COMMONWEALTH OF VIRGINIA

Meeting of the Board of Pharmacy

Perimeter Center, 9960 Mayland Drive, Second Floor
Henrico, Virginia 23233

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Tentative Agenda of Meeting
Compounding Workgroup

August 26, 2014

9:00AM

TOPIC	PAGES
Call to Order: Jody H. Allen, Chairman • Welcome & Introductions • Reading of Emergency Evacuation Script	
Call for Public Comment	
Approval of Draft Minutes	1-6
Response from Counsel regarding Pharmacists Compounding in Physician's Office	
Discuss and Approve Draft Report	7-10
Adjournment	

******The workgroup will have a working lunch at approximately 11:45am.*****

DRAFT/UNAPPROVED

VIRGINIA BOARD OF PHARMACY
MINUTES OF COMPOUNDING WORKGROUP

July 31, 2014
Second Floor
Board Room 2

Perimeter Center
9960 Mayland Drive
Henrico, Virginia 23233-1463

CALL TO ORDER: The meeting was called to order at 9:05 A.M.

PRESIDING: Jody H. Allen, PharmD, Board of Pharmacy member

MEMBERS PRESENT:
Ellen Shinaberry, PharmD, Board of Pharmacy chairman
R. Crady Adams, RPh, Board of Pharmacy member
Syed Salman Ali, MD, Board of Medicine member
Sarah Colgan, PharmD, Representing Virginia Society of Health System Pharmacists
Kelly Gattschalk, DVM, Board of Veterinary Medicine member
Jamin Engel, PharmD, Participated at the request of Board of Pharmacy chairman
David W. Newton, PhD, 2010-2015 USP Compounding Expert Committee member (serving in lieu of Eric Kastango)
Claudia True, DVM, Representing Virginia Veterinary Medicine Association (serving in lieu of Steve Escobar, DVM)
Alexander Pytlarz, PharmD, Representing Virginia Pharmacists Association
Gary Cook, MD, Representing Virginia Society of Eye Physicians and Surgeons (serving in lieu of Alan Wagner, MD)

MEMBER NOT PRESENT: Brian Mitchell, MD, Representing Medical Society of Virginia

STAFF PRESENT:
Caroline D. Juran, RPh, Executive Director
J. Samuel Johnson, Jr., RPh, Deputy Executive Director
Beth O'Halloran, RPh, Individual Licensing Manager
Elaine J. Yeatts, Senior Policy Analyst, DHP
James Rutkowski, Assistant Attorney General
David Brown, DC, Director, DHP
Jaime Hoyle, Esq., Chief Deputy Director, DHP

PUBLIC COMMENT:
There were no public comments offered.

BACKGROUND MATERIALS: Dr. Allen provided a summary of the background materials provided in the agenda packet and reviewed the requirement in the enactment clause of HB 1035 for this workgroup to convene for the purpose of exploring and clarifying issues related to compounding of drugs for human and animal use. She indicated staff will prepare a draft report based on discussion and present it to the workgroup for consideration at the August 26, 2014 meeting. A third meeting will be held on September 10, 2014 if necessary to finalize the report. The report will be provided to the

Chairmen of the House of Delegates' Committee on Health, Welfare, and Institutions and the Senate Committee on Education and Health by November 1, 2014.

BRIEF OVERVIEW OF FEDERAL COMPOUNDING ALLOWANCES:

Ms. Juran provided a brief overview of federal compounding allowances.

COMPOUNDING PERFORMED IN PHARMACIES:

As each agenda item was discussed in this section, consideration was given for amending Board of Pharmacy Guidance Document 110-36 by either including additional guidance on the discussed item or clarifying existing guidance on the discussed item.

Dr. Engel raised concern that USP requires surface sampling to be performed periodically and that board guidance recommends performing it at least annually. Dr. Newton indicated USP is discussing how often surface sampling should be performed, as well as the frequency for which gloved fingertip testing must be performed. Dr. Newton stated that breaches in aseptic technique are the most common source of contamination.

RECOMMENDATION:

There was consensus to recommend to the Board of Pharmacy that it consider amending question #23 in Guidance Document 110-36 to advise that surface sampling should be performed at least quarterly.

There was discussion regarding the importance of appropriate incubation periods and temperatures when performing media fill testing and that it's dependant on the media used. Dr. Engel suggested requiring two temperatures for incubation. Mr. Johnson indicated USP provides an allowance for the use of two temperatures under specific conditions, but does not require it. Dr. Newton indicated USP is currently considering this matter. No recommendation was made at this time.

