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State Board of Pharmacy
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Subject: Proposed Rule Making Relating to Compounding (Reference No. 16A-5419)

To Whom It May Concern:

It is wonderful that the Pennsylvania State Board is putting forth regulations to protect the patients in our state. I am a Pennsylvania-licensed pharmacist with almost 15 years of sterile compounding experience, 10 years of which have been focused on chemotherapy and other hazardous drug compounding. I am the Assistant Director of Pharmacy at my hospital and also travel around the US and Canada giving programs on sterile, non-sterile and hazardous drug compounding safety and compliance. I am really passionate about the safety of compounded products for the patients and the healthcare workers.

Thank you for a great job. I have listed suggestions and points for clarification on the wording published in the 3/11/17 edition of the Pennsylvania Bulletin.

§ 27.601. Compounding of preparations.

The compounding of sterile and nonsterile preparations shall be done in accordance with the current version of the USP chapters governing compounding.

This is great language as the US Pharmacopeia consistently works with a national team of experts to improve their standards and allows for public commentary as well as provides classes and education to interpret and implement standards!

The PA regulations become complicated because they do not consistently use the same wording as USP.

First the use of the term "bulk" and/or "bulk compounding" is confusing and needs clarification.

§ 27.604. Dispensing compounded drugs.

A compounded drug shall only be dispensed pursuant to a prescription or drug order by the prescriber for a specific patient. Pharmacists may compound drugs in anticipation of receiving a valid prescription based on a history of receiving valid prescriptions generated solely within an established practitioner/patient/pharmacist relationship. Bulk compounding shall comply with §§ 27.603 and 27.623 (relating to bulk drug substances: and production record for drugs compounded in bulk quantities).

- In the PA regulations: "Bulk" is referred to as both a type of product and a volume of product – which is confusing and I recommend should be avoided.
- Bulk drug is commonly used to refer to non-sterile, active pharmaceutical ingredients (aka API or bulk powder) and thus is related to non-sterile compounding or non-sterile to sterile compounding (current USP version considers this "high risk compounding"). I recommend that the word "bulk" should be limited to this term, or preferably the more specific term "Active Pharmaceutical Ingredients (API)" be used only.
- Compounding a drug in "bulk" means a larger quantity, which could also be called batching. The use of the term "batching" is more specific and would improve clarity.
- Batching products made from commercially manufactured sterile ingredients is well established and often daily occurrence, such as making batches of IV antibiotics from sterile starting ingredients prior to filling the orders for many hospital patients. This is deemed as a different risk level as defined by USP 797 (low or medium risk compounding).
- **May I suggest that Pennsylvania Regulations employ the terms and the associated beyond-use-dating and product requirements that are used in the USP.**
- **To decrease confusion, eliminate the sections in the Pennsylvania document that attempt to paraphrase USP and instead refer directly to USP per the original statement in § 27.601.**

USP 797 Proposed Draft (Sept 2015) uses two terms: "Master Formulation Record" and "Compounding Record."

- Recommend not using "formula record" or "production record" as they are not in USP and are ambiguous

- USP lists all the components for both documents (below see cuts from the USP 797 Proposed revisions for 2015 , so can the PA regulation just refer to USP?

9.2 Creating Master Formulation Records

A Master Formulation Record must be created for CSPs prepared in a batch for multiple patients or for CSPs prepared from nonsterile ingredients. Any changes or alterations to the Master Formulation Record must be performed only by authorized personnel and must be documented. *Box 9-1* lists the information that must be included in a Master Formulation Record.

Box 9-1 Master Formulation Record

A Master Formulation Record must include at least the following information:

- Name, strength, and dosage form of the CSP
- Physical description of the final preparation
- Identities and amounts of all ingredients and appropriate container–closure systems
- Complete instructions for preparing the CSP, including equipment, supplies, and a description of the compounding steps
- BUD and storage requirements
- Quality control procedures (e.g., pH, filter integrity, and visual inspection)
- Sterilization method, if applicable (e.g., filter, steam, or dry heat)
- Any other information needed to describe the operation and ensure its repeatability (e.g., adjusting pH and tonicity and temperature)

9.3 Creating Compounding Records

A Compounding Record must be created by the compounder preparing the CSP to document the compounding process. The Compounding Record or inventory control system must permit traceability of all ingredients. The Master Formulation Record (when used) can be used as the basis for preparing the Compounding Record. For example, a copy of the Master Formulation Record can be made that contains spaces for recording the information needed to complete the Compounding Record. It is critical that the Compounding Record document in detail any deviations from the process outlined in the Master Formulation Record and any problems or errors experienced during the compounding of the CSP. *Box 9-2* lists the information that must be included in a Compounding Record.

Each Compounding Record must be reviewed and approved before the CSP is released (signature or initials and date).

Box 9-2 Compounding Records

§ 27.608. Protective apparel.

Pharmacy personnel engaged in the compounding of drugs shall wear clean clothing appropriate to the operation being performed. Protective apparel, such as a coat or jacket, apron, or hand or arm coverings, shall be worn as necessary to prote drug products from contamination. For a sterile compounding operation involving one or more aseptic manipulations, steril gowning components are necessary as required by the USP chapter on sterile compounding.

- **Strongly suggest adding "Pharmacy personnel engaged in handling and compounding sterile and non-sterile hazardous drug preparations must wear proper personnel protective equipment as defined in USP for the drugs listed on the National Institute of Occupational Safety and Health (NIOSH) Hazardous Drug list, which is peer-reviewed and updated through the Federal Registry.**

§ 27.605. Resale of compounded drug products.

(a) The wholesale distribution of compounded drug products to other pharmacies, commercial entities or prescribers is considered manufacturing and is prohibited, except for distribution to a medical practitioner to administer to an individual patient if the medical practitioner has an administrative system whereby the product can be tracked through the medical practitioner to the individual patient.

- Consider editing the above statement to include "Except for distribution within a health system to be administered to patients within that health system" to ensure that products compounded at one facility within a health system, may be distributed to other institutions within that system. (ie. Hospital A compounds certain products for the anesthesia department since many potent drugs need to be diluted prior to administration during anesthesia. Pharmacy in Hospital A provides these drugs to the same anesthesia group that supports the hospital at their main campus and staff the Hospital owned Surgery Center just down the road)

§ 27.606. Compounding prohibited.

Pharmacists may not compound any of the following:

(1) Drugs that have been identified by the FDA as withdrawn or removed from the market because the drugs were found to be unsafe or ineffective as set forth in 21 CFR 216.24 (relating to drug products withdrawn or removed from the market for reasons of safety or effectiveness).

- Ensure that this statement does not conflict with a clinical trial where a drug that has been removed from the market is now being investigated
- Consider editing the above statement and include " The exception is when a drug is removed from the market for safety reasons may be included but is then used for investigational purposes, and approved by Institutional Review Board."

§ 27.617. Standard operating procedures required.

(b) The pharmacist shall establish standard operating procedures in accordance with applicable USP chapters that are designed to prevent microbiological contamination of compounded drug products purported to be sterile, including validation of any sterilization process.

- Validation of sterilization is described in detail in USP 797
- Recommend it is not included here and instead refer to the original USP document

Thank you for your time and consideration. I am happy to support the board in any way I can.

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