

## **Compounding Task Force Meeting**

**May 19, 2015**

DOPL Building North Conference Room 7 am

Attendance: Attached

Next Meetings: August 18, 2015 and November 10, 2015

Agenda: Attached

### **Domperidone Update:**

Letter created by Task Force and approved by Board and DOPL was sent out to all pharmacies on May 15<sup>th</sup>. The letter was sent to inform Utah compounders of the current regulatory landscape and to inform that domperidone is not an approved drug for compounding by the FDA and now also by our State. The letter is attached. PCCA also sent out a letter stating they will sell domperidone for veterinarian use only.

### **Facilities (503b): Outsourcing:**

These entities will be registered and inspected by the FDA as well as licensed and inspected by DOPL. There are 50 registered outsourcing facilities currently in the country. Isomeric Pharmacy (led by Bryan Horne and Jake Corsi) is opening our first in Utah soon and in the process of becoming license have had some issues come up. The main issue is what category of licensure would be the best fit. They will need a Class C (manufacturing license) as well as a Class A (retail pharmacy). A facility is not able to have Class A and manufacturing license at the same address (location). DEA wants them registered as a manufacturer because they will be providing controlled substances for in office use. It was discussed to create a licensure under Class E with appropriately defining its operational setting.

Note: FDA has sent 483 warning letters to all but one of the 50 outsourcing facilities. These are concerns that need to be addressed by the outsourcing facilities.

### **New DOPL Pharmacy Bureau Manager:**

Dane Ishihira. [dishihira@utah.gov](mailto:dishihira@utah.gov)

### **Compounding (non-sterile) self-inspection form:**

This form has been revamped and updated. DOPL has worked hard to create this new document to enable pharmacies to prepare for inspections. This new form has material that is exactly from our Rules and USP 795. It is recommended to perform your own gap analysis with this form to become ready for inspections. Class B inspection forms will be similar to the Class A with a few added questions. Travis will send out a sample of the Class B. All the inspection forms will be posted to the DOPL website once they are all finished. Koby had an issue with question #52 with the wording of active vs inactives. Our Rules still state both, so we need to change our Rules so they better reflect what USP 795 states and that is only actives. Trip will talk with Board in June concerning this issue.

**NCPA Capitol Hill meeting with legislators:**

Dean Jolley met with all 6 of the Utah delegates. Main topics of discussion were allowance of “for office use” compounding, MOUs, and the positive and negative lists in regard to the DQSA. Also, see attachment.

**Vet FOU:**

Trip has taken several questions regarding veterinarian compounding for office use and whether it is allowed. There was discussion about legality of vet FOU compounding. The DQSA at this time has not addressed animal compounding. No consensus was reached but DOPL isn't currently taking action. There is a draft from the FDA just recently released regarding compounding for animals (Guidance for Industry: Compounding Animal Drugs from Bulk Drug Substances) and can be found at [www.fda.gov/AnimalVeterinary/.../UCM446862](http://www.fda.gov/AnimalVeterinary/.../UCM446862)

- o Cached

There will need to be discussion on this draft as it was just released on May 18<sup>th</sup>. Written comments can be sent regarding the draft on the FDA's website or as stated in the above document.

**Prescriber script pads created by pharmacies:**

DOPL has had discussion about these pads and would like this to be addressed by the Board for a decision. Task Force discussed approach to take. Rx pads are appropriate as long as patients have freedom of choice of pharmacy and no controlled substances are listed. A motion was made by Dean Jolley and properly seconded to have the Task Force prepare an educational letter to the State Board and DOPL in regards to pre-printed prescription forms. Then a letter can be sent out to all pharmacies from the three entities. The vote was taken and was unanimously passed by all members present. Koby Taylor will lead on this task.

**DQSA positive and negative lists:**

Jim Ruble led this discussion. There were 6 medications to be approved at the Feb. meeting. Four were approved and 2 were not added to the positive list. There were 24 medications added to the do not compound list or the negative list. See attachments.

