COMMONWEALTH of VIRGINIA

David E. Brown, D.C.
Director

Department of Health Professions
Perimeter Center
9960 Mayland Drive, Suite 300
Henrico, Virginia 23233-1463

www.dhp.virginia.gov
TEL (804) 367- 4400
FAX (804) 527- 4475

MEMORANDUM

TO: The Honorable Robert D. Orrock, Sr.
Chairman, House Committee on Health, Welfare & Institutions

The Honorable Stephen H. Martin
Chairman, Senate Committee on Education and Health

FROM: Caroline D. Juran, RPh
Executive Director
Board of Pharmacy

DATE: October 29, 2014

RE: **Report of the Compounding Workgroup pursuant to Chapter 147 of the 2014 Acts of the Assembly**

As specified in the second enactment of House Bill 1035 (Chapter147 of the 2014 Acts of the Assembly), we are submitting a report from the workgroup convened to "explore and clarify issues related to the compounding of drugs for human and animal use." The workgroup was required to provide a report 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. Accordingly, we are providing a copy of the report for your review.

The workgroup, composed of 12 representatives from medicine, pharmacy and veterinary medicine, held two very productive meetings in July and August. From those meetings, a consensus report has been drafted and circulated among the workgroup. The report outlines the discussion and recommendations for revisions to the Board of Pharmacy's guidance document on compounding, legal advice on the role of a pharmacist who is compounding within a physician's office, discussion of the Board of Medicine's regulations on mixing, diluting and reconstituting drugs, and a legislative proposal for the 2015 Session of the General Assembly.

We appreciate your review of the report and are available to answer any questions you may have or provide additional information if necessary.

REPORT OF THE

VIRGINIA BOARD OF PHARMACY

DEPARTMENT OF HEALTH PROFESSIONS

Report on Actions Workgroup on Compounding Drugs Pursuant to Chapter 147 (2014)

To the House Committee on Health, Welfare and Institutions and the Senate Committee on Education and Health

COMMONWEALTH OF VIRGINIA

RICHMOND

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TABLE OF CONTENTS

Report of the Workgroup on Compounding Drugs

I. Introduction.

This report summarizes the actions taken by a workgroup convened by the Board of Pharmacy pursuant to the enactment clause of Chapter 147 (HB1035) of the 2014 Acts of the Assembly. The charge to the workgroup was to explore and clarify issues related to the compounding of drugs for human and animal use. The 12-member 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 nine hours over two meetings held on 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.

II. Discussion on Compounding Performed in Pharmacies.

Through consensus the workgroup recommended that the Board of Pharmacy consider amending Guidance Document 110-36 on *Compounding for Compliance with USP Standards* 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 undiluted multi-dose vials (e.g., insulin) into multiple syringes is a medium-risk level manipulation when puncturing the vial more than 3 times (Note: this guidance addresses repackaging, not administration);
- Including the following guidance for the beyond use date (BUD) for a single dose vial:
    - a single dose vial punctured outside of an ISO class 5 environment shall not exceed 1 hour, unless specified otherwise by the manufacturer;
    - a single dose vial punctured and stored in an ISO class 5 environment shall not exceed 6 hours;
    - a punctured single dose vial that is removed from the ISO class 5 environment such as for final verification purposes 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 Center for Disease Control (CDC) and USP Appendix);
    - a closed system transfer device (CSTD) cannot be used to extend the BUD of a single-dose vial to exceed the 1 hour BUD when punctured outside of an ISO Class 5 environment or 6 hour BUD when punctured within and not removed from an ISO Class 5 environment.
- Providing guidance that sterile and non-sterile drug stability is formulation-specific and that stability information may only be used when the drug has been prepared using the same formulation (USP-NF equivalent ingredients) as used in either at least one peer-reviewed article or other reliable reference source;
- Providing guidance that stability could be estimated for an aqueous or 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 the same formulation (USP-NF equivalent ingredients) as used in the peer-reviewed articles or reference sources.

