analysis Review and Action Plan Recommendations
Relative to USP Chapter <797>
Prepared for XX Medical Center**

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Overview

XX Medical Center
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On August 24, 2005, Eric S. Kastango, MBA, RPh, FASHP, and Jim Wagner visited with XX, QA Pharmacist of XX Medical Center (XX). The purpose of the visit was to conduct a one-day tour of the XX and XX Divisions of XX with the following objectives:

- Review current compounding operations, processes, and quality systems as they relate to the requirements detailed in USP Chapter <797>, Pharmaceutical Considerations: Sterile Preparations;
- Review the gap analyses that were conducted by XX;
- Provide a report and recommendations for an action plan in order to meet both short-term and long-term goals for compliance with the requirements of USP Chapter 797. The report will also include suggestions on engineering controls and/or optimized cleanroom floor plans that can be provide to hospital engineering and/or contractors.

Time was spent touring both campuses, during which the compounding, main pharmacy, and warehouse areas were inspected. Time was also spent in extensive conversation with XX Smith. The aseptic compounding behaviors of pharmacy personnel were observed at both hospital campuses, and policies and procedures and quality assurance documentation were reviewed.

Direct observations of personnel compounding procedures and the discussions with XX provided insight relative to the departments' understanding of the required elements of USP Chapter <797>. XX has conducted an extremely accurate gap analysis and identified several issues that were confirmed by the consultants along with other opportunities for improvement, included in this report.

Pharmacies in the State of XX are in a unique situation in terms of compliance with state and USP regulations. They are required to comply with both USP Chapter <797> and with the XX Board of Pharmacy Practice Act and Regulations. However, there are discrepancies between these two documents that need to be considered. The XX Board is in the process of reviewing the subchapter and determining how to harmonize the XX regulations with those in the USP chapter.

It must be stressed that the failure to comply with the requirements in USP Chapter <797> places patients at greater risk of injury or death and makes the hospital system more liable to litigation in the event of such an occurrence. Although there has been little or direct punitive actions taken against hospital pharmacies to date, there continues to be a significant number of cases concerning patient morbidity and mortality from contaminated sterile preparations. Compliance should not be viewed as optional.

Operational Analysis

The overall impression of hospital pharmacy is that while significant progress has already been made towards compliance and a blueprint for success has been laid out in the hospital's policies and procedures, there exists a lack of employee compliance with these policies and procedures and a lack of true understanding of professional responsibility relative to the principles of contamination control and aseptic compounding as they are clearly defined in USP Chapter <797>.

In any quality system, the most important factor is management commitment. The management and employees need to have the correct attitude if their quality system program is to be effective. Quality consciousness should be developed in every employee. Each employee should be made aware of the importance of his or her individual contributions in the overall effort to achieve an acceptable level of quality. For each of the requirements within the USP chapter there are evidence-based practices known to minimize the risks associated with aseptic compounding, many that requires employee compliance.

After a quality system is in place and checked, it should not be allowed to stagnate -- it should continue to be dynamic. The system remains dynamic through continuous feedback, "big-picture" monitoring by system audits, management review, and corrective and preventive action.

There are several other areas of concern that were discovered during this visit. They include the following:

- The physical space of the XX pharmacy is inadequate to perform the critical tasks in both the compounding and general pharmacy work areas. There was inadequate room for gowning, product staging and checking, labeling of compounded sterile preparations (CSPs), and storage of the CSPs prior to their delivery to the patient care units.
- The personnel observed compounding CSPs did not follow standards of practice relative to procedures for hand washing, garbing, and gloving. Operators working at the XX facility gown up outside the room prior to entry. Gowning included a smock, face mask, hair net, and booties, all of which were done outside the room. Gowning should be occurring inside of the anteroom where the environment conditions (particles, etc) are controlled. Hand-washing was not part of the gowning process.
- Compounding personnel, in full garb, were observed walking around outside of the compounding room in the XX division pharmacy talking with other employees.
- A pharmacist at the XX Division was observed compounding medications without first washing her hands or removing jewelry and makeup.
- The maximum beyond-use dating (BUD) for CSP formulations under frozen conditions ($\leq 20^{\circ}\text{C}$) is 45 days. There were XX syringes found labeled with BUD of 6 months. Although, there may be chemical stability data to support this six month dating, USP Chapter <797> requires those CSPs whose BUD exceeds published ranges be sterility tested according to the requirements of USP Chapter <71> Sterility Testing.
- The LED temperature display on the XX Freezer read -21°C , but the temp-scribe read -10°C to -14°C .