**Compounding Task Force Meeting****May 19, 2015**

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DOPL Building 7 am

North Conference Room

**AGENDA:**

Item:	Lead:	Notes:
I. Domeperidone update	Trip	
II. Outsourcing Facilities	Trip	
III. New DOPL Bureau Manager	Trip	
IV. Compounding Self-Inspection Reports-Review	Trip	
V. DC Meeting with Legislators	Dean	
VI. VET Compounding FOU	Trip	
VII. Prescriber script pads created by pharmacies	Trip	
VIII. DQSA Positive and Negative Lists	Trip/Jim	

Next Meeting: August 18<sup>th</sup>, 2015



## Compounding Task Force

May 13, 2015

Re: Domperidone Compounding Regulatory Landscape

The Compounding Task Force held a meeting on March 17, 2015 to discuss domperidone and its current regulatory landscape. The following are the items concerning domperidone reviewed by the Compounding Task Force and the Utah Board of Pharmacy:

1. In 2004, the FDA released a public warning that distributing any domperidone-containing product is illegal.
2. Domperidone is currently not a component of an FDA-approved human drug.
3. Domperidone does not have a USP/NF monograph.
4. It is being considered for the positive list and it is not on the negative list in respect to the Federal Food, Drug, and Cosmetic Act (FDCA), as amended by section 503a of the Drug Quality and Security Act (DQSA) of 2013.
5. DOPL has issued one subpoena to a Utah compounding pharmacy for compounding domperidone-containing prescriptions.
6. The FDA has sent 2 warning letters to pharmacies regarding compounded domperidone within the last year.
7. The FDA has a mechanism in place to provide domperidone to qualified patients with gastroparesis through an IND expanded access program.  
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/ucm368736.htm>
8. Several state boards of pharmacy have specifically instructed licensees that compounding of domperidone is not permitted in their state.

Based on the current status of domperidone, the Compounding Task Force, the Utah Board of Pharmacy and the Division of Occupational and Professional Licensing would like to communicate to all compounding pharmacies that continued compounding with domperidone may place a licensee in immediate and substantial risk of administrative enforcement actions at Federal and State agency levels.

We will keep you informed and educated as changes occur at Federal and/or State regulations regarding domperidone.

Thank you for your time and cooperation in this issue.

Sincerely,

The Compounding Task Force  
Utah Board of Pharmacy  
Utah Division of Occupational and Professional Licensing

To view this email as a web page, click [here](#).



## Public Affairs News: Current Regulatory Landscape Regarding Domperidone

Dear PCCA Member:

Since the passage of the Drug Quality and Security Act in November 2013, and the Food and Drug Administration (FDA) enforcement of the new Section 503A of the Federal Food, Drug, and Cosmetic Act, the FDA has considered items for use in compounding which are important for patient care but do not qualify as a permissible bulk drug ingredient under the federal law. Domperidone is an important drug which many human and veterinary patients depend on for relief from their suffering. PCCA has continued to sell the drug to our membership with the expectation that the FDA would either quickly make a decision regarding adding it to the "positive list" or provide for enforcement discretion until it could be considered. This expectation has not been met. Now, the FDA and some state boards of pharmacy have undertaken enforcement action against pharmacies that fill prescriptions for domperidone based on a prescriber's decision that the medication would be the best course of treatment to serve their patient's needs.

Section 503A permits compounding using "bulk drug ingredients" (APIs) which:

- Have a USP or NF monograph, OR
- Are part of an FDA-approved human drug product, OR
- Appear on FDA's (yet-to-be-established) list of bulk drug substances that pharmacies may use in compounding (FDA's "positive list").

PCCA sells domperidone for several reasons, including the following:

1. Domperidone serves numerous compelling patient needs;
2. PCCA nominated domperidone for inclusion on FDA's "positive list" of bulk substances that may be used in compounding;
3. PCCA sponsored the submission to USP of a proposed monograph for domperidone; and
4. Veterinarians may still compound preparations using domperidone for veterinary (not just equine) use.