- Providing guidance for the assignment of BUDs that stability information for multiple drugs may be considered when combining the drugs in a compound, assuming the shortest BUD is used to assign stability to the compound. Peer-review or reference source literature shall be consulted and the professional judgment of the pharmacist exercised when assigning the BUD of a compound containing multiple drugs. Any extended BUD must also comply with the applicable USP Chapter <795> or <797>;
- Clarifying that nasal sprays and nasal irrigations may be prepared as a non-sterile compound while nasal inhalations for the lungs shall be prepared as a sterile compound; and,
- Removing reference to USP Chapter <51> from question #2, repeal question #25, and provide a reason for the repeal using the following explanation from USP: currently USP Chapter <797> does not contain specific requirements for compounding multiple-dose containers, such as the need for a preservative, nor requirements for testing, labeling, and container closures for compounded multiple-dose containers; and, that Chapter <797> references Chapter <51> for informational purposes as the source of the 28-day BUD after initially entering or opening a multiple-dose container, unless otherwise specified by the manufacturer.

Additionally, the workgroup briefly discussed the differences in federal oversight for compounding for animals versus humans and the recent allowance in state law for pharmacists to provide a veterinarian a supply of compounded drug to dispense to his clients under limited circumstances. If there is a need for clarity in interpretation of the statute, the Board of Pharmacy, in conjunction with the Board of Veterinary Medicine, should consider adopting guidance on the subject.

III. Discussion on Compounding Performed in Physician Offices.

There was discussion regarding the existence of differences in requirements for mixing, diluting and reconstituting under Board of Medicine regulations and USP standards as required in law for compounding. The work group was advised that the Board of Medicine Legislative Committee

intends to review what constitutes compounding and the current regulations governing mixing, diluting, and reconstituting performed in physician offices. Additionally, there was discussion as to which standards pharmacists must comply when combining two or more drugs in a physician's office. Hence the following information was requested of board counsel:

- 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?

At its meeting on August 26, 2014, the workgroup received the following advice from the assistant attorney general who provides counsel to the Board of Pharmacy:

- A pharmacist must comply with laws and regulations overseeing pharmacists, regardless of the environment in which he practices and therefore, must always compound in compliance with USP-NF standards as required in §54.1-3410.2;
- The exception in the definition of "compounding" (§54.1-3401) for mixing, diluting, and reconstituting when performed by a practitioner of medicine or osteopathy licensed under Chapter 29 (§ 54.1-2900 et seq.), a person supervised by such practitioner pursuant to subdivision A 6 or A 19 of § 54.1-2901, or a person supervised by such practitioner or a licensed nurse practitioner or physician assistant pursuant to subdivision A 4 of § 54.1-2901 does not apply to pharmacists;
- A physician may supervise a pharmacist as an employer, but the pharmacist must compound on his own and not under the physician's supervision;

- A pharmacist would not be advised to perform verification of a drug that was mixed, diluted, or reconstituted as referenced in the definition of "compounding" (§54.1-3401); and,
- A pharmacist performing compounding at a physician's practice location may do so pursuant to a pharmacy permit and may not perform compounding under the supervision of a physician maintaining a physician selling permit.

IV. Discussion of Compounding Performed in Outsourcing Facilities.

During the July 31st meeting, the workgroup reviewed a draft legislative proposal approved by the Board of Pharmacy for the 2015 General Assembly addressing outsourcing facilities 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.

Upon further consideration at the August 26th meeting and following information received from the Virginia Society of Eye Physicians and Surgeons, the workgroup concluded that there appears to be a legitimate need for pharmacists to provide a reasonable amount of compounded human drugs to a physician's office for administration to a patient if there is a critical need to treat an emergency condition. Therefore, the Department has included in its legislative proposal an exception to the restriction on compounding human drugs for office use to allow a reasonable amount of drugs to be compounded for office administration when there is a critical need to treat an emergency condition. For example, an ophthalmologist may need to have small quantities of non-patient specific compounded antibiotics for emergency use in the treatment of acute infectious endophthalmitis. A delay in treatment of this eye infection of several hours can result in severe visual loss or blindness. There may be other examples of the need for reasonable amounts of a compounded drug to be available for administration in a physician's office in an emergency situation.

The workgroup further concluded that the workgroup should provide written comment to the Food and Drug Administration (FDA) regarding its prohibition for compounding human drugs for office use. Specifically, the workgroup will advise the FDA of the need for pharmacists to provide a reasonable amount of compounded human drugs to a physician's office for administration to a patient if there is a critical need to treat an emergency condition. There is concern that any conflict between state and federal law on this subject may place health care providers in the difficult situation of meeting patient needs as authorized under state law versus complying with federal law.