There was brief discussion regarding whether a pharmacist supervising the performance of compounding and performing the final verification must complete and pass media fill testing. Ms. Juran stated that the Board of Pharmacy advises that the pharmacist supervising the performance of compounding and performing the final verification must also pass media fill testing.

Dr. Colgan raised the question of how to determine competency of pharmacy technicians performing compounding and whether additional training should be required.

RECOMMENDATION:

There was consensus to recommend to the Board of Pharmacy that it include additional guidance in Guidance Document 110-36 regarding personnel competency by referencing the training and educational requirements in USP Chapter <797> and the requirement for a site-specific training program in Regulation 18VAC110-20-111.

RECOMMENDATION:

There was consensus to recommend to the Board of Pharmacy that it provide the following guidance:

- **repackaging of insulin into multiple syringes is a medium-risk level manipulation when puncturing the vial more than 3 times;**
- **beyond use date for a single dose vial punctured outside of an ISO class 5 environment shall not exceed 1 hour;**
- **beyond use date for a single dose vial punctured and stored in an ISO class 5 environment shall not exceed 6 hours; and,**
- **if the single dose vial is removed from the ISO class 5 environment such as for final verification purposes, then the beyond use date for the single dose vial shall not exceed 1 hour from being removed from the ISO class 5 environment or the originally assigned BUD of 6 hours within the ISO class 5 environment, whichever is shorter (reference the CDC and USP Appendix).**

Dr. Pytlarz raised concern for question #20 within Guidance Document 110-36 advising pharmacists have at least two articles to justify assigned stability. Dr. Newton agreed that it is uncommon for a second peer-reviewed article to be published on the same subject.

Dr. Newton confirmed that drug stability is formulation specific and explained when existing stability information may be used to estimate the stability for non-aqueous compounds.

RECOMMENDATION:

There was consensus to recommend to the Board of Pharmacy that it take the following action:

- **amend question #20 in Guidance Document 110-36 to advise that pharmacists should have at least one peer-reviewed article which justifies the assigned stability;**
- **provide guidance that references the USP 33-point screening tool to evaluate the quality of a peer-reviewed article and the importance of using quality reference sources to determine stability;**
- **provide guidance that drug stability is formulation-specific and that stability information may only be used when the drug has been prepared using an identical formulation (in all aspects) as used in the peer-reviewed article or reference source;**
- **provide guidance that stability could be estimated for a non-aqueous compound under the following conditions:**
  - **stability information exists in peer-reviewed articles or reference sources indicating stability at a low concentration and high concentration and therefore, stability for concentrations in-between could be estimated;**
  - **stability is not concentration-dependent; and,**
  - **the drug is compounded using an identical formulation (in all aspects) as used in the peer-reviewed articles or reference sources.**
- **provide guidance that the estimation of stability cannot be performed for an aqueous compound (containing any amount of water). Stability information for the exact**

concentration and formulation of an aqueous compound must exist or the beyond use date must not exceed the recommended beyond use dates in USP Chapters <795> or <797>; and,

- **provide guidance that stability information for two individual non-aqueous drugs may be considered when combining the drugs in a compound, assuming the shorter timeframe is used to assign stability to the compound.**

Dr. Engel expressed concern for the use of single-dose vials with a dispensing pin possibly being used as a multi-dose vial.

RECOMMENDATION:

There was consensus to recommend to the Board of Pharmacy that it provide guidance indicating there is currently no allowance for the beyond use date of a single-dose vial with a dispensing pin to exceed a 1 hour beyond use date when punctured outside of an ISO Class 5 environment or 6 hours when punctured within and not removed from an ISO Class 5 environment.

RECOMMENDATION:

There was consensus to recommend to the Board of Pharmacy that it provide guidance indicating nasal sprays and nasal drops may be prepared as a non-sterile compound while nasal inhalations for the sinus cavity shall be prepared as a sterile compound.

Dr. Pytlarz questioned the reference to USP Chapter <51> in Guidance Document 110-36. Ms. Juran agreed that information on page 93 of the agenda packet would support the removal of this reference.

RECOMMENDATION:

There was consensus to recommend to the Board of Pharmacy that it remove reference to USP Chapter <51> from question #3 in Guidance Document 110-36, repeal question #25, and provide a reason for the repeal using the explanation from USP on page 93 of the agenda packet regarding the role of Chapter <51>.

There was consensus that the workgroup did not need to discuss the use of closed system transfer devices since it is being addressed by USP in the proposed USP Chapter <800>.