However, in the last couple of months, FDA and several states have engaged in increased enforcement activity relating to domperidone. FDA issued warning letters to at least four pharmacies in the last year after FDA observed compounded domperidone preparations during inspections. FDA has also recently updated its website addressing the drug to state as follows: "Domperidone is not currently a legally marketed human drug and it is not approved for sale in the U.S." However, FDA "continues to recognize that there are some patients with severe gastrointestinal motility disorders that are difficult to manage with available therapy for which domperidone's potential benefits may justify its potential risks." FDA concludes, "While there are currently no pharmacies that are authorized to compound domperidone under the expanded access program, domperidone may be obtained under certain circumstances..." through an expanded access investigational new drug application (IND). (Information available at: <http://1.usa.gov/1ITxBsc>)

Additionally, at least five state boards of pharmacy have asserted that domperidone is an unapproved drug, and if dispensed outside the IND process, is adulterated and misbranded under both state and federal law. This may well be the position of any state that has adopted Section 503A; a similarly worded state statute addressing new drugs, misbranding or adulterated drug products; or the uniform Food, Drug, and Cosmetic Act (which has been adopted in every state). Given FDA's current regulatory position concerning domperidone and

coupled with state boards of pharmacy actions regarding the drug, starting today, we will be labeling domperidone as "For Veterinary Use Only."

Our members must be aware of the potential regulatory risks associated with providing domperidone to patients in the absence of a veterinary prescription or obtaining an expanded access IND for use in humans. If you have any additional questions regarding domperidone, including questions about treatment alternatives or places where patients can acquire domperidone, please contact the Pharmacy Consulting Department (PCD) at 800.331.2498. If you have any patients negatively impacted by decreased accessibility to the medication, please contact the Public Affairs team either at the phone number above or via e-mail at [publicaffairs@pccarx.com](mailto:publicaffairs@pccarx.com)

Sincerely,

Jim Smith  
PCCA President

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## Reminder: Public Affairs Free Monthly Call TOMORROW, Wednesday, April 22 at 11 a.m. Central

Please join us tomorrow for our monthly Public Affairs call -- we will be discussing:

- Domperidone
- Office Use
- TRICARE
- Memorandum of Understanding (MOU)
- And much more

And, as always, will open up the call for questions from our members.

Call In: 1.877.273.4202

PIN: 874.400.930#



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State of Utah  
Department of Commerce

Division of Occupational and Professional Licensing

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NON STERILE  
COMPOUNDING

INSPECTION

New Opening  Regular

INFORMATION

Pharmacy Name: \_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Pharmacy License Number: \_\_\_\_\_ Expiration Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Controlled Substance License Number: \_\_\_\_\_ Expiration Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

DEA Registration Number: \_\_\_\_\_ Expiration Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Pharmacist-in-Charge (PIC): \_\_\_\_\_

Pharmacist-in-Charge License Number: \_\_\_\_\_ Expiration Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Compounding Facilities engaged in simple, moderate or complex non-sterile or any level of sterile compounding activities shall be required to maintain proper records and procedure manuals and establish quality control measures to ensure stability, equivalency where applicable and sterility. The following requirements shall be met: (a) Shall follow USP-NF Chapter 795, compounding of non-sterile preparations, and USP-NF Chapter 797 if compounding sterile preparations [UAC R156-17b-614a (3)]