- Although it was stated that daily cleaning was occurring in the XX pharmacy, the floor and the legs of the XX pharmacy compounding isolator were soiled with a brownish residue (suspected to be dextrose). The room did not look clean. Dedicated pharmacy cleaning supplies (mops and buckets) were found sitting in an unsanitary area, with a mop sitting in a bucket of dirty water. The handle of the mop was wood, which is a prime source of microbial contamination.

Facility Recommendations

Existing Sterile Compounding Room – XX

The primary sterile compounding room is a relatively small room, approximately 14' x 9' x 8', employing a positive pressure compounding isolator as the primary engineering control. Supply air to the room is provided by an unfiltered outlet positioned in the ceiling close to the entry door. The return is located in the ceiling toward the back of the room away from the entry door. There is no record of room particle counts for estimation of facility cleanliness. A sink is located in the room toward the front near to the entry door. Counters with shelving are positioned on the wall opposite and across from the compounding isolator.

The compounding isolator is an XX positive pressure unit. This model employs a unidirectional pass-through chamber in the center with a unidirectional compounding chamber on either side. It appears to be set up for one person to feed supplies and material to operators on either side for processing. Three people can work together as a team. In addition, the center unidirectional pass-through section is being used as a vertical laminar flow hood for stat preparations.

Short term recommendations – sterile compounding room

The following facility recommendations are based on the current version of USP Chapter <797> and assume the operations are to be performed in compounding barrier isolators. Conversion to a cleanroom would require a major renovation. Currently, there are no standards in existence for isolators used for compounding so any comments relating to these devices are strictly the opinion of the consultants (based on years of experience and actively working with NIOSH and USP to address the issue).

The compounding isolator should be adequate for compounding in its current setting according to the standard. It employs unidirectional airflow, so used properly it should offer adequate isolation and particle free “first air” as needed for good aseptic technique. The particle counts are currently performed under “at-rest” conditions. Particle counts should be taken under simulated “operational” conditions to verify that ISO class 5 is maintained when you need it – during actual manipulations. No sterile compounding, however, should ever be done in the center pass-through section of this isolator unless it was placed in a cleanroom.

Although not necessary for compliance with USP requirements, we recommend swapping the locations for the return and the supply to the room. Additionally, the return would be in a better position to remove any particulate burden introduced to the room when the door is opened.

Hazardous Drug Prep Room – XX

The hazardous drug prep room, like the main compounding room, is a small room with an isolator as the primary engineering control. In this case, a negative pressure aseptic containment XX model X. It was reported that the hazardous drug room is negative pressure to the X pharmacy but the certification report that was reviewed did not confirm this statement. Supply air to the room is provided by an unfiltered outlet positioned in the ceiling toward the back of the room away from the

entry door. The return is located in the in the ceiling the back of the room away from the entry door. There is no record of room particle counts for estimation of room cleanliness.

Short term recommendations – Hazardous Drug Prep Room

The room should be maintained under negative pressure. This would ideally be 0.05" w.c. negative relative to adjacent spaces but anything below 0.02" w.c. would be adequate. A real-time monitor can be easily and inexpensively installed. This can be as simple as a magnehelic gauge mounted on the wall.