Ms. Juran stated that FDA prohibits a pharmacy under section 503A to compound human drugs for office-use and therefore, a legislative proposal adopted by the Board of Pharmacy proposes striking this allowance in 54.1-3410.2. She indicated the Board does not propose striking the ability for a pharmacy to compound animal drugs for office use as this does not appear to be prohibited under federal law. Dr. Cook expressed concern for certain drugs used in office administration such as intravitreal antibiotics that could no longer be provided by compounded pharmacies under the legislative proposal. Dr. Newton agreed that FDA intends for compounded human drugs for office use to be provided by outsourcing facilities under section 503B.

Ms. Juran reviewed the new allowance in law for pharmacies to provide compounded animal drugs to veterinarians intended to be dispensed by

the veterinarian under specific, emergent conditions. She and Leslie Knachel, Executive Director for the Board of Veterinary Medicine, indicated it was unclear at this time if joint guidance from the boards would be necessary.

COMPOUNDING PERFORMED IN PHYSICIAN OFFICES:

William Harp, MD, Executive Director of the Board of Medicine provided an overview of the mixing, diluting, and reconstituting regulations. There was discussion regarding the differences between the law for compounding and the law and regulations for mixing, diluting, and reconstituting. Ms. Juran stated there appears to be a national trend, including in Virginia, for pharmacists to perform compounding within physician offices for both office administration and dispensing. There was discussion regarding how the laws and regulations are applied to a pharmacist compounding in a physician's office.

RECOMMENDATION:

There was consensus that legal guidance should be obtained from counsel on the following subjects:

- **May a pharmacist compound in a physician's office? If so, is he being supervised by the physician? Is it "compounding" when the drug is intended to be dispensed to the patient vs. administered? Who must perform the final verification of accuracy? Must he comply with USP standards as required in §54.1-3410.2? Who is liable for a compounding error and what might be the violation?**

- **May a pharmacist mix, dilute, and reconstitute drugs in a physician's office? If so, is he being supervised by the physician? Is it "mixing, diluting, and reconstituting" when the drug is intended to be administered to the patient vs. dispensed? Who must perform the final verification of accuracy? Must he fully comply with USP standards when combining two or more drugs together as required in §54.1-3410.2 or are there conditions under which the mixing, diluting, and reconstituting regulations would apply? Who is liable for a compounding error and what might be the violation? What are the standards for mixing, diluting, and reconstituting non-sterile drugs?**

RECOMMENDATION:

There was consensus to recommend to the Board of Medicine to fully adopt USP standards when mixing, diluting, and reconstituting sterile and non-sterile drugs.

COMPOUNDING PERFORMED IN OUTSOURCING FACILITIES:

Ms. Juran briefly explained the intent of the legislative proposal to create a new licensing category for outsourcing facilities based on the new federal law.

MISCELLANEOUS TOPICS:

Dr. Newton indicated it is possible that USP may have a second public comment period for the proposed Chapter <800>.

Regarding the MOU being drafted by NABP and the FDA, Dr. Pytlarz stated the Virginia Pharmacists Association would like the Board to consider greater than a 5% allowance for those pharmacies located less than 50 miles from a neighboring state. Ms. Juran indicated that she was recently told by the FDA that it cannot currently release a draft copy of the MOU or discuss the draft concepts.

ADJOURNMENT: With all business concluded, the meeting adjourned at 3:10pm.

JODY H. ALLEN,
WORKGROUP CHAIRMAN

CAROLINE D. JURAN, EXECUTIVE DIRECTOR

DATE

DATE

Draft Report of the Compounding Workgroup

This report summarizes the actions taken by a workgroup convened by the Board of Pharmacy pursuant to the enactment clause of HB 1035 passed during the 2014 General Assembly Session to explore and clarify issues related to the compounding of drugs for human and animal use. The workgroup included representation from the Boards of Pharmacy, Medicine, and Veterinary Medicine, the Virginia Pharmacists Association, the Virginia Society of Health System Pharmacists, the Virginia Veterinary Medicine Association, the Virginia Society of Eye Physicians and Surgeons, a practicing hospital pharmacist who participated at the request of the Board chairman, and a member of the 2010-2015 United States Pharmacopeia (USP) Compounding Expert Committee. Jody H. Allen, PharmD, Board of Pharmacy member presided over the workgroup. The workgroup met for approximately _____ hours over July 31, 2014 and August 26, 2014.

Board staff solicited feedback for agenda topics from the workgroup members prior to the first meeting and received several suggestions. During the first meeting, the workgroup had in-depth discussions on the agenda topics which were divided into the following subtopics: compounding performed in pharmacies; compounding performed in physician offices; compounding performed in outsourcing facilities; and miscellaneous topics. During the discussions, state and federal law, board regulations, board guidance, and current and proposed USP chapters were taken into consideration.