**GENERAL OPERATIONS AND INFORMATION**

- |    | Yes                      | No                       |  |
|----|--------------------------|--------------------------|--|
| 1. | <input type="checkbox"/> | <input type="checkbox"/> | Compounders shall acquire and maintain knowledge and skills in all areas (e.g., dosage form, patient population, and medical specialty) for which they compound. [USP-NF Chapter 795— <i>Categories of Compounding</i> ]   |
| 2. | <input type="checkbox"/> | <input type="checkbox"/> | Which categories of compounding does the facility perform?   |
|    | <input type="checkbox"/> | <input type="checkbox"/> | <b>Simple</b> - Making a preparation that has a <i>United States Pharmacopeia (USP)</i> compounding monograph or that appears in a peer-reviewed journal article that contains specific quantities of all components, compounding procedure and equipment, and stability date for that formulation with appropriate BUDs; or reconstitution or manipulation commercial products that may require the addition of one or more ingredients as directed by the manufacturer. Examples include <i>Captopril Oral Solution</i> , and <i>Indomethacin Topical Gel</i> , and <i>Potassium Bromide Oral Solution, Veterinary</i> . [USP-NF Chapter 795— <i>Categories of Compounding—Description of Categories</i> ] |
|    | <input type="checkbox"/> | <input type="checkbox"/> | <b>Moderate</b> - Making a preparation that requires special calculations or procedure (such as calibration of dosage unit mold cavities) to determine quantities of components per preparation or per individualized dosage units; or making a preparation for which stability data for that specific formulation are not available. Examples include <i>Morphine Sulfate Suppositories</i> , diphenhydramine hydrochloride troches, and mixing two or more manufactured cream products when the stability of the mixture is not known. [USP-NF Chapter 795— <i>Categories of Compounding—Description of Categories</i> ]   |
|    | <input type="checkbox"/> | <input type="checkbox"/> | <b>Complex</b> - Making a preparation that requires special training, environment, facilities, equipment, and procedures to ensure appropriate therapeutic outcomes. Examples of possible complex preparation types include transdermal dosage forms, modified-release preparations, and some inserts and suppositories for systemic effects. [USP-NF Chapter 795— <i>Categories of Compounding—Description of Categories</i> ]  |
| 3. | <input type="checkbox"/> | <input type="checkbox"/> | The preparation, mixing, assembling, altering, packaging, and labeling of a drug, drug-delivery device, or device is accordance with a licensed practitioner's prescription, medication order, or initiative based upon the practitioner/patient/pharmacist/compounder relationship in the normal course of professional practice [USP-NF Chapter 795— <i>Definitions—Compounding</i> ]  |
| 4. | <input type="checkbox"/> | <input type="checkbox"/> | Does the facility compound nonsterile prescriptions which are then delivered to a practitioner for administration to the patient in the office, clinic or facility?  |



5.  Yes  No A pharmacy licensed under this chapter may, subject to rules established by the Division, repackage or compound a prescription drug for sale to a practitioner if: the prescription drug: does not include a compounded drug; or includes a compounded drug; and is not a controlled substance; the pharmacy labels the prescription drug "for office use only"; the practitioner administers the drug to a patient in the practitioner's office or facility; and except in accordance with Title 58, Chapter 17b, Part 8, Dispensing Medical Practitioner and Dispensing Medical Practitioner Clinic Pharmacy, the practitioner does not dispense the drug to the patient. [UCA 58-17b-624(1)(a)(i)(ii)(A)(B)(b)(c)(d)]
6.   Does the facility distribute nonsterile compounded preparations to hospitals, clinics, or surgery centers?
7.   Does the facility have a sales force that distributes samples containing active ingredients? List.
8.   Does the facility provide nonsterile compounded preparations to other pharmacies for dispensing?
9.   What does the facility compound?  
 Tablets  Liquids  Troches  Ointments  
 Capsules  Lozenges  Creams  Suppositories  
 Patches  Sprays  Powders  Oral Pastes  
 Transdermals  \_\_\_\_\_  \_\_\_\_\_  \_\_\_\_\_
10.   Does the facility compound vitamins or nutritional supplements? List.
11.   Does the facility compound investigational drugs? List.
12.   The facility does not prepare a prescription drug in a dosage form which is regularly and commonly available from a manufacturer in quantities and strengths prescribed by a practitioner. [UCA 58-17b-502 (13)]
13.   Does the facility perform compounding with hazardous drugs?
14.   Does the facility segregate hazardous drugs from normal compounding stock?
15.   MSDSs shall be readily accessible to all employees working with drug substances or bulk chemicals located on the compounding facilities premises. Employees should be instructed on how to retrieve and interpret needed information. [USP-NF Chapter 795—*Compounding Documentation—Material Safety Data Sheets File*]
16.   Does the facility make nonsterile compounded preparations using bulk powder active pharmaceutical ingredients?
17.   All significant procedures performed in the compounding area should be covered by written standard operating procedure (SOPs). Implementing SOPs establishes procedural consistency and also provides a reference for orientation and training of personnel. To ensure accountability, accuracy, quality, safety and uniformity in compounding procedures should be developed for the following: [USP-NF Chapter 795—*Compounding Documentation—Standard Operating Procedures*]  
 Facility  Equipment  Personnel  
 Packaging  Storage  Preparation
18.   A *United States Pharmacopeia (USP)*, *National Formulary (NF)*, or *Food Chemical Codex (FCC)* substance is the recommended source of all ingredients for compounding all preparations. [USP-NF Chapter 795—*Component Selection, Handling, and Storage(1)*]
19.   Bulk active ingredients must be procured from a facility registered with the federal Food and Drug Administration and must not be listed on the federal Food and Drug Administration list of drug products withdrawn or removed from the market for reasons of safety or effectiveness. [R156-17b-614a (3)(c)(i)(ii)]
20.   Bulk containers are labeled with appropriate Occupational Safety and Health Administration (OSHA) hazard communication labels (see OSHA.gov), and Material Safety Data Sheets (MSDSs) are available to compounding personnel for all drugs and chemicals used in compounding. [USP-NF Chapter 795—*Responsibilities of the*



