BRIEFING

⟨**795**⟩ **Pharmaceutical Compounding—Nonsterile Preparations.** To improve clarity and respond to stakeholder input, the Compounding Expert Committee proposes to revise this chapter with the following major edits:

1. Expand guidance for assigning beyond-use dates (BUDs) for compounded nonsterile preparations (CNSPs) in the absence of stability information.
2. Elaborate on the role of water activity (a_w) in determining BUD limits for preparations.
3. Add a table of commonly compounded dosage forms and their respective a_w values to aid compounders in determining BUD limits for CNSPs.
4. Clarify the requirements for identifying the need for a recall and related procedures.

A copy of this proposal and additional supplementary materials are posted online here.
Please submit comments using the electronic submission form here.
Additionally, minor editorial changes have been made to update this chapter to current *USP* style.
(CMP: S. Mitiche)
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Change to read:

⟨795⟩ PHARMACEUTICAL COMPOUNDING—NONSTERILE PREPARATIONS

1. INTRODUCTION AND SCOPE

This chapter describes the minimum standards to be followed when preparing compounded nonsterile preparations (CNSPs) for humans and animals. For purposes of this chapter, nonsterile compounding is defined as combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug or bulk drug substance to create a nonsterile medication.

The requirements in this chapter must be followed to minimize harm, including death, to human and animal patients that could result from 1) excessive microbial contamination, 2) variability from the intended strength of correct ingredients (e.g., ±10% of the labeled strength), 3) physical and chemical incompatibilities, 4) chemical and physical contaminants, and/or 5) use of ingredients of inappropriate quality.

Handling of nonsterile hazardous drugs (HDs) must additionally comply with *Hazardous Drugs—Handling in Healthcare Settings* ⟨800⟩.

1.1 Scope

1.1.1 CNSPs subject to the requirements in this chapter: CNSPs that must comply with this chapter include but are not limited to the following dosage forms:

- Solid oral preparations
- Liquid oral preparations
- Rectal preparations
- Vaginal preparations

- Topical preparations (i.e., creams, gels, and ointments)
- Nasal and sinus preparations intended for local application (i.e., nasal sprays and nasal irrigation)
- Otic preparations (excluding use in perforated eardrums)

1.1.2 Practices not subject to the requirements in this chapter: The following practices are not considered compounding and are not required to meet the requirements of this chapter:

- *Administration*: Preparation of a single dose for a single patient when administration will begin within 4 h of beginning the preparation is not required to meet the standards in this chapter.
- *Nonsterile radiopharmaceuticals*: Compounding of nonsterile radiopharmaceuticals is not required to meet the standards in this chapter and is subject to the requirements in *Radiopharmaceuticals—Preparation, Compounding, Dispensing, and Repackaging* ⟨825⟩.
- *Reconstitution*: Reconstitution of a conventionally manufactured nonsterile product in accordance with the directions contained in the manufacturer approved labeling is not required to meet the standards in this chapter.
- *Repackaging*: Repackaging of conventionally manufactured drug products is not required to meet the standards in this chapter (see *Good Repackaging Practices* ⟨1178⟩).
- *Splitting tablets*: Breaking or cutting a tablet into smaller portions is not required to meet the standards in this chapter.

1.1.3 Personnel and settings affected: This chapter applies to all persons who prepare CNSPs and all places where CNSPs are prepared. This includes but is not limited to pharmacists, technicians, nurses, physicians, veterinarians, dentists, naturopaths, and chiropractors in all places including but not limited to pharmacies, hospitals and other healthcare institutions, patient treatment sites, and physicians' or veterinarians' practice sites.

The compounding facility's leadership and all personnel involved in preparing, storing, packaging, dispensing, and transporting CNSPs are responsible for 1) ensuring that the applicable practices and quality standards in this chapter are continually and consistently applied to their operations, and 2) proactively identifying and remedying potential problems within their operations. Personnel engaged in the compounding and dispensing of CNSPs must also comply with laws and regulations of the applicable regulatory jurisdiction.

The compounding facility must designate one or more individuals to be responsible and accountable for the performance and operation of the facility and personnel for the preparation of CNSPs. The responsibilities of the designated person(s) include but are not limited to:

- Overseeing a training program to ensure competency of personnel involved in compounding, handling, and preparing CNSPs
- Selecting components
- Monitoring and observing compounding activities and taking immediate corrective action if deficient practices are observed
- Ensuring that standard operating procedures (SOPs) are fully implemented. The designated person(s) must ensure that follow-up is carried out if problems, deviations, or errors are identified
- Establishing, monitoring, and documenting procedures for the handling and storage of CNSPs and/or components of CNSPs

The designated person(s) must be identified in an SOP. If the compounding facility has only one person responsible for all compounding in the facility, then that person is the designated person.

2. PERSONNEL TRAINING AND EVALUATION

All personnel involved in, or the direct oversight of, preparing and dispensing CNSPs must be initially trained, must demonstrate competency before being allowed to perform their job functions, and must undergo training at least every 12 months. Training and competency of personnel must be documented as described in *15. Documentation*.

Designated person(s) must oversee a training program that describes the required training, the frequency of training, and the process for evaluating the competency of personnel involved in nonsterile compounding and handling of CNSPs. This program must equip personnel with knowledge and training in the required skills necessary to perform their assigned tasks.

Before beginning to prepare CNSPs independently, all compounding personnel must complete training and be able to demonstrate knowledge competency in the principles and hands-on skills of nonsterile manipulations as applicable to their assigned tasks. Knowledge competency must be demonstrated at least every 12 months in at least the following core competencies:

- Hand hygiene
- Garbing
- Cleaning and sanitizing
- Handling and transporting components and CNSPs
- Measuring and mixing
- Proper use of equipment and devices selected to compound CNSPs
- Documentation of the compounding process (e.g., *7. Master Formulation and Compounding Records*)

Steps in the training procedure must include the following:

- Read and understand this chapter, other applicable standards, and other relevant literature
- Understand and interpret safety data sheets (SDSs) and, if applicable, certificates of analysis (COA)
- Read and understand procedures related to their compounding duties

Designated person(s) must oversee the training of personnel. Training and observation may be performed by the designated person(s) or an assigned trainer. Personnel must be observed and guided throughout the training process. The personnel will then be expected to repeat the procedures independently while under the direct supervision of the designated person(s) and/or trainer. Personnel will be permitted to perform the procedure without direct supervision only after independently demonstrating understanding and competency. Upon completion of the training program, the designated person(s) and/or trainer must document that the personnel has been trained and successfully completed competency assessments (see *15. Documentation*).

In addition to the initial and annual competency training and evaluation described in this section, the designated person(s) should monitor and observe compounding activities and must take immediate corrective action if deficient practices are observed. SOPs must describe procedures for monitoring and observing compounding activities and personnel.

If the facility has only one person in the compounding operation, that person must document that they have obtained training and demonstrated competency, and they must comply with the other requirements of this chapter.

3. PERSONAL HYGIENE AND GARBING

Individuals entering the compounding area must maintain appropriate personal hygiene. Individuals must evaluate whether they have a personal risk of potentially contaminating the compounding environment and CNSP (e.g., personnel with rashes, recent tattoos, oozing sores, conjunctivitis, or active respiratory infection). Individuals must report these conditions to the designated person(s). The designated person(s) is responsible for evaluating whether these individuals should be excluded, because of the risk of contaminating the CNSP and the environment, from working in compounding areas until their conditions have resolved.

3.1 Personnel Preparation

Personnel engaged in compounding must maintain appropriate hand hygiene and maintain appropriate cleanliness required for the type of compounding performed.

Before entering the compounding area, compounding personnel must remove any items that are not easily cleanable and that might interfere with garbing. At a minimum, personnel must:

- Remove personal outer garments (e.g., bandanas, coats, hats, and jackets)
- Remove all hand, wrist, and other exposed jewelry, including piercings that could interfere with the effectiveness of garbing or hand hygiene (e.g., watches or rings that may tear gloves)
- Remove earbuds or headphones

The designated person(s) may permit accommodations provided that the quality of the environment and CNSP will not be affected. All accommodations should be documented.

3.2 Hand Hygiene

Personnel must perform procedures necessary for appropriate hand hygiene when entering the compounding area to compound as described in *Box 1*.

The use of alcohol hand sanitizers alone is not sufficient.

Box 1. Hand Hygiene Procedures

- Wash hands with soap and water for at least 30 s
- Dry hands completely with disposable towels or wipers
- Allow hands to dry thoroughly before donning gloves

To minimize the risk of cross contaminating other CNSPs and contaminating other objects (e.g., pens and keyboards), gloves should be wiped or replaced before beginning a CNSP that has different components.

All gloves must be inspected for holes, punctures, or tears and must be replaced immediately if such defects are detected.

3.3 Garb and Glove Requirements

Gloves must be worn for all compounding activities. Other garb (e.g., shoe covers, head or hair covers, facial hair covers, face masks, and gowns) must be appropriate for the type of compounding performed and should be worn as needed for the protection of personnel from chemical exposures and for prevention of preparation contamination. Garbing requirements and frequency of changing garb must be determined by the facility and documented in the facility's SOPs.

Garb must be stored in a manner that minimizes contamination (e.g., away from sinks to avoid splashing). Visibly soiled garb or garb with tears or punctures must be changed immediately.

Garb should be removed when leaving the compounding area. If gowns are worn, they may be re-used if not soiled. If gowns are to be re-used, they must remain in the compounding area. If used, gloves, shoe covers, head or hair covers, facial hair covers, and face masks may not be re-used and

must be replaced with new ones. If used, non-disposable garb, such as goggles, should be cleaned then sanitized with 70% isopropyl alcohol before re-use.

4. BUILDINGS AND FACILITIES

4.1 Compounding Space

Space must be specifically designated for nonsterile compounding. The method of designation (e.g., visible perimeter) must be described in the facility's SOPs. Other activities must not be occurring in the space at the same time as compounding. The compounding space must be well lit and must be maintained in a clean, orderly, sanitary condition and in a good state of repair. There must not be carpet in the compounding space. Surfaces should be resistant to damage from cleaning and sanitizing agents.

The space must provide for the orderly placement of equipment and materials to prevent mix-ups among components, containers, labels, in-process materials, and finished CNSPs. The space should be designed, arranged, and used in a way that minimizes cross contamination from noncompounding areas.

4.2 Storage Area

Compounding personnel must monitor temperatures in the storage area(s) either manually at least once daily on days that the facility is open, or continuously with a temperature recording device to ensure the temperature remains within the appropriate range for the CNSPs and components. The results of the temperature readings must be documented on a temperature log or stored in the continuous temperature recording device and must be retrievable. All temperature monitoring equipment must be calibrated or verified for accuracy as recommended by the manufacturer or every 12 months if not specified by the manufacturer.

The compounding facility must adhere to SOPs to detect and reduce the risk of temperature excursions within the storage area(s).

When it is known that a CNSP or component has been exposed to temperatures either below or above the storage temperature limits for the CNSP or component, personnel must determine whether the CNSP or component integrity or quality has been compromised, and, if so, the CNSP or component must be discarded.

All CNSPs, components, equipment, and containers must be stored off the floor in a manner that prevents contamination and permits inspection and cleaning of the storage area(s).

4.3 Water Sources

A source of hot and cold water and an easily accessible sink must be available for compounding. The sink must be emptied of all items unrelated to compounding and must be cleaned if visibly soiled before being used to clean any equipment used in nonsterile compounding. The plumbing system must be free of defects that may contribute to the contamination of any CNSP. *Purified Water* (see *Water for Pharmaceutical Purposes ⟨1231⟩, 3.1.1 Purified Water*), distilled water, or reverse osmosis water should be used for rinsing equipment and utensils.

5. CLEANING AND SANITIZING

Cleaning and sanitizing the surfaces in the nonsterile compounding area(s) must occur on a regular basis at the minimum frequencies specified in *Table 1* or, if compounding is not performed daily, cleaning and sanitizing must be completed before initiating compounding. Cleaning and sanitizing must be repeated when spills occur and when surfaces are visibly soiled. Each occurrence of cleaning and sanitizing must be documented.

Cleaning and sanitizing agents must be selected and used with consideration of compatibilities, effectiveness, and minimal potential to leave residues.

If cleaning and sanitizing are performed as separate steps, cleaning must be performed first.

Table 1. Minimum Frequency for Cleaning and Sanitizing in Nonsterile Compounding Area(s)—Surfaces

Site	Minimum Frequency
Work surfaces	• At the beginning and end of each shift, after spills, and when surface contamination (e.g., from splashes) is known or suspected • Between compounding CNSPs with different components
Floors	• Daily, after spills, and when surface contamination (e.g., from splashes) is known or suspected
Walls	• Every 3 months, after spills, and when surface contamination (e.g., from splashes) is known or suspected
Ceilings	• When visibly soiled and when surface contamination (e.g., from splashes) is known or suspected
Storage shelving	• Every 3 months, after spills, and when surface contamination (e.g., from splashes) is known or suspected

6. EQUIPMENT AND COMPONENTS

6.1 Equipment

The equipment and components used for compounding a CNSP must be suitable for the specific compounding process.

Equipment surfaces that contact components must not be reactive, additive, or sorptive, and must not alter the quality of the CNSP. Disposable or dedicated equipment may be used to reduce the chance of bioburden and cross contamination.

Equipment must be stored in a manner that minimizes the risk of contamination and must be located to facilitate equipment use, maintenance, and cleaning. Equipment and devices used in the compounding or testing of compounded preparations must be inspected prior to use and, if appropriate, verified for accuracy as recommended by the manufacturer at the frequency recommended by the manufacturer or at least every 12 months, whichever is more frequent. After compounding, the equipment must be cleaned to prevent cross contamination of the next preparation.

Weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles (e.g., active pharmaceutical ingredients [APIs], added substances, and conventionally manufactured products) must be assessed to determine if these activities must be performed in a closed-system processing device to reduce the potential exposure to personnel or contamination of the facility or CNSPs. Examples of closed-system processing devices include containment ventilated enclosures (CVEs), biological safety cabinets (BSCs), and single-use containment glove bags. The process evaluation must be carried out in accordance with the facility's SOPs, and the assessment must be documented.

If a BSC or CVE is used, it must be certified at least every 12 months according to requirements such as the current Controlled Environment Testing Association (CETA), NSF International, or American

Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE) guidelines or other laws and regulations of the applicable regulatory jurisdiction.

If a BSC, CVE, or other nondisposable device is used, it must be cleaned as described in *Table 2*.

Table 2. Minimum Frequency for Cleaning and Sanitizing in Nonsterile Compounding Area(s)—Equipment

Site	Minimum Frequency
CVE	• At the beginning and end of each shift, after spills, and when surface contamination (e.g., from splashes) is known or suspected • Clean and sanitize the horizontal work surface of the CVE between compounding CNSPs with different components
BSC	• At the beginning and end of each shift, after spills, and when surface contamination (e.g., from splashes) is known or suspected • Clean and sanitize the horizontal work surface of the BSC between compounding CNSPs with different components • Clean and sanitize under the work surface at least monthly
Other devices and equipment used in compounding operations	• Before first use and thereafter in accordance with the manufacturer's recommendations • If no recommendation is available, between compounding CNSPs with different components

6.2 Components

The compounding facility must have written SOPs for the selection and inventory control of all components from receipt to use in a CNSP.

SDSs must be readily accessible to all personnel working with components located in the compounding facility. Personnel must be instructed on how to retrieve and interpret needed information.

6.2.1 Component selection: Designated person(s) must be responsible for selecting components to be used in compounding.

APIs:

- Must comply with the criteria in the *USP–NF* monograph, if one exists
- Must have a COA that includes specifications and test results and shows that the API meets the specifications
- In the United States, must be obtained from an FDA-registered facility
- Outside of the United States, must comply with the laws and regulations of the applicable regulatory jurisdiction

All components other than APIs:

- Should be accompanied by a COA that verifies that the component meets the criteria in the USP–NF monograph, if one exists, and any additional specifications for the component
- In the United States, should be obtained from an FDA-registered facility (If an API cannot be obtained from an FDA-registered facility, the designated person(s) must select a component that is suitable for the intended use)
- Outside of the United States, must comply with the laws and regulations of the applicable regulatory jurisdiction

Water:

- *Purified Water* (see monograph) or better quality, e.g., *Sterile Water for Irrigation*, must be used for compounding nonsterile drug preparations when formulations indicate the inclusion of water.

6.2.2 Component receipt: Upon receipt of components other than conventionally manufactured products, the COA must be reviewed to ensure that the component has met the acceptance criteria in an appropriate *USP–NF* monograph, if one exists, and the following information must be documented: receipt date, quantity received, supplier name, lot number, expiration date, and results of any in-house or third-party testing performed.

For all components that lack a vendor expiration date, the date of receipt by the compounding facility must be clearly and indelibly marked on each packaging system. Packaging systems of components (i.e., API and added substances) that lack a vendor's expiration date must not be used by the compounding facility after 3 years from the date of receipt. A shorter expiration date must be assigned according to *Pharmaceutical Compounding—Sterile Preparations ⟨797⟩, 9.3 Components, Component Receipt* if the same component container is also used in sterile compounding or if the ingredient is known to be susceptible to degradation.

Any component found to be of unacceptable quality must be promptly rejected, clearly labeled as rejected, and segregated from active stock to prevent use before appropriate disposal. Any other lots of that component from the same vendor must be examined to determine whether the other lots have the same defect.

6.2.3 Component evaluation before use: Before use, compounding personnel must visually re-inspect all components. Each packaging system must be inspected to detect any container breakage, looseness of the cap or closure, or deviation from the expected appearance or texture of the contents that might have occurred during storage.

Compounding personnel must ascertain before use that components are of the correct identity based on the labeling and have been stored under required conditions in the facility.

If the correct identity, strength, purity, and quality of components intended for preparation of CNSPs cannot be confirmed (e.g., containers with damaged or incomplete labeling), the components must be immediately rejected. Any component found to be of unacceptable quality must be promptly rejected, clearly labeled as rejected, and segregated from active stock to prevent use before appropriate disposal.

6.2.4 Component handling: All components must be handled in accordance with the manufacturer's instructions or per laws and regulations of the applicable regulatory jurisdiction. The handling must minimize the risk of contamination, mix-ups, and deterioration (e.g., loss of identity, strength, purity, or quality). For each use, the lot must be examined for evidence of deterioration and other aspects of unacceptable quality. Once removed from the original container, any component not used in compounding (e.g., excess after weighing) should be discarded and not returned to the original container to minimize the risk of contaminating the original container.

6.2.5 Component spill and disposal: The facility must maintain chemical hazard and disposal information (e.g., SDSs) and must document the review and update of its chemical hazard and disposal

information at least every 12 months. Such information must be made accessible to compounding personnel.

The facility must have an SOP for the management of nonhazardous component spills and disposal. If required by the SOP, these activities must be documented, and corrective action must be taken.

The facility must have a readily accessible spill kit in the compounding area. The contents of the spill kit should be affixed to its packaging system if not readily visible on the manufacturer's label.

All personnel who may be required to remediate a spill must receive training in spill management of chemicals used and stored at the compounding facility. Training must be conducted at least every 12 months and documented for all personnel who may be required to clean up a spill.

Waste of any component must be disposed of in accordance with laws and regulations of the applicable regulatory jurisdiction. For information on the handling of HDs, see ⟨800⟩.

7. MASTER FORMULATION AND COMPOUNDING RECORDS

7.1 Creating Master Formulation Records

A master formulation record (MFR) is a detailed record of procedures that describes how the CNSP is to be prepared. An MFR must be created for each unique formulation of a CNSP. CNSPs are prepared according to the MFR, and the details of each preparation are documented on a compounding record (see *7.2 Creating Compounding Records*). Any changes or alterations to the MFR must be approved and documented according to the facility's SOP. See *Box 2* for information that must be included in an MFR.

Box 2. Master Formulation Record

An MFR must include at least the following information:

- Name, strength or activity, and dosage form of the CNSP
- Identities and amounts of all components; if applicable, relevant characteristics of components (e.g., particle size, salt form, purity grade, solubility)
- Container closure system(s)
- Complete instructions for preparing the CNSP including equipment, supplies, and description of compounding steps
- Physical description of the final CNSP
- Assigned beyond-use date (BUD) and storage requirements
- Reference source to support the assigned BUD and storage requirements
- If applicable, calculations to determine and verify quantities and/or concentrations of components and strength or activity of the API(s)
- Labeling requirements (e.g., shake well)
- Quality control (QC) procedures (e.g., pH testing, visual inspection) and expected results
- Other information needed to describe the compounding process and ensure repeatability (e.g., adjusting pH, temperature)

7.2 Creating Compounding Records

A compounding record documents the compounding of each CNSP. A compounding record must be created for all CNSPs. Each compounding record must be reviewed for completeness before the CNSP is released. The name or other unique identifier of the person completing the review and the date of the review must be documented on the compounding record. The compounding record must permit traceability of all components in the case of a recall or known quality issue. The MFR can be used as the basis for preparing the compounding record. For example, a duplicate can be made of the MFR with

blank fields for recording the information necessary to complete the compounding record. See *Box 3* for information that must be included in a compounding record.

Box 3. Compounding Record

A compounding record must include at least the following information:

- Name, strength or activity, and dosage form of the CNSP
- Date and time of preparation of the CNSP
- Assigned internal identification number (e.g., prescription, order, or lot number)
- A method to identify the individuals involved in the compounding process and individuals verifying the final CNSP
- Name, vendor or manufacturer, lot number, and expiration date of each component
- Weight or measurement of each component
- Total quantity of the CNSP compounded
- Assigned beyond-use date (BUD) and storage requirements
- If applicable, calculations to determine and verify quantities and/or concentrations of components and strength or activity of the API(s)
- Physical description of the final CNSP
- Results of quality control procedures (e.g., pH testing and visual inspection)
- MFR reference for the CNSP

8. RELEASE INSPECTIONS

At the completion of compounding and before release, the CNSP must be visually inspected to determine whether the physical appearance is as expected. Inspections must also confirm that the CNSP and its labeling match the compounding record and the prescription or medication order. Some CNSPs, as noted in their MFR, also must be visually checked for certain characteristics (e.g., emulsions must be checked for phase separation). All checks, inspections, and, if required, any other tests necessary to ensure the quality of the CNSP must be detailed in the facility's MFR. Checks and inspections must be documented for each instance. See *12. Quality Assurance and Quality Control* for additional quality assurance (QA) and quality control (QC) activities. Prerelease inspection also must include a visual inspection of container closure integrity (e.g., checking for leakage, cracks in the container, or improper seals). Any CNSP found to be of unacceptable quality (e.g., observed defects) must be promptly rejected, clearly labeled as rejected, and segregated from active stock to prevent use before appropriate disposal.

9. LABELING

Every dispensed CNSP must be labeled with appropriate, legible identifying information to prevent errors during storage, dispensing, and use. The term *labeling* designates all labels and other written, printed, or graphic matter on the immediate container or on (or in) any packaging system or wrapper in which the article is enclosed, except any outer shipping container. The term *label* designates the part of the labeling on the immediate container. See *Labeling ⟨7⟩*.

All labeling must be in compliance with laws and regulations of the applicable regulatory jurisdiction.

The label on each immediate container of the CNSP must, at a minimum, display prominently and legibly the following information:

- Assigned internal identification number (e.g., barcode, prescription, order, or lot number)
- Active ingredient(s), and their amount(s), activity(ies), or concentration(s)
- Storage conditions if other than controlled room temperature
- BUD
- Dosage form
- Total amount or volume if it is not obvious from the container

The labeling on the CNSP should display the following information:

- Route of administration
- Indication that the preparation is compounded
- Any applicable special handling instructions
- Any applicable warning statements
- Name, address, and contact information of the compounding facility if the CNSP is to be sent outside of the facility or healthcare system in which it was compounded

Labeling procedures must be followed as described in the facility's SOPs to prevent labeling errors and CNSP mix-ups.

The label of the CNSP must be verified to ensure that it confirms with the:

1. Prescription or medication order;
2. MFR, if required (see *7.1 Creating Master Formulation Records*); and
3. Compounding Record (see *7.2 Creating Compounding Records*)

All labels must also comply with laws and regulations of the applicable regulatory jurisdiction.

10. ESTABLISHING BEYOND-USE DATES

10.1 Terminology

Each CNSP label must state the date, or the hour and date, beyond which the preparation cannot be used and must be discarded (i.e., the BUD). BUDs for CNSPs are calculated in terms of hours, days, or months.

BUDs and expiration dates are not the same. An expiration date identifies the time during which a conventionally manufactured drug product, active ingredient, or added substance can be expected to meet the requirements of a compendial monograph, if one exists, or maintain expected quality, provided it is kept under the prescribed storage conditions. The expiration date limits the time during which a conventionally manufactured product, API, or added substance may be dispensed or used (see *⟨7⟩, Labels and Labeling for Products in Other Categories, Expiration Date and Beyond-Use Date*).

10.2 Parameters to Consider in Establishing a BUD

BUDs for CNSPs should be established conservatively to ensure that the preparation maintains its required characteristics to minimize the risk of contamination or degradation.

When establishing a BUD for a CNSP, compounders must consider parameters that may affect stability, including but not limited to:

- Chemical and physical stability properties of the API and any added substances in the preparation (e.g., if the API and added substances in the preparation are known to rapidly degrade over time and/or under certain storage conditions, reduce the strength of the preparation, or produce harmful impurities)
- Compatibility of the container closure system with the finished preparation (e.g., leachables, interactions, adsorption, and storage conditions)

- Degradation of the container closure system, which can lead to a reduction in integrity of the CNSP
- Potential for microbial proliferation in the CNSP
- Significant deviations from essential compounding steps and procedures; changes to essential compounding steps may have an impact on the stability of the formulation

10.3 Establishing a BUD for a CNSP

BUDs indicate the days after the CNSP is prepared and beyond which the CNSP must not be used. The BUDs in *Table 4* are based on the ability of the CNSP to maintain chemical and physical stability and to suppress microbial growth. These BUDs represent the limit for CNSPs that are packaged in tight, light-resistant containers unless conditions under *10.4 CNSPs Requiring Shorter BUDs* or *10.5 Extending BUDs for CNSPs* apply.

The aqueous and nonaqueous dosage forms in *Table 4* are defined based on the water activity (a_w) of the most similar drug preparation described in *Table 3* or *Application of Water Activity Determination to Nonsterile Pharmaceutical Products ⟨1112⟩*. In general, the use of water activity aids in assessing the susceptibility of CNSPs to microbial contamination and the potential for API degradation due to hydrolysis. Water activity is different from water content and may be considered as the available water to support microbial growth and hydrolytic reactions. Nonaqueous dosage forms will not support spore germination or microbial growth due to their low water activity. Reduced water activity greatly assists in the prevention of microbial proliferation in conventionally manufactured products and is expected to convey the same benefit to CNSPs.

The manufactured products in ⟨1112⟩, *Table 2* and compounded preparations in *Table 3* below are not exhaustive. However, they provide guidance on the a_w value of a particular CNSP and can assist personnel in determining the BUD by dosage form using *Table 4*. CNSPs need not be tested for water activity unless necessary to determine if the preparation is aqueous or nonaqueous.

When preparing CNSPs, raw materials and equipment contribute a bioburden to the final preparation. CNSPs with $a_w \geq 0.6$ should contain suitable antimicrobial agents to protect against the proliferation of bacteria, yeast, and mold contamination if inadvertently introduced during or after the compounding process. Careful consideration should be taken when selecting a preservative to ensure microbiological effectiveness and stability. When antimicrobial preservatives are clinically contraindicated in a CNSP, storage of the preparation in a refrigerator is required if such storage does not change the physical or chemical properties of the CNSP (i.e., precipitation).

Table 3. Water Activity (a_w) of Common Compounded Nonsterile Dosage Forms[a]

Nonaqueous Dosage Forms: $a_w < 0.60$			Aqueous Dosage Forms: $a_w \geq 0.60$		
Dosage Form	**Description**	**a_w**	**Dosage Form**	**Description**	**a_w**
Animal treat	Animal treat (oil flavor)	0.507	Animal treat	Animal treat with 15%–18% aqueous flavor	0.716
Capsule (oil filled)	Olive oil encapsulated	0.468	Cream	Cream vehicle (oil in water emulsion, petrolatum free)	0.968

Nonaqueous Dosage Forms: a_w < 0.60			Aqueous Dosage Forms: a_w ≥ 0.60		
Dosage Form	**Description**	**a_w**	**Dosage Form**	**Description**	**a_w**
Capsule (powder filled)	Powder base encapsulated	0.435	Cream	Emollient cream (petrolatum and mineral oil)	0.984
Gel (glycol based)	Propylene glycol, ethoxy diglycol, or hydroxypropyl cellulose gel	0.056	Cream	Cream (oil in water emulsion with natural oils)	0.989
Lollipop	Lollipop	0.460	Foam	Foaming surfactant solution	0.983
Ointment	Hydrophilic petrolatum	0.396	Gel (water based)	Alcohol-free aqueous gel	0.990
Ointment	Polyethylene and mineral oil gel base	0.459	Gel (water based)	Hydroxypropyl methylcellulose (HPMC) gel	1.000
Oral solution (glycol based)	20% Polyethylene glycol and 80% propylene glycol	0.009	Lotion	Lotion (oil in water emulsion)	0.986
Oral solution (oil based)	Medium chain triglycerides oil	0.338	Nasal spray	Nasal spray	0.991
Oral suspension (fixed oil)	Fixed oil with thickener	0.403	Oral solution (water based)	Low sucrose syrup vehicle	0.906
Powder for inhalation	Encapsulated powder for inhalation	0.402	Oral solution (water based)	90% Water and 10% glycerin	0.958
Stick	Lip balm	0.181	Oral suspension (water based)	Oral suspension base	0.992
Suppository	Polyethylene glycol base	0.374	Rinse	Polymer gel with 30% water	0.960
Suppository	Fatty acid base	0.385	Shampoo	Shampoo	0.976
Tablet (compressed)	Compressed tablet	0.465	Simple syrup	Simple syrup	0.831
Tablet (triturate)	Tablet triturate (lactose and/or sucrose)	0.427	—	—	—

Nonaqueous Dosage Forms: a_w < 0.60			Aqueous Dosage Forms: a_w ≥ 0.60		
Dosage Form	**Description**	**a_w**	**Dosage Form**	**Description**	**a_w**
Troche (gelatin)	Gelatin troche with NMT 3% aqueous flavor	0.332	—	—	—
Troche (glycol based)	Polyglycol troche with NMT 3% aqueous flavor	0.571	—	—	—

[a] The measured water activities in *Table 3* for the different dosage forms are intended to be representative examples. The descriptions listed are details about the tested formulation and are provided to assist personnel in determining whether their CNSPs are aqueous or nonaqueous.

Table 4. BUD Limit by Type of Preparation in the Absence of a *USP–NF* Compounded Preparation Monograph or CNSP-Specific Stability Information

Type of Preparation	BUD (days)	Storage Temperature[a]
Aqueous Dosage Forms (a_w ≥ 0.60)		
Non-preserved aqueous dosage form[b]	14	Refrigerator
Preserved aqueous dosage form[b]	35	Controlled room temperature or refrigerator
Nonaqueous Dosage Forms (a_w < 0.60)		
Oral liquids (nonaqueous)[c]	90	Controlled room temperature or refrigerator
Other nonaqueous dosage forms[d]	180	Controlled room temperature or refrigerator

[a] See *Packaging and Storage Requirements* ⟨659⟩

[b] An aqueous preparation is one that has an a_w ≥ 0.6 (e.g., emulsions, gels, creams, solutions, sprays, or suspensions).