Through consensus the workgroup recommended that the Board of Pharmacy consider amending Guidance Document 110-36 by:

- Revising the response to question #23 to advise that surface sampling should be performed at least quarterly;
- including additional guidance regarding personnel competency by referencing the training and educational requirements in USP Chapter <797> and the requirement for a site-specific training program in Regulation 18VAC110-20-111;
- adding guidance indicating the repackaging of insulin into multiple syringes is a medium-risk level manipulation when puncturing the vial more than 3 times;

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- including language that the beyond use date for a single dose vial punctured outside of an ISO class 5 environment shall not exceed 1 hour;
- adding guidance that the beyond use date for a single dose vial punctured and stored in an ISO class 5 environment shall not exceed 6 hours;
- including guidance stating that if the single dose vial is removed from the ISO class 5 environment such as for final verification purposes, then the beyond use date for the single dose vial shall not exceed 1 hour from being removed from the ISO class 5 environment or the originally assigned BUD of 6 hours within the ISO class 5 environment, whichever is shorter (reference the CDC and USP Appendix);
- amending question #20 to advise that pharmacists should have at least one peer-reviewed article which justifies the assigned stability;
- providing guidance that references the USP 33-point screening tool to evaluate the quality of a peer-reviewed article and the importance of using quality reference sources to determine stability;
- providing guidance that drug stability is formulation-specific and that stability information may only be used when the drug has been prepared using an identical formulation (in all aspects) as used in the peer-reviewed article or reference source;
- providing guidance that stability could be estimated for a non-aqueous compound under the following conditions:
    - stability information exists in peer-reviewed articles or reference sources indicating stability at a low concentration and high concentration and therefore, stability for concentrations in-between could be estimated;
    - stability is not concentration-dependent; and,
    - the drug is compounded using an identical formulation (in all aspects) as used in the peer-reviewed articles or reference sources.
- including guidance that the estimation of stability cannot be performed for an aqueous compound (containing any amount of water). Stability information for the exact concentration and formulation of an aqueous compound must exist or the beyond use date must not exceed the recommended beyond use dates in USP Chapters <795> or <797>;

- providing guidance that stability information for two individual non-aqueous drugs may be considered when combining the drugs in a compound, assuming the shorter timeframe is used to assign stability to the compound;
- including guidance indicating there is currently no allowance for the beyond use date of a single-dose vial with a dispensing pin to exceed a 1 hour beyond use date when punctured outside of an ISO Class 5 environment or 6 hours when punctured within and not removed from an ISO Class 5 environment;
- clarifying that nasal sprays and nasal drops may be prepared as a non-sterile compound while nasal inhalations for the sinus cavity shall be prepared as a sterile compound; and,
- removing reference to USP Chapter <51> from question #3, repeal question #25, and provide a reason for the repeal using the explanation from USP on page 93 of the agenda packet regarding the role of Chapter <51>.

By consensus, the workgroup recommended that board counsel provide answers to the following questions:

- May a pharmacist compound in a physician's office? If so, is he being supervised by the physician? Is it "compounding" when the drug is intended to be dispensed to the patient vs. administered? Who must perform the final verification of accuracy? Must he comply with USP standards as required in §54.1-3410.2? Who is liable for a compounding error and what might be the violation?
- May a pharmacist mix, dilute, and reconstitute drugs in a physician's office? If so, is he being supervised by the physician? Is it "mixing, diluting, and reconstituting" when the drug is intended to be administered to the patient vs. dispensed? Who must perform the final verification of accuracy? Must he fully comply with USP standards when combining two or more drugs together as required in §54.1-3410.2 or are there conditions under which the mixing, diluting, and reconstituting regulations would apply? Who is liable for a compounding error and what might be the violation? What are the standards for mixing, diluting, and reconstituting non-sterile drugs?

Additionally, there was consensus to recommend that the Board of Medicine revise its regulations for mixing, diluting, and reconstituting to fully adopt USP standards for both sterile and non-sterile drugs.

Lastly, the Committee reviewed a draft legislative proposal approved by the Board of Pharmacy for the 2015 General Assembly that includes a provision prohibiting pharmacies from providing compounded human drugs for office use. There was some concern expressed by one member about that provision, but it was acknowledged that the legislation would conform state law to federal law which already prohibits pharmacies from providing compounded human drugs for office use. Other workgroup members supported the concept since compounding for office use would potentially place pharmacies in violation of federal law. There was also an acknowledgement that compounded drugs for office use could be provided by outsourcing facilities.