Compounder—General Principles of Compounding (3)]

Yes No

**BEYOND USE DATING**

- 21.   All components used in the compounding of preparations must be store as directed by the manufacturer or according to *USP, NF, or FCC* monograph requirements, in a clean area, and under appropriation temperatures and humidity conditions (controlled room temperature, refrigerator, or freezer). All components shall be stored off the floor, handled and stored to prevent contamination, and rotated so that the oldest stock is used first. All containers shall be properly labeled. [USP-NF Chapter 795—*Component Selection , Handling, and Storage (11)*]
- 22.   For components that do not have expiration dates assigned by the manufacture or supplier, the compounder shall label the container with the date of receipt and assign a conservative expiration date, not to exceed three years after receipt, to the component (see the *General Notices and Requirements, Preservation, Packaging, Storage, and Labeling, Labeling, Expiration Date and Beyond-Use Date*) based on the nature of the component and its degradation mechanism, the container in which it is packaged, and the storage conditions. [USP-NF Chapter 795—*Component Selection, Handling, and Storage(6)*]
- 23.   If the component has been transferred to a different container, that container shall be indentified with the component name, lot or control number, transfer date, and expiration date and shall provide integrity that is equivalent to or better than that of the original container. [USP-NF Chapter 795—*Component Selection, Handling, and Storage(5)*]
- 24.   The compounder shall ensure that the container and container closures used in packaging compounded preparations meet *USP* requirements (see the *General Notices and Requirements, Preservation, Packaging, Storage, and Labeling, Containers; Containers—Glass <660>; Containers—Plastics<661>; Containers—Performance Testing <671>; Chapter <681>; Chapter <1136>; Packaging Practice—Repackaging a Single Solid Oral Drug Product into a Unit-Dose Container<1146>*); and when available, compounding monographs. Compounders are not expected to perform the tests described in these chapters but should be knowledgeable about the stands described in them. [USP-NF Chapter 795—*Packaging and Drug Preparation Containers*]
- 25.   The containers and closures shall be stored off the floor, handled and stored to prevent contamination, and rotated so that the older stock is used first. The containers and container closures shall be stored in such a way as to permit inspection and cleaning of the storage area. [USP-NF Chapter 795—*Packaging and Drug Preparation Containers*]
- 26.   The BUD is the date after which a compounded preparation shall not be used and is determined from the date when the preparation is compounded. [USP-NF Chapter 795—*Stability Criteria and Beyond-Use Dating*]
- 27.   The beyond use date assigned shall be based on currently available drug stability information and sterility considerations or appropriate in-house or contract service stability testing. [R156-17b-614a (3)(g)]
- 28.   Sources of drug stability information shall include the following: [R156-17b-614a (3)(g)(i)(A)(B)(C)]  
References can be found in Manufacturer recommendations Reliable, published research  
 "Trissel's Handbook on Injectable Drugs", 17<sup>th</sup> Edition, October 31, 2012
- 29.   These maximum BUDs (shown below) are recommended for nonsterile compounded drug preparations in the absence of stability information that is applicable to a specific drug or preparation. The BUD shall not be later than the expiration date on the container of any component. [USP-NF Chapter 795—*Stability Criteria and Beyond-Use Dating—General Guidelines for Assigning Beyond-Use Dates*]  
  BUDs for Nonaqueous Formulations—The BUD is not later than the time remaining until the earliest expiration date of any API or 6 months, whichever is earlier.  
  BUDs for Water-Containing Oral Formulations—The BUD is not later than 14 days when stored at controlled cold temperatures.