[c] A nonaqueous oral liquid is one that has an a_w < 0.6.

[d] Capsules, tablets, granules, powders, nonaqueous topicals, suppositories, and troches.

10.4 CNSPs Requiring Shorter BUDs

The BUDs in *Table 4* are the BUD limits for CNSPs in the absence of specific stability information. This does not absolve the designated person(s) from performing due diligence to determine if there is existing stability data that would require a shorter BUD.

A shorter BUD must be established under the following circumstances:

- If the components in the CNSP have an expiration date that is earlier than the BUD that could be assigned from *Table 4*, then the BUD of the CNSP must not exceed the shortest remaining expiration date of any component
- If the CNSP includes components from other compounded preparations, then the BUD of the final CNSP must not exceed the shortest remaining BUD of any of those compounded preparations

- If the formulation is known to require a shorter BUD

10.5 Extending BUDs for CNSPs

CNSPs with a *USP–NF* monograph: When compounding from a *USP–NF* compounded preparation monograph for the CNSP, the BUD must not exceed the BUD specified in the monograph.

CNSPs with stability information: The BUDs specified in *Table 4* for aqueous and nonaqueous dosage forms may be extended up to a maximum of 180 days if there is a stability study (published or unpublished) using a stability-indicating analytical method for the API(s), CNSP, and type of container closure that will be used.

If the BUD of the CNSP is extended beyond the BUDs in *Table 4*, an aqueous CNSP must be tested for antimicrobial effectiveness (see *Antimicrobial Effectiveness Testing* ⟨51⟩). The designated person(s) may rely on antimicrobial effectiveness testing that is conducted (or contracted for) once for each formulation in the particular container closure system in which it will be packaged. Alternatively, the designated person(s) may rely on antimicrobial effectiveness testing results provided by an FDA-registered facility or published in peer-reviewed literature as long as the CNSP formulation (including any preservative) and container closure materials of composition are the same as those tested (unless a bracketing study is performed). Antimicrobial effectiveness testing may be performed on a low concentration and a high concentration of the active ingredient in the formulation to establish preservative effectiveness across various strengths of the same formulation (e.g., bracketing). The concentration of all other ingredients (including preservatives) must fall within the bracketed range.

11. SOPS

Facilities preparing CNSPs must develop SOPs on all aspects of the compounding operation. All personnel who conduct or oversee compounding activities must be trained in the SOPs and be responsible for ensuring that they are followed.

One or more person(s) must be designated to ensure that SOPs are fully implemented. The designated person(s) must ensure that follow-up occurs if problems, deviations, or errors are identified.

12. QUALITY ASSURANCE AND QUALITY CONTROL

Quality assurance and quality control programs are necessary to ensure that consistently high-quality CNSPs are prepared. QA is a system of procedures, activities, and oversight that ensure that the compounding process consistently meets quality standards. QC is the sampling, testing, and documentation of results that, taken together, ensure that specifications have been met before release of the CNSP. See *Quality Assurance in Pharmaceutical Compounding* ⟨1163⟩.

A facility's QA and QC programs must be formally established and documented in SOPs that ensure that all aspects of the preparation of CNSPs are conducted in accordance with this chapter ⟨795⟩, and laws and regulations of the applicable regulatory jurisdiction. Designated person(s) must ensure that the facility has formal, written QA and QC programs that establish a system of:

- Adherence to procedures
- Prevention and detection of errors and other quality problems
- Evaluation of complaints and adverse events
- Appropriate investigations and corrective actions such as:
    - Determination of when recalls must be initiated, which should include procedures to immediately notify the prescriber of a failure of specifications with the potential to cause patient harm (e.g., strength, purity, or other quality attributes)
    - Determination of the distribution of any affected CNSP, including other affected lots, and the date and quantity of distribution
    - Identification of patients who have received the CNSP
    - Recall any unused dispensed stock and quarantine any stock remaining

- Disposal of the recalled CNSP and documentation thereof

The implementation of recall procedures must be documented and reported to appropriate regulatory bodies as required by laws and regulations of the applicable regulatory jurisdiction.

The SOPs must describe the roles, duties, and training of the personnel responsible for each aspect of the QA program. Designated person(s) responsible for the QA program must have the training, experience, responsibility, and authority to perform these duties. The overall QA and QC program must be reviewed at least once every 12 months by the designated person(s). The results of the review must be documented, and appropriate action must be taken if needed.

13. CNSP PACKAGING AND TRANSPORTING

13.1 Packaging of CNSPs

SOPs must describe packaging of CNSPs. Personnel should select and use packaging materials that will maintain the physical and chemical integrity and stability of the CNSPs. Packaging materials must protect CNSPs from damage, leakage, contamination, and degradation, while simultaneously protecting personnel from exposure.

13.2 Transporting CNSPs

If transporting CNSPs, the facility must have written SOPs to describe the mode of transportation, any special handling instructions, and whether temperature monitoring devices are needed.

14. COMPLAINT HANDLING AND ADVERSE EVENT REPORTING

Compounding facilities must develop and implement SOPs for complaint and adverse event report receipt, acknowledgment, and handling and designate one or more person(s) to be responsible for handling them. Complaints may include concerns or reports on the quality and labeling of, or possible adverse reactions to, a specific CNSP.

14.1 Complaint Handling

The designated person(s) must ensure that all complaints are reviewed to determine whether the complaint indicates a potential quality problem with the CNSP. If it does, a thorough investigation into the cause of the problem must be initiated and completed. The investigation must consider whether the quality problem extends to other CNSPs. Corrective action, if necessary, must be implemented for all potentially affected CNSPs. Consider whether to initiate a recall of potentially affected CNSPs and whether to cease nonsterile compounding processes until all underlying problems have been identified and corrected.

A readily retrievable written or electronic record of each complaint must be kept by the facility, regardless of the source of the complaint (i.e., email, telephone, or mail). The record must contain the name of the complainant or other unique identifier, the date the complaint was received, the nature of the complaint, and the response to the complaint. In addition, to the extent that the information is known, the following should be recorded: the name and strength of the CNSP, the prescription or medication order number, and the lot number if one is assigned.

The record must also include the findings of any investigation and any follow-up. Records of complaints must be easily retrievable for review and evaluation for possible trends and must be retained in accordance with the record-keeping requirements described in *15. Documentation*. A CNSP that is returned in connection with a complaint must be quarantined until it is destroyed after completion of the investigation and in accordance with laws and regulations of the applicable regulatory jurisdiction.

14.2 Adverse Event Reporting

The designated person(s) must ensure that reports of potential adverse events involving a CNSP are reviewed. If the investigation into an adverse event reveals a quality problem with a CNSP that is likely to affect other patients, those patients and prescribers potentially affected must be informed. The

designated person(s) must review all adverse event reports as part of the QA and QC programs (see *12. Quality Assurance and Quality Control*). Adverse events potentially associated with the quality of CNSPs must be reported in accordance with the facility's SOPs and all laws and regulations of the applicable regulatory jurisdiction.

15. DOCUMENTATION

All facilities where CNSPs are prepared must have and maintain written or electronic documentation to demonstrate compliance with the requirements in this chapter. This documentation must include, but is not limited to, the following:

- Personnel training, competency assessments, and qualification records including corrective actions for any failures
- Equipment records (e.g., calibration, verification, and maintenance reports)
- COAs and all documentation required for components not conventionally manufactured
- Receipt of components
- SOPs, MFRs, and compounding records
- Release inspection and testing records
- Information related to complaints and adverse events including corrective actions taken
- Results of investigations and corrective actions
- Records of cleaning and sanitizing the designated compounding area
- Temperature logs
- Accommodations to personnel compounding CNSPs
- Any required routine review (e.g., yearly review of QA and QC programs, yearly review of chemical hazard and disposal information)

Documentation must comply with all laws and regulations of the applicable regulatory jurisdiction. Records must be legible and stored in a manner that prevents their deterioration and/or loss. All required compounding records for a particular CNSP (e.g., MFR, compounding record, and release inspection and testing results) must be readily retrievable for at least 3 years after preparation or as required by the laws and regulations of the applicable regulatory jurisdiction, whichever is longer.

GLOSSARY

Active pharmaceutical ingredient (API): Any substance or mixture of substances intended to be used in the compounding of a preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or animals or affecting the structure and function of the body

Added substance: An ingredient that is necessary to compound a preparation but is not intended or expected to cause a pharmacologic response if administered alone in the amount or concentration contained in a single dose of the compounded preparation. The term is used synonymously with *inactive ingredient*, *excipient*, and *pharmaceutical ingredient*.

ASHRAE: American Society of Heating, Refrigerating, and Air-Conditioning Engineers

Biological safety cabinet (BSC): A ventilated cabinet that may be used for compounding. These cabinets are divided into three general classes (Class I, Class II, and Class III). Class II BSCs are further divided into types (Type A1, Type A2, Type B1, and Type B2).

Beyond-use date (BUD): The date or time after which a CNSP shall not be used, stored, or transported. The date is determined from the date or time the preparation is compounded.

CETA: Controlled Environment Testing Association

Certificate of analysis (COA): A report from the supplier of a component, container, or closure that accompanies the supplier’s material and contains the specifications and results of all analyses and a description of the material.

Cleaning: The process of removing soil (e.g., organic and inorganic material) from objects and surfaces, normally accomplished by manually or mechanically using water with detergents or enzymatic products.
Component: Any ingredient used in the compounding of a preparation, including any API, added substance, or conventionally manufactured product.
Compounded nonsterile preparation (CNSP): A preparation intended to be nonsterile created by combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug or bulk drug substance.
Compounding personnel: Personnel trained to compound or oversee compounding of preparations.
Compounding: The process of combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug or bulk drug substance to create a nonsterile medication.
Compounding area: A space that is specifically designated for nonsterile compounding.
Container closure system: Packaging system components that together contain and protect the dosage form. This includes primary packaging system components and secondary packaging system components if the latter are intended to provide additional protection.
Containment glove bag: A single-use disposable glove bag that is capable of containing airborne chemical particles.
Containment ventilated enclosure (CVE): A full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through high-efficiency particulate air (HEPA) filtration and to prevent their release into the work environment.
Conventionally manufactured product: A pharmaceutical dosage form, usually the subject of an FDA-approved application, that is manufactured under current good manufacturing practice conditions.
Designated person(s): One or more individuals assigned to be responsible and accountable for the performance and operation of the facility and personnel for the preparation of CNSPs.
FDA: Food and Drug Administration of the United States
Hazardous drug (HD): Any drug identified by at least one of the following criteria: carcinogenicity, teratogenicity or developmental toxicity; reproductive toxicity in humans; organ toxicity at low dose in humans or animals; genotoxicity or new drugs that mimic existing HDs in structure or toxicity. See ⟨800⟩
Label: A display of written, printed, or graphic matter on the immediate container of any article.
Labeling: All labels and other written, printed, or graphic matter that are 1) on any article or any of its containers or wrappers or 2) accompanying such an article.
MFR: Master formulation record.
Purified water: The minimal quality of source water for the production of *Purified Water* is drinking water whose attributes are prescribed by the US Environmental Protection Agency (EPA), the European Union, Japan, or the World Health Organization (WHO). This source water may be purified using unit operations that include deionization, distillation, ion exchange, reverse osmosis, filtration, or other suitable purification procedures. (See ⟨1231⟩, *3.1.1 Purified Water*.)
Preservative: A substance added to inhibit microbial growth.
Quality assurance (QA): A system of procedures, activities, and oversight that ensures the compounding process consistently meets quality standards.
Quality control (QC): The sampling, testing, and documentation of results that, taken together, ensure that specifications have been met before release of the CNSP.
Reconstitution: The process of adding a diluent to a conventionally manufactured product to prepare a solution or suspension.
Release inspection and testing: Visual inspection and testing performed to ensure that a preparation meets appropriate quality characteristics.
Sanitizing agent: An agent for reducing, on inanimate surfaces, the number of all forms of microbial life including fungi, viruses, and bacteria.
SDS: Safety data sheet.

SOP: Standard operating procedure.

Specification: The tests, analytical methods, and acceptance criteria to which any components, CNSP, container closure system, equipment, or other material used in the compounding of CNSPs must conform to be considered acceptable for its intended use.

Stability: The extent to which a product or preparation retains physical and chemical properties and characteristics within specified limits throughout its expiration or BUD.

Water activity (a_w): A measure of the fraction of total water that is unbound and freely available to participate in chemical, biochemical, or physicochemical reactions or provide an environment that can support microbial growth. Water activity is not water content. ▲ (USP 1-May-2023)

Page Information:

Not Applicable

DocID:

On Aug 5, 2021, at 4:17 PM, A. J. Day <ADay@pccarx.com> wrote:

Matt and I reviewed the document and came up with some comments for your consideration. Let me know what you think.
-A.J.

I'd like them to explain their expectations for "testing" of preparations. Many pharmacies may interpret this to allow some form of in-house testing based on weights or final pharmacist verification. Testing by an accredited laboratory is likely your intent, so perhaps there needs to be more specific language? Eagle may wish to contribute thoughts on which accreditation or certifications might be most appropriate to list.

<image001.jpg>
Line 250, I don't think you want the manufacturer's specification for minimum weighable quantity, because that would point to USP <41> which would create a minimum quantity of 840mg. USP <41> is not mentioned in USP compounding chapters, and therefore does not apply to compounding per USP General Notices. Suggest ending the sentence after MAWQ for that balance.

<image002.png>

I also think the CVE should be certified in compliance with the manufacturer's instructions, or at a minimum every 12 months. Line 271 just says Q12m. Also, line 270 appears to have a page number or line number from USP copied into it. See the random "249"?

<image003.jpg>

Line 373-375: IPA is a disinfectant, but not known to remove drugs. I'm not sure the best phrasing to suggest apart from "appropriate agent" which is pretty nebulous.
<image005.png>

Line 393 complaints, I'd like them to add investigations, corrective and preventative actions.

<image004.jpg>

A.J. Day, PharmD | Vice President of Clinical Services

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From: Lee,Yunkyung <s6685m@heb.com>
Sent: Friday, October 1, 2021 11:43 AM
To: Tim Tucker
Subject: Compounding pharmacy rules

To whom it may concern,

We're literally filling MULTIPLE magic mouth wash prescriptions for patients with sore throat, mouth sores, GI cancer and indigestion every day coming from hospitals and urgent cares. Our competitor Walmart cannot fill these prescriptions due to their company policy and rules so many of the customers in Texas are relying on us to assist them in the very timely manner so their pain can be relieved as soon as possible. Modifying the current compounding rules will not benefit but only delay the treatment of their symptoms. Please reconsider amending this rules.

Thanks for all your help,

Yunkyung Lee
Pharmacist in Charge at HEB in Copperas Cove

From: Kitchens,Paul <kitchens.paul@heb.com>
Sent: Friday, October 1, 2021 12:13 PM
To: Tim Tucker
Cc: Kitchens,Paul
Subject: Please Modify the Proposed Compounding Rules

Mr. Tucker:
Please consider modifying the proposed compounding rule changes which will severely impact the availability of simple non-sterile preparations that the patients in my stores need.
Requiring a special designation for a pharmacy to flavor liquid products which increases compliance with everyone, especially children, will limit this to primarily specialized practices and will make it unavailable for the majority of Texans as well as increase costs for families with children. The net result will be less compliance and discontinuance of therapy before completion.
Another widely compounded product that would be impacted is the simple addition of approved items where a torsion balance is not required such as a combination of creams for a diaper rash or mixing of liquids for mouth sores for cancer treatments. Both of these type preparations are items that have impacted me personally- the former for my grandchildren and the later for myself when undergoing cancer treatment.
I've been a pharmacist since 1977 and a large percentage of the prescriptions in my initial practice would not be possible with the newly proposed rules. I urge the Board to reconsider and modify these overly stringent requirements.
Thanks.

Paul Kitchens, RPh
Pharmacy Director, **H-E-B** North West Food Drug Division
office 254-662-7510 | cell 254-855-7091 | fax 254-662-7518 | kitchens.paul@heb.com

From: Guerra,Thomas RPh <guerra.thomas@heb.com>
Sent: Wednesday, October 13, 2021 3:08 PM
To: Tim Tucker
Subject: TSBP Proposed Compounding Rules

Mr. Tim Tucker,

I would like to submit my comments in regards to the proposed TSBP Compounding Rules. The proposed rules would severely affect the level of healthcare that retailers (Chain and Independent) are able to provide to our Customers in Texas. A change in the compounding rules would also affect the convenience factor for many patients which we know is key when it comes to adherence/compliance. Below are some key points to consider:

- Simple compounding, as described below, has been done in the Texas by a trained and licensed Pharmacist SAFELY and EFFECTIVELY for decades. The proposed change to the definition of Compounding would have negative effects on our patients ability to conveniently acquire the medications that they need.
- Flavoring of commercially available products should be completely excluded from the proposed definition of compounding. As you are aware, many commercially available preparations such as antibiotic suspensions, cough syrups, or other liquid formulations may not be palatable to certain patients. Flavoring those preparations makes those medication much more suitable and likely to be taken. Additionally, the flavoring process does not change the effectiveness/efficacy of the medication.
- Compounding of simple products such cream/ointment mixtures, liquids (which may include "magic mouthwash/pink magic", etc.) should be excluded from the definition of compounding.
- If the type of simple compounding or flavoring just described is included in the proposed definition of Compounding, there will be a detrimental effect on the availability of those medications and in turn there will be a significant effect on adherence/compliance.

Perhaps the biggest impact will be that if ALL compounding is included in the Rules, every Class A Pharmacy in Texas which performs the simple compounding described above will need to be re-licensed as a Class A-N Pharmacy and the various onerous requirements of §291.131 would have to be implemented. These **onerous** requirements would include:

1. Training requirements for Technicians and Pharmacists which is not necessary for the simple compounding performed today under the current definition of compounding
2. Sample product testing
3. Possible requirement to add a hood in Pharmacies, many of which are already cramped for space.
4. Designation of a dedicated space in the pharmacy for a non-sterile compounding area
5. Addition of a balance in every Pharmacy which must be inspected and calibrated EVERY 12 MONTHS by a "qualified independent individual" OUTSIDE of the company that is being inspected. Balance check will no longer be performed by the TSBP compliance inspector
6. Employees performing compounding duties will be required to wear gloves and other bodily cover (shoe covers, head and facial hair covers, face masks, and gowns)

Thank you for your consideration.

Thomas Guerra, RPh
H-E-B Pharmacy Sr. Director of Operations-HFD, NWFD, Contact Call Center, & RxOC
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October 18, 2021

Mr. Eamon D. Briggs
Assistant General Counsel
Texas State Board of Pharmacy
333 Guadalupe Street, Suite 3-500
Austin, Texas 78701

Public Comment in Connection with Proposed Rules Regarding Non-Sterile Compounding as set forth in 22 TAC §§ 291.36 and 291.131.

Dear Mr. Briggs:

FLAVORx is pleased to provide comments to the Texas State Board of Pharmacy on the proposed rule amendments to 22 TAC §§291.36 and 291.131 concerning the classification of pharmacies engaged in compounding non-sterile preparations.

Introduction

For decades, pharmacies in Texas have utilized the FLAVORx program to improve the palatability of conventionally manufactured liquid medications for children in a safe and uniform manner. Over the years, the process of flavoring liquid medications with FLAVORx has improved and become more efficient, to the point where we now supply pharmacies in Texas with machines that flavor liquid medications automatically at the push of a button. FLAVORx flavoring and additives are inert. They are tested to ensure the stability and pH of conventionally manufactured medications is maintained, and they are proven safe with an estimated 1 million children in Texas benefiting from the widespread availability of the service each year.

Concerns with the Published Proposed Rule Language

Under the proposed rules as drafted, the simple flavoring of commercially available medications (such as amoxicillin, prednisolone, and Tamiflu) will be subjected to a new set of detailed, specific requirements for non-sterile compounding. These new requirements will force pharmacies engaged in flavoring to install a hood or have a closed-system processing device, implement hours of additional employee training that is unrelated to the flavoring process, and increase costs by requiring expensive and unnecessary testing of the flavored product. **Simply put, if the proposed rules are adopted as written, thousands of pharmacies in Texas will be forced to stop offering the flavoring service to their patients.** This would greatly diminish patient access to a valuable and trusted service and be catastrophic to pediatric patient care.

Suggested Modifications in the Published Proposed Rule Language

We feel the Board should not adopt the proposed amendments to the rules. If, however, the Board believes that the process of implementing more specific rules on non-sterile compounding should not be delayed, then we respectfully request the Board modify the proposed rules as described below to make clear that flavoring of conventionally manufactured medications is exempted from the new licensing and other requirements. This will provide assurances to pharmacies in Texas that they may continue to provide the flavoring service to their patients in the same manner as they have for years.

FLAVORx proposes the following revisions, indicated in red, to §291.36 (b) and §291.131 (d)(1)(H) to ensure flavoring continues to be readily available to children in Texas and is performed in a safe and effective manner, without subjecting pharmacies to unnecessary and onerous licensure and operational requirements.

1. §291.36 (b)

"§291.36 (b) Licensing Requirements for Class A-N. A community pharmacy engaged in the compounding of non-sterile preparations that use bulk API or excipients or manipulation beyond the FDA labeling of a commercial product (e.g., crushing a tablet or opening a capsule), shall be designated as a Class A-N pharmacy. The addition of a flavoring to a conventionally manufactured medication shall be excluded from the aforesaid requirements to the extent it is performed in accordance with the conditions specified in §291.131 (d)(1)(H)."

The best way to address any concerns the Board may have regarding the safety of the actual flavoring process would be to set clear, specific standards for flavoring, as many other State Boards have done. Since the Texas Administrative Code directly addresses flavoring prescriptions in paragraph (d)(1)(H) of 22 TAC §291.131 (*Pharmacies Compounding Non-Sterile Preparations*), that language should be revised as follows to ensure the safety and efficacy of flavorings being added to medications.

2. §291.131

"(H) A pharmacist may add flavoring to a prescription at the request of a patient, the patient's agent, or the prescriber, and it shall be exempt from the other requirements of this section, provided the following conditions are met:

(i) The flavoring agents are therapeutically inert and nonallergenic, do not exceed five (5) percent of a drug product's total volume, and produce no effect other than the instillation or modification of flavor.

Conclusion

In summary, the revisions to §291.36 (b) and §291.131 (d)(1)(H) that we have suggested above would ensure that medication flavoring is administered safely and effectively in Texas without reducing patient access to this valuable pharmacy service. By incorporating this language, pharmacists and technicians in Texas would be able to continue to add flavorings to conventionally manufactured medications regardless of any non-sterile compounding requirements that may be otherwise beneficial and warranted.

Thank you once again for this opportunity to comment on the proposed rule. We would be pleased to further discuss this matter should the Board have any questions and we look forward to providing oral comments at the Board's upcoming meeting.

Sincerely,

Chad Baker
Senior Vice President
FLAVORx, Inc.

Copy:

Mr. Tim Tucker, Executive Director, Texas State Board of Pharmacy
Texas State Board of Pharmacy

FLAVORx
HEALTHY KIDS • HAPPY FAMILIES

TIM,

WE PUT TOGETHER THESE PACKETS TO HELP YOU AND THE BOARD MEMBERS AS YOU DISCUSS FLAVORING AND NON-STERILE COMPOUNDING. I HOPE YOU FIND THEM INFORMATIVE AND USEFUL.

BEST REGARDS,

FLAVORx
HEALTHY KIDS • HAPPY FAMILIES

CHAD BAKER
Senior VP Marketing

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Cell: 301-512-0784
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Columbia, MD 21046

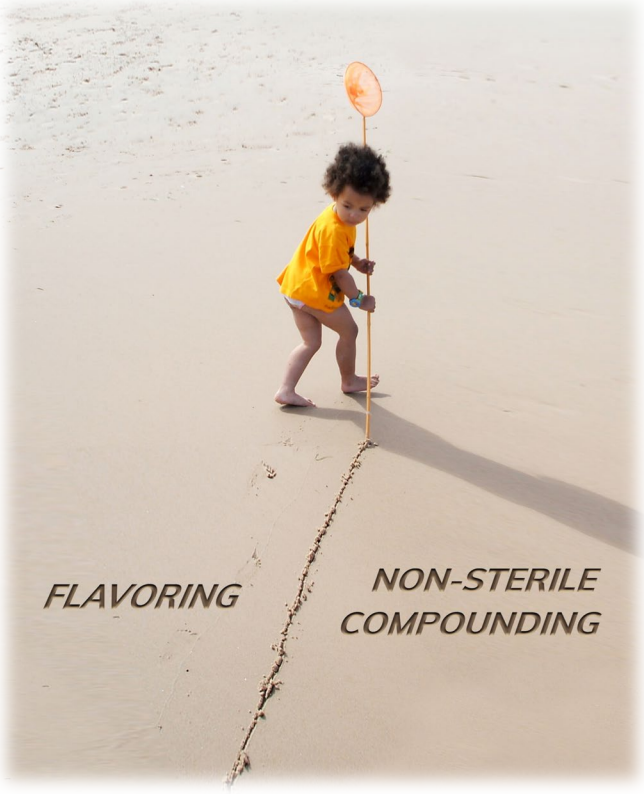
Flavoring Kids Medicine in Texas

Allowing children to choose the taste of their liquid medicine is one of the most effective tools pharmacists have at their disposal to improve pediatric compliance and adherence.

Access to this proven, safe service is widely available to children and parents across Texas *now* and has been for decades.

“Drugs don’t work in patients who don’t take them”

- C. Everett Coop



Flavoring Kids Medicine in Texas

Currently

- The Texas State Board of Pharmacy (TSBP) currently allows pharmacies to flavor conventionally manufactured liquid medications for a child to their preferred taste without subjecting the pharmacy to requirements associated with non-sterile compounding.

- In 2007, the TSBP adopted specific language to allow taste changes to be made in pharmacies "at the request of the patient, patient's caregiver or the prescriber".

- Because of the TSBP's stance on flavoring, each year over 1 million children in Texas have an easier time taking their medicine – in fact, it is estimated that 15 million children in Texas have benefitted from being able to choose the taste of their medicine since the TSBP adopted their common-sense approach to flavoring 14 years ago.

- **TSBP's 2007 ruling has since been viewed as a model for other states to follow, with 24 additional State Boards of Pharmacy now explicitly excluding the simple act of flavoring medications from non-sterile compounding in either rule or guidance.**

  (Of note - Washington is the only state in the country that strictly regulates flavoring as compounding. Many pharmacies there have ceased to offer the service to children and parents there.)

Flavoring Kids Medicine in Texas

Safety First

- As you will see in the attached appendices, allowing pharmacies to customize the taste of children's medications is safe and widely regarded as so by many State Boards of Pharmacy.

- We, FLAVORx, provide over 38,000 pharmacies in the U.S. and 3,200 pharmacies across Texas with a standardized, uniform, and automated way for children to choose the taste of their liquid medicine using flavors that have been tested to ensure the efficacy, potency, pH, and BUD of the drug remains intact.

- Over 160 million liquid medications have been flavored using the FLAVORx program since we were founded in 1995, with at least 15 million of those flavorings occurring in pharmacies located in Texas.

- The alternative to safely flavoring medications in the pharmacy is to leave parents to their own devices using untested, home-cooked methods that could very well impact how medicines work in children.

Flavoring Kids Medicine in Texas

Changes Under Consideration

- The TSBP has proposed new language that, if not revised, would subject the simple act of flavoring conventionally manufactured medications to non-sterile compounding requirements.

- If the current proposed language is adopted as written, pharmacies will be required to do the following, and more, in order to simply flavor a medication:

    - Remodel the pharmacy
    - Install a hood in the pharmacy or have a closed-system processing device
    - Sit through hours and hours of training that is irrelevant to the task of flavoring medications
    - Perform extensive and expensive testing
    - Wear gloves and garb up each time they flavor a medication
    - Receive authorization from a physician, physician's assistant, or nurse practitioner

- Because compliance with these regulations is tremendously costly and time-consuming, most pharmacies will cease to offer the flavoring service, taking a valuable compliance-boosting tool out of pharmacist's hands, limiting access to this much needed service to compounding pharmacies only, and negatively impacting children's health.

Flavoring Kids Medicine in Texas
A Recommended Approach Going Forward

To maintain widespread access to such a valuable service, we respectfully request the Texas State Board of Pharmacy continue to exclude patient-preferred flavoring of conventionally manufactured medications from the requirements of non-sterile compounding, as it has for the past 14 years.

To ensure patient safety, we request the Board adopt language that provides clear guidelines under which the addition of flavorings to conventionally manufactured drugs can be performed safely, while preserving the widespread availability of the service to children & parents.

Many State Boards of Pharmacy use a version of the following language in law:

> "The addition of flavoring to a drug shall not be considered non-sterile compounding when such additive is inert, nonallergenic, and produces no effect other than the instillation or modification of flavor and is not greater than five (5) percent of the drug's total volume."

We request the Texas State Board of Pharmacy adopt this language as well.

In Summary

- Flavoring of pediatric liquid medications is an important tool in the pharmacist's toolbox to improve compliance and children's health.

- Flavoring of pediatric liquid medications is proven safe, both in independent laboratory testing and in over 160 million actual use cases.

- Flavoring of pediatric liquid medications is widely regarded by State Boards of Pharmacy as separate from non-sterile compounding.

- The Texas State Board of Pharmacy excludes flavoring from non-sterile compounding requirements in its existing rules.

- Subjecting the simple flavoring of conventionally manufactured medications to burdensome non-sterile compounding regulation will severely limit access to this valuable service and ultimately have a negative impact on children's health.

- For this reason, it is important that the Texas State Board of Pharmacy continue to allow non-compounding pharmacies to flavor medications for children without additional oversight or regulation.

Thank you for your attention to this serious matter. We share your commitment to protecting patient safety while maintaining access to helpful pharmacy services. Should you have any questions, please do not hesitate to reach out.

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Appendix A
FLAVORx Bio

FLAVORx
Who We Are & What We Do

- We provide pharmacies with a standardized, uniform, automated way for children to choose the taste of their liquid medicine to improve adherence and compliance, using flavors that have been tested to ensure the safety, efficacy, potency, BUD, and pH of the drug remains intact (see Appendix B for sample test reports)
- We were established in 1995 and have been working with pharmacies in Texas since 1996.
- Over 38,000 pharmacies in the U.S. now carry FLAVORx, with 3,200 of those hailing from Texas.
- 160+ million liquid medications have been custom-flavored using the FLAVORx program since our inception.

We estimate over 1 million Texan children benefit from this service every year

- Our products are predominantly used with conventionally manufactured liquid medications, like amoxicillin, Cleocin, and Tamiflu, and are always added by a pharmacist or technician at the time of dispensing.
- The addition of FLAVORx flavors does not exceed 5% of total volume and typically amounts to 1% – 3% of total volume, with no change in concentration for medications requiring reconstitution.
- Our flavors are HPLC/UV assay tested in medications to ensure there is no impact on the API's potency, pH of the preparation, and organoleptics.
- We are regulated and inspected by the FDA.
- No adverse events related to the use of our product have been reported to us in our 26 years of supplying pharmacies.

Appendix B
Sample Studies

ACETAMINOPHEN

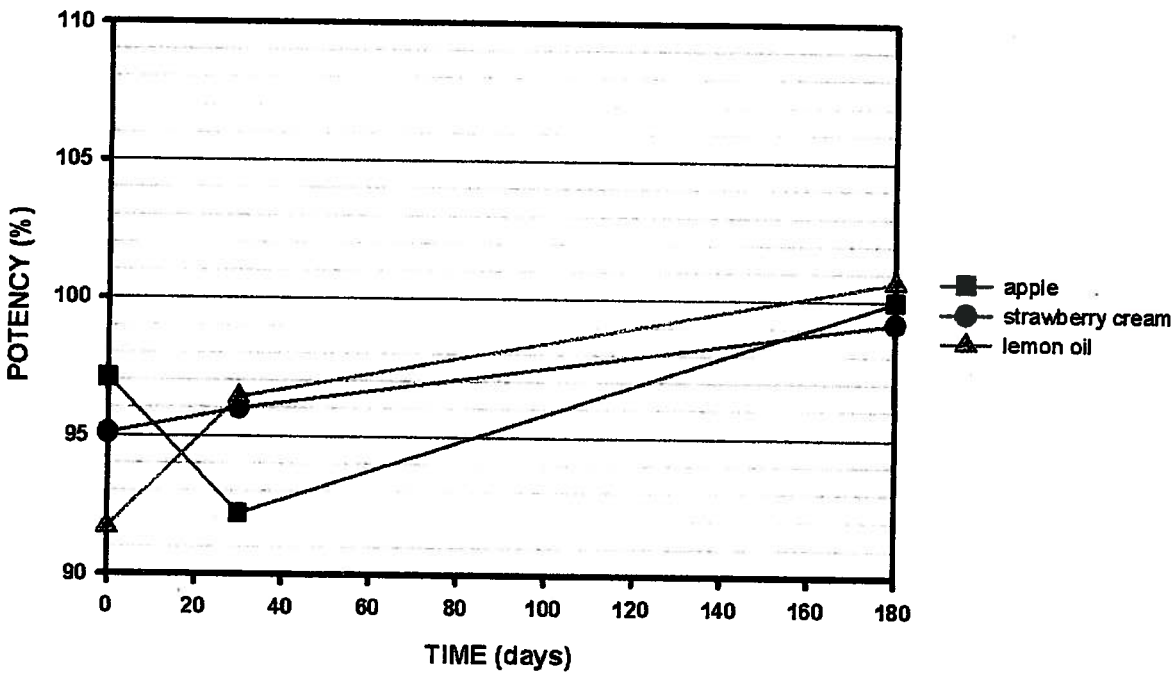
Materials: Tylenol® Extra Strength Adult Rapid Blast Liquid, NDC#50580-111-08, Lot#128364 (BCAM)

Physical Appearance: Clear, homogeneous, red solution

Preparation Methods: Apple sample bottle contained 25mL Sample, 0.4mL FlavoRx™ Apple flavor and 0.1mL FlavoRx™ Watermelon flavor. Strawberry sample bottle contained 25mL Sample, 0.3mL FlavoRx™ Strawberry Cream flavor and 0.1mL FlavoRx™ Watermelon flavor. Lemon sample bottle contained 25mL Sample and 0.1mL FlavoRx™ Lemon Oil flavor. In addition, 0.3mL FlavoRx™ Sweetness Enhancer was added to all three bottles. Sample solutions of 0.1mg/mL were then prepared in 25% methanol. Standard solutions were prepared from 0.01mg/mL-0.1mg/mL in 25% methanol.

Test Method & Materials: The samples were assayed based on USP 31 (2008) assay method for Acetaminophen Oral Solution. The assay was done on a Hitachi L-7000 system with UV-detector (243nm). The column used was a Zorbax Rx-C18, 4.6mm X 15cm. The flow rate was 1.5mL/min and run time 5min. The mobile phase was deionized water:methanol (75:25).

ACETAMINOPHEN POTENCY RELATIVE to CONTROL



ACETAMINOPHEN CONTINUED

Table A: Potency of Medication in the Presence of Flavorants Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	---	---	---
Apple	97.1	92.2	100.0
Stawberry Cream	95.1	96.0	99.2
Lemon Oil	91.7	96.4	100.7

Table B: Potency of Medication in the Presence of Flavorants

Sample	% of Potency (%RSD) Relative to Label vs. Time after FlavoRx™ Flavorant Addition			%Gain/ (Loss) in Potency
	0 days	30 days	180 days	
Control	104.7(0.3)	100.7(0.2)	99.5(0.7)	(5.2)
Apple	101.6(0.2)	92.9(0.2)	99.5(0.3)	(2.1)
Stawberry Cream	99.5(0.5)	96.7(0.7)	98.7(1.8)	(0.8)
Lemon Oil	96.0(0.2)	97.0(0.4)	100.2(1.0)	4.2

Table C: pH of Medication

Sample	pH vs.Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	4.98	5.08	5.32
Apple	4.78	5.00	5.01
Stawberry Cream	5.22	4.92	4.97
Lemon Oil	5.24	5.18	5.23

Conclusion: The results of this testing showed no variation in potency, pH or physical appearance between the control sample and the flavored samples. The changes in potency for acetaminophen are comparable in all samples. pH showed stability throughout the trial. The physical appearance of all samples was consistent. The smell of the flavored samples was also consistent over the entire trial.

Tested by: Ronald Schneider Date: 5/4/10

Reviewed by: _____ Date: 5/5/10

AMOXICILLIN

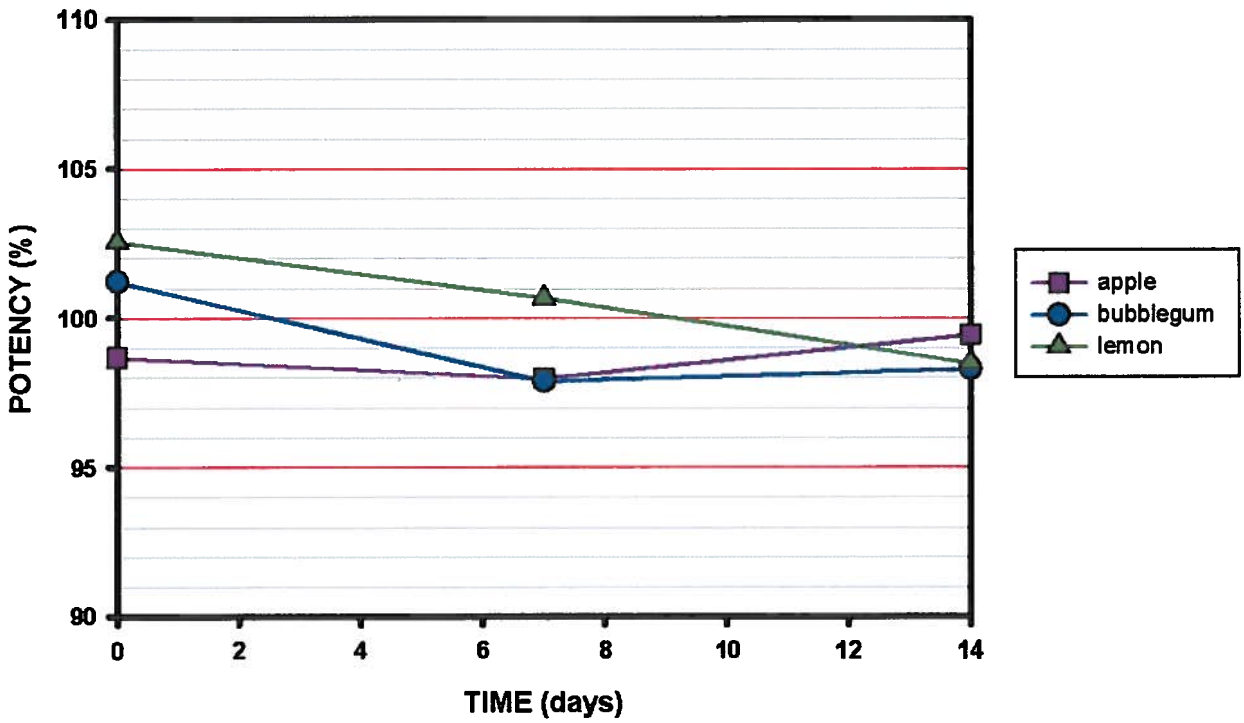
Materials: Amoxicillin for Oral Suspension USP, NDC#0781-6039-55, Lot#159104

Physical Appearance: Cloudy, homogeneous, pink solution

Preparation Methods: Prepared Sample as stated on bottle reducing water added based on flavor additions. Apple sample bottle contained 25mL Sample and 0.4mL FlavoRx™ Apple flavor. Bubblegum sample bottle contained 25mL Sample and 0.3mL FlavoRx™ Bubblegum flavor. Lemon sample bottle contained 25mL Sample and 0.1mL FlavoRx™ Lemon Oil flavor. Sample solutions of 0.25mg/mL were then prepared in deionized water. Standard solutions were prepared from 0.025mg/mL-0.25mg/mL in deionized water.

Test Method & Materials: The samples were assayed based on USP 31 (2008) assay method for Amoxicillin and Potassium Clavulanate. The assay was done on a Hitachi L-7000 system with UV-detector (220nm). The column used was a Zorbax Rx-C18, 4.6mm X 15cm. The flow rate was 2mL/min and run time 4min. The mobile phase was monobasic sodium phosphate buffer (7.8g/1000mL):methanol (95:5) to pH 4.4 with phosphoric acid.

AMOXICILLIN POTENCY RELATIVE to CONTROL



AMOXICILLIN CONTINUED

Table A: Potency of Medication in the Presence of Flavorants Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlavoRx™ Flavorant Addition		
	0 days	7 days	14 days
Control	---	---	---
Apple	98.7	97.9	99.5
Bubblegum	101.2	97.9	98.3
Lemon Oil	102.6	100.7	98.5

Table B: Potency of Medication in the Presence of Flavorants

Sample	% of Potency (%RSD) Relative to Label vs. Time after FlavoRx™ Flavorant Addition			%Gain/ (Loss) in Potency
	0 days	7 days	14 days	
Control	97.9(0.8)	103.8(0.4)	105.0(0.8)	7.1
Apple	96.6(0.5)	101.7(1.0)	104.4(1.1)	7.8
Bubblegum	99.1(1.8)	101.6(0.6)	103.2(1.0)	4.1
Lemon Oil	100.4(0.9)	104.5(1.0)	103.4(0.6)	3.0

Table C: pH of Medication

Sample	pH vs.Time after FlavoRx™ Flavorant Addition		
	0 days	7 days	14 days
Control	5.33	5.18	5.19
Apple	5.35	5.25	5.26
Bubblegum	5.26	5.26	5.28
Lemon Oil	5.26	5.26	5.27

Conclusion: The results of this testing showed no variation in potency, pH or physical appearance between the control sample and the flavored samples. The increases in potency for amoxicillin are comparable in all samples. pH showed stability throughout the trial. The physical appearance of all samples was consistent. The smell of the flavored samples was also consistent over the entire trial.

Tested by: Ronald Schneider Date: 2/1/10

Reviewed by: [signature] Date: 2/1/10

CEPHALEXIN

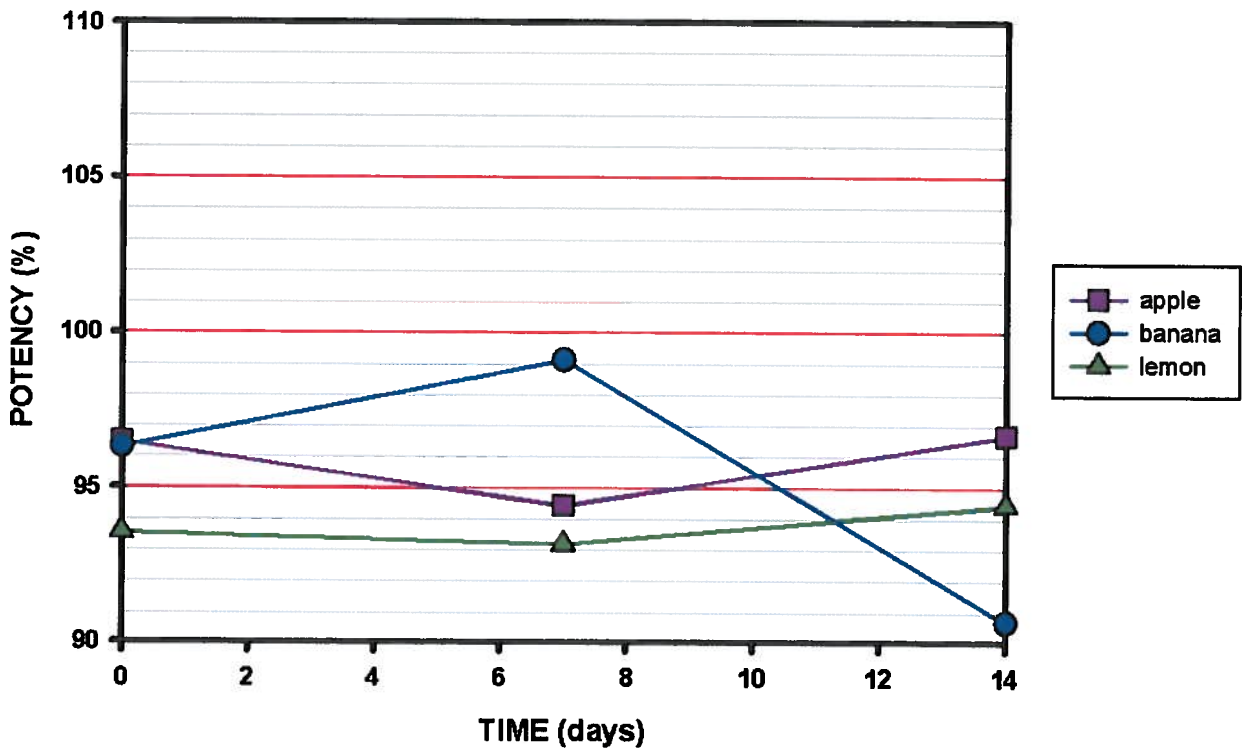
Materials: Cephalexin for Oral Suspension USP, NDC#0093-4177-73, Lot#30301142A

Physical Appearance: Cloudy, homogeneous, pink solution

Preparation Methods: Prepared Sample as stated on bottle reducing water added based on flavor additions. Apple sample bottle contained 25mL Sample, 0.3mL FlavoRx™ Apple flavor, and 0.1mL FlavoRx™ Watermelon flavor. Banana sample bottle contained 25mL Sample, 0.3mL FlavoRx™ Banana flavor, and 0.1mL FlavoRx™ Bubblegum flavor. Lemon sample bottle contained 25mL Sample and 0.3mL FlavoRx™ Lemon Oil flavor. In addition, 0.3mL FlavoRx™ Sweetness Enhancer and Bitterness Suppressor were added to all three bottles. Sample solutions of 0.2mg/mL were then prepared in mobile phase. Standard solutions were prepared from 0.02mg/mL-0.2mg/mL in mobile phase.

Test Method & Materials: The samples were assayed based on USP 31 (2008) assay method for Cephalexin. The assay was done on a Hitachi L-7000 system with UV-detector (254nm). The column used was a Zorbax Rx-C18, 4.6mm X 15cm. The flow rate was 1.5mL/min and run time 4min. The mobile phase was (85:10:5:1.5) deionized water:acetonitrile:methanol:triethylamine to pH 5.1 with phosphoric acid.

CEPHALEXIN POTENCY RELATIVE to CONTROL



CEPHALEXIN CONTINUED

Table A: Potency of Medication in the Presence of Flavorants Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlavoRx™ Flavorant Addition		
	0 days	7 days	14 days
Control	---	---	---
Apple	96.5	94.4	96.7
Banana	96.3	99.1	90.7
Lemon Oil	93.6	93.2	94.4

Table B: Potency of Medication in the Presence of Flavorants

Sample	% of Potency (%RSD) Relative to Label vs. Time after FlavoRx™ Flavorant Addition			%Gain/ (Loss) in Potency
	0 days	7 days	14 days	
Control	119.5(1.0)	114.6(0.05)	114.8(0.7)	(4.7)
Apple	115.3(0.3)	108.2(0.5)	111.0(0.7)	(4.3)
Banana	115.1(0.3)	113.6(1.2)	104.1(3.6)	(9.0)
Lemon Oil	111.8(0.9)	106.8(0.4)	108.4(2.6)	(3.4)

Table C: pH of Medication

Sample	pH vs.Time after FlavoRx™ Flavorant Addition		
	0 days	7 days	14 days
Control	4.53	4.62	4.71
Apple	4.25	4.18	4.40
Banana	4.58	4.55	4.56
Lemon Oil	4.38	4.69	4.73

Conclusion: The results of this testing showed no variation in potency, pH or physical appearance between the control sample and the flavored samples. The decreases in potency for cephalexin are comparable in all samples given the larger %RSD for the banana sample. pH showed stability throughout the trial. The physical appearance of all samples was consistent. The smell of the flavored samples was also consistent over the entire trial.

Tested by: Ronald Schneider Date: 2/1/10

Reviewed by: [signature] Date: 2/1/10

Stability Report

Clindamycin Palmitate HCl for Oral Solution, USP

Materials

Flavors		Lot#	Expiration
Strawberry Cream		W292132	11/1/2019
Lemon Aqueous		N012977	10/1/2016
FLAVORx, INC **9475 Gerwig Lane, Columbia, MD 21046**			
Standards	**Part #**	**Lot #**	
Clindamycin Palmitate HCl	C4534	0000405-K	
LKT Laboratories, Inc. **545 Phalen Blvd.St. Paul, MN 55130**			
Reagents	**Part #**	**Lot #**	
Methanol	135267	Various	
Acetonitrile		Various	
Fisher Scientific			
Formic Acid	56302-50ML-F	BCBF1432V	
Fluka Analytical			
Water (House DI System)	Last Service 3/11/2014		
Pharmaceutical	**NDC #**	**Lot #**	**Expiration**
Clindamycin Palmitate HCL for Oral Solution	59762-0016-1	G37974	8/1/2015
Greenstone LLC **Peapack NJ, 07977**			

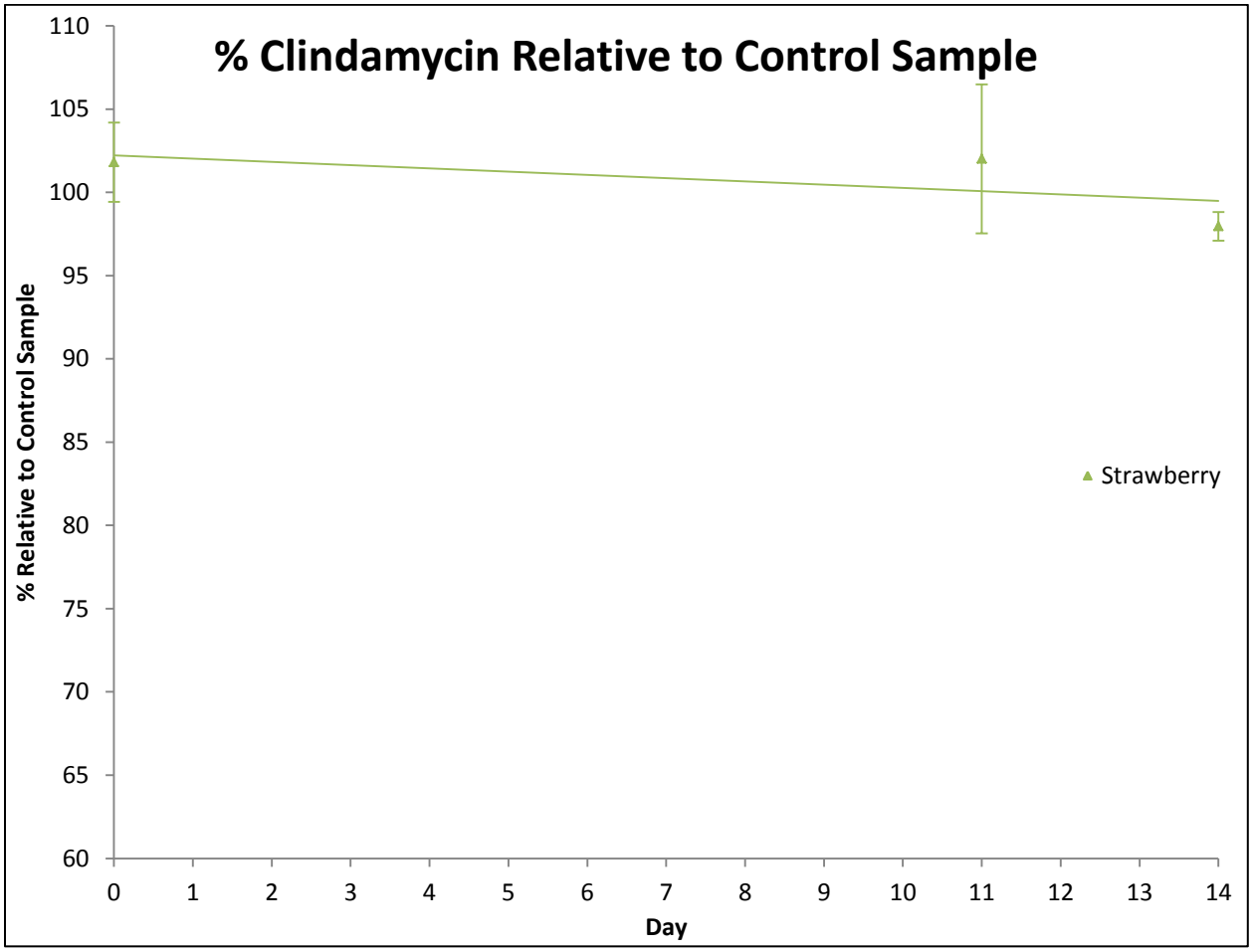
Results

Table 1: Average % Potency Relative to Bottle Value Sample

Sample	Average % Potency Relative to Bottle Value (75mg/5mL) vs. Time after FLAVORx Flavor Addition (± 95%)		
	Day 0	Day 11	Day 14
Control	125.78 (1.71)	107.97 (2.97)	100.75 (1.10)
Strawberry	127.92 (0.84)	110.03 (2.81)	98.71 (1.27)

Table 2: Average % Potency Relative to Control Sample

Sample	Average % Potency Relative to Control vs. Time after FLAVORx Flavor Addition (± 95%)		
	Day 0	Day 7	Day 14
Control	-	-	-
Strawberry	101.81 (2.39)	102.02 (4.47)	97.97 (0.86)



Physical Appearance/Observations

When reconstituted, the medication had clear, viscous appearance. The physical appearance of each of the samples remained unchanged over the time period of the study.

Mobile Phase Composition:

The mobile phase consisted of water and acetionitrile both with 0.1% Formic Acid added.

Diluent Composition:

The Diluent consisted of 10% Water, 90% Methanol

Instrument:

PerkinElmer Flexar FX-15 UHPLC with SQ300D single quadrupole mass spectrometer. Also included PerkinElmer Flexar Column oven and Flexar Cool Only autosampler.

Column:

Phenomenex Gemini-NX 5µm C18, 250x4.60mm
Part #: 00G-4454-E0
S/N: 612008-10

Guard Column:

Phenomenex SecurityGuard Cartridge System
Part #: KJO-4282
Cartridge: Gemini-NX C18 4x3.0mm
Part #: AJO-8368

HPLC Method:

AutoSampler:
Injection Volume: 10µL
Tray Temperature: 20°C

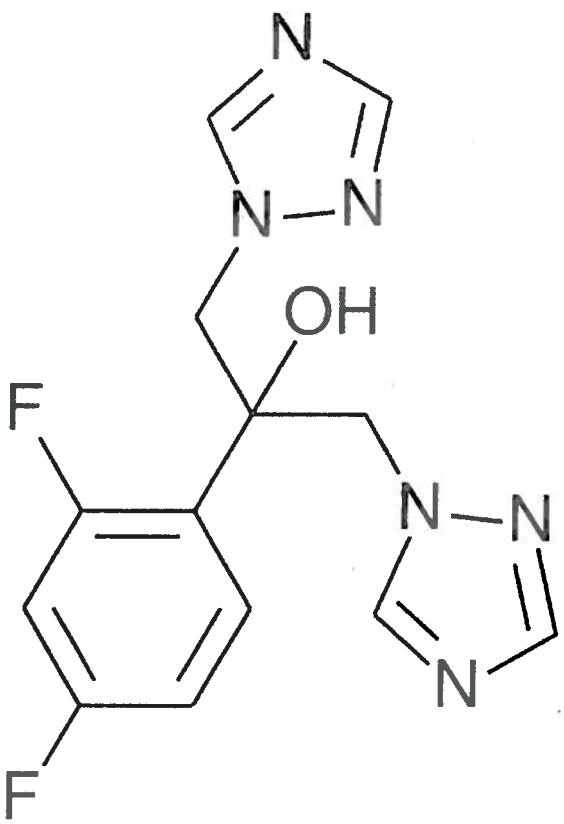
Pump:
Gradient: 95% Water, 5% Acetonitrile to 5% water, 95% Acetonitrile
Equilibration: 7 minutes
Run Time: 20 minutes

Column Oven:
Isothermal: 35°C

Detector:
Single Quadrupole Mass Spectrometer with positive mode Electrospray Ionization.

Stability Report

Fluconazole



$C_{13}H_{12}F_2N_6O$

Materials

Flavors		Lot#	Expiration
Bubblegum		W158177	7/2019
OrangeCream		W292126	11/2019
Banana		W237067	9/2019
Apple		R0927	9/2019
FLAVORx, INC			
9475 Gerwig Lane, Columbia, MD 21046			
Standards	**Part #**	**Lot #**	
Fluconazole	F4682	2597499	
LKT Laboratories, Inc.			
545 Phalen Blvd.St. Paul, MN 55130			
Reagents	**Part #**	**Lot #**	
Acetonitrile	A955-4	126501	
Formic Acid	A117-50	116758	
Fisher Scientific			
Water	9152-2.5	2207714	
Ricca Chemical Company			
Pharmaceutical	**NDC #**	**Lot #**	**Expiration**
Fluconazole for Oral Suspension(40mg/mL)	16714-696-01	UF4012003-A	3/2014
Manufactured For:			
Northstar Rx LLC			
Memphis, TN 38141			
1-800-206-7821			
Manufactured By:			
Aurobindo Pharma Limited			
Hyderabad-500-072, India			

Results

Table 1: Average % Potency Relative to Bottle Value Sample

Sample	Average % Potency Relative to Bottle Value (40mg/mL) vs. Time after FLAVORx Flavor Addition (±95%)		
	Day 0	Day 7	Day 14
Control	100.42 (4.98)	110.97 (0.88)	113.78 (3.23)
Apple	101.01 (1.51)	101.43 (1.69)	106.84 (0.55)
Bubblegum	109.86 (1.03)	96.37 (1.52)	110.02 (4.99)
OrangeCream	107.57 (2.37)	105.40 (2.31)	111.94 (2.50)

Table 2: Average % Potency Relative to Control Sample

Sample	Average % Potency Relative to Control vs. Time after FLAVORx Flavor Addition (±95%)		
	Day 0	Day 7	Day 14
Control	-	-	-
Apple	100.80 (3.94)	91.40 (0.99)	93.97 (2.46)
Bubblegum	109.67 (4.72)	86.84 (0.69)	96.89(7.68)
OrangeCream	107.54 (7.67)	94.98 (1.94)	98.52 (4.86)

Table 3: Sample pH over 14 day period

Sample	pH On Day of Testing		
	Day 0	Day 7	Day 14
Control	4.12	4.06	4.08
Apple	4.13	4.08	4.10
Bubblegum	4.16	4.09	4.11
OrangeCream	4.13	4.09	4.11

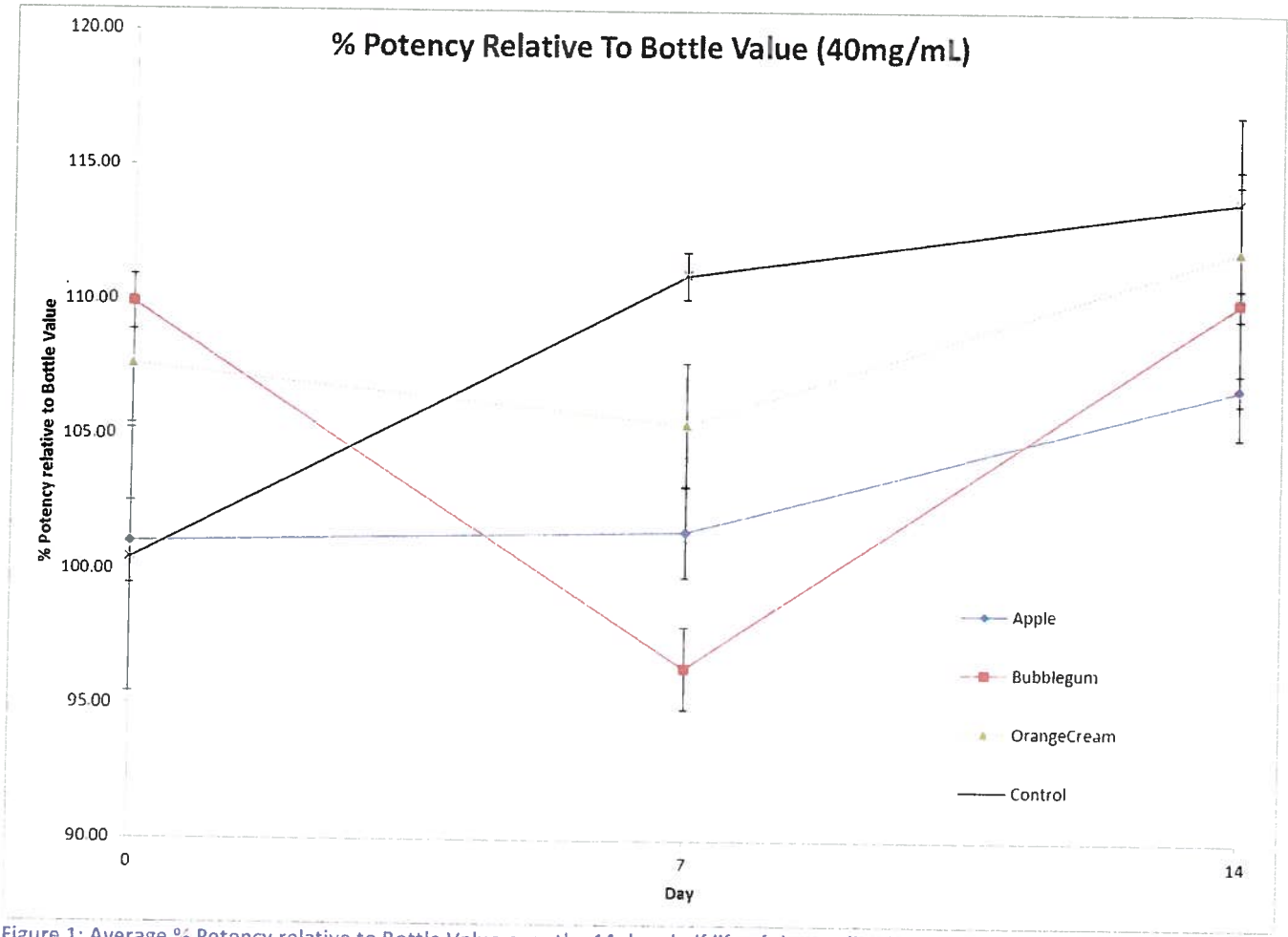


Figure 1: Average % Potency relative to Bottle Value over the 14 day shelf life of the medication. Lines do not represent a fit to an algorithm, they are presented for data clarity. Error bars represent ±95% confidence interval.