Unlike the sterile compounding room, the main concern and priority is hazardous drug/vapor containment. The supply and exhaust locations should be left as they are in the current configuration. Air should be pulled away from the door entry to aid in containment. Due to its role as a containment room, a minimum of 12 air changes per hour in this space should be achieved.

Recommendations – Certification

Room particle counts should be performed to understand the current state of control. These are not cleanrooms but it would be helpful to understand the current particulate burden of the rooms.

The hazardous drug room will ideally be maintained under negative pressure. This should be confirmed and documented at the time of certification. I also recommend verifying the level of the positive pressure in the sterile compounding room as well.

Particle counts should be taken under "operational conditions".

Determine the air change rate of the hazardous drug prep room to verify a minimum of 12 ACPH is maintained.

The Controlled Environment Testing Association (CETA) will be publishing a guide for certification of compounding isolators later this year. It is recommended that all isolators be tested to that guide. Depending on the results, it may be necessary to reevaluate the use of the existing devices.

XX Compounding Room – XX Division

The XX division operation is based on a cleanroom with an anteroom employing traditional laminar flow equipment (not barrier isolators). The XX compounding room is used for both hazardous and non-hazardous compounding. The anteroom is used for compounding stat preparations as well as support activities of the main compounding room. Both rooms were certified to be well within class 10,000 (ISO class 7) for "as built" conditions at 0.5µm particles. The counts were low enough that the sterile compounding room will most likely maintain ISO class 7 and the anteroom ISO class 8 under "operational" conditions.

Air is delivered to both rooms through ceiling mounted HEPA filters (3 filters in the sterile compounding room and 1 filter in the anteroom). The sterile compounding room currently operates at approximately 72 Air Changes per Hour (ACPH) the anteroom operates at approximately 13 ACPH. I did not see a return in the main compounding room but the Biological Safety Cabinet does exhaust approximately 270 cfm from the room. The anteroom has a small exhaust vent in the ceiling by the entry door.

The sterile compounding room is approximately 11' x 14' with an 8' ceiling. Sterile compounding is done in a 6' XXHLF (horizontal laminar flow hood). This particular unit is very old and is showing signs of age including some rust spots. The hazardous drug preparations are done in a XX Biological Safety Cabinet (BSC) vented outside of the building. This hood is also approximately 25 years old. Consideration should be given to replacing both existing primary engineering controls.

The anteroom has a sink for hand washing. The drain in the cabinet under the sink has an open drain. Open drains are potential sources of contamination.

A XX vertical laminar flow hood in the anteroom is used for stat preparations. The anteroom is approximately 13.5' x 13' with 8' ceilings.

SAMPLE

Operational Recommendations

The focus of pharmacy management as a result of this report and the gap analysis should be on implementing the attached action plan within an achievable timeline. JCAHO will be surveying hospital organizations against their gap analysis and will be looking for a definitive action plan that has been approved by the organization’s leadership. In addition to the action plan, there will be a need to develop a budget to address the capital expenditures required to comply with USP <797>. Organizations that fail to comply with the action plan and established timeline will be cited failing to comply with JCAHO standards that have been cross-walked to the USP Chapter <797> requirements.

The following table will identify recommendations prioritized as either short-term action items or long-term action items in order to address the USP Chapter <797> operational and regulatory gaps identified during this visit. Recommendations include the following:

Action item priority	Recommendations
S	Read and review this report with pharmacy staff and hospital administration in order initiate the necessary corrective actions
S	Require all pharmacy department employees to reread the following references: a. ASHP Discussion Guide for Compounding Sterile Preparations: Summary and Implementation of USP Chapter <797> b. Blueprint for Implementing USP Chapter <797> for compounding sterile preparations. <i>Am J Health-Syst Pharm.</i> 2005; 62:1271-88
S	Remove excess inventory, supplies, old narcotics records, and other items from the pharmacy and place in storage in order to reduce the clutter and provide more space to employees to perform their job duties.
S	Implement a microbial environmental monitoring program for all areas of the pharmacy, which would include both non-hazardous and hazardous engineering controls (hoods)
S	Routine cleaning and sanitizing procedures should be reviewed, since it an important part of the hospital pharmacy’s environmental monitoring program. Since cleaning services are delivered from another department, trained personnel and equipment that is used and stored correctly should be used to ensure that the cleaning requirements of the pharmacy are being met on a daily basis.
S	Eliminate the practice of compounding in the pass-through chamber of the compounding isolator in the sterile compounding room at the XX facility.
S	Discontinue the preparation of hazardous drugs at the XX Division facility and outsource compounding from the XX facility
S/L	Evaluate the facility options available to the hospital relative to the renovation of the cleanroom that have been included in this report.
S/L	Enforce a proper employee hand washing and garbing program. All garbing apparel must meet USP requirements (e.g. powder-free gloves and appropriate smocks or gowns with elastic cuffs at the wrist. There must be ramifications for personnel who fail to comply.

S=short-term action items (require attention and resolution within 6 months)

L=long-term action items (require significant planning and fiscal/human resources and resolution will take longer than 6 months).

Handling and preparation of hazardous drugs

A reminder regarding the preparation of antineoplastics: Based on the new OSHA recommendations relative to the compounding of antineoplastic agents, all compounding for these types of medications should occur in a dedicated and properly designed area where optimal environmental controls can be maintained. See the NIOSH Alert, *Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings*, for specific recommendations that must be considered (www.cdc.gov/niosh).

Some of the recommendations include:

- Read all information and material safety data sheets (MSDS) your employer provides to you for the hazardous drugs you handle.
- Participate in any training your employer provides on the hazards of the drugs you handle and the equipment and procedures you should use to prevent exposure.
- Be familiar with and able to recognize sources of exposure to hazardous drugs. Sources of exposure include:
 - All procedures involving hazardous drugs (including preparation, administration, and cleaning), and
 - All materials that come into contact with hazardous drugs (including work surfaces, equipment, personal protective equipment [PPE], intravenous [IV] bags and tubing, patient waste, and soiled linens).
- Prepare hazardous drugs in an area that is devoted to that purpose alone and is restricted to authorized personnel.

Summary

Overall, there are several opportunities for process and procedure improvement in the area of aseptic compounding at XX Medical Center. It is important to recognize that the principles of contamination control and good aseptic compounding have not been nor are today an inherent part of a pharmacist's didactic education and experiential training in pharmacy school. Morris, et. al. (2002) conducted and published a national survey in the December 15, 2003 issues of the American Journal of Health-System Pharmacists regarding the compliance of hospital pharmacies with the 1993/2000 ASHP QA Guidelines. The overall rate of compliance was poor and speaks to an overall failure of the education and training system of pharmacy vs. the failure of any one individual.

There is now a significant awareness of the importance of good aseptic compounding procedures and a multitude of resources are available to help pharmacists and technicians address gaps and deficiencies that may exist. Using the issues identified and recommendations noted in this report, immediate and measurable results can be achieved, all which will have a direct and positive impact in the delivery of pharmaceutical care at XX Medical Center.

It is the opinion of the consultants that the pharmacy management will need to actively engage in this endeavor and support the current efforts by the pharmacist working on this project. The greatest challenge that will be faced in correcting the issues will come from two areas:

- a. Lack of physical space available in the pharmacy and in the immediate area to expand the pharmacy operations.
- b. Direct and indirect employee resistance to change. There is a significant amount of dogma and misinformation relative to good aseptic compounding practices that can only be addressed through intensive education and objective qualitative testing.

If there are any questions that you may have regarding this report, please contact me. If desired, Clinical IQ, LLC, can assist XX in this matter as deemed necessary. Thank you for the opportunity to provide the pharmacy management of XX Medical Center with this service.