Yes No

BUDs for Water-Containing Topical/Dermal and Mucosal Liquid and Semisolid Formulations—The BUD is not later than 30 days.

30.   These maximum BUDs recommended for nonsterile compounded drug preparations that are packaged in tight, light-resistant containers and stored at controlled room temperature, unless otherwise indicated; and for sterile preparations for which a program of sterility testing is in place (see *General Notices and Requirements, Preservation, Packaging, Storage, and Labeling*). [USP-NF Chapter 795—*Stability Criteria and Beyond-Use Dating—General Guidelines for Assigning Beyond-Use Dates*]

**ENVIRONMENT**

31.   Compounding facilities shall have an adequate space that is specifically designated for compounding of prescriptions. This space shall provide the orderly placement of equipment and materials to prevent mixups among ingredients, containers, labels, in-process materials and finished preparations and is designed, arranged and used to prevent adventitious cross-contamination. [USP-NF Chapter 795—*Compounding Facilities*]

32.   Areas used for sterile preparations shall be separated and distinct from the nonsterile compounding area (see Chapter <797>, *Environmental Quality and Control*). [USP-NF Chapter 795—*Compounding Facilities*]

33.   Compounding is done in an appropriately clean and sanitized area dedicated to this activity (see section *Compounding Facilities*). [USP-NF Chapter 795—*Compounding Process—Criteria When Compounding Each Drug Preparation (4)*]

34.   Only one preparation is compounded at one time in a specific workspace. [USP-NF Chapter 795—*Compounding Process—Criteria When Compounding Each Drug Preparation (5)*]

35.   The entire compounding and storage area should be well lighted. [USP-NF Chapter 795—*Compounding Facilities*]

36.   Heating, ventilation, and air conditioning systems shall be controlled to avoid decomposition and contamination of chemicals (see the *General Notices and Requirements, Preservation, Packaging, Storage, and Labeling, Storage Temperature and Humidity*; and the manufacturers' labeled storage conditions). [USP-NF Chapter 795—*Compounding Facilities*]

37.   Potable water shall be supplied for hand washing and equipment washing. *Purified Water* (see *Purified Water* monograph) shall be used for compounding nonsterile preparations when formulations indicate the inclusion of water. *Purified Water* should be used for rinsing equipment and utensils. [USP-NF Chapter 795—*Compounding Facilities*]

38.   Hazardous drugs shall be stored, prepared, and handled by appropriately trained personnel under conditions that protect the healthcare workers and other personnel. [USP-NF Chapter 795—*Compounding Facilities*]

39.   Disposal of all hazardous drugs wastes shall comply with all applicable federal and state regulations. All personnel who perform routine custodial waste removal and cleaning activities in storage and preparation areas for hazardous drugs shall be trained in appropriate procedure to protect themselves and prevent contamination. [USP-NF Chapter 795—*Compounding Facilities*]

**TRAINING**

40.   Personnel are appropriately trained and are capable of performing and qualified to perform their assigned duties. Such training should be documented. [USP-NF Chapter 795—*Responsibilities of the Compounder—General Principles of Compounding (1)*]

41.   All employees involved in pharmaceutical compounding shall read and become familiar with the chapter (USP-NF Chapter 795). They should also become familiar with the contents of the *USP Pharmacists' Pharmacopoeia* and other relevant publications, including how to read and interpret MSDSs. [USP-NF Chapter 795—*Training*]

42.   All employees shall read and become familiar with each of the procedures related to compounding, including those involving the facility, equipment, personnel, actual compounding, evaluation, packaging, storage, and dispensing. [USP-NF Chapter 795—*Training*]



Yes No

**COMPOUNDING EQUIPMENT**

- 43.   All equipment used in compounding is clean, properly maintained, and used appropriately. [USP-NF Chapter 795—Responsibilities of the Compounder—General Principles of Compounding (4)]
- 44.   Equipment shall be stored to protect it from contamination and shall be located to facilitate its use, maintenance and cleaning. Automated, mechanical, electronic, and other types of equipment used in compounding or testing of compounded preparations shall be routinely inspected, calibrated as necessary, and checked to ensure proper performance. Immediately before compounding operations, the equipment shall be inspected by the compounder to determine its suitability for use. After use, the equipment shall be appropriately cleaned. [USP-NF Chapter 795—Compounding Equipment]

**DOCUMENTATION**

- 45.   A master worksheet shall be developed and approved by a pharmacist for each batch of sterile or non-sterile pharmaceuticals to be prepared. Once approved, a duplicate of the master worksheet shall be used as the preparation worksheet from which each batch is prepared an on which all document for that batch occurs. The master worksheet may be stored electronically and shall contain at a minimum: [UAC R156-17b-614a (3)(d)(i)(ii)(iii)(iv)(v)(vi)(vii)(viii)]
 

<input type="checkbox"/> The formula <input type="checkbox"/> Sample label information <input type="checkbox"/> Specific equipment used during compounding such as specific compounding device <input type="checkbox"/> Calculations needed to determine and verify quantities of components and doses of active pharmaceutical ingredients [USP-NF Chapter 795—Compounding Documentation—Master Formulation Record]	<input type="checkbox"/> The components <input type="checkbox"/> Evaluation and testing requirements <input type="checkbox"/> Storage requirements <input type="checkbox"/> Compatibility and stability information, including references when available [USP-NF Chapter 795—Compounding Documentation—Master Formulation Record] <input type="checkbox"/> Description of final preparation [USP-NF Chapter 795—Compounding Documentation—Master Formulation Record]	<input type="checkbox"/> The compounding directions <input type="checkbox"/> Sterilization methods, if applicable <input type="checkbox"/> Container used in dispensing [USP-NF Chapter 795—Compounding Documentation—Master Formulation Record] <input type="checkbox"/> Packaging and storage requirements [USP-NF Chapter 795—Compounding Documentation—Master Formulation Record] <input type="checkbox"/> Quality control procedures and expected results [USP-NF Chapter 795—Compounding Documentation—Master Formulation Record]
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- 46.   A preparation worksheet for each batch of sterile or non-sterile pharmaceuticals shall document the following: [UAC R156-17b-614a (3)(e)(i)(ii)(iii)(iv)(v)(vi)(vii)(viii)(ix)(x)(xi)]
 

<input type="checkbox"/> Identity of all solutions and ingredients and their corresponding amount, concentrations, or volumes <input type="checkbox"/> Beyond use date of batch prepared products <input type="checkbox"/> Names, initials or electronic signature of the responsible pharmacist or DMP <input type="checkbox"/> Master formulation record reference for the preparation [USP-NF Chapter 795—Compounding Documentation—Compounding Record]	<input type="checkbox"/> Manufacturer lot number for each component <input type="checkbox"/> Component manufacturer or suitable identifying number <input type="checkbox"/> Date of preparation <input type="checkbox"/> Names, initials, or electronic signature of the person or persons involved in the preparation <input type="checkbox"/> Description of final preparation [USP-NF Chapter 795—Compounding Documentation—Compounding Record] <input type="checkbox"/> Documentation of any quality control issues and any adverse reactions or preparation problems reported by the patient or caregiver [USP-NF Chapter 795—Compounding Documentation—Compounding Record]	<input type="checkbox"/> Container specification (e.g., syringe, pump cassette) <input type="checkbox"/> Unique lot or control number assigned to batch <input type="checkbox"/> End product evaluation and testing specifications, if applicable <input type="checkbox"/> Comparison of actual yield to anticipated yield, when appropriate <input type="checkbox"/> Results of quality control procedures (e.g., weight range of filled capsules, pH of aqueous liquids) [USP-NF Chapter 795—Compounding Documentation—Compounding Record]
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Yes No