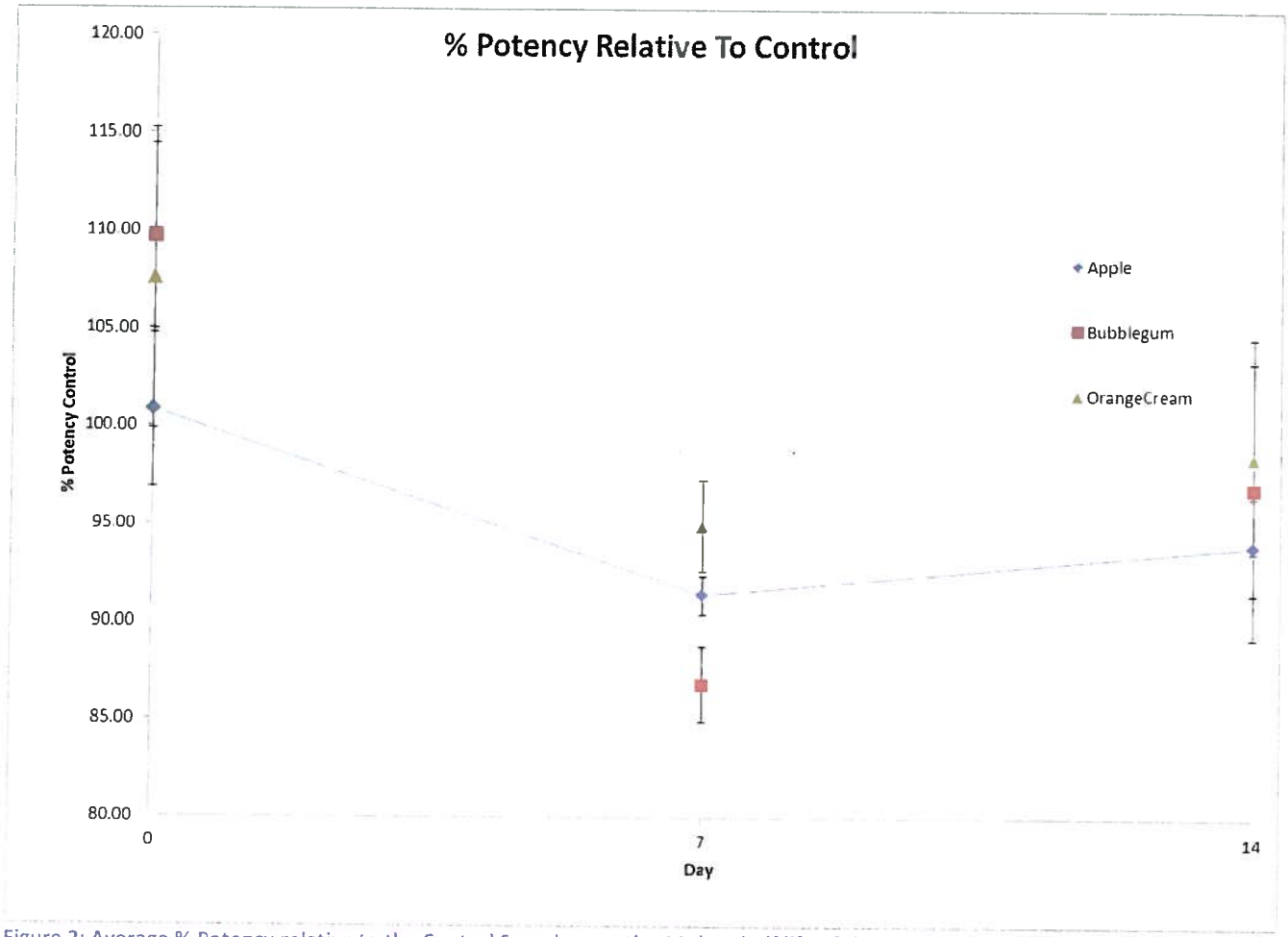


Figure 2: Average % Potency relative to the Control Sample over the 14 day shelf life of the medication. Lines do not represent a fit to an algorithm, they are presented for data clarity. Error bars represent ±95% confidence interval.

Physical Appearance/Observations

When reconstituted, the medication had a white, viscous appearance. When diluted in the sample preparation step prior to analysis each sample was cloudy. The smell and appearance of each sample was consistent over the two week trial.

Standards Preparation

The initial standard solution was prepared to approximately 1.0 $mg \cdot mL^{-1}$. The remaining standard solutions were prepared by serial dilution from this standard. Each solution was thoroughly mixed and visually inspected to ensure no standard remained un-dissolved. The concentration range included 1.0 $mg \cdot mL^{-1}$, 0.8 $mg \cdot mL^{-1}$, 0.6 $mg \cdot mL^{-1}$, 0.4 $mg \cdot mL^{-1}$ and 0.1 $mg \cdot mL^{-1}$. An aliquot of each standard was transferred to a 2mL glass sample vial to be used with the HPLC.

Sample Preparation

The Fluconazole for Oral Suspension was reconstituted as directed on the bottle. The reconstitution directions instruct that the medication be reconstituted with 24mL of water. The medication was then shaken to ensure proper mixing. From the medication bottle, 4 equal aliquots of medication were removed and placed into 4 separate containers. Three of the containers will contain the three flavor formulations to be tested. The fourth will contain no flavor and act as the control. The flavors were prepared according to the FLAVORx formulation, adjusted for the decreased sample size. To prepare the Apple flavor, 0.100mL of Apple was added to one container. To prepare the Bubblegum flavor, 0.100mL of Bubblegum, 0.050mL of Banana were added to the second container. To prepare the Orange Cream flavor, 0.100mL of Orange Cream was added to the third container. The final concentration of each solution was approximately 40 $mg \cdot mL^{-1}$ fluconazole.

To prepare the samples for analysis by HPLC each sample needed to be diluted. To prepare these dilutions, 0.300 mL of each sample was quantitatively transferred into a 25mL volumetric flask. The flask was then brought to volume using water. The final concentration was approximately .48 $mg \cdot mL^{-1}$. At this concentration fluconazole is completely soluble in water. After vigorous mixing the solutions still remained cloudy as a result of other excipients in the pharmaceutical formulation. A portion of the solution was removed and placed in a 2mL centrifuge tube. The tubes were centrifuged for 3 minutes at 12,400 rpm. The supernatant of each sample was transferred to a 2mL glass sample vial to be used with the HPLC.

The samples were stored at room temperature. On each day of testing the samples were thoroughly mixed followed by a pH measurement.

Blank Preparation

A blank sample was prepared with the water used in the dilutions.

Mobile Phase Composition:

The mobile phase consisted of water and acetonitrile each containing 0.1% formic acid.

Column:

Phenomenex Gemini-NX 5µm C18, 250x4.60mm
Part #: 00G-4454-E0
S/N: 612008-10

Guard Column:

Phenomenex SecurityGuard Cartridge System
Part #: KJO-4282
Cartridge: Gemini-NX C18 4x3.0mm
Part #: AJO-8368

Conclusion

The results of this testing showed no significant variation in potency or physical appearance between the control sample and the flavored samples. USP does not have a monograph for Fluconazole for Oral Suspension. However, other oral suspension monographs state that the formulation must contain between 90% and either 110%, 115% or 120% of the stated amount. The results above show that the formulation test with flavors stayed between 90% and 115% of the stated value over the course of the trial. Also, the physical appearance and pH of the flavored and control samples were consistent over the entire trial. Based on this analysis, Fluconazole for Oral Suspension from any manufacture that has the same formulation and concentration as the medication tested is appropriate to use with the flavors tested.

Tested By: _____ Date 2/19/2014
Greg Winter

Reviewed By: _____ Date 2/4/2014
William R. LaCourse, Ph.D.

MICROBAC LABORATORIES, INC.
PITTSBURGH DIVISION

Testing completed Oct. 03, 2016

STABILITY STUDY REPORT

FLUOXETINE

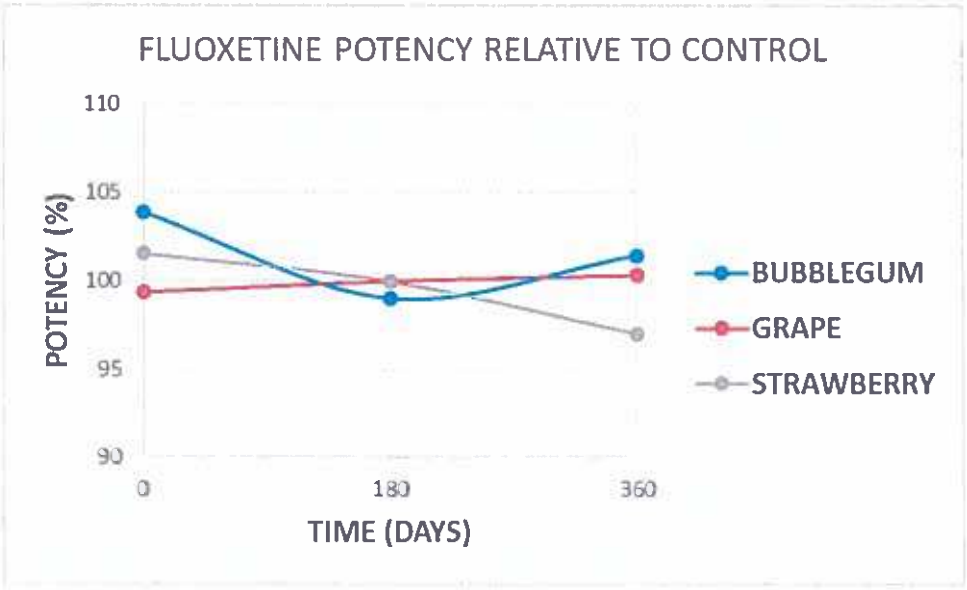
Materials: Fluoxetine for Oral Suspension USP NDC 0121-0721-04, Bitterness Suppressor (Lot F181021), Sweetening Enhancer (Lot 1893340), Bubblegum flavoring (Lot F182035), Grape flavoring (Lot W0715), Strawberry flavoring (Lot F181024), Watermelon Flavoring (Lot W0526).

Physical Appearance: Clear, homogenous solution.

Preparation Method: Fluoxetine Solution Samples were submitted to the laboratory at 20mg/5mL. The Control Sample was analyzed as is. The samples were analyzed using three flavors: bubblegum, grape, and strawberry. The Bubblegum container contained 120mL of 20mg/5mL Fluoxetine Solution, 0.7mL sweetening enhancer, and 1.3mL bubblegum flavoring. The Grape container contained 120mL of 20mg/5mL Fluoxetine Solution, 0.7mL sweetening enhancer, 0.7mL grape flavoring, and 0.7mL watermelon flavoring. The Strawberry container contained 120mL of 20mg/5mL Fluoxetine Solution, 0.7mL sweetening enhancer, 0.7mL strawberry flavoring, and 0.7mL watermelon flavoring. Standard solutions were prepared at 100ppb, 250ppb, 500ppb, 750ppb, and 1000ppb.

Test Method & Material:
The samples were assayed on by Ultra Performance Liquid Chromatography (Vanquish UPLC) coupled to an electrospray ionization triple quadruple mass spectrometer (Thermo Scientific Endura Triple Quad ES-LC/MS/MS). HPLC Columns was Agilent Eclipse XDB-C18, 5µm, 47.6 x 150mm. The flow rate is 0.50mL/min. and run time 15min. HPLC mobile phase A: is 0.1 % formic acid. Mobile phase B is mthanol with 0.1 % formic acid.

Potency of Medication in the presence of Flavorant Relative to Control



MICROBAC LABORATORIES, INC.
PITTSBURGH DIVISION

STABILITY STUDY REPORT

FLUOXETINE

Table A: Potency of Medication in the presence of Flavorant Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlvoRx TM Flavorant Addition		
	0 days	180 days	360 days
Control	-	-	-
Bubblegum	103.9	99.0	101.4
Grape	99.3	100.0	100.3
Strawberry	101.5	100.0	97.0

Table B: Potency of Medication in the presence of Flavorants

Sample	% of Potency of Medication Relative to Bottle Value vs. Time after FlvoRx TM Flavorant Addition		
	0 days	180 days	360 days
Control	98.6	109.1	100.6
Bubblegum	102.5	108.0	102.1
Grape	98.0	109.0	100.9
Strawberry	100.1	109.0	97.6

Table C: pH of Medication

Sample	pH vs. Time after FlvoRx TM Flavorant Addition		
	0 days	180 days	360 days
Control	3.92	3.89	3.94
Bubblegum	3.85	3.85	3.83
Grape	3.62	3.65	3.61
Strawberry	3.69	3.75	3.70

Conclusion: The results of this testing showed that no variation in potency, pH or physical appearance between the control sample and the flavored samples. The USP monograph for Fluoxetine oral solution stated that oral solution contains NLT 90.0% and NMT 110.0% of the labeled amount of Fluoxetine. The results above showed that the formulation test with flavored stayed between 90% and 110% of the stated value over the course of the trial. Also, the physical appearance, and pH of the flavored samples and the control sample were consistent over the entire trial.

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Mohamed Hamad, PHD
Tested By

Lauren Zeleny
QA Manager

IBUPROFEN

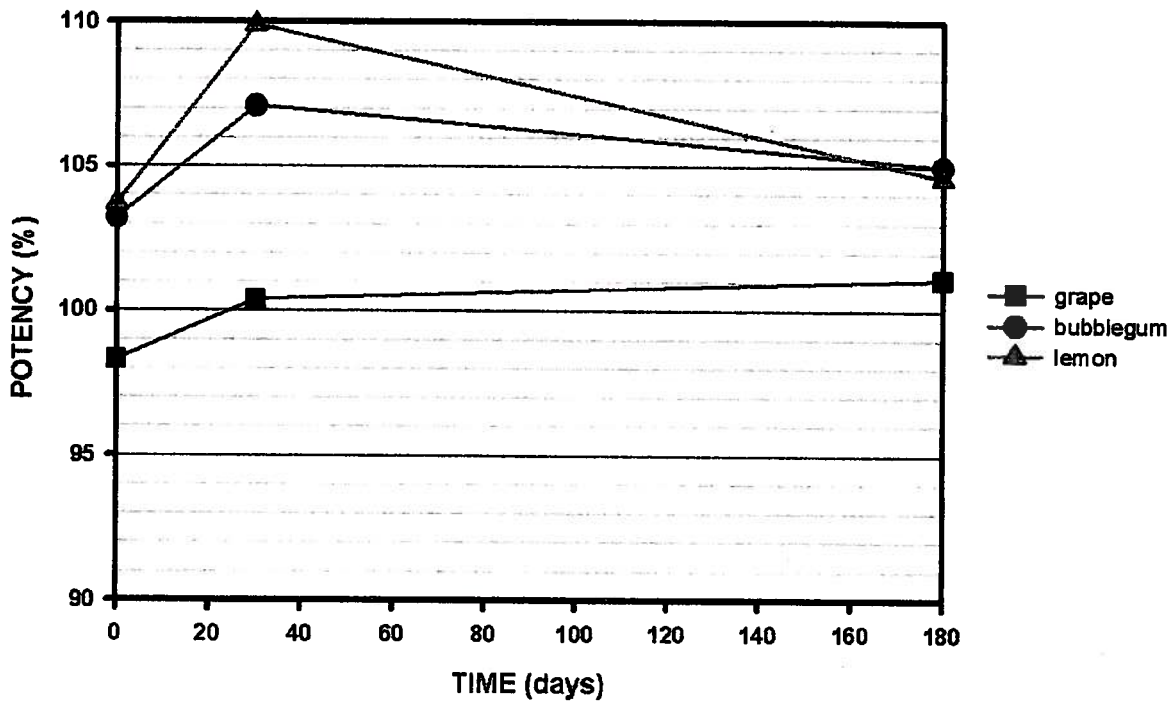
Materials: Ibuprofen Oral Suspension USP, NDC#0472-1270-16, Lot#L904009

Physical Appearance: Cloudy, homogeneous, orange suspension

Preparation Methods: Grape sample bottle contained 25mL Sample, 0.1mL FlavoRx™ Grape flavor and 0.1mL FlavoRx™ Watermelon flavor. Bubblegum sample bottle contained 25mL Sample, 0.3mL FlavoRx™ Bubblegum flavor. Lemon sample bottle contained 25mL Sample and 0.1mL FlavoRx™ Lemon Oil flavor. Sample solutions of 0.25mg/mL were then prepared in 50% acetonitrile. Standard solutions were prepared from 0.025mg/mL-0.25mg/mL in 50% acetonitrile.

Test Method & Materials: The samples were assayed based on USP 31 (2008) assay method for Ibuprofen Oral Suspension. The assay was done on a Hitachi L-7000 system with UV-detector (220nm). The column used was a Zorbax Rx-C18, 4.6mm X 15cm. The flow rate was 2mL/min and run time 6min. The mobile phase was 0.01M phosphoric acid:acetonitrile (50:50).

IBUPROFEN POTENCY RELATIVE to CONTROL



IBUPROFEN CONTINUED

Table A: Potency of Medication in the Presence of Flavorants Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	---	---	---
Grape	98.3	100.4	101.1
Bubblegum	103.2	107.1	105.0
Lemon Oil	103.7	109.9	104.6

Table B: Potency of Medication in the Presence of Flavorants

Sample	% of Potency (%RSD) Relative to Label vs. Time after FlavoRx™ Flavorant Addition			%Gain/ (Loss) in Potency
	0 days	30 days	180 days	
Control	91.8(0.9)	97.5(0.9)	100.7(0.8)	8.9
Grape	90.3(1.7)	97.9(1.1)	101.8(1.4)	11.5
Bubblegum	94.8(1.5)	104.4(0.6)	105.7(1.1)	10.9
Lemon Oil	95.2(1.0)	107.1(2.2)	105.3(1.2)	10.1

Table C: pH of Medication

Sample	pH vs.Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	3.85	3.82	3.65
Grape	3.84	3.80	3.62
Bubblegum	3.90	3.93	3.75
Lemon Oil	3.91	3.90	3.75

Conclusion: The results of this testing showed no variation in potency, pH or physical appearance between the control sample and the flavored samples. The increases in potency for ibuprofen are comparable in all samples. pH showed stability throughout the trial. The physical appearance of all samples was consistent. The smell of the flavored samples was also consistent over the entire trial.

Tested by: Ronald Schneider Date: 5/4/10

Reviewed by: [signature] Date: 5/5/10

MICROBAC LABORATORIES, INC.
PITTSBURGH DIVISION

Testing completed Sept. 30, 2016

STABILITY STUDY REPORT

LEVETIRACETAM (KEPPRA)

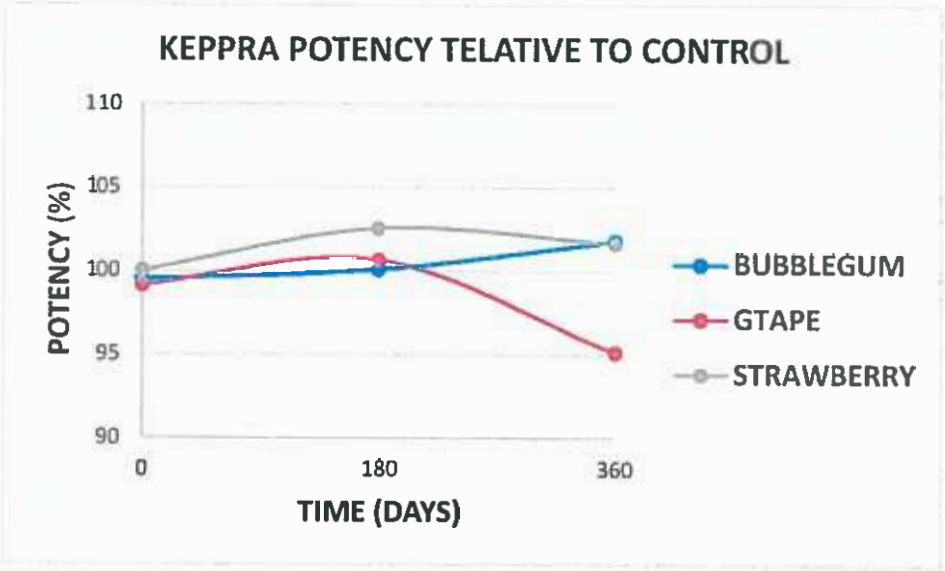
Materials: Levetiracetam for Oral Suspension NDC 50383-241-16, Bitterness Suppressor (Lot F181021), Sweetening Enhancer (Lot 1893340), Bubblegum flavoring (Lot F182035), Grape flavoring (Lot W0715), Strawberry flavoring (Lot F181024), Watermelon Flavoring (Lot W0526).

Physical Appearance: Clear, homogenous solution.

Preparation Method: Keppra Solution Samples were submitted to the laboratory at 100mg/mL. A Control Sample was analyzed as is; 120mL of Control Keppra was placed into a labeled amber jar. The samples were analyzed using three flavors: bubblegum, grape, and strawberry. The Bubblegum jar contained 120mL of 100mg/mL Keppra Solution, 0.7mL bitterness suppressor, 1.3mL sweetening enhancer, and 1.3mL bubblegum flavoring. The Grape jar contained 120mL of 100mg/mL Keppra Solution, 0.7mL bitterness suppressor, 1.3mL sweetening enhancer, 1.3mL grape flavoring, and 0.7mL watermelon flavoring. The Strawberry jar contained 120mL of 100mg/mL Keppra Solution, 0.7mL bitterness suppressor, 1.3mL sweetening enhancer, 1.3mL strawberry flavoring, and 0.7mL watermelon flavoring. Standard solutions were prepared at 100ppb, 250ppb, 500ppb, 750ppb, and 1000ppb.

Test Method & Material:
The samples were assayed on by Ultra Performance Liquid Chromatography (Vanquish UPLC) coupled to an electrospray ionization triple quadruple mass spectrometer (Thermo Scientific Endura Triple Quad ES-LC/MS/MS). HPLC Columns was Agilent Eclipse XDB-C18, 5µm, 47.6 x 150mm. The flow rate is 0.50mL/min. and run time 15min. HPLC mobile phase A: is 0.1 % formic acid. Mobile phase B is mthanol with 0.1 % formic acid.

Potency of Medication in the presence of Flavorant Relative to Control



MICROBAC LABORATORIES, INC.
PITTSBURGH DIVISION

STABILITY STUDY REPORT

LEVETIRACETAM (KEPPRA)

Table A: Potency of Medication in the presence of Flavorant Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlvoRx TM Flavorant Addition		
	0 days	180 days	360 days
Control	-	-	-
Bubblegum	99.5	100.1	101.8
Grape	99.1	100.7	95.1
Strawberry	100.0	102.6	101.7

Table B: Potency of Medication in the presence of Flavorants

Sample	% of Potency of Medication Relative to Bottle Value vs. Time after FlvoRx TM Flavorant Addition		
	0 days	180 days	360 days
Control	107.6	106.1	98.81
Bubblegum	107.1	106.2	100.6
Grape	106.7	106.8	94.0
Strawberry	107.6	108.8	100.4

Table C: pH of Medication

Sample	pH vs. Time after FlvoRx TM Flavorant Addition		
	0 days	180 days	360 days
Control	5.42	5.44	5.43
Bubblegum	5.43	5.43	5.45
Grape	5.40	5.42	5.41
Strawberry	5.43	5.40	5.41

Conclusion: The results of this testing showed that no variation in potency, pH or physical appearance between the control sample and the flavored samples. The USP monograph for Levetiracetam oral solution stated that oral solution contains NLT 90.0% and NMT 110.0% of the labeled amount of levetiracetam. The results above showed that the formulation test with flavored stayed between 90% and 110% of the stated value over the course of the trial. Also, the physical appearance, and pH of the flavored samples and the control sample were consistent over the entire trial.

12/7/16

X _____ X _____ 12/7/16

Mohamed Hamad, PHD
Tested By

Lauren Zeleny
QA Manager

MICROBAC LABORATORIES, INC.
PITTSBURGH DIVISION

Testing completed Nov. 28, 2016

STABILITY STUDY REPORT

OMEPRAZOLE

Table A: Potency of Medication in the presence of Flavorant Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlvoRx TM Flavorant Addition				
	0 days	7 days	14 days	29 days	34 days
Control	-	-	-	-	-
Grape	90.28	93.69	95.04	102.5	97.63

Table B: Potency of Medication in the presence of Flavorants

Sample	% of Potency of Medication Relative to Bottle Value vs. Time after FlvoRx TM Flavorant Addition				
	0 days	7 days	14 days	29 days	34 days
Control	101.1	99.97	105.7	103.2	97.98
Grape	91.24	93.67	100.5	105.8	91.45

Table C: pH of Medication

Sample	pH vs. Time after FlvoRx TM Flavorant Addition				
	0 days	7 days	14 days	29days	34 days
Control	8.48	8.43	8.47	8.52	8.53
Grape	8.48	8.46	8.56	8.51	8.51

Conclusion: The results of this testing showed that no variation in potency, pH or physical appearance between the control sample and the flavored sample. The USP monograph for Omeprazole oral solution stated that oral solution contains NLT 90.0% and NMT 110.0% of the labeled amount of Omeprazole. The results above showed that the formulation test with flavored sample stayed between 90% and 110% of the stated value over the course of the trial. Also, the physical appearance, and pH of the flavored sample and the control sample were consistent over the entire trial.

X _____ X _____

Mohamed Hamad, PHD
Tested By
1/17/17

Lauren Zeleny
QA Manager
1/17/17

MICROBAC®

CERTIFICATE OF ANALYSIS

Work Order Number:
6090807

FLAVORx, INC.
Ursula Chizhik, PharmD
9475 Gerwig Lane
Columbia ,MD 21046

Date Reported	1/17/2017
Date Received	09/08/2016
Customer #	AF671
Customer P.O.	4768

30 Day Stability Study/Omeprazole

THIS REPORT HAS BEEN REVIEWED AND APPROVED FOR RELEASE:

Account Manager, Microbac Laboratories Inc., Pittsburgh Division

Report released by Claudia Boerner

The data and information on this, and other accompanying documents, represents only the sample(s) analyzed. This report is incomplete unless all pages indicated in the footnote are present and an authorized signature is included.

For any feedback concerning our services, please contact Claudia Boerner, Project Manager at claudia.boerner@microbac.com. You may also contact Hesham A. Elgaali, Ph.D, Division Manager at hesham.elgaali@microbac.com or Robert Crookston, President at robert.crookston@microbac.com.

PREDNISOLONE

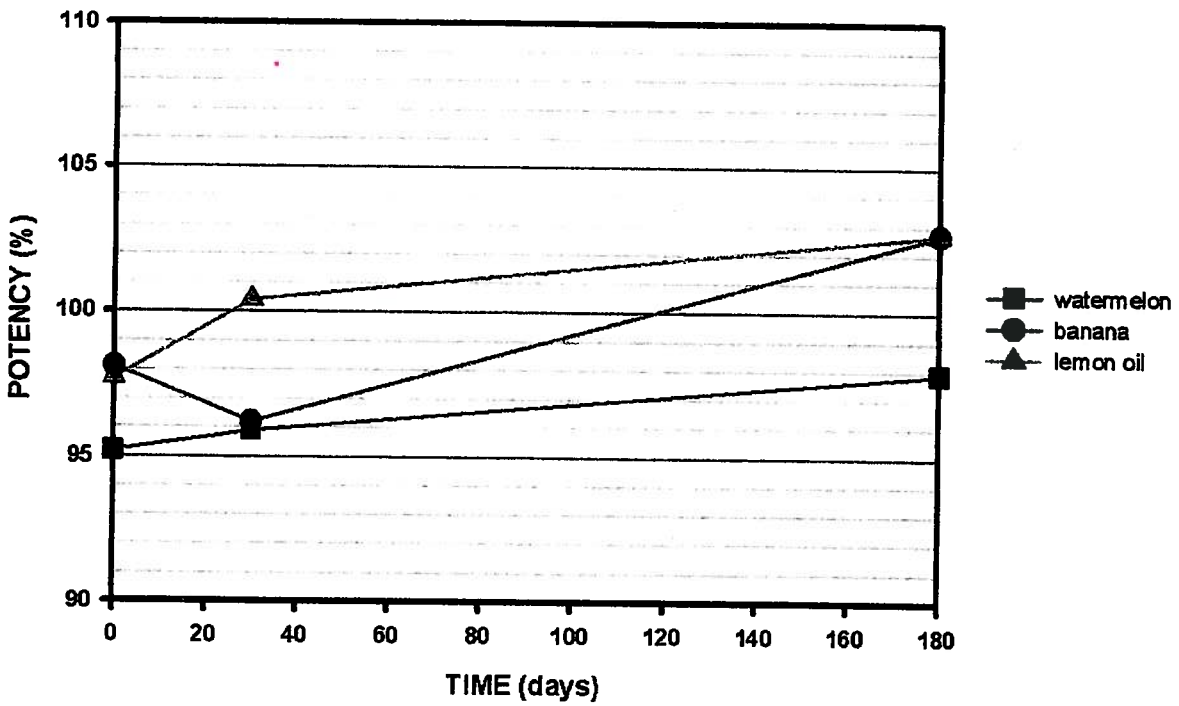
Materials: PrednisoLONE Oral Solution USP, NDC#0603-1567-56, Lot#L004L07A

Physical Appearance: Clear, homogeneous, pink solution

Preparation Methods: Watermelon sample bottle contained 25mL Sample, 0.3mL FlavoRx™ Watermelon flavor and 0.1mL FlavoRx™ Apple flavor. Banana sample bottle contained 25mL Sample and 0.3mL FlavoRx™ Banana flavor. Lemon sample bottle contained 25mL Sample and 0.3mL FlavoRx™ Lemon Oil flavor. In addition, 0.4mL FlavoRx™ Sweetness Enhancer and 0.3mL Bitterness Suppressor were added to all three bottles. Sample solutions of 0.1mg/mL were then prepared in 50% methanol. Standard solutions were prepared from 0.01mg/mL-0.1mg/mL in 50% methanol.

Test Method & Materials: The samples were assayed based on USP 31 (2008) assay method for Prednisolone Oral Solution. The assay was done on a Hitachi L-7000 system with UV-detector (254nm). The column used was a Zorbax Rx-C18, 4.6mm X 15cm. The flow rate was 1mL/min and run time 8min. The mobile phase was citrate buffer (0.63g Citric Acid/1000mL):methanol (50:50) to pH 6.2 with sodium hydroxide.

PREDNISOLONE POTENCY RELATIVE to CONTROL



PREDNISOLONE CONTINUED

Table A: Potency of Medication in the Presence of Flavorants Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	---	---	---
Watermelon	95.2	95.9	97.9
Banana	98.1	96.2	102.7
Lemon Oil	97.7	100.4	102.7

Table B: Potency of Medication in the Presence of Flavorants

Sample	% of Potency (%RSD) Relative to Label vs. Time after FlavoRx™ Flavorant Addition			%Gain/ (Loss) in Potency
	0 days	30 days	180 days	
Control	104.2(0.6)	97.3(0.6)	97.1(0.5)	(7.1)
Watermelon	99.3(0.4)	93.3(0.8)	95.0(1.7)	(4.3)
Banana	102.2(0.7)	93.6(1.0)	99.7(1.2)	(2.5)
Lemon Oil	101.8(0.3)	97.7(1.0)	99.7(2.2)	(2.1)

Table C: pH of Medication

Sample	pH vs.Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	3.67	3.87	3.84
Watermelon	3.55	3.71	3.73
Banana	3.65	3.79	3.80
Lemon Oil	3.73	3.76	3.75

Conclusion: The results of this testing showed no variation in potency, pH or physical appearance between the control sample and the flavored samples. The decreases in potency for prednisolone are comparable in all samples. pH showed stability throughout the trial. The physical appearance of all samples was consistent. The smell of the flavored samples was also consistent over the entire trial.

Tested by: Ronald Schneider Date: 5/4/10

Reviewed by: [signature] Date: 5/5/10

Testing Completed: January 13, 2010 Stability Report Tested by: UMBC (R.Schneider)

RANITIDINE HYDROCHLORIDE

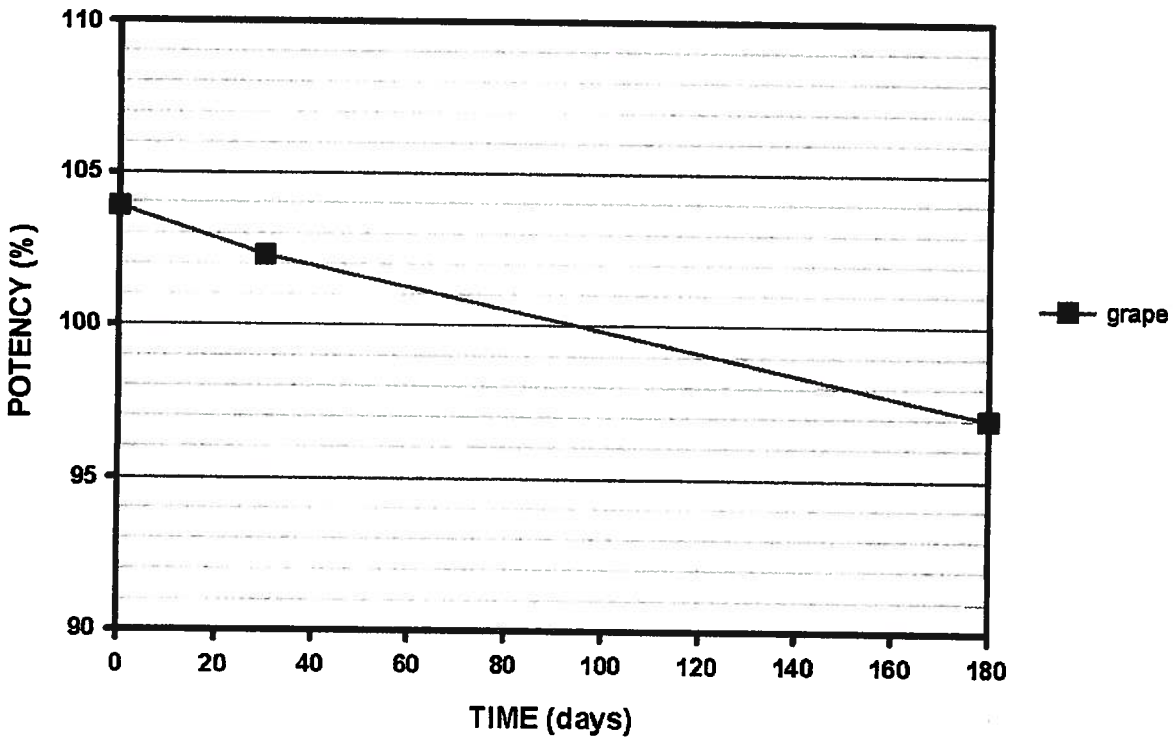
Materials: Ranitidine Oral Solution USP, NDC#60505-0351-1, Lot#JC7122

Physical Appearance: Clear, homogeneous, colorless solution

Preparation Methods: Grape sample bottle contained 25mL Sample, 0.3mL FlavoRx™ Grape flavor and 0.1mL FlavoRx™ Sweetness Enhancer. Sample solutions of 0.1mg/mL were then prepared in mobile phase. Standard solutions were prepared from 0.01mg/mL-0.1mg/mL in mobile phase.

Test Method & Materials: The samples were assayed based on USP 31 (2008) assay method for Ranitidine Oral Solution. The assay was done on a Hitachi L-7000 system with UV-detector (322nm). The column used was a Zorbax Rx-C18, 4.6mm X 15cm. The flow rate was 2mL/min and run time 5min. The mobile phase was 0.1M ammonium acetate:methanol (15:85).

RANITIDINE POTENCY RELATIVE to CONTROL



RANITIDINE CONTINUED

Table A: Potency of Medication in the Presence of Flavorants Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	---	---	---
Grape	103.9	102.3	97.0

Table B: Potency of Medication in the Presence of Flavorants

Sample	% of Potency (%RSD) Relative to Label vs. Time after FlavoRx™ Flavorant Addition			%Gain/ (Loss) in Potency
	0 days	30 days	180 days	
Control	85.8(1.2)	92.9(1.0)	98.5(1.6)	12.7
Grape	89.2(1.3)	95.1(0.9)	95.5(2.0)	6.3

Table C: pH of Medication

Sample	pH vs.Time after FlavoRx™ Flavorant Addition		
	0 days	30 days	180 days
Control	7.06	7.05	7.03
Grape	7.13	7.08	7.08

Conclusion: The results of this testing showed no variation in potency, pH or physical appearance between the control sample and the flavored samples. The increases in potency for ranitidine are comparable in all samples. pH showed stability throughout the trial. The physical appearance of all samples was consistent. The smell of the flavored samples was also consistent over the entire trial.

Tested by: Ronell Schneider Date: 5/4/10

Reviewed by: [signature] Date: 5/5/10

Oseltamivir Phosphate (Tamiflu®)

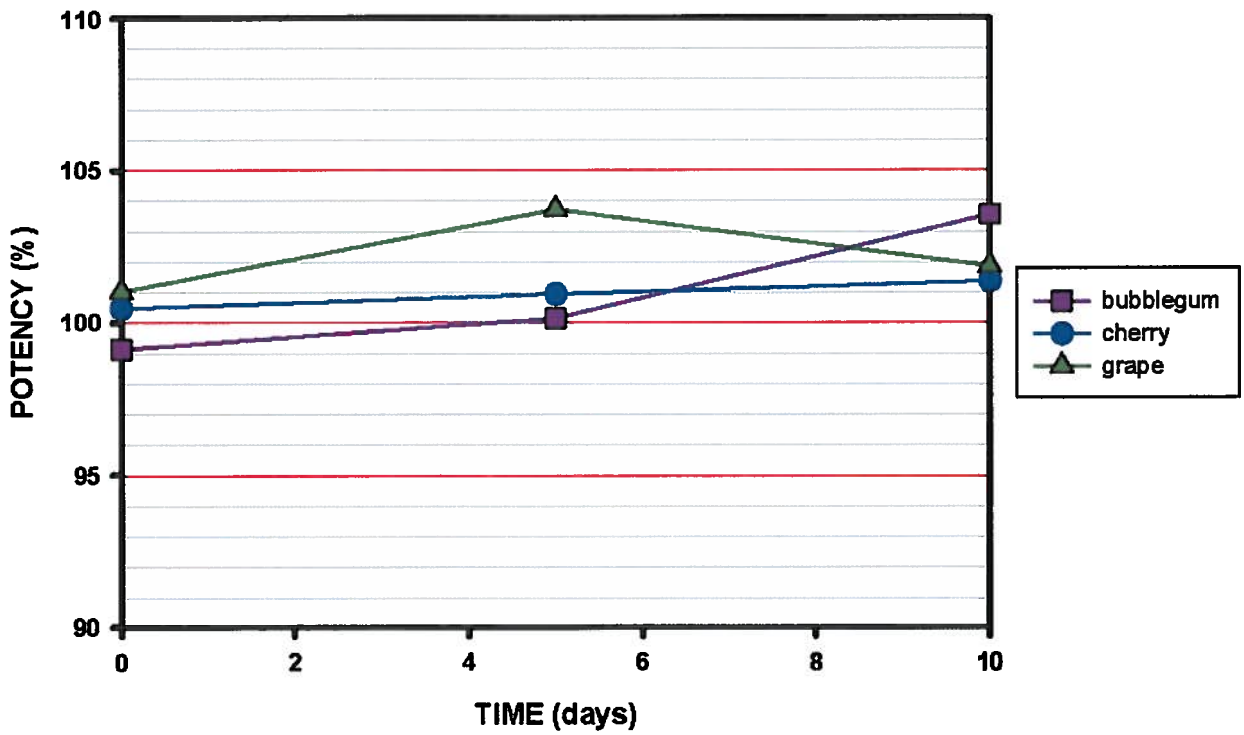
Materials: Oseltamivir phosphate for Oral Suspension, NDC#0004-0810-95, Lot#FOH431

Physical Appearance: Cloudy, homogeneous, white solution

Preparation Methods: Prepared Sample as stated on bottle. Transferred to Bubblegum sample bottle 6mL Sample, 4 drops FlavoRx™ Bubblegum flavor and 1 drop FlavoRx™ Banana flavor. Cherry sample bottle contained 6mL Sample, 1 drop FlavoRx™ Cherry flavor and 1 drop FlavoRx™ Watermelon flavor. Grape sample bottle contained 6mL Sample, 2 drops FlavoRx™ Grape flavor and 1 drop FlavoRx™ Watermelon flavor. All three flavored sample bottles also contained 2 drops FlavoRx™ Sweetness Enhancer and 1 drop Bitterness Suppressor. Sample solutions of 0.24mg/mL were then prepared in 25% acetonitrile. Standard solutions were prepared from 0.024mg/mL-0.24mg/mL in 25% acetonitrile.

Test Method & Materials: The samples were assayed based on assay method for Oseltamivir phosphate developed by Narasimhan B.[1] The assay was done on a Hitachi L-7000 system with UV-detector (215nm). The column used was a Zorbax Rx-C18, 4.6mm X 15cm. The flow rate was 1.0mL/min and run time was 7min. The mobile phase was (75:25) 0.2% triethylamine: acetonitrile to pH 3.0 with phosphoric acid.

OSELTAMIVIR POTENCY RELATIVE to CONTROL



OSELTAMIVIR CONTINUED

Table A: Potency of Medication in the Presence of Flavorants Relative to Control

Sample	% of Potency Relative to Control vs. Time after FlavoRx™ Flavorant Addition		
	0 days	5 days	10 days
Control	---	---	---
Bubblegum	99.1	100.2	103.6
Cherry	100.5	101.0	101.4
Grape	101.0	103.7	101.9

Table B: Potency of Medication in the Presence of Flavorants

Sample	% of Potency (%RSD) Relative to Label vs. Time after FlavoRx™ Flavorant Addition			%Gain/ (Loss) in Potency
	0 days	5 days	10 days	
Control	126.1(1.1)	126.0(1.4)	123.6(1.1)	(2.5)
Bubblegum	125.0(1.2)	126.2(0.7)	128.0(0.4)	3.0
Cherry	126.7(0.9)	127.2(0.7)	125.3(0.6)	(1.4)
Grape	127.4(0.2)	130.7(0.9)	125.9(0.3)	(1.5)

Table C: pH of Medication

Sample	pH vs.Time after FlavoRx™ Flavorant Addition		
	0 days	5 days	10 days
Control	N/T	N/T	3.75
Bubblegum	N/T	N/T	3.72
Cherry	N/T	N/T	3.18
Grape	N/T	N/T	3.29

Conclusion: The results of this testing showed no significant variation in potency or physical appearance between the control sample and the flavored samples. The changes in potency for oseltamivir phosphate are comparable in all samples. pH was tested only at 10 days due to the small sample volumes. The physical appearance of all samples was consistent. The smell of the flavored samples was also consistent over the entire trial.

1) Narasimhan B, Khan A, and Kona S. Stability indicating RP-HPLC method development and validation for Oseltamivir API. *Chem. Pharm. Bull.* 2008:56(4):413-417.

Tested by: Ronald Schneider Date: 2/1/10

Reviewed by: [signature] Date: 2/1/10

Appendix C
Board of Pharmacy Language on Flavoring

STATE SPECIFIC MENTION OF FLAVORING + NABP MODEL ACT
24 STATES AS OF AUGUST 2021

ARIZONA https://pharmacy.az.gov/practice-flavoring-medications

The Arizona General Assembly established a law allowing flavoring on July 2, 2011. Policy Statement still holds true:

POLICY:

1. A pharmacist may add flavoring agents, up to a maximum of five (5) percent (%) of the total volume, to a prescription at the request of a patient, the patient's care-giver, or the prescriber. The pharmacist shall label the flavored prescription with a beyond-use-date that shall be no longer than fourteen days if stored in a refrigerator unless otherwise documented and maintain electronic or manual documentation of the flavoring agent and quantity added. Documentation of beyond-use-dates longer than fourteen days, including the flavoring agent and quantity added, shall be maintained by the pharmacy electronically or manually and made available to agents of the Board on request.

2. The addition of flavoring agents over five (5) percent (%) of the total volume to a prescription requires the permission of the prescriber and compliance with the requirements of the Current Good Compounding Practices rule (A.A.C. R4-23-410).

3. A pharmacist may not add flavoring to an over-the-counter product at the request of a patient or patient's care-giver unless the pharmacist first obtains a prescription for the over-the-counter product from the patient's medical practitioner.

CALIFORNIA https://www.pharmacy.ca.gov/laws_regs/lawbook.pdf

Article 4.5 Compounding 1735. Compounding in Licensed Pharmacies (a) "Compounding" means any of the following activities occurring in a licensed pharmacy, by or under the supervision of a licensed pharmacist, pursuant to a prescription: (1) Altering the dosage form or delivery system of a drug (2) Altering the strength of a drug (3) Combining components or active ingredients (4) Preparing a compounded drug preparation from chemicals or bulk drug substances (b) "Compounding" does not include reconstitution of a drug pursuant to a manufacturer's direction(s), nor does it include the sole act of tablet splitting or crushing, capsule opening, or the addition of flavoring agent(s) to enhance palatability.

COLORADO

https://www.sos.state.co.us/CCR/GenerateRulePdf.do?ruleVersionId=9470&fileName=3%20CCR%2071 9-1

3.00.55 Prescription Flavoring. A flavor additive may be incorporated into a non-sterile prescription under

the following conditions:

a. The patient, patient's caregiver, or practitioner who authorized the original prescription

shall authorize the flavoring of each new and, if applicable, refilled prescription;

b. The flavor additive shall in no way compromise the stability, safety, or efficacy of the dispensed drug.

c. No expired flavor additive shall be incorporated into a prescription. No flavor additive shall be incorporated which will expire prior to utilization by the patient, based on the practitioner's directions for use.

d. For flavoring additives that do not have expiration dates assigned by the manufacturer or supplier, a pharmacist shall clearly and legibly label the container with the date of receipt and assign a conservative expiration date, not to exceed three years after receipt, to the flavoring additive. In no event shall the labeled date of receipt or assigned expiration date be later altered after originally labeling the container.

e. The following information shall be recorded and maintained in a suitable hard-copy or electronic dispensing record for a period of two years from the date of flavoring the corresponding new or refilled prescription. This record shall be made available, in printed form, for the Board or its representatives immediately upon the request of the Board or its representatives.

1) Additive's flavor;

2) Flavor additive's manufacturer

3) Flavor additive's lot number (if available); and

4) Flavor additive's expiration date.

f. The pharmacist responsible for conducting the final evaluation of a new or refilled prescription shall also be responsible for the flavoring of the prescription as specified in subsections a., b., and c. of this Rule 3.00.55.

g. The pharmacist manager shall be responsible for subsection d. of this Rule 3.00.55 and the maintenance of records as specified in subsection e. of this Rule 3.00.55.

CONNECTICUT https://www.cga.ct.gov/current/pub/chap_400j.htm#sec_20-617a

Sec. 20-617a. Flavoring agent added to prescription product. (a) For purposes of this section, "flavoring agent" means an additive used in food or drugs when such additive: (1) Is used in accordance with good manufacturing practice principles and in the minimum quantity required to produce its intended effect, (2) consists of one or more ingredients generally recognized as safe in food and drugs, has been previously sanctioned for use in food and drugs by the state or the federal government, meets United

States Pharmacopeia standards or is an additive permitted for direct addition to food for human consumption pursuant to 21 CFR 172, (3) is inert and produces no effect other than the instillation or modification of flavor, and (4) is not greater than five per cent of the total weight of the product.

(b) A flavoring agent may be added to a prescription product by: (1) A pharmacist upon the request of the prescribing practitioner, patient for whom the prescription is ordered or such patient's agent, or (2) a pharmacist acting on behalf of a hospital, as defined in section 19a-490.

(P.A. 12-12, S. 1.)

IDAHO https://bop.idaho.gov/wp-content/uploads/sites/99/2020/07/BOP-Complete-Law-Book-2020.pdf

700. COMPOUNDING DRUG PREPARATIONS. Any compounding that is not permitted herein is considered manufacturing. (3-20-20)T 01. Application. This rule applies to any person, including any business entity, authorized to engage in the practice of non-sterile compounding, sterile compounding, and sterile prepackaging of drug products in or into Idaho, except these rules do not apply to: (3-20-20)T a. Compound positron emission tomography drugs; (3-20-20)T b. Radiopharmaceutics; (3-20-20)T c. The reconstitution of a non-sterile drug or a sterile drug for immediate administration; (3-20-20)T IDAHO ADMINISTRATIVE CODE IDAPA 24.36.01 DOPL – State Board of Pharmacy Rules of the Idaho State Board of Pharmacy Section 700 Page 23 d. The addition of a flavoring agent to a drug product; and (3-20-20)T e. Product preparation of a non-sterile, non-hazardous drug according to the manufacturer's FDA approved labeling. (3-20-20)T

ILLINOIS
https://ilga.gov/legislation/ilcs/ilcs3.asp?ActID=1318&ChapAct=225%26nbsp%3BILCS%26nbsp%3B85%2F&ChapterID=24&ChapterName=PROFESSIONS+AND+OCCUPATIONS&ActName=Pharmacy+Practice+Act%2E

(o) "Compounding" means the preparation and mixing of components, excluding flavorings, (1) as the result of a prescriber's prescription drug order or initiative based on the prescriber-patient-pharmacist relationship in the course of professional practice or (2) for the purpose of, or incident to, research, teaching, or chemical analysis and not for sale or dispensing.

IOWA https://www.legis.iowa.gov/docs/iac/chapter/657.20.pdf

Compounding does not include the use of a flavoring agent to flavor a drug pursuant to rule 657—20.13(124,126,155A), nor does it include mixing or reconstituting a drug according to the product's manufacturer label.

"Flavoring agent" means a therapeutically inert, nonallergenic substance consisting of inactive ingredients that is added to a drug to improve the drug's taste and palatability.

657—20.13(124,126,155A) Use of flavoring agents. A flavoring agent may be added to a drug at the discretion of the pharmacist or upon the request of the prescriber, the patient, or the patient's agent. The pharmacist may add flavoring agents not to exceed 5 percent of the total volume of the drug to which the flavoring agents are added. The pharmacist shall label the flavored drug with a beyond-use

date no greater than 14 days past the date the flavoring agent is added if the drug is required to be stored in a refrigerator. A different beyond-use date or alternate storage conditions may be indicated if such variation is supported by peer-reviewed medical literature. The pharmacist shall electronically or manually document that a flavoring agent was added to a drug, and such documentation shall be made available for inspection and copying upon the request of the board or an agent of the board.

KANSAS

https://pharmacy.ks.gov/docs/default-source/statues-regulations/full-version-pdf.pdf?sfvrsn=66fca701_8

Compounding does not include reconstituting any oral or topical drug according to the FDA approved labeling for the drug or preparing any sterile or nonsterile preparation that is essentially a copy of a commercially available product.

KENTUCKY

https://pharmacy.ky.gov/statutesandregulations/Documents/201%20KAR%202%20076%20Compounding.pdf

Exclusion of flavoring in USP 795 has been adopted (confirmed at the July 2021 board meeting) and will be filed with the new revision.

be compounded pursuant to United States Pharmacopeia (USP) 795, unless specified portions submitted by a pharmacist have been waived by the board. Notwithstanding any USP guidance to the contrary, the addition of flavoring to a drug shall not be considered non-sterile compounding, when such additive:

(a) is inert, nonallergenic, and produces no effect other than the instillation or modification of flavor; and

(b) is not greater than five [5] percent of the drug product's total volume.

STATE SPECIFIC MENTION OF FLAVORING + NABP MODEL ACT
24 STATES AS OF AUGUST 2021

LOUISIANA
http://www.pharmacy.la.gov/assets/docs/GuidanceDocuments/PPM_I.A.31_AdditionFlavorsMedications_2019-1113.pdf

Louisiana Board of Pharmacy | **Policies & Procedures**

Title: Addition of Flavors to Medications | Policy No. I.A.31

Approved: 11-13-2019 | Revised:

1. The Board received a request from a representative of FlavoRx, a firm which manufactures flavoring agents used by pharmacists to customize prescription medications, to exempt the addition of flavoring agents to medications from the definition of compounding. The representative indicated his understanding that USP would include in the new update to *USP General Chapter <795> Pharmaceutical Compounding – Nonsterile Preparations* the guidance that the addition of flavoring agents would require compliance with the provisions of that chapter. It was suggested a requirement for compliance with USP standards might deter pharmacists from performing that service and might inhibit patient access to such services. The company requested the Board to promulgate a rule to exempt flavoring of commercially available liquid medications from the definition of compounding. The representative suggested limitations for the proposed rule such as requiring the flavoring agents to be nonallergenic and inert and for the flavoring agent not to exceed 5% of the drug product's total volume.

2. Following their review of the pharmacy law and rule, the Board determined a rule was not necessary and that an enforcement policy statement would be appropriate. The following motion was adopted after a unanimous vote in the affirmative.

Resolved, that the Board adopt an enforcement policy, such that the addition of nonallergenic and inert flavoring agents to commercially available liquid oral products resulting in a change in the final product volume of less than 5% shall not require a prescriber's order or a full compounding log.

MASSACHUSSETTS https://www.mass.gov/advisory/advisory-on-levels-of-non-sterile-compounding#advisory

THE BOARD OF REGISTRATION IN PHARMACY ADVISORY ON LEVELS OF NON-STERILE COMPOUNDING
Simple non-sterile compounding: Making a preparation that: (1) is the subject of a *United States Pharmacopeia* (*USP*) compounding monograph; or (2) appears in a peer-reviewed journal article that contains specific quantities of all components, compounding procedure and equipment, and stability data for that formulation with appropriate BUDs. (USP <795>)

- Please note carefully, the Board does not consider reconstitution of commercially available FDA approved preparations to be "compounding."
- It is highly recommended that pharmacies maintain a reconstitution log for the preparation of commercially available products (e.g., antibiotic suspensions, erythromycin-benzoyl peroxide gel, etc.) If utilized, any flavoring agents should be recorded either on this log or a compounding log.

MICHIGAN https://www.michigan.gov/documents/lara/4-8-2020_Pharmacy_Full_Approved_Minutes_with_attachments_693458_7.pdf

(e)"Compounding" does not include any of the following:

(i)Except as provided in section 17748c of the code, MCL 333.17748c, the compounding of a drug product that is essentially a copy of a commercially available product.

(ii)The reconstitution, mixing, or other similar act that is performed pursuant to the directions contained in approved labeling provided by the manufacturer of a commercially available product.

(iii)The compounding of allergenic extracts or biologic products.

(iv)Flavoring agents added to conventionally manufactured and commercially available liquid medications. Flavoring agents must be nonallergenic and inert, not exceeding 5% of a drug product's total volume.

MISSOURI https://pr.mo.gov/boards/pharmacy/practiceguide.pdf

H.10 FLAVORING

Licensees may flavor a legend product unless the prescriber indicates otherwise, however, OTC products may only be flavored by prescription. Licensees should indicate that the product was flavored on the patient's container and the added flavoring must be documented in the pharmacy's prescription record (e.g., in a flavoring book or in the prescription record). As defined by the Board's rules, flavoring does not constitute compounding. Licensees may not flavor a prescription dispensed by another pharmacy.

The Board is aware that USP is reviewing whether flavoring constitutes compounding. The Board has not adopted USP's proposed revision at this time but may reconsider this approach in the future. Flavoring does not constitute compounding under Missouri law.

NEBRASKA http://dhhs.ne.gov/licensure/Documents/Pharmacy.pdf

(4) Any authorized person splitting a scored tablet along scored lines or adding flavoring to a commercially available drug product is not engaged in compounding.

NEW HAMPSHIRE https://www.oplc.nh.gov/pharmacy/documents/nh-phcy-law-rule-book-10-29-19.pdf

"Compounding" shall not include the reconstitution of powdered formulations before dispensing or the addition of flavoring. "Compounding" shall not include the simple addition of flavoring, nor shall it include the preparation of a single dose of a nonhazardous commercially available drug or licensed biologic for administration within 2 hours of preparation to an individual patient when done in accordance with the manufacturer's approved labeling or instructions consistent with that labeling.

NEW JERSEY https://www.njconsumeraffairs.gov/regulations/Chapter-39-State-Board-of-Pharmacy.pdf

c) A compounding record shall not be required for: 1) Mixing, reconstituting, or assembling a drug according to the product's labeling or the manufacturer's directions; and 2) Product flavoring.

NORTH CAROLINA http://www.ncbop.org/faqs/pharmacist/faq_compoundedproducts.htm

Pharmacist FAQs

Frequently Asked Questions for Pharmacists on Compounded Products/Compounding

STATE SPECIFIC MENTION OF FLAVORING + NABP MODEL ACT
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Q: Is adding flavoring to a conventionally manufactured product considered compounding?

A: USP considers adding flavoring to a conventionally manufactured product to fall within the scope of compounding, because there are known instances when flavoring components have destabilized a product. If a pharmacy adds flavoring to a manufactured product it must take into account the manufacturer's Beyond Use Date (BUD) and the effect on stability caused by adding flavoring. If a flavoring component is added to a manufactured product that does not contain a preservative (e.g.: reconstitution of amoxicillin oral suspension) the BUD is 14 days refrigerated or shorter if indicated in the manufacturer's labeling. If a flavoring component is added to a manufactured product that contains a preservative (e.g. pyridostigmine oral solution), then the BUD is 35 days in controlled room temperature or refrigerated or shorter if indicated in the manufacturer's labeling. The addition of flavoring including the flavor manufacturer or product, lot number, and expiration date must be documented in the patient record notes for the prescription.

OREGON

https://www.oregon.gov/pharmacy/Documents/OBOPCurrent_Laws_Rules.pdf

https://olis.oregonlegislature.gov/liz/2019R1/Downloads/MeasureDocument/SB698/A-Engrossed

(c) Coloring agents, emulsifiers, excipients, flavorings, lubricants, preservatives and other like

inactive ingredients used in the manufacture of drugs.

PENNSYLVANIA
https://www.dos.pa.gov/ProfessionalLicensing/BoardsCommissions/Pharmacy/Pages/default.aspx

The Board voted to adopt the following position and will be amending its regulations to reflect this information: The definition of "compounding" does not include the unencumbered flavoring of conventionally manufactured medications provided that the flavors used are inert, tested and do not alter a medication's concentration beyond USP's accepted level of variance.

SOUTH DAKOTA https://doh.sd.gov/boards/pharmacy/minutes/9-12-19minutes.pdf

USP 795 and USP 797 published June 1, 2019 for go live date of December 1, 2019.

• USP 795 clarifications – Flavoring antibiotic suspensions is not compounding, simple reconstitution of antibiotics with water is not compounding; however, combining two creams or preparing a magic mouthwash is compounding and USP 795 must be followed including the restriction for carpet in the compounding area (Board may propose to allow extra time for compliance) and the BUD changes

TEXAS https://www.pharmacy.texas.gov/files_pdf/TSBP%20Rules_MASTER%20FILE.pdf

(H) A pharmacist may add flavoring to a prescription at the request of a patient, the patient's agent, or the prescriber. The pharmacist shall label the flavored prescription with a beyond-use-date that shall be no longer than fourteen days if stored in a refrigerator unless otherwise documented. Documentation of beyond-use-dates longer than fourteen days shall be maintained by the pharmacy electronically or manually and made available to agents of the board on request. A pharmacist may not add flavoring to an over-the-counter product at the request of a patient or patient's agent unless the pharmacist obtains a prescription for the over-the-counter product from the patient's practitioner.

UTAH

Flavoring Rule Proposal Utah Admin Code R156-17b-102

R156-17b-102

(13) "Compounding," as defined in Section 58-17b-102(18), in accordance with 21 U.S.C. 353a(e) does not include;

(a) mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with that labeling; and

(b) the addition of flavoring agents to conventionally manufactured and commercially available liquid medications so long as flavoring agents are therapeutically inert and do not exceed five (5) percent of a preparation's total volume.

WEST VIRGINIA

http://apps.sos.wv.gov/adlaw/csr/readfile.aspx?DocId=53617&Format=PDF

2.1.7.c. The following are not "compounding" and are exempt from USP 795 Compounding Standards:

2.1.7.c.1. the reconstitution of a drug pursuant to a manufacturer's directions;

2.1.7.c.2. the act of tablet splitting, crushing, or capsule opening, including those hazardous medications listed in NIOSH List Tables 2 and 3;

2.1.7.c.3. upon the request of the prescribing practitioner and/or the patient for whom the prescription is ordered or such patient's agent, the addition of therapeutically inert, nonallergenic flavoring agents to a commercially manufactured product, not in excess of five percent (5%) of the preparation's total volume;

WYOMING https://drive.google.com/file/d/1uZ68rYnnStHnVOFD0Rku8pFZCse5gzrb/view

(iv) Compounding does not include mixing, reconstituting, adding flavoring or other such acts that are performed in accordance with directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with the labeling.

STATE SPECIFIC MENTION OF FLAVORING + NABP MODEL ACT
24 STATES AS OF AUGUST 2021

NABP MODEL ACT

Section 105. Definitions.

(a) "Active Ingredients" refer to chemicals, substances, or other Components of articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases in humans or animals or for use as nutritional supplements.

(b) "Added Substances" mean the ingredients necessary to prepare the Drug Product but are not intended or expected to cause a human pharmacologic response if administered alone in the amount or concentration contained in a single dose of the Compounded Drug Product or alter the composition and effectiveness of the Compounded Drug Product. The term "added substances" is used synonymously with the terms "inactive ingredients," "excipients," "flavoring agents," and "pharmaceutic ingredients.

(c3) "Equivalent Drug Product" means a Drug Product that has the same established name, active ingredient(s), strength or concentration, dosage form, and route of Administration and which is formulated to contain the same amount of active ingredient(s) in the same dosage form and to meet the same compendial or other applicable standards (eg, strength, quality, purity, and identity), but which may differ in characteristics, such as shape, scoring, configuration, packaging, excipients (including colors, flavors, and preservatives), and expiration time.

October 20, 2021

Timothy Tucker, PharmD
Executive Director
Texas State Board of Pharmacy
333 Guadalupe Street, Suite 3-500
Austin, TX 78701

Re: 22 TAC Sections 291.36 and 291.131 Non-Sterile Compounding

Dear Dr. Tucker,

On behalf of Albertsons Companies, we extend our gratitude for the Board's continued work during the COVID-19 Public Health Emergency. Albertsons Companies operates 194 pharmacies in Texas under 6 different banners (Albertson's, Amigos, Market Street, Randalls, Tom Thumb, and United). We have worked diligently to keep sites open to serve patient needs during this emergency. Patient access to pharmacy care is paramount and has been proven with each step during the COVID-19 pandemic.

Albertsons Companies appreciates the opportunity to provide comments on the proposed regulations related to non-sterile compounding recently filed in the Texas Register. It is from the perspective of patient access to pharmacy care that we would like to deliver these comments. In general, adding regulations and additional requirements will inherently decrease patient access to compounding services. It is the position of Albertsons Companies that layering on regulations is altogether unnecessary and we request that the Board take steps to cancel the rule making process. The basis of our conclusion is outlined in the following paragraphs.

22 TAC Sections 291.36

Creating a new designation for Class A pharmacies relative to non-sterile compounding adds a new unnecessary regulatory hurdle that pharmacies will need to overcome to offer compounding services to their patients. The COVID-19 pandemic has taught us that additional regulatory burden hinders prompt reaction to a public health emergency and impedes public safety. Depending on the nature of a public health emergency, even waiting for the Governor or Board of Pharmacy to issue a waiver could be too long.

Additionally, we believe this will create a burden for Board staff as they will be required to relicense numerous community retail pharmacies to grant them the A-N designation. A pharmacy may unnecessarily apply for the designation while not routinely providing these services in an attempt to avoid failing to meet the needs of a patient. This has the potential to further burden Board staff with an increased workload due to the large number of applications they will have to process. If there is a need

for inspectors to know in advance if a pharmacy is engaging in compounding, this can be accomplished by including a question on the renewal form or a self-attestation survey and would not require reclassifying a pharmacy. Albertsons Companies would not be in favor of a required Class A-N designation to perform compounding.

TAC 22 Section 291.131

A majority of compounding that occurs in a community pharmacy today is limited to simple routine compounds. A simple routine compound is very different than performing complex compounds or even compounds related to hazardous medications. Performing these compounds is often as basic as mixing a steroid cream into a lotion or mixing a few ingredients to make a mouthwash. Neither of these scenarios require specialized equipment that a standard community pharmacy lacks. The proposed regulations seek to regulate the act of non-sterile compounding with the expectation that all compounds are complex and dangerous.

It is also our observation that many of the requirements added to this section have been drawn from the draft USP 795 guidelines. These guidelines are controversial and have been met with much opposition. So much so that they were pulled back to be amended after several successful appeals were filed. USP has recently reposted these guidelines for public comment, which is open until January 2022. Pulling requirements from a draft document that could change based on public comments or future appeals can be problematic. We recommend that the board table these regulations until the USP 795 guidelines have been finalized to ensure the regulations do not conflict with nationally recognized guidance.

Furthermore, when considering the potential effects on patient access to routine simple compounds, there are additional unnecessary requirements within the proposed regulation. For example, a simple nonsterile compound routinely provided in community pharmacies is “Magic Mouthwash.” This medication is provided to patients who experience pain from undergoing radiation, chemotherapy, strep throat, etc. The benefit to these patients having access to this nonsterile compound far outweighs any risk and does not warrant additional training for the pharmacy staff beyond what is provided today with on-the-job training or during a pharmacist’s professional training. Another example of the benefit of easy access to these simple nonsterile compounds are the liquid formulations for treatment of influenza that were previously unavailable in the market. Pharmacists had to resort to compounding a liquid formulation from capsules to respond to the needs of pediatric patients. We cannot predict patient demands during a public health crisis, and we know that increased regulation leads to the increased need for waivers. Under these circumstances, time is of the essence and the Board cannot afford to delay treatment to a patient in need. This goes against the mission of the Board to protect public safety.

Alternatively, if the Board chooses to move forward with these regulations, we recommend that the Board consider an exemption to the extensive requirements for simple compounds. These regulations should be limited to complex compounds, compounding that requires the use of hazardous medications, or the use of airborne generating chemicals.

We appreciate the opportunity to provide feedback on these regulations and their significance to patient access to pharmacy care. If you have questions, please reach out to me at Rob.Geddes@albertsons.com or (208) 513-3470.

Sincerely,

Rob Geddes, PharmD
Director, Pharmacy Legislative and Regulatory Affairs

From: LEdmundson@brookshirebros.com
Sent: Thursday, October 21, 2021 3:09 PM
To: Tim Tucker
Subject: Proposed Amendments to §291.131 – Pharmacies Compounding Non-Sterile Preparations

Good afternoon, Mr. Tucker,

I am writing in regards to the proposed amendments to §291.131, which relates to pharmacies that compound non-sterile preparations. As a retail pharmacy chain with 67 locations across many rural areas of Central and East/Southeast Texas, we see our fair share of prescriptions for compounded medications, the majority of which, I would consider 'simple' compounding. We would like to request that there be some clarification of the proposed language starting with lines 79 through 82. The examples of crushing a tablet or opening a capsule are provided for "manipulation beyond the FDA labeling of a commercial product". Is this rule also meant to include the mixing of two or more commercially available creams, ointments, or liquids? By mixing one product with one or more others, is that considered "manipulation"? If the combining of one or more commercially available products is within the realm of this definition, then these proposed amendments will greatly limit the general public's access to some of the most commonly compounded preparations.

The proposed space and equipment requirements that are outlined for a Class A-N pharmacy license may, unfortunately, lead to compounding services no longer being offered at the majority of our locations. This would require a significant cost investment for such a small part of our pharmacy operation. As I mentioned previously, our pharmacy footprint across Texas tends to cover many small towns where we may be the only pharmacy for 20-30 miles. If we were to cease compounding some of these common preparations (Magic Mouthwash, topicals mixed with other topicals, etc), I could see many patients not being willing to travel to another city or wait for their compound to come in the mail. Oftentimes, the preparation being compounded is being used to treat an acute condition or illness in which the patient wants and/or needs to get started using their compound sooner rather than later.

Again, some clarification on specifically which types of compounds are included and/or excluded (and whether or not flavoring of a medication is also included) will be very helpful in determining the true potential impact to community pharmacies and to the communities they serve.

On another note, we request that the rule language also clarify that the prescription balance only be required for pharmacies that are compounding products that need to be weighed, hence those that would qualify to receive a Class A-N license.

Thank you for your time and attention.

Laura

Laura Edmundson

Director of Pharmacy
Brookshire Brothers, Inc.
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Lufkin TX
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From: jacob c
Sent: Friday, October 22, 2021 9:45 AM
To: Tim Tucker
Subject: Pharmacist concern for §291.131

Hello,
I would like to express my concern for §291.131 which would require all pharmacies to be re-licensed as a class A-N pharmacy. I am emailing on behalf of myself and my employer (HEB) to re-consider these rules which would make the pharmacy world more complicated and, in my opinion, would not benefit the patient. In retail pharmacy we are expected to provide safe and quick service. We interact with thousands of patients per week who expect their medication to be of value to their health in a reasonable time frame. These rules would create additional training, sample product testing, and addition of compounding hoods and garbing procedures. This would be unreasonable in a retail pharmacy due to space limitations and increased wait time for patients. These simple compounds and flavoring have been done safely and effectively for years, and providing these limitations, in my opinion, is unnecessary and impractical. This increased burden would add weight to retail pharmacy which is not needed. Retail focuses on dispensing, providing immunizations, and patient care. Time is limited in the work place, and less physical space and more lengthy procedures would not benefit the pharmacy or the patient.

Sincerely,
Jacob Colbath
[redacted]

HOUSTON Methodist LEADING MEDICINE

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Houston, Texas 77030
Office: 346-356-1758
neverett@houstonmethodist.org

October 20, 2021

Eamon D. Briggs, Assistant General Counsel
Texas State Board of Pharmacy
333 Guadalupe Street, Suite 3-500
Austin, TX 78701
eamon.briggs@pharmacy.texas.gov

Re: Proposed Rule Amendment §291.1 Pharmacies Compounding Non-Sterile Preparations

Houston Methodist is a non-profit health care system serving the greater Houston area through its seven community hospitals, academic medical center ranked as the number one hospital in Texas and among the top twenty hospitals in the nation, and primary and specialty physician organizations. In 2020, Houston Methodist cared for over 120,000 inpatient admissions and almost 632,000 outpatient visits. Houston Methodist's highest priority is patient safety, quality, and service, which have been recognized by national awards in these areas.

We appreciate the opportunity to submit comments to the Texas State Board of Pharmacy regarding the proposed rule announced in the September 24, 2021 edition of the Texas Register on compounding of non-sterile preparations as a service provided by pharmacies.

Pharmacy leaders have reviewed the proposed amendment and offer the follow comments for consideration pending rulemaking in upcoming board session(s).

I. Initial training: We support the idea of an initial competency training requirement for pharmacy personnel responsible for preparation of non-sterile compounding. However, there are areas of concern that merit additional clarity and information prior to the implementation date.

   a. The scope of training as listed in the proposed rule is as follows: Training shall include instruction, experience and demonstrated proficiency in the following areas: *(i)* hand hygiene; *(ii)* garbing; *(iii)* cleaning and sanitizing; *(iv)* handling and transporting components and compounded non-sterile preparations; *(v)* measuring and mixing; *(vi)* proper use of equipment and devices selected to compound non-sterile preparations". There are considerable safety differences between sterile compounding and non-sterile compounding and these are covered in-depth during training for sterile compounding. For the categories proposed in the rule, we believe there would be significant overlap in the training content. The scope and breadth of the non-sterile compounding training may not necessitate a full 20 hours for pharmacists and 40 hours for technicians for successful training and skills validation. It would be helpful for the board to provide its rationale for proposing such a large amount of time dedicated to training that is duplicative.

   b. Unlike the 20-hour and 40-hour initial training requirements for pharmacists and pharmacy technicians for sterile IV certification – which are well defined with regards to scope, content and availability of training resources – there are currently few training resources for non-sterile compounding. Content within training resources that are currently available vary and include content that is not specific to practice settings. For example, review of the content for the non-sterile compounding program offered by PCCA suggests that only 8 hours of the program is significantly geared towards items that are typically seen in a hospital setting. The remaining content of PCCA training has other focus areas such as veterinarian non-sterile preparations which is not needed in hospital pharmacy. We request that the board provide a list of companies or organizations beyond solely PCCA that are equipped to provide such training as most hospitals

do not have resources and/or bandwidth to facilitate an independent, in-house training course for non-sterile compounding in addition to our ongoing training on sterile compounding.

c. The proposed rule suggests that standardization of training is a desired outcome. To do so, further clarity should be provided on the various components that must be included in the training as relative to the practice setting. We currently have clearly listed knowledge domains that must be covered for IV certification. To ensure that pharmacy personnel are exposed to similar or comparable training, the board should clearly define essential domains for non-sterile compounding certification.

d. With regards to initial training, further clarification is needed regarding which hospital staff are required to complete such training. Will tenured hospital staff be required to complete an initial training or will skills validation and competency assessment support waiver of some or all parts of the initial training? Additionally, further clarification of the term "involvement" would be helpful as there are several moving parts and contributors to all processes within hospital pharmacy.

II. With regards to the subsequent annual 1-hour CE requirement: The PIC remains accountable for all pharmacy services including duties which are delegated to lead staff. Monitoring the compliance of employees' CE is a task that can be reasonably delegated without eliminating the overall accountability of the PIC. We encourage consistency among regulations and suggest alignment with <USP 795> to allow delegation to a "designated pharmacy staff".

III. With regards to the board's proposed initial and subsequent testing: We support the purpose of testing, however, there is a need for clarification about subsequent testing (e.g. Would three tests be required in the subsequent annual testing as in the initial testing?).

IV. Under the "environment" section: Further clarity of "designated space" is needed. We ask for consideration of flexibilities for lower volume hospitals that may not be able to have a segregated area for non-sterile compounding within the work area, but could have a "designated space" that would not be used for other pharmacy functions.

V. With regard to the pharmacist's role in pre-preparation, in-process, and post-preparation checks: Further clarification and/or explanation of the details, similar to that which is stated in <USP 795>, and how these processes would meet inspection requirements would be appreciated.

VI. We support the board's recommendation on the equipment and supplies section, including the standard calibration of equipment.

VII. We support the board's recommendation on the gloving and garbing section.

VIII. We support the board's recommendation on the development and implementation of SOPs supporting quality assurance.

We appreciate review and consideration of all collective comments from pharmacy practitioners in the field.

Sincere Regards,

Nichelle S. Everett, RPh, MHA
Houston Methodist Hospital System
Director, Pharmacy Med Policy & Regulatory Compliance

Mark Johnston, R.Ph
Senior Director, Pharmacy Regulatory Affairs
One CVS Drive
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10/18/2021

Dr. Timothy Tucker
Texas State Board of Pharmacy
William P. Hobby Building
Tower 3, Suite 500
333 Guadalupe Street
Austin, TX 78701
tim.tucker@pharmacy.texas.gov

Dear Director Tucker,

I am writing to you in my capacity as Senior Director of Regulatory Affairs for CVS Health and its family of pharmacies in Texas and across the United States. CVS Health, the largest pharmacy health care provider in the United States, through our integrated offerings across the spectrum of pharmacy care, is uniquely positioned to provide diverse access points of care to patients. CVS Health commends the Texas Board of Pharmacy for its progressive approach to protecting public safety.

CVS Health's purpose is to help people on their path to better health. We are committed to patient safety, technological and process advances, and expanded pharmacy services that will assist in achieving our stated purpose. Our pharmacists have evolved from the traditional dispensing practices of data entry, counting, pouring and labeling to become a health care provider within a culture of patient centered care.

CVS Health appreciates the opportunity to comment on the proposed amendments to **22 TAC §291.131**

As community pharmacy providers we believe these regulations will negatively affect patient access to simple, traditional non-sterile compounding, that have been conducted and dispensed by community pharmacies as a normal part of the practice of pharmacy. Evidence has not been provided to justify over-regulation of non-sterile compounding as deterring a known patient safety concern, especially if smaller volumes are compounded. CVS Health recommends that the Board consider the volume compounded for traditional non-sterile compounding and allow community pharmacies to continue to maintain patient access to non-sterile compounded products. Additionally, we believe the fiscal impact analysis, which focused primarily on rural pharmacies and did indeed state that there would be an impact, underestimated the fiscal impact these proposed regulations will have on all community pharmacies. If these proposed regulations were to be promulgated, of paramount concern is the great number of pharmacies that would likely cease providing non-sterile compounding services, which would greatly impact patient access to non-sterile compounded products. This is due to significant burdens placed on pharmacies, which would surpass USP requirements, without a documented patient safety nexus. Therefore, CVS Health provides the following comments.

" Completing testing of three preparations compounded by compounding pharmacists and technicians for accuracy of correct identities and amounts of ingredients within the first six months of engaging in compounding non-sterile preparations intended for patient use does not align with current or proposed USP standards, does not afford the pharmacist to utilize their professional judgment, is not appropriate in all cases and is overly burdensome and impractical."

Proposed 795 defers to USP 1163 as it pertains to quality control procedures. USP 1163 outlines the importance of SOPs that describe how to perform routine and expected tasks in the compounding environment. As such, testing is but a single component of proper SOPs, which include quality assurance, safety, and training amongst several other components. As it pertains to testing specifically, the USP states that a quality assurance program for compounded preparations should include testing during the compounding process and of the finished compounded preparation, when appropriate, as described in chapters ⟨795⟩ and ⟨797⟩. There are 2 important points with this USP standard. First, the standard states that testing "should" occur rather than "shall" occur. Second, the standard is clear that that testing should be conducted "when appropriate". This gives the pharmacist the ability to utilize discretion and professional judgment in whether testing is utilized or not. Furthermore, the USP has stated that testing every compounded preparation is neither practical nor officially required, but compounders should conduct visual inspections and know: (1) the importance of testing in the overall quality program in the compounding facility, (2) when to test, (3) what to test, (4) what appropriate method(s) and equipment to use, (5) how to interpret the results, (6) the limits of the test, and (7) specific actions required when a preparation does not meet specifications. Investigative and corrective action should extend to other preparations that may have been associated with the specific failure or discrepancy. We believe this USP guidance applies to the assessment of compounding personnel as well.

Therefore, CVS Health proposes striking the following sections as it would be extremely difficult for every pharmacist engaging in non-sterile compounding to comply, place a large burden on the practice of non-sterile compounding and ultimately, create a patient access issue because pharmacies will discontinue the practice of non-sterile compounding.

§291.131. Pharmacies Compounding Non-Sterile Preparations.

(2)(B) ~~complete testing of three preparations compounded by the pharmacist for accuracy of correct identities and amounts of ingredients within the first six months of engaging in compounding non-sterile preparations intended for patient use; and~~

(3)(B) ~~(i) complete testing of three preparations compounded by the pharmacy technician or pharmacy technician trainee for accuracy of correct identities and amounts of ingredients within the first six months of engaging in compounding non-sterile preparations intended for patient use~~

" Excessive training hours for pharmacists are not required as they should only be performing non-sterile compounding based on their knowledge, skills and abilities, which are adequately

provided in a Doctor of Pharmacy program. Additionally, a static training requirement for all pharmacy technicians performing non-sterile compounding does not account for the variable knowledge, skills and abilities of different technicians"

A regulatory requirement, placing excessive training requirements for pharmacists and technicians, who wish to perform non-sterile compounding, will create a barrier for pharmacies and thereby result in pharmacies not providing non-sterile compounds because they do not have the professionals available with the requisite training requirements.

Therefore, CVS Heath proposed striking the training hours requirement for the pharmacist and technicians.

(C) All personnel involved in the preparation and mixing of compounded non-sterile preparations that use bulk API or excipients or manipulation beyond the FDA labeling of a commercial product (e.g., crushing a tablet or opening a capsule) shall complete initial training in the areas listed in subparagraph (D) of this paragraph through:

> *~~(i) a single course with a minimum of 40 hours for the pharmacy technician or 20 hours for the pharmacist of instruction and hands-on, in-person experience. Such training shall be obtained through completion of a recognized course in an accredited college of pharmacy or a course sponsored by an ACPE-accredited provider; or~~*

"The requirement for a closed system device goes far beyond the necessary safety requirements of USP 795 additionally placing a large burden on the practice of non-sterile compounding and ultimately, creating a patient access issue because pharmacies will discontinue the practice of non-sterile compounding."

The currently "proposed" USP Chapter 795, nor the current 795, do not mandate the use of a closed system device. Rather, the USP allows for an assessment of the APIs used and allows the compounder to decide on whether a CVE or BSC is necessary or should be used. This regulation would mandate the use of a closed system device for all non-sterile compounding and take away any professional or clinical decision making by the pharmacist overseeing the compounding operation. In an effort to maintain patient access to common non-sterile compounds, as most pharmacies have done throughout history, CVS Health proposes striking the following proposed regulation.

~~C) use a closed system processing device, used to reduce the potential exposure to personnel, or contamination of the pharmacy, or compounded non-sterile preparations, to perform activities such as weighing, measuring, or otherwise manipulating components that generate airborne chemical particles (e.g., active pharmaceutical ingredients (APIs), added substances, conventionally manufactured products). Examples of closed system processing devices include containment ventilated enclosures (CVEs), 249 biological safety cabinets (BSCs), powder containment hoods, or single-use containment glove bags. If a BSC or CVE is used, the BSC or CVE shall be certified every 12 months by a qualified independent individual~~

"Mandating garbing for all non-sterile compounding activities is unnecessary, not supported by evidence to promote safety for most products compounded by community pharmacies and also does not align with the USP."

The current and newly proposed USP Chapter 795 do allow for "appropriate" garbing for the type of compounding conducted. We feel this is reasonable as it allows for the pharmacist to utilize their professional judgement on when garbing should be worn based on the specific compound. Therefore, CVS Health proposes the following changes.

(D) Gloves and other garb (e.g., shoe covers, head and facial hair covers, face masks, gowns) ~~shall~~ may be worn for ~~all~~ compounding activities, as appropriate and as determined by the pharmacy, for prevention of preparation and facility contamination and must be appropriate for the type of compounding performed. The garbing requirements and frequency of changing the garb shall be determined by the pharmacy and documented in the pharmacy's SOPs. Garb shall be stored in a manner that minimizes contamination (e.g., away from sinks to avoid splashing). Visibly soiled garb or garb with tears or punctures, including gloves, shall be changed immediately. Gloves, shoe covers, hair covers, facial hair covers, face masks, or head coverings may not be re-used if worn outside of the compounding area and must be replaced with new ones. To minimize the risk of cross-contaminating other compounded non-sterile preparations and contaminating other objects (e.g., pens and keyboards), gloves should be wiped with 70% isopropyl alcohol or replaced before beginning a compounded non-sterile preparation with different components

"While it is understood that the newly proposed USP 795 also mandates the removal of carpeting, the TX Board of Pharmacy is not required to follow all aspects of the USP. Additionally, this mandate would place pharmacies in the position to decide whether to remodel all of their pharmacies at a great expense or discontinue non-sterile compounding."

The requirement to remove all carpeting would create a negative work environment as most pharmacies utilize "fatigue carpeting" to relieve stress for the pharmacists standing on their feet all day. Also, USP has provided no scientific data to justify the removal of carpeting and would be an unnecessary expense. Therefore, CVS Health proposes the following change.

(3) Environment.

(A) Pharmacies regularly engaging in compounding shall have a designated and adequate area for the safe and orderly compounding of non-sterile preparations, including the placement of equipment and materials. Space in the pharmacy shall be specifically designated for non-sterile compounding. The method of designation (e.g., visible perimeter) must be described in the pharmacy's SOP. Other activities shall not occur in the space at the same time as compounding. The compounding space shall be secure, well-lighted and shall be maintained in a clean, orderly, and sanitary condition, and in a good state of repair. ~~Carpet is not allowed in the compounding space~~. Surfaces should be resistant to damage by cleaning and sanitizing agents. The space shall allow for the orderly placement of equipment and materials to prevent confusion among components, containers, labels, in-process materials, and finished compounded non-sterile preparations. The space shall be designed, arranged, and used in a way that minimizes cross-contamination from non-compounding areas

Thank you again for the opportunity to comment on these regulations, and feel free to contact me for any reason.

Sincerely,

Mark Johnston, R.Ph

Senior Director

Pharmacy Regulatory Affairs

CVS Health

From: RGriffith@brookshirebros.com
Sent: Friday, October 22, 2021 5:26 PM
To: Tim Tucker
Subject: Proposed Amendments to §291.131 - Non-Sterile Compounding in Pharmacies

Dear Mr. Tucker,

I am writing regarding the proposed amendments to §291.131, relating to non-sterile compounding in pharmacies. As a retail pharmacy in rural Deep East Texas, Hemphill (Sabine County) to be specific, there are a limited number of pharmacies accessible to our patients. In our pharmacy we see a fair number of compounded prescriptions of which the majority consist of mixing readily available ingredients, Magic Mouth Wash being the most common.

Given my community consists of many retired patients it would burden them to drive outside the area for a simple compounded prescription. The closest pharmacy that would potentially offer compounding services would require my patients to drive over an hour one way which limits access to some of these common compounded prescriptions. Many of my patients depend on medical transportation to access medical services and would not have access to pharmacies outside our community.

Thank you for your time,

Robyn Griffith, PharmD
Brookshire Brothers Pharmacy #1020
2075 Worth St Hemphill, TX 75948

Robyn Griffith

Pharmacy Manager #1020
Brookshire Brothers, Inc.
2075 Worth St.
Hemphill, TX TX
75948

Phone: 409-787-2356
Mobile:
Fax: 409-787-4775
Email: RGriffith@brookshirebros.com
Web:

From: Jd Fain
Sent: Sunday, October 24, 2021 1:34 PM
To: Eamon Briggs
Subject: Non- Sterile Compounding rules

Dear President Spier and Board Members,

I am writing to you to share my concerns with the proposed compounding changes. I would implore you to vote "no"on the proposed rules.
I cannot foresee a reason to change the rules that are currently in place. I don't know why there would need to be a non-sterile compounding license when pharmacists have been making non-sterile patient products for as long as pharmacy has been practicing as a profession. I do believe pharmacists should keep up with new concepts and products concerning their practice however, "requiring" continuing education for something we learned from pharmacy school that makes us the only profession that performs such tasks, doesn't make sense to me. As I understand the new rules concerning non-sterile compound , combining two liquids or creams together requires a sterile hood. I cannot express how illogical that sounds.

I own a rural independent pharmacy that supplies cancer patients and others with simple mouthwash and commonly known "Magic Mouthwash" which is usually an acute condition and needs immediate treatment. The new rules would delay or eliminate my patients their ability to acquire relief. I am sure there are other examples of simple, easy preparations that are utilized in community pharmacies.

Sterile compounding is another subject as they represent more potential for permanent adverse events. Non-sterile compounding should continue under the current rules to allow pharmacies to continue to provide for their patients.

Thank you for your time and attention.

Sincerely,

JD Fain BSPharm, PharmD, R.Ph.
PIC Pieratt's Pharmacy
233 S. Manse
Giddings, Tx
78942

From: Kunal N
Sent: Sunday, October 24, 2021 2:20 PM
To: Eamon Briggs
Subject: tsbp proposed compounding rules comments

Hello,

I have reviewed the proposed rule changes for non-sterile compounding. I am an independent pharmacy owner and have the following comments/concerns;

-it is very costly to send compounding samples for testing. The additional cost incurred to comply would burden small pharmacies and ultimately reduce access by increasing costs to patients especially since the majority of compounds are paid for out of pocket

-Pharmacists with a PharmD should be exempt from additional training and testing requirements as non-sterile compounding techniques are thoroughly taught in school

Thank you for your time.

Sincerely,
Kunal Nagarsheth, PharmD, RPh

--
Sent from Gmail Mobile

Tim Tucker, Pharm D
Executive Director
Texas State Board of Pharmacy
William Hobby Building
333 Guadalupe Street, Suite 3-500
Austin, Texas 78701-3943

CC: Julie Spier, President
Megan Holloway, General Counsel

Re: Proposed non-sterile compounding 291.131

Dr. Tucker and Board Members:

I have great concerns about the proposed rules addressing pharmacy non-sterile compounding that imposes new requirements on both the Class A pharmacy and all personnel in the pharmacy that are involved in the non-sterile compounding of a prescription order. It appears the driver for adopting these numerous rules is "public safety". My experience as a past Board member for twelve years involved in numerous disciplinary actions is that there is little to no concerns for non-sterile compounding as it relates to complaints or adverse results stemming from a non-sterile compounded medication, especially when compared to dispensing errors in general in Class A pharmacies. And when comparing that to sterile compounding which has had a number of adverse issues resulting from a failure to follow current rules and regulations which were designed to create policies and procedures including training, environment requirements, specific record keeping, and more. In fact, the issue has been a failure for the pharmacy to follow their own policies and procedures.

The proposed rules will create substantial financial hardship for the typical community pharmacy (Class A) to meet all these proposed requirements to be able to fill a non-sterile compound prescription order. For the vast number of community pharmacies, non-sterile compounds are probably less than 1% of prescriptions filled compared to a sterile pharmacy compounding pharmacy who has made a business decision to be licensed as a sterile compounding pharmacy and indicate that on their license. What are the likely results if this proposed rule passes? First and foremost, this will impact patients who are used to going to their community pharmacy for all their prescription needs, including nonsterile compounding prescription orders. Pharmacists are trained to perform this activity as part of their pharmacy education and stay current through existing education requirements. I envision pharmacies will opt out and not be a non-sterile compounding pharmacy leading to a hardship for patients in identifying which pharmacy can fulfill a compounded prescription order.

All rules and regulations need to be reviewed prior to adoption to identity any unintended consequences that might result and weigh that against the proposed benefit. That includes enforcement of the rule and what resources the Board staff needs to enforce compliance. The focus must always be on the patient to not only include safety issues but accessibility to pharmacy services. The only exception is a statute change which is the result of legislative action.

Rules and regulations are created to address pharmacy practice needs, especially as the practice of pharmacy evolves and expands to included expanded clinical activities. At the same time, the Board needs to be cautious about being “too” prescriptive, with the end result not being beneficial to the patients.

As I have stated in my comments, it is necessary to weigh the impact of the proposed regulations to Class A pharmacies and patient access to this service. Currently there are approximately 5,800 Class A pharmacies in Texas, with around 290 being sterile compounding pharmacies, who already operate under sterile compounding rules. This would result in around 5,500 or 95% of current Class A pharmacies forced to decide whether they can continue to serve their patients as it relates to non-sterile compounding under the new proposed regulations.

During your discussion, it would be helpful to understand rules other states have implemented addressing non-sterile compounding. I would add for more clarity during the discussion, how does this rule align with USP nonsterile compounding definitions? Additionally, what is the anticipated additional cost to the Board to address the new requirements to ensure compliance and what new disciplinary cost to address non-compliance violations.

My last comment in reviewing the proposed rule is that I initially planned to comment on each proposed change. I decided that would be non-productive but rather focus on the bigger picture and ask that you take a step back and revisit the need for this change and the cost of this change to everyone involved, especially the citizens of Texas.

I would encourage the Board to not move forward with adopting these proposed rules at this time.

Your truly,

Dennis Wiesner R.Ph. Texas 18697

[redacted]
7901 Southwest Parkway, Unit 14
Austin, Texas 78735

October 25, 2021

Mr. Eamon D. Briggs
Assistant General Counsel
Texas State Board of Pharmacy
333 Guadalupe Street, Ste. 3-500
Austin, Texas 78701

Dear Mr. Briggs:

The Alliance for Pharmacy Compounding is the voice for pharmacy compounding, representing compounding pharmacists and technicians in both 503A and 503B settings, as well as prescribers, educators, researchers, and suppliers. In traditional compounding, pharmacists create a customized medication, most often from pure ingredients, for an individual patient pursuant to a prescription. Pharmacists' ability to compound medications from pure ingredients is authorized in federal law and for good reason: Manufactured drugs don't come in strengths and dosage forms that are right for everyone, and prescribers need to be able to prescribe customized medications when, in their judgment, a manufactured drug is not the best course of therapy for a human or animal patient.

Founded in 1898, the National Community Pharmacists Association is the voice for the community pharmacist, representing over 21,000 pharmacies that employ approximately 250,000 individuals nationwide. Community pharmacies are rooted in the communities where they are located and are among America's most accessible health care providers.

We write today in strong support of the amendments proposed by the Texas State Board of Pharmacy to 22 TAC 291.131 concerning pharmacies compounding non-sterile preparations as published in the September 24, 2021, issue of the *Texas Register* at 46 TexReg 6350. APC and NCPA believe these proposed amendments are directly aligned with the authority given the Board under Sections 551.002 and 554.051 of the Texas Pharmacy Act that authorize effective control and regulation of the practice of pharmacy in Texas to protect the public.

APC supports amending the regulations to add definitions of "cleaning" and "sanitizing", update requirements for all personnel engaged in non-sterile compounding, add additional requirements for personnel engaged in certain types of non-sterile compounding, and update environmental and equipment requirements for non-sterile compounding. These proposed changes are consistent with our desire to see state boards of pharmacy better align their regs with pharmacy compounding best

practices as listed in USP 795 on non-sterile compounding. It is critical for both public safety and for public trust in the compounded medications they are prescribed that the regulations in Texas be amended to recognize the evolving best practice standards of the industry.

For these reasons, we ask that the Board adopt the proposed rules concerning pharmacies compounding non-sterile preparations. If you have questions or concerns, please feel free to reach out to APC's Scott Brunner at scott@a4pc.org or 404.844.8607.

Sincerely,

Scott Brunner, CAE
Chief Executive Officer
Alliance for Pharmacy Compounding

Ronna Hauser, PharmD
SVP Policy & Pharmacy Affairs
National Community Pharmacists Association

TEXAS Pharmacy Association
Together Pharmacy Advances

October 25, 2021

Julie Spier, President, and Members
Texas State Board of Pharmacy
333 Guadalupe St., Suite 3-500
Austin, TX 78701

Via email: Eamon.Briggs@pharmacy.texas.gov

Re: Proposed Rules for Final Adoption – Non-Sterile Compounding

Dear President Spier and Board Members,

On behalf of the thousands of pharmacists, student pharmacists, and pharmacy technicians represented by the Texas Pharmacy Association (TPA), we thank the Texas State Board of Pharmacy (TSBP) for the opportunity to comment on the proposed rules for final adoption concerning non-sterile compounding. TPA represents pharmacy professionals in all practice settings and knows firsthand the value pharmacists bring to improving health outcomes, with patient safety of utmost concern.

TPA does not support the proposed non-sterile compounding rules as published and does not believe they should be adopted as written. Pharmacists have been compounding medications since the beginning of time, and have performed non-sterile compounding safely and effectively for many years. While we totally understand and support the need for sterile compounding rules, we feel that similar rules are not necessary for non-sterile compounding. The proposed rules as written are overly prescriptive and overreaching. We feel that rules in the current pharmacy regulations adequately address non-sterile compounding. The proposed additional rules will cause confusion and significantly reduce patient access to much-needed non-sterile compounding preparations. Many pharmacies will likely be unable or unwilling to meet the new requirements and will therefore be unable to meet their patients' medication needs.

We do not believe there is a need for a separate pharmacy license to perform non-sterile compounding. Pharmacists should be able to compound non-sterile medications for any of the licensed settings in which they practice. Additional training is not necessary. Pharmacists' years in pharmacy school with their pharmacy education provides them with the training to compound. Compounding is part of being a pharmacist and non-sterile compounded preparations should be available in any pharmacy. Current Board rules already require training and require the proficiency necessary to properly and safely perform compounding duties. Therefore, the Board should enforce current rules on the books if there is cause or concern for patient safety.

The current rules also require continuing education appropriate for the type of compounding done by a pharmacist or pharmacy technician. Pharmacists are obligated and able to use their professional judgement to

select the continuing education courses necessary to fill gaps in knowledge to enhance their skills, improve their practice, and enhance patient care. A specific non-sterile compounding CE requirement during each renewal period could become repetitive, as guidelines aren't changed frequently as evidenced with the current version of USP 795 for Non-Sterile Compounding being from 2014.

Current rules already require a designated and adequate area for the safe and orderly compounding of non-sterile preparations. We do not believe that additional rules are needed in this level of granularity. Pharmacists/pharmacists-in-charge should be able to include in their Standard Operating Procedures, or SOP, what is specific to their practice area. We believe that the proposed rules as written are onerous for less difficult or less complex non-sterile compounding and are definitely not required for adding flavoring. The rules should not attempt to list every possible exception, as inevitably something will arise in the future that has not been included. Again, pharmacists should be able to compound non-sterile preparations that they are comfortable doing and that meet the requirements in the rules today.

In closing, we appreciate the Compounding Advisory Group's hard work and expertise. We ask the Board members and the Advisory Group to look at compounding through the eyes of the many pharmacists whose core business is not compounding, and ask them to consider the unintended consequences such rules can have on patient access to care by limiting the ability for such pharmacists to compound needed medications. Texas already has solid rules for non-sterile compounding in current pharmacy regulations. Perhaps the Advisory Group should look at best practices and tips to help Board inspectors when inspecting pharmacies and enforcing current rules.

We respectfully ask this Board to vote "no" and not adopt these rules as written.

Sincerely,

Debbie B. Garza, R.Ph.

Debbie B. Garza, R.Ph.
Chief Executive Officer
dgarza@texaspharmacy.org
512-615-9170

tshp Pharmacy Leaders. Transforming Patient Care.

October 25, 2021

Eamon D. Briggs
Assistant General Counsel
Texas State Board of Pharmacy
333 Guadalupe Street, Suite 3-500
Austin, TX 78701

Re: Proposed Rule Amendments to 22 TAC §291.77 and 22 TAC §291.131 – Institutional Pharmacies Compounding Non-Sterile Preparations

Dear Mr. Briggs,

On behalf of our members, the Texas Society of Health-System Pharmacists (TSHP) appreciates the continued opportunity to work with the Texas State Board of Pharmacy (Board) on ensuring patient safety. As such, we would like to offer the following comments related to proposed Rule Amendments to 22 TAC §291.77 and 22 TAC §291.131, which establish new non-sterile compounding institutional pharmacy classes (Class C-N and Class C-SN) and their respective licensing requirements.

TSHP believes that Board Rules should ensure patient safety while making certain that burdensome and costly requirements do not adversely affect access to care without measurable evidence of improved patient safety. Based on the information available related to the compounding of non-sterile preparations, TSHP has significant concerns regarding the impact of these rules on patient safety and access to care. It is unclear how the proposed Rule Amendments would improve patient safety, especially since non-sterile compounding is currently regulated under the general services provided by pharmacies.

In addition, TSHP believes that the economic impact included in the published proposed rule amendments *significantly underestimates* both the extent of the impact as well as the overall cost to be incurred by institutional pharmacies, many of which provide on-site services to community hospitals throughout the state.

<u>Extent of the Impact</u>
The Economic Impact Statement for Proposed Rule Amendment 22 TAC §291.131 states that the Board "anticipates a possible adverse economic impact on some small or micro-businesses (pharmacies) or rural communities as a result of the proposed amendments…."[1] With regards to the extent of the impact, the Economic Impact Statement recognizes that the Board does not have information regarding the number of pharmacies that compound non-sterile preparations but

[1] "Recent Proposed Rule Changes," Texas State Board of Pharmacy, https://www.pharmacy.texas.gov/Rules_Recent_Proposed_Changes.asp, p. 35.

estimates that approximately 365 rural communities contain pharmacies that perform some form of non-sterile compounding that could be potentially impacted.[2] TSHP believes that the number of pharmacies and communities impact will be much greater. The proposed Rule Amendments would impact the vast majority of institutional pharmacies, including those in urban settings and those within a pediatric hospital.

TSHP believes that the definition of compounding of non-sterile preparations as that which uses "bulk API or excipients or manipulation beyond the FDA labeling of a commercial product (e.g., crushing a tablet or opening a capsule" is too broad and would require most institutional pharmacies to either seek licensure as a Class C-N/C-SN pharmacy or outsource all non-sterile compounding to another pharmacy.[3] Both of these scenarios, when considering our feedback below regarding estimated costs, will significantly increase costs to the pharmacy and, ultimately, the patient, which could then result in decreased access to care without evidence to support these changes as needed to ensure patient safety.

Anticipated Economic Impact of Proposed Rule Adoption

The cost estimates included in the Economic Impact Statement are significantly lower than the anticipated market cost of implementing all of the required components. For instance, the cost of a closed-system processing device is often much higher than the range of $1,000 to $11,000 included in the Economic Impact Statement.[4] Hospitals, where most institutional pharmacies reside, often have limited pharmacy space since the vast majority of hospital space is utilized for direct patient care. The Economic Impact Statement fails to capture the added costs to hospitals to ensure that a significant amount of additional space is provided to pharmacies to accommodate required equipment and dedicated non-sterile compounding space. In addition, environmental costs for maintaining a pharmacy compounding area and costs for equipment, garb, and supplies have exponentially increased, with costs often overwhelming institutional pharmacy budgets.

These significant added expenses, if the institutional pharmacy is unable to justify the significantly increased costs to now prepare non-sterile compounded drugs, will most likely cause a shift with institutional pharmacies needing to outsource the preparation of compounded drugs. This will lead to an increase in the cost of patient care, especially in rural areas, which are often limited by compounding pharmacy service areas.

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[2] "Recent Proposed Rule Changes," Texas State Board of Pharmacy, https://www.pharmacy.texas.gov/Rules_Recent_Proposed_Changes.asp,, p. 35.
[3] "Recent Proposed Rule Changes," Texas State Board of Pharmacy, https://www.pharmacy.texas.gov/Rules_Recent_Proposed_Changes.asp,, p. 29.
[4] "Recent Proposed Rule Changes," Texas State Board of Pharmacy, https://www.pharmacy.texas.gov/Rules_Recent_Proposed_Changes.asp,, p. 35

Environmental Requirements

The proposed Rule Amendments are too broad to specifically address specific handling differences between non-sterile, non-hazardous drugs (in compliance with USP 795) and non-sterile, hazardous drugs (USP 800). TSHP believes that the cost of compliance should be weighed with the risks associated with handling the compounding materials. For instance, an ISO-7 appropriate bench not located under a hood may be considered acceptable for certain types of non-sterile, non-hazardous preparations, while a closed-system processing device may be required for the preparation of non-sterile hazardous drugs. Applying these proposed Rule Amendments with precision will ensure that access to care is not adversely affected by overly burdensome requirements.

Personnel Testing and Training Requirements

The proposed personnel testing requirements outlined in the proposed Rule Amendments appear to exceed those required in 22 TAC §291.133 (Sterile Compounding Regulations). TSHP believes that the process of testing personnel should correspond with the risks associated with the type of compounding being completed (i.e., non-hazardous versus hazardous; non-sterile versus sterile).

In addition, the training requirements present a significant financial and staffing barrier to institutional pharmacies who already struggle with maintaining a sufficient technician workforce. TSHP recommends that additional data be gathered to demonstrate the need for additional training, especially for Class C-SN pharmacies who are already required to provide training for preparing sterile products.

Other Comments

Some of the proposed Rule Amendment language appears to conflict with USP 800 standards for non-sterile hazardous drug compounding. TSHP recommends that the Board consider the implementation of Rules related to hazardous compounding (both sterile and non-sterile) before attempting the implementation of non-sterile compounding regulations.

With regards to the "Sanitizing" definition included in 22 TAC §291.131, TSHP believes that this definition is incomplete and requires revision.[5] Isopropyl alcohol sanitizes against viral and bacterial organisms but generally has less activity against fungal origins. To be complete, TSHP recommends adding a sporicidal solution requirement, such as Peridox RTU or sodium hypochlorite.

[5] "Recent Proposed Rule Changes," Texas State Board of Pharmacy, https://www.pharmacy.texas.gov/Rules_Recent_Proposed_Changes.asp,, p. 37.

TSHP Recommendations

TSHP respectfully requests that these proposed Rule Amendments be postponed until the Board can conduct a survey on the true impact of the proposed Rule Amendments as well as gather evidence to support the need for these Rule Additions. This would also potentially allow the proposed Rule Amendments to be considered for adoption after the implementation of any changes to the USP 795 Standards.

TSHP is willing to assist the Board in gathering additional feedback and information and would be happy to provide additional information regarding our comments.

Thank you for your consideration. We appreciate the opportunity to continue working with the Board to improve patient safety and advance patient care in Texas.

Sincerely,

Latresa Billings, PharmD, BCPS
President, 2021-2022

tfds
TEXAS FEDERATION OF
DRUG STORES

October 25, 2021

Via Facsimile – 512-305-8061
Via Email – eamon.briggs@pharmacy.texas.gov

Mr. Eamon D. Briggs
Assistant General Counsel
Texas State Board of Pharmacy
333 Guadalupe Street
Suite 3-500
Austin, Texas
78701

Re: Public Comment in Connection with Proposed Rules Regarding Non-Sterile Compounding as set forth in 22 TAC §§ 291.36 and 291.131.

Dear TSBP Board Members;

I am submitting these comments today on behalf of the Texas Federation of Drugs Stores (TFDS). We would like to thank the members of the Compounding Advisory Group for their time reviewing the current regulations of non-sterile compounding in a retail pharmacy setting. While the TFDS members adhere to and comply with the current regulations, we cannot support the proposed rule changes to 22 TAC §§ 291.36 and 291.131. As currently proposed, we would ask that the Texas State Pharmacy Board members VOTE NO to adopting the changes, or at a minimum, postpone consideration until a later date and after a thorough review is completed by the agency staff and board members on the impact and need of the proposed regulations.

These proposed rules will impact access and adherence. After California implemented new non-sterile compounding rules that placed additional costs on retail pharmacies, several chain pharmacies stopped providing all medications that required non-sterile compounding at most of their pharmacies. At least one chain pharmacy stopped providing compounded medications at all of their locations in the state. This forces many patients to seek a pharmacy, other than their regular pharmacy, that will provide the medication and has caused delays to patients in obtaining the medications while they are compounded at a less convenient facility, that may require the mailing or delivery of the medication one or two days after being prescribed. Several reports on adherence have noted transportation and access as key issues on patient adherence to taking medications. The additional costs and burdens will most negatively impact pharmacies with lower volumes such as those typically found in rural and underserved areas of Texas.

TSBP staff cited convenience for the inspectors. No written report was provided by the Compounding Advisory Group ("Group") detailing the need and cost benefit of the proposed regulations and only minimal notes were reported in the minutes of the Group. TSBP staff in discussing the rule at the August 4, 2021 TSBP Board meeting and in the September 2020 and November 2020 minutes of the Group noted that the rules were being drafted so it would be easier for an inspector to inspect a pharmacy and to know if a pharmacy performs non-sterile compounding. TFDS member retail pharmacies keep logs of each compounded medication and at the request of the inspector those logs will be produced. Having or not

having a scale on site does not provide the inspector with any information on the level, amount or safety of non-sterile compounding being performed.

The cost to comply with the new regulations far exceed the scope and quantity of non-sterile compounding at chain retail pharmacies. The vast majority of chain pharmacies prepare a limited number of simple and fewer moderate non-sterile compounds onsite at the retail pharmacy locations, offering only the most frequently prescribed and basic of compounded medications. In most instances, basic medication compounding is a very small percentage of a chain retail pharmacies business, only increasing slightly when located near a hospital, hospice provider or other. No complex non-sterile compounding is performed at chain pharmacy retail locations. The proposed rule requires all pharmacies to set aside space and to meet specifications, such as vent hoods and 20 hours of additional training of all pharmacists, in order to even provide simple non-sterile compounding such as flavorings for a child's amoxicillin, magic mouthwash for painful sores and ulcers in a patient's mouth, and butt paste for severe diaper rash.

The proposed rules are overregulation and cannot be fixed with one amendment.

> **Education** -TFDS agrees that complex and hazardous non-sterile compounding should be more heavily regulated. However, that type of compounding is not being performed in the chain retail pharmacies. The proposed rule requires an additional 20 hours of training for a pharmacist (40 hours for a pharmacy technician). Compounding has been part of the education requirements for a pharmacist before it was regulated in the United States and from the beginning of Texas' pharmacy school requirements in 1925. Current ACPE standards require a minimum of two courses specifically on compounding which are considered central to contemporary, high quality pharmacy education.
>
> **Facilities** – Designating space that isn't carpeted, contains scales and has a closed system processing device such as a vent hood or safety cabinets are just a few of the requirements listed in the rule. Every layer of regulation to date has added to the congestion behind the counter at a pharmacy. Even the newest pharmacies designed to meet all the current regulations will be pressed to find the budget to create and the space to retrofit and set aside to meet the rule requirements. The proposed additional regulations are not necessary for the most basic compounding performed at retail chain pharmacies. This additional cost and burden will most negatively impact pharmacies with lower volumes such as those typically found in rural and underserved areas of Texas.
>
> **Testing** - the cost and time required to independently test added flavors to a child's prescription, or the Simple Non-Sterile Compounded cream is excessive and does not draw a distinction between the different levels of compounding. TFDS supports independent testing of Sterile Compounds and Hazardous non-sterile compounds but does not support such a requirement for the types of simple and moderate compounding performed at a retail facility.

TFDS members support regulation that meets the level of the work being performed. However as written, the proposed rule requires excessive costs and regulation for simple and some moderate non-sterile compounding that is likely to create a void in the number of locations a patient may fill such prescriptions. As health care providers, consumer safety is a number one priority for TFDS member companies. If we believed these measures were addressing widespread safety concerns and were requiring the implementation of regulations to address those specific concerns, we would not be opposing the proposed rules. As written these regulations far exceed safety concerns. If implemented it is most likely that patients will have to seek out limited pharmacies to fill even the most basic products, such as steroids added to topical creams for chronic itching, wait 24 hours or more to receive the prescription, and longer if the prescription must be mailed. TFDS does not support measures that make pharmacy care less accessible for the receipt of simple and moderate non-sterile compounded medications.

In summary, TFDS urges the Texas State Pharmacy Board members to VOTE NO to adopting the changes, or at a minimum, postpone consideration until a later date and after a thorough review is completed by the agency staff and board members on the impact and need of the proposed regulations. Thank you for your time and attention on this matter. We look forward to working with the TSBP Board and staff as the proposed rules are amended.

Yours Very Truly,

Jeff Loesch, PharmD, RPh
TFDS President
Director of Pharmacy – Dallas Division
Kroger Health
751 Freeport Parkway
Coppell, TX 75019
(469) 645-7909

The Texas Federation of Drug Stores is an association of ten (10) chain pharmacies which operate in Texas. The Federation's activities are focused on pharmacy- specific legislative and regulatory matters. Our members are Albertsons Companies (Randall's and Tom Thumb), Brookshire Brothers, Inc., Brookshire's Grocery, H-E-B, Kroger, Genoa, ReCept Pharmacy, United Supermarkets, Walgreens and Walmart.

From: Brian Hettler
Sent: Monday, October 25, 2021 9:20 AM
To: Tim Tucker
Subject: TSBP Proposed law change
Attachments: Document.docx

Good morning Tim,

I have attached my letter to the state board regarding flavoring and compounding. Have a great day!

Thank you,

Brian A. Hettler, PharmD

To whom it may concern,

The proposed TSBP law change regarding prescription flavoring can negatively affect many patients over the course of time. As a pharmacist and parent of a child with special needs, this is a concerning proposal that I believe will take us in the wrong direction. My son has both a speech and learning disability. Flavoring his medication, that he takes daily, truly helps him take it with ease. This is just one of the many examples. There are many children we do this for and would also negatively impact them, not just children with special needs.

Another group that would be negatively impacted by this proposed change would be patients that receive simple compounds (pink magic, etc). My pharmacy fills pink magic on a daily basis for dental patients and also for patients with cancer. The proposed change would make it extremely costly to retrofit every pharmacy with the needed hood and needed materials. This would restrict access to patients since they would need to possibly drive to a pharmacy that has the correct hood and materials.

Flavoring and simple compounding have been performed safely and routinely for many years in the state of Texas. If these proposed laws are voted in; this will negatively impact the lives of many individuals, including patients, pharmacists and small pharmacy owners. FlavorRx auto dispensing machines have made it extremely accurate and quick for pharmacies to help patients for years now.

I truly hope you consider voting against this proposed law. This change will have a detrimental effect on various patient populations, which include: children, children and adults with special needs, cancer patients, general patient population.

From: Aaron Gibson <prescriptionshopandrews@gmail.com>
Sent: Monday, October 25, 2021 9:47 AM
To: Eamon Briggs
Subject: Comments on the proposed rule changes regarding compounding

Good Morning Eamon,

I would like to submit my comments on the proposed rules that will affect compounding that will be voted on at the next meeting of the State Board. My request is that the Board vote no on these proposed changes. I am an Independent pharmacy owner of 6 pharmacies in rural parts of Texas (western and southern) parts of the state. Compounding is not a major component of my business, but we do simple compounds on occasion. My understanding is that the proposed rules would prevent me from doing that.

My objections are 2-fold. The first is that there are already laws/rules on the books that govern compounding. I'm assuming there are reports of "bad actors" not following these regulations being the reason for the proposed rule. My thought is that implementing these proposed rules would simply make simple compounding impossible for the good actors. My training and CE have prepared me to do simple compounds. It has also prepared me to know when I'm not capable of preparing a compound safely, and thus refer the prescription to a compounding store. The bad actors don't follow current rules/laws so I'm guessing these new rules won't be followed either. I believe it would be far more effective to educate compliance officers to recognize problems with compounding and enforce the laws on the books rather than add more rules to the books.

My second objection deals with the rural nature of all of my stores. There isn't a compounding pharmacy within 1 hour of any of my stores. Removing the capability of my pharmacists to do simple compounds would present a significant barrier to most of my patients who cannot easily get to a compounding store for a magic mouthwash or butt paste prescription.

I'm all for protecting patients and pharmacy employees, but I don't think these proposed rules would accomplish that. Thank you for giving me the opportunity to present my comments in this format. Unfortunately I'm 6 hours from Austin and working the counter the day of the next meeting where these rules will be discussed.

Kind Regards,

Aaron Gibson
Prescription Shop
Andrews, TX 79714
[redacted]

From: Crystal McEntire
Sent: Monday, October 25, 2021 11:20 AM
To: Eamon Briggs
Subject: Non-Sterile Compounding Rules

Greetings President Spier and Board Members,

I am writing to you today to graciously ask you to vote "NO" on the proposed rules for compounding.

As an independent pharmacy owner I see that this could cause great harm for patients access to medication that they might need. I believe that we have solid rules for non-sterile compounding and the added mandates/requirements/licenses are not needed. I feel like a separate non-sterile pharmacy license is not needed, this falls under the realm of my knowledge and training that I received in pharmacy school.

First and for most I am not a compounding pharmacy. I am a pharmacy in a rural area that is here for the needs of my patients. If this proposed rules for compounding becomes law then it will greatly affected the way I can take care of my patients. For example, I have patients that don't even realize that they have a prescription that is a compound. The receive the prescription in Amarillo, drive two hours back home to their hometown pharmacy for it to be filled. If it is a non-sterile compound, which it is 99.9% of the time, I simply just take care of them so they don't have to drive the two hours back to Amarillo to get the prescription filled. A lot of the times it is just simply Magic Mouth Wash for a cancer patient.

Another example is when doctors prescribe Questran powder to be put in aquaphor for diaper rash. A child receives an antibiotic that causes diarrhea. The Doctor calls in above compound and with the new proposed rules patient's mom will have to take off of work, drive two hours one way to Amarillo for a simple compound.

Another example is we have a Flavor RX machine to add flavoring to children's medication to help with compliance and the child taking his/her medication. This has been a huge success for us in getting kids to take their medication. They feel involved! We let the child choose his/her flavor for the medication and then let them watch us mix their medication. The kids love this! However, if the proposed rules become law, I will hate to inform our parents and kids that the State Board felt like that was out of the scope of our current practice and took that away from us.

My last example that I would like to give is one that was for a newborn baby that was a life or death situation. Two young parents present a prescription to us for Coreg suspension. They had just been discharged from the hospital in Amarillo with their newborn baby. The baby had been in ICU for a week and they were so excited to be getting to bring him home but knew that they had a long road ahead of them. They had an appointment with a pediatric cardiologist in the coming week. When I looked at the prescription, my heart sank! It was a compounded prescription. What was I going to do. They just drove two hours from Amarillo for me to take care of them not realizing that the medication that they needed for their newborn baby was a compound. When I went to talk to the parents and told them what was going on the mom started crying. We don't have the money for gas to go back to Amarillo, what are we going to do. I immediately was like, just sit here and let me make some calls and see what I can do for you. So I immediately called the pharmacy at BSA Hospital where the baby had been in the hospital. I spoke with the pharmacy manager and told him what was going on. I explained to him that I wasn't a compounding pharmacy and that the parents didn't have the money to drive back to Amarillo to a compounding pharmacy. He was like oh no problem. That is an easy compound to make. All you have to do is crush some Coreg 3.125 dissolve and then mix with some Cherry Suspension. Don't need anything fancy he said. I took a deep sigh of relief and thought Crystal you can do this! We did this in pharmacy school! Did exactly as the pharmacy manager told me too, and took the parents the prescription for their new baby. What a great feeling of joy I had to be able to take care of them. I was able to go back to my roots, my training from pharmacy school and take care of the patients. However, under the proposed new rules I will not be able to make a simple compound by just crushing tablets.
So this brings to mind, crushing tablets is simply just a form of how we can help administer medication to a patient. What about nurses that crush tablets in the hospital setting or nursing home setting and place the medication on applesauce in order for the patient to take the medication. Are they compounding?

I feel like for simple or less difficult/less complex non-sterile compounding, the proposed required designated area with the granular details and containment hoods or negative pressure is NOT needed.

Please take into consideration the simple, common practice each day the we do to take care of our patients. Don't take away our basic compounding practices, that is pharmacy. That is what we were trained for in pharmacy school.

Sincerely,

Crystal McEntire, PharmD

Owner Hyland's Pharmacy, Wheeler, Texas

Owner Hyland's Pharmacy, Shamrock, Texas

From: Shamrock Pharmacy <shamrockrx1@gmail.com>
Sent: Monday, October 25, 2021 2:11 PM
To: Eamon Briggs
Subject: Non-Sterile Compounding Rules

To President Spier and Board Members:

Greetings from Northwest Texas. Thank you for taking the time to consider comments concerning the proposed rule changes affecting the compounding of non-sterile products in the pharmacy. I will keep my comments brief as I know your time is limited and valuable.

There are two strong arguments that I believe can be made AGAINST the proposed changes to the current non-sterile compounding rules:

1) First, patient accessibility to quality pharmacy services is something that the board and all pharmacists in the state of Texas can agree upon. With the current pandemic, pharmacies have become an essential and highly accessible resource for trusted information and services. Pharmacies, in conjunction with the State of Texas, have been able to vaccinate more patients against Covid-19 faster than almost any other state in the nation. We have been able to aid the overwhelmed medical community by taking on services that previously were available only in clinics or hospitals, and we have continued to provide medications in a safe and timely manner as we have always done. But with these extra services has also come the extra burden on staff and pharmacists to perform these services and to be well trained for them. The additional requirements for pharmacy compounding areas and the training of pharmacy personnel set forth in the rule changes for non-sterile compounding would add even more burden to an already burdened system. The result would not, as some would argue, shift that burden to pharmacies dedicated solely to compounding, but would cause those services previously available in rural communities to disappear. Patients in rural Texas communities often live 20 or more miles from their nearest pharmacy and, as is the case here in Shamrock, Texas, almost 100 miles from a compounding-only pharmacy. We provide simple compounding services for many of our patients, including Magic Mouthwash and Promethazine gel. I can assure the board that if additional requirements are added for these products, it is doubtful that we will continue to offer them to the public. In the end, the patient will have to choose between driving 100 miles for their medication or going without it.
2) Secondly, patient safety has always been and will always be a high priority of the Board and of every good pharmacy. Sterile compounding is a complicated process with many chances for error that can adversely affect a patient. Oversight of these processes and adequate training is without reservation a necessity for pharmacies involved in sterile compounding. However, non-sterile compounding should not be included in the umbrella of strict requirements for sterile compounding. Non-sterile compounding involves products already approved for safety and effectiveness by the FDA and prepared in ways that do not affect their safety or efficacy. Crushing a tablet or opening a capsule (as allowed by the manufacturer) to create another dosage form for the better use by a patient is essential to the practice of pharmacy and is one of the first skills we are taught as pharmacists. Even the combination of FDA approved bulk products to assist doctors in the best treatment of their patients is withing the normal training and practice of a pharmacist. When I first graduated from pharmacy school, our nation experienced the H1N1 epidemic. Tamiflu, the main treatment for our patients, was in short supply, especially for our hard-hit pediatric population. We used our training as pharmacists to compound thousands of prescriptions for oseltamivir liquid, using non-sterile products, and were able to supplement a drug shortage that would have adversely affected thousands of people.

Again, I believe that the Board of Pharmacy currently has in place an excellent system of oversight for the compounding of non-sterile products. Our goals as pharmacists are the same as the Board's: we want give our patients safe and accessible care. Our patients are our neighbors, our family members and our friends. They are our community and we

are proud to serve them the best we can. I ask the Board to vote against burdensome regulations and for the enabling of pharmacists to continue serving their patients.

Thank you for your time and consideration,

Erin Raber, PIC
Hyland's Pharmacy
1814 Bill Mack Rd
Shamrock, TX 79079
(806)256-3111

These comments are in opposition of two proposed rules for the November meeting

OPPOSE with suggestions: 22 TAC §291.34, concerning Records. The amendments, if adopted, clarify that a pharmacist may provide an emergency refill of insulin or insulin-related equipment or supplies under certain conditions, in accordance with House Bill 1935.

Let me begin this comment by saying I support the change allowing us to give emergency refills of insulin and insulin-related supplies to patients. My opposition is to wording that singles out certain patients. The line is as follows:

"The quantity of an emergency refill of insulin may not exceed a 30-day supply. The quantity of an emergency refill of insulin-related equipment or supplies may not exceed the lesser of a 30-day supply or the smallest available package."

Notice the difference in what is allowed with insulin vs the insulin related supplies. The emergency supply of insulin may not exceed a 30 day supply but the supplies have an allowance to "the smallest available package". Why is this wording not being applied to insulin? Although there are some insulin products that have a shelf life of 30 days or less while in use, many of the modern insulin products last longer than that. Here is a list of brand name insulin products in vial form with their expiration dates according to the manufacturer

Novolin N	**42 days**
Humulin N	**31 days**
Tresiba	**8 weeks**
Levemir	**42 days**
Humulin 70/30	**31 days**
Novolin 70/30	**42 days**
Humulin R	**31 days**
Humulin R U-500	**40 days**
Novolin R	**42 days**

If I have a patient injecting 25 units a day of Novolin N, that vial will last 40 days. Per this proposed change, an emergency refill of insulin for this patient will be in violation of the law. Allow me to address some potential responses to my comments.

"Insulin pens have more flexibility so this change would not affect them. Just dispense enough pens to get under the 30 day limit and the patient will receive the insulin they need."

On October 13, 2020, the Food and Drug Administration clarified labeling on insulin pens stating they are only approved to be dispensed in their original sealed carton. If a brand of insulin comes in a box of 5 pens and the 30 day limit is hit with 4 pens, I will be unable to dispense an emergency refill.

"Just do what is right for the patient and dispense the insulin anyway."

This is a dangerous suggestion. Violating state law for the betterment of the patient might look good to government officials but it doesn't look good to insurance companies. It's my belief that if I did this for a patient and billed the insulin to their insurance, I would be committing fraud and risk recoupment of any billed claims. I have asked a compliance company about this scenario and they agree with my interpretation. An obvious follow up would be to just fill it off insurance and have the patient pay the cash price. I have a lot of patients who are low income or retired living on a fixed income. This isn't fair to them.

The obvious fix for this would be to match the language of insulin-related supplies to insulin and all of this goes away. If these changes are approved anyway, I hope the Board makes this information available to pharmacies so they know which patients will benefit from it. Until then, these are rules that don't apply to everyone. My patients deserve the equal protection of board regulation.

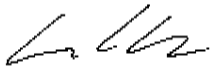
OPPOSE: 22 TAC §291.131, concerning Pharmacies Compounding Non-Sterile Preparations. The amendments, if adopted, add definitions of "cleaning" and "sanitizing", update requirements for all personnel engaged in non-sterile compounding, add additional requirements for personnel engaged in certain types of non-sterile compounding, and update environmental and equipment requirements for non-sterile compounding.

I would understand why the Board would want to regulate sterile compounding, especially considering the reputation it's had in the media over the last decade. Pharmacies performing sterile compounding in non-sterile conditions put patients at risk. But to use vague language and enforce rules about non-sterile compounding that are facially absurd, I wonder why this is being proposed.

A great example of this absurdity is the compound known as magic mouthwash. It's prepared with liquid diphenhydramine, antacid, and viscous lidocaine in equal parts. If

passed, these rules will prevent me from doing the most common compound in pharmacy today. Magic mouthwash doesn't require calibrated balances or a closed system device such as a containment hood but these proposed rules will change that. But there is a work around to the proposed rules. Instead of compounding magic mouthwash like pharmacies have been doing for nearly a century, we can just dispense the ingredients to the patient in separate bottles and have them mix it at home. At that point the compounding goes from the clean but not sterile pharmacy to the unpredictable environment of the patient's home. The unintended consequence of these vague rules is the inevitable decline of quality in the final product

These rules need major work before they're approved. As they stand today, compounding in pharmacy will come to a complete halt unless you already have the facility in place for sterile compounding. Magic mouthwash will go away. Antibiotic flavoring will go away. Where is the proof that these rules will protect the public? What are we protecting the public from exactly? I urge the board to, at a minimum, reexamine this issue and delay the implementation of this rule.



Craig Chapman, PharmD, RPh

From: rx0112@brookshirebros.com
Sent: Monday, October 25, 2021 2:31 PM
To: Tim Tucker
Subject: FW: Compounding of " simple " non-sterile compounds

From: Pharmacy 0112 <rx0112@brookshirebros.com>
Sent: Monday, October 25, 2021 2:00 PM
To: tim.tucker@pharmacy.texas.gove
Cc: Pharmacy 0112 <rx0112@brookshirebros.com>
Subject: Compounding of " simple " non-sterile compounds

Dr. Tucker,

I am writing in regards to the proposed amendments to §291.131, which relate to pharmacies that compound non-sterile preparations.

I do have some concerns regarding the restrictions as they relate to “simple” compounds in which we are mixing commercially available products. This includes preparations such as Magic Mouthwash, Cholestyramine Ointment, and Kenalog with Lubriderm in which the medication would provide immediate relief for an acute and often uncomfortable condition. In choosing to work in the rural, medically underserved area of Grapeland, I take great pride in being able to provide these preparations to my community without delay or disruption.

However, I am concerned that the proposed amendments to §291.131 could have a negative impact on the public health of Grapeland and many communities like it. The required physical changes to my pharmacy and purchase of equipment unnecessary to the preparation of these simple compounds would most likely prohibit us from offering compounded medications. For many of my patients, a participating compounding pharmacy could be in excess of 30 miles away, but due to financial or physical limitations, the trip would not be a viable option for them. Most would be reliant on having compounded medications delivered to them via mail, which could extend their condition by days.

I understand and appreciate the role of the Texas State Board of Pharmacy in ensuring the safety of the public, but I am afraid if these simple compounds and mixtures are not excluded from the proposed amendments, we may very well end up providing additional discomfort or harm to our most vulnerable populations.

Thank you for your time and consideration.

Thor Traylor R.Ph. – Brookshire Brothers #112 – Grapeland, Texas

From: Lee Ann Hampton <leeann@paris-apothecary.com>
Sent: Monday, October 25, 2021 4:10 PM
To: Eamon Briggs
Subject: Non-sterile Compounding Rules

President Spier and Board members,
Thank you for your time today and everyday serving the great state of Texas. I am writing to you today as an Independent Pharmacist. I'm asking that you vote no to the proposed non-sterile compounding rules.
Currently, we have solid rules for non-sterile compounding. If they are not being enforced then that is an issue to work on with education of compliance officers but generating more rules just hinders your honest pharmacists and does nothing to the outliers.
A separate non-sterile pharmacy license is not needed and comes across as a way to tax and add yet another burden to the pharmacy industry.
It's well known that pharmacists are the most over-educated, underutilized healthcare professionals. We are trained during our schooling on compounding. Therefore, additional training is not necessary.

Thank you for your time and consideration,

--
Lee Ann Hampton, PharmD
Paris Apothecary
707 Lamar
Paris, TX 75460
(903) 785-4208
Texas Pharmacy Association's Pharmacist of the Year 2021

From: KathleenF Jackson
Sent: Monday, October 25, 2021 4:46 PM
To: Eamon Briggs
Subject: Comment on Non-sterile Compounding Rules
Attachments: Electronic Balances from Revised MWAQ.docx

To: M.Briggs

I am very pleased to see that our state is taking the initiative to improve patient safety and efficacy, with powder containment requirements (even in non-hazardous compounding this reduces cross contamination), training, and potency testing.

In addition, I offer a suggestion for the removal of one phrase. (4)(A)(ii) inspected and calibrated at least every 12 months by a qualified independent individual. The balance shall not be used to weigh any amount less than the minimum accurate weighable quantity (MAWQ)of that bal ance
or the manufacturer's specifications for the smallest weighable quantity; and

The phrase "or the manufacturer's specifications for the smallest weighable quantity" should not be included in this rule.
The minimum accurate weighable quantity that can be weighed is based on the accuracy of the electronic balance. I have attached a document to explain. The manufacturer provides the value for the sensitivity and that is used along with the desired percent error in a calculation to determine MAWQ. Balances may be used in many different industries; however, the use of a balance in the pharmaceutical industry should be based on accuracy that is determined by this calculation. It is not the same as the smallest amount a balance can weigh.
For example, if a balance can weigh 0.001 (1 mg) but the manufacturer provides (0.002) 2 mg is the sensitivity, then using the formula MAWQ = Sensitivity ÷ Desired Percent Error (5%) , the pharmacy should not weigh less than 40 mg or (0.040) on the balance.
My personal experience as an accreditation surveyor and non-resident sterile inspector have led me to review many potency tests over the years and around the US. I have personally seen potencies of as much as 237% when only 9 mg was weighed, because this was not an accurate weight. I believe that overall, this is a good rule if this phrase is removed.

Thank you for allowing my input.
Kathleen Jackson, RPh, PhD (H.C), FIAPC
2836 County Road 962d
Alvin, Texas 77511
[redacted]

Electronic Balances

A typical electronic prescription balance is an instrument that provides essential readability for materials weighed within the range of capacities for the balance. The display should have prompts to guide users through the balance function, as well as an output port for printing if necessary. Most balances sold for prescription compounding meet or exceed Class I or II accuracy requirements according to NIST Handbook 44 and come with certificates issued under the National Type Evaluation Program (NTEP) of the National Conference on Weights and Measures.

Calibration/certification of the balance should be performed according to the standard operating procedures of the facility. Many electronic balances contain internal calibration programs that automatically calibrate the balance daily. If there is no internal calibration feature, external calibration may be conducted using a calibration weight, according to the procedure supplied by the manufacturer. Weights for use in calibrating an electronic balance should be kept in a special rigid and compartmentalized box and handled with plastic or plastic-tipped forceps, or gloves that are provided with the weights, to prevent scratching or soiling. These calibration weights should meet or exceed ASTM Class 1 criteria. In addition, there are companies that offer calibration services to certify that the balance is performing adequately.

For more information regarding the use of electronic balances, see ⟨41⟩ and *Weighing on an Analytical Balance* ⟨1251⟩.

1.1 Minimum Accurately Weighable Quantity on the Balance

The minimum accurately weighable quantity (MAWQ) is the smallest weight or mass that will produce no greater than a predetermined fraction of error on a properly calibrated, situated, and operated balance. The predetermined weighing error is assigned based on either a professional standard (such as NMT 0.05 or 5% error in the weight of any prescription ingredient) or scientific rigor, for example, NMT 0.005 or 0.5% error in the weight of an ingredient that is in limited supply. The compounder should use professional judgment when assigning the acceptable error for each process.

The formula for determining MAWQ for a typical Class III torsion balance is:

$$\text{MAWQ} = \text{Sensitivity requirement}/\text{Acceptable error}$$

Example: Calculate the MAWQ for a Class III torsion balance with a sensitivity requirement of 6 mg and an acceptable error of 5% or 0.05.

$$\text{MAWQ} = 6\ \text{mg}/0.05 = 120\ \text{mg}$$

For electronic balances, the MAWQ is calculated using the linearity or the absolute error over the range of the balance. This value is provided by the balance manufacturer. Note that the balance linearity and the readability of the smallest mass unit may not be the same.

Example: Calculate the MAWQ for an electronic balance with a linearity of 0.002 g and an acceptable error of 5% or 0.05.

$$\text{MAWQ} = 0.002\ \text{g}/0.05 = 0.04\ \text{g or } 40\ \text{mg}$$

HILLCREST PHARMACY 1015 Hillcrest Suite B Vernon, TX 76384

Phone: 940-552-9501 Fax: 940-552-2075

October 25th, 2021:

President Spier and Board Members,

I am writing to you today to ask you to vote "NO" on the proposed rules for compounding.

As the PIC and owner of Hillcrest Pharmacy, I see that these proposed rules could cause great harm for patients access to medication that they may need. We already have sufficient rules for non-sterile compounding and the added mandates, requirements, and licenses are not necessary. I feel like a separate non-sterile pharmacy license is simply not needed.

Hillcrest Pharmacy is located in a rural area and if these proposed rules for compounding become law, then it will greatly affect the way I can take care of my patients.

Our patients should not have to drive 50+ miles to Wichita Falls or 200 miles to Dallas/Fort Worth to have prescriptions filled for non-sterile compounds like Magic Mouthwash, Cholestyramine in Aquaphor, Carvedilol tablets crushed and suspended in Orasweet, etc.

We as pharmacists go to school for years to learn all the complex intricacies of pharmacy practice. I am more than confident that any licensed PharmD has the ability to provide these simple services to their patients. There is no need for added regulation and oversight and in these rural areas it creates a real burden to the patient to receive the medications and care that they need in a timely manner.

For non-sterile compounding, the proposed required designated area, containment hoods, special air ventilation systems are NOT needed as well. Pharmacies that primarily compound have this equipment already. But for regular, small-town, retail pharmacies who do small amounts of non-sterile compounding this is just an added expense and burden on the pharmacy to purchase unnecessary and EXPENSIVE equipment.

This is primarily about allowing pharmacists to practice without additional unnecessary regulation. More regulation does not help the pharmacy, pharmacist, or the patient. We as pharmacists are very well educated and can handle the basic compounding practices that we have already been doing for years. Patients are always our first priority and we want to be able to take care of them and eliminate any unnecessary burdens that prevent them from receiving the care that they need.

Thanks for your consideration in this matter.

Sincerely,

Adam Bayer, PharmD

October 25, 2021

Texas State Board of Pharmacy
333 Guadalupe Street, Suite 3-500
Austin, TX 78701

Re: Proposed non-sterile compounding rules for final adoption

Dear President Spier and Board Members,

As a pharmacist, I do not support the proposed non-sterile compounding rules as published. Providing a vital service to their patients, pharmacists have performed non-sterile compounding safely for many years. I feel that the proposed rules as written are overreaching and limiting. Pharmacists will be unable to meet their patients' needs by not being able to comply with the onerous additional requirements as proposed. The current pharmacy regulations adequately address non-sterile compounding and require a proficiency and training for pharmacists to perform compounding duties in a safe and effective manner.

The proposed rules for adoption require all pharmacies to designate a space for non-sterile compounding with many additional and more restrictive requirements, some of which include a non-carpeted assigned space for compounding, devices such as safety cabinets or vent hoods, and scales inspected and calibrated by an independent party. The current rules already require a designated and adequate area for the safe compounding of non-sterile preparations, and the proposed rules are prescriptive and not needed.

I believe that a separate pharmacy license to perform non-sterile compounding is unwarranted. With my pharmacy school education and experience, I feel that I should be able to compound non-sterile preparations in any licensed setting. I respectfully ask this Board to vote "NO" and not adopt these rules as written.

Sincerely,

Sheila Dawson, R.Ph.

Sheila Dawson, R.Ph.
Brookshire Pharmacy #74
Greenville, TX 75402

October 25, 2021

Tim Tucker, PharmD, Executive Director
Texas State Board of Pharmacy
333 Guadalupe S., Ste 3-500
Austin, TX 78701

Via email: tim.tucker@pharmacy.texas.gov

Dear Executive Director and Board Members,

I write today as a retail pharmacist concerned with the proposed rules for final adoption regarding non-sterile compounding. I do not support the proposed rules as written. I have worked in various retail settings over the last ten years that perform compounding services to varying degrees for patients. Compounding is by no means the core of our business; however, the impact would be on patient access and the ability to effectively serve our patients.

The proposed rules attempt to define and impose cost-prohibitive measures for non-sterile compounding that include flavoring and simple mixtures, services that should be accessible to all patients at any pharmacy willing and qualified to provide them. Our patients are then impacted by way of treatment abandonment or having to travel unnecessary distances in many parts of our state, limiting timely patient access and the ability for pharmacists to serve our patients.

Additionally, the rules as proposed mandate unnecessary education requirements. The schooling and experience of a pharmacist qualifies us to compound non-sterile preparations for our patients, just as the schooling and experience of a physician qualifies them prescribe these medications. As highly educated professionals, additional training and continuing education should be encouraged to supplement rather than required.

I encourage the Board to vote **against** adoption of the proposed rules. If adopted as written, these rules will have unintended consequences on our patients and the integrity of our profession.

Sincerely,

Lauren Hayden, PharmD
[redacted]
[redacted]

512 305 8061

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Mr. Eamon D. Briggs
Assistant General Counsel
Texas State Board of Pharmacy
333 Guadalupe Street, Ste 3-500
Austin, TX 78701

For TSBP regarding the proposed non-sterile compounding rules:

The human brain is predictable in its response to change stimuli. When the brain is presented with change, it does not like change which it interprets as possible "danger or threat". Also, to accomplish "change", a great expenditure of energy would be required, which is also undesirable to the brain. Therefore, the brain will typically take the easy way out- "no change, no pain".

For Texas Compounding Pharmacies, we have to weigh the pain of doing nothing against the pain of change. Should we allow unethical or simply low-performing compounders to continue operating at sub-standard levels of safety and care –or-- should we establish minimum standards of practice to elevate under-performing practices, thereby reducing the chances of patient harm?

Maintaining access to compounded medications which are critical to the health of millions of Texas patients has been an overriding personal objective of mine for many years. I fully recognize that it will only take the actions of a few bad actors to cause a regulatory knee-jerk reaction that could effectively eliminate access to vital compounded medications for Texans. If we don't act now to help TSBP inspectors recognize low-performing or unethical practices, then patient harm is much more like to occur.

In our practice, it was "painful" to increase safety and quality by creating safe & dedicated compounding areas within our pharmacy, buying expensive powder containment hoods to create safer compounds, to send finished compounded preparations for pricy potency testing to validate our processes, to develop Standard Operating Procedure manuals for our compounding operation and abide by those S.O.Ps, to adhere to the national standards for Beyond Use Dating, to understand and establish the Minimum Accurate Weighable Quantity for our Analytical balances, and prove that our techs and pharmacists are properly trained to produce safe and effective compounded preparations.

Why do we do all this "painful" stuff? Because our patients trust us and deserve our very best effort. We must earn that trust with ethical and compassionate care. So I ask you- what is more painful, establishing and maintaining minimum standards of care in Texas compounding practices –or— greater risk of bad patient outcomes?

Kind Regards,
Jim Hrncir RPh

Kroger Dallas Division – Pharmacy Department 751 Freeport Parkway, Coppell, TX 75019 (469) 645-7908

October 25, 2021

Mr. Eamon D. Briggs, Assistant General Counsel
Texas State Board of Pharmacy
William P. Hobby Building, Tower 3, Suite 500
333 Guadalupe Street
Austin, TX 78701

RE: Public Comment on Proposed Rules Regarding Non-Sterile Compounding

Dear Texas State Board of Pharmacy Board Members,

I would first like to thank the Texas State Board of Pharmacy staff members, and the Board's Compounding Advisory Group for the time and work involved in reviewing the Board's current regulations concerning non-sterile compounding. However, the current proposal that is now before the Board for consideration creates several concerns and barriers for pharmacies that could lead to significant access issues for patients.

Overall, non-sterile compounding constitutes a small percentage of the total prescriptions prepared at our pharmacies. However, in situations where a commercially available product is unable to fulfill a patient's needs, the ability to perform simple compounding enables a pharmacist to potentially fill this need and can often enhance patient adherence. The most common preparation, which appears to fall under the current proposal, is the flavoring of liquid medications. In our pharmacies, this is performed using a commercially available flavoring program (FlavoRx) which is frequently used to improve pediatric adherence and decrease resistance to taking medication. This program provides significant value to these pediatric patients and to their parents.

Additionally, most of our pharmacies prepare medications following the receipt of prescriptions for commonly compounded medications using FIRST "unit-of-use" compounding kits, which provide pre-measured quantities of bulk drug substances. These kits are a simple, easy to use solution that enables pharmacists to meet the needs of these patients without significant dedicated equipment and training. The same physical processes are also utilized in the preparation of commercially available products such as Benzamycin and Benzaclin.

An additional consideration is the need to avoid delays in the patient's initiation of therapy. While it infrequently occurs, drug shortages of Tamiflu suspension have occurred in past years. In these

situations, pharmacists follow provided instructions for the compounding of Tamiflu suspension by opening capsules. Additional simple to moderate compounds that are prepared by our pharmacies include mixtures for “magic mouth wash” for oncology patients who are seeking prompt relief for their oral and throat pain, and simple steroid suspension mixes into topical creams. Pharmacists must be able to retain the ability to perform this level of compounding to avoid delays which could be harmful to patients.

Under the current proposal a pharmacy that compounds less than twenty compounds in its Master Formulation Record, even if all similar and relatively simple in process and difficulty, is subject to the same minimum training requirements as a pharmacy that compounds several hundred medications involving far more complex compounding processes along with the use of multiple pieces of specialized equipment that each requires its own training on use and sanitation. While training in proper compounding is a necessity, a one size fits all approach to training for compounding may not adequately address complex situations and may overcomplicate and create barriers that limit access in less complicated situations.

The specified level of training for pharmacists (20 hours) and technicians (40 hours), as well as the inclusion in the proposal for complete testing of identities and amounts in three prepared compounds for each pharmacist creates additional barriers for pharmacies. These barriers will prevent pharmacists from providing care for patients and will limit patient access to these medications, potentially delaying treatment. Additionally, the specified training and compound testing requirements exceed the current proposed updates to USP 795 that have been approved by USP’s compounding committee.

As currently proposed, I would ask that the Texas State Pharmacy Board members vote “no” to adopting the changes, or at a minimum, postpone consideration until a later date and after a thorough review by the agency staff and board members is completed on the impact and need of the proposed regulations.

Thank you for your dedication to Texas pharmacy, to the safety of Texas citizens, and for your time and attention to this request for consideration.

Sincerely,

Jeff Loesch, PharmD, RPh

Director of Pharmacy – Dallas Division

Kroger Health

TO: Texas State Board of Pharmacy
c/o Eamon D. Briggs, Assistant General Counsel
333 Guadalupe Street, Suite 3-500
Austin, Texas 78701

FROM: Ted Menard, RPh|License #31249
[redacted]

Dear Sir,
I am writing regarding the proposed amendments concerning pharmacies that compound non-sterile preparations. While I appreciate the State Board of Pharmacy proactively addressing the current state of non-sterile compounding, I do believe that the Board has unnecessarily gone beyond both current and proposed federal/USP guidelines.

I do not have an issue with the bulk of the proposed amendments and so I will only address those areas that I believe to create an unnecessary burden, either financially or administratively, on the profession of pharmacy as it is practiced in Texas.

Concerning lines 166-173 and 190-199: Pharmacists and technicians shall *complete testing of three preparations compounded...for accuracy of correct identities and amounts of ingredients....*
This requirement is not included in either the current or proposed versions of <795>. USP has dedicated significant resources to the creation, maintenance, review and updating of <795> and they did not see the need to add this requirement to a federal standard. I assume the Board has added this requirement as sort of an equal competency measure akin to the aseptic media fill test for sterile compounding. If so, I understand the intent, but the logic is faulty. With aseptic technique you can not tell if you contaminated a product unless you test it – even if you have a trainer overseeing your technique. With nonsterile compounding, if we are testing for *correct identities and amounts of ingredients* as the proposed amendments say we are, the identities and amounts can be verified by the trainer prior to the compounding of the product. There is no need for testing to verify those data points.

Concerning lines 205-216: Pharmacists and technicians shall be required to complete *a single course with a minimum of 40 hours for the pharmacy technician or 20 hours for the pharmacists of instruction and hands-on, in-person experience.*
Again, this requirement is not included in either the current or proposed versions of <795>. Both USP <795> and ><797> have extensive requirements for the training and evaluation of personnel both initially and annually. USP <797> further requires pharmacists and technicians to complete a similar 40hr/20hr course prior to compounding sterile products, but USP did not believe this was necessary for <795>. They seem to believe that individual pharmacies have both the expertise and professional integrity to devise and implement their own training program. I further submit that this requirement constitutes an undo financial burden on both the individual employee and the individual pharmacy. While those at the Board may see this as a one-time expense that would ignore the current state of

employment where employees change jobs often due to reasons that are both varied and uncontrollable.

Concerning lines 349-357: The pharmacy shall: *use a closed system process device, used to reduce the potential exposure to personnel, or contamination of the pharmacy, or compounded non-sterile preparations, to perform activities such as weighing, measuring, or otherwise manipulating components that generate airborne chemical particles.*
Once again, I must go back to the current and proposed USP <795> guidelines. According to <795> the use of a closed system processing device is determined by the professional expertise of the pharmacist involved in the compounding process. <795> says that this evaluation and decision 'must' be made, but they do leave the decision to the pharmacist. I am concerned about the safety and well-being of my staff and I appreciate that the Board has very clearly demonstrated that they too care about the people that they represent, but I believe the mandated use of a closure system is overkill. This again will create a financial burden for both the pharmacy and the patient.

I ask that the Board reconsider these concerns before voting on these amendments. I understand that the Board must balance the safety of the patient with the impact the proposed rule has on the profession itself, but in the concerns raised above I do not believe that the safety of the patient or of the staff is affected.

Thank you for your consideration.

Sincerely,

Ted W. Menard

Jeenu Philip, R.Ph.
Director, Pharmacy Affairs
Walgreen Co.
p: 904-386-6776
jeenu.philip@walgreens.com

October 25, 2021
Via Email

Texas Board of Pharmacy
Attention: Tim Tucker, Executive Director/Secretary
333 Guadalupe, Ste #3-500
Austin, TX 78701
Email: tim.tucker@pharmacy.texas.gov
Cc: eamon.briggs@pharmacy.texas.gov

Re: Comments to proposed rule changes, §291.131 Texas Pharmacies Compounding Non-Sterile Preparations & §291.36. Pharmacies Compounding Sterile Preparations (Class A-S).

Dear Mr. Tucker and respected members of the Texas Board of Pharmacy,

On behalf of all pharmacies owned and operated by Walgreen Co. in the state of Texas, we thank the board for the opportunity to comment on proposed changes to rule §291.131, Texas Pharmacies compounding non-sterile preparations and §291.36. Pharmacies Compounding Sterile Preparations.

We believe that combining commercially manufactured, ready-to-use products *that have not been manipulated* should be exempt from the many onerous requirements within this rule. There are many simple compounds that pharmacists have been combining for years with no complaints and **extremely** low risk of patient harm. We also believe the Board's inspectors time is better served focusing on those pharmacies that are performing more complex sterile and non-sterile compounding. We would point to Mississippi's compounding rule as an example of a state that has carved these types of compounds from USP 795 standards. We believe the Texas Board can do something similar within its proposed rules.

MS 30-030-3001, Article XXXI Compounding guidelines

C. For the purpose of this Article, the combining of commercially manufactured, ready-to-use products shall be exempt from USP 795 compounding standards under the following conditions:

i. No more than four (4) commercially manufactured ready-to-use products (that have not been manipulated) are used;

ii. Compounding is not done in anticipation of medication orders;

iii. Must follow USP 795 beyond use dates (BUDs);

iv. A valid prescription shall serve as the compounding record;

We believe pharmacies performing compounds within limited to these products should NOT be required to obtain a Class A-N compounding license and all of the onerous requirements associated with it.

Walgreens

§291.131 Texas Pharmacies Compounding Non-Sterile Preparations

In general, we believe these new regulations within 291.131 are overly burdensome and a direct governmental overreach intended to push the practice of compounding closer to the regulations associated with manufacturing. We believe the Board's proposed rules lack current and supported data, but rather rely heavily on speculation and opinion. With the dramatic increase in the number of non-sterile compounds made in the United States over the past 2 decades, any specific issues with current regulations would have stood out through mass drug errors and been referenced, as was the case when the regulations creating 503b criteria. In short, if accepted as written, these regulations will dramatically limit patient access to vital simple and complex compounds alike and place an undue burden on the compounding pharmacies who try to comply. The Board has not provided any evidence of an extreme spike in non-sterile compounded related cases, nor evidence of why these additional requirements are necessary.

Personnel:

Line 77:

*(ii) obtain **one hour of ACPE accredited** continuing education **during each renewal period as** appropriate for the type of compounding done by the pharmacist.*

Line 99:

***(ii)**[(B)] obtain **one hour of ACPE accredited** continuing education **during each renewal period as** appropriate for the type of compounding done by the pharmacy technician or pharmacy technician trainee; and*

We believe these additional 1 hour specific CE requirements are unnecessary. Pharmacists should be more than qualified to perform these compounds through their education and training. Creating training requirements for individual activities creates a bad precedent and is an onerous and unnecessary requirement.

Line 83 & 109

All Pharmacists involved…:

(ii) complete testing of three preparations compounded by the pharmacist for accuracy of correct identities and amounts of ingredients within the first six months of engaging in compounding non-sterile preparations intended for patient use; and

All technicians involved…:

(ii) complete testing of three preparations compounded by the pharmacist for accuracy of correct identities and amounts of ingredients within the first six months of engaging in compounding non-sterile preparations intended for patient use; and

As written, this appears to impact each new pharmacist and each new technician. Requiring 3 preparations to be tested appears to be an arbitrary quantity. In addition, testing is not defined. If the Board intends independent testing, independent testing would be onerous and expensive. A Quality Assurance process is already required by USP and Walgreens adds additional existing internal processes. As a potential estimate, independent testing could be as much as $140 per test = $840 for just 2 people (i.e. 1 pharmacist and 1 technician) annually.

Walgreens

Line 123

(i) a single course with a minimum of 40 hours for the pharmacy technician or 20 hours for the pharmacist of instruction and hands-on, in-person experience. Such training shall be obtained through completion of a recognized course in an accredited college of pharmacy or a course sponsored by an ACPE accredited provider;

We believe that 40 hours is an arbitrary hour's requirement. This is an extremely expensive and burdensome requirement. Pharmacists are provided compounding training in pharmacy school and additional board mandated training is unnecessary. Instead, we believe that the specific hours requirement be stricken and there should instead be an internal competency review. Pharmacists and technicians should instead be proficient before proceeding to perform any compounding beyond their knowledge, skills or abilities.

Environment:

Line 218:

The compounding space shall be secure, well-lighted and shall be maintained in a clean, orderly, and sanitary condition, and in a good state of repair.

We believe this language is highly subjective. As an example, hot plates that appear to have stains will occasionally see inspectors insist on replacement even though these are fine to use. We recommend striking.

Equipment and Supplies:

Line 248:

Re: Class A prescription balance:

(ii) inspected and calibrated at least every 12 months by a qualified independent individual.

This requirement is different from USP 795. Independent inspection have a cost associated with them of at least $100 per scale. 500 stores x $100 = $50000+ annually. In addition, some locations have more than one scale. Scales are intended to be used for long-term use. Manufacturers of scales utilize simple methodology for personnel to calibrate the scales. In addition, personnel log calibrations that are being performed. In addition, these are NTEP certified scales. Our recommendation is to strike "Qualified independent individual." One option is to require that the scale be certified prior to use.

Compounding Process

Line 364

(D) Gloves and other garb (e.g., shoe covers, head and facial hair covers, face masks, gowns) shall be worn for all compounding activities for prevention of preparation and facility contamination and must be appropriate for the type of compounding performed. The garbing requirements and frequency of changing the garb shall be determined by the pharmacy and documented in the pharmacy's SOPs. Garb shall be stored in a manner that minimizes contamination (e.g., away from sinks to avoid splashing).

We believe the 1st sentence to be sufficient. There are too many variables from a compounding perspective to add all scenarios into an SOP.

Walgreens

Line 369:
Visibly soiled garb or garb with tears or punctures, including gloves, shall be changed immediately. Gloves, shoe covers, hair covers, facial hair covers, face masks, or head coverings may not be re-used if worn outside of the compounding area and must be replaced with new ones. To minimize the risk of cross-contaminating other compounded non-sterile preparations and contaminating other objects (e.g., pens and keyboards), gloves should be wiped with 70% isopropyl alcohol or replaced before beginning a compounded non-sterile preparation with different components.

This is highly prescriptive language. We recommend striking as this is normal standard of care. Regarding reuse of PPE: "Replace when deemed necessary" type language is sufficient.

Walgreens believes that the additional requirements within this rule are unnecessary from a public protection standpoint and recommend sending both sets of these rules back to committee and engage with stakeholders to identify how to craft rules that will permit much needed access to basic compounds while still protecting the public. We appreciate the Board reading these comments and appreciate the opportunity to comment.

If the Board would like additional information, please feel free to contact me.

Sincerely,

Jeenu Philip R.Ph.

October 25, 2021

Tim Tucker, PharmD, Executive Director

Texas State Board of Pharmacy

333 Guadalupe S., Ste 3-500

Austin, TX 78701

Email: tim.tucker@pharmacy.texas.gov

Dear Executive Director Tim Tucker,

I write to you today as a concerned pharmacist with the proposed rules up for final adoption regarding non-sterile compounding. I ask for your support and for you to **vote NO the proposed rules** in the sections listed below. These proposed rules would negatively affect our patients by creating unnecessary barriers to our ability as pharmacist to offer our compounding services to the community. Most of our pharmacies would have to stop offering many pharmacy services (flavoring and simple compounding) due to the cost and additional training needed to implement the needed changes.

- §291.36 concerning Pharmacies Compounding Sterile Preparations (Class A-S)
- §291.77 concerning Pharmacies Compounding Sterile Preparations (Class C-S)
- §291.106 concerning Pharmacies Compounding Sterile Preparations (Class E-S)
- §291.131 concerning Pharmacies Compounding Non-Sterile Preparations

Thank you for your leadership and support in the profession of pharmacy!

Sincerely,

Chuck Sinn | PharmD