- 47.   Compounding records including the master worksheet, preparation worksheet, and prescription files, including refill information shall be maintained for a minimum of five years and be immediately retrievable in written or electronic format. [UAC R156-17b-612 (4)]
- 48.   There shall a documented, ongoing quality control program that monitors and evaluates personnel performance, equipment and facilities that follow USP-NF Chapters 795 and 797 standards. [R156-17b-614a (3)(h)]

**COMPOUNDING PROCEDURES**

- 49.   Only authorized personnel are allowed in the immediate vicinity of the compounding operations. [USP-NF Chapter 795—Responsibilities of the Compounder—General Principles of Compounding(6)]
- 50.   Personnel engaged in compounding maintain good hand hygiene and wear clean clothing appropriate to the type of compounding performed (e.g., hair bonnets, coats, gowns, gloves, face masks, shoes, aprons, or other items) as needed for protection of personnel from chemical exposures and for preventions of drug contamination. [USP-NF Chapter 795—Compounding Process—Criteria When Compounding Each Drug Preparation (8)]
- 51.   Critical processes (including but not limited to weighing, measuring, and mixing) are verified by the compounder to ensure that procedures, when used, will consistently result in the expected qualities in the finished preparation. [USP-NF 795—Compounding Process—Criteria When Compounding Each Drug Preparation]

**LABELING OF FINISHED PREPARATIONS**

- 52.   The label of each batch prepared of sterile or non-sterile pharmaceuticals shall bear at a minimum; [UAC R156-17b-614a (3)(f)(i)(ii)(iii)(iv)(v)(vi)]
 

<input type="checkbox"/> The unique lot number assigned to the batch	<input type="checkbox"/> all solution and ingredient names, amounts, strengths and concentrations, when applicable	<input type="checkbox"/> Quantity
<input type="checkbox"/> Beyond use date and time, when applicable	<input type="checkbox"/> Device-specific instructions, where appropriate	<input type="checkbox"/> Appropriate ancillary instructions, such as storage instructions or cautionary statements, including cytotoxic warning labels where appropriate

**ADDITION OF PRESCRIPTION LABEL REQUIREMENTS—WHEN AVAILABLE**

**PATIENT COUNSELING AND COMMUNICATION**

- 53.   At the time of dispensing the prescription, the patient or the patient’s agent shall be counseled about proper use, storage, handling, and disposal of the compounded preparation. The patient or the patient’s agent shall also be instructed to report any adverse event and to observe and report to the compounder any changes in the physical characteristics of the compounded preparation (see Chapter <1191>, Responsibility of the Pharmacist). The compounder shall investigate and document any reported problem with a compounded preparation and shall take corrective action. [USP-NF Chapter 795—Patient Counseling]

**VETERINARY COMPOUNDING**

- 54.   Does the facility compound for veterinary use?
- 55.   If compounding for both humans and animals, are the API’s or other components that are labeled for veterinary use only are segregated or marked in such way to prevent them from being used for human compounding?
- 56.   The pharmacist shall be knowledgeable about the individual species’ limitation in physiology and metabolic capacity that can result in toxicity when certain drugs or excipients are used in compounded preparations. For this reason, compounders making preparations for animals should use, when possible, formulations specifically developed for animal patients. If such formulations are not available, the compounder shall conduct a literature review to determine whether a specific component of the formula is toxic to the target species. [USP-NF Chapter 795—Compounding For Animal Patients]

**COMMENTS**





# Preserving Patient Access to Medications

## Overview of Office-use

Compounded medications are available for use by medical professionals and patients from a compounding pharmacy in one of two ways: (1) patient-specific prescriptions, or (2) office-use as provided by state law. Under office-use, a medical professional must submit a medical order to a compounding pharmacy. This order must include all information required under and specified by state law. The medical professional writing the office-use “prescription” is then responsible for the control and administration of the compounded medication.

## Why Office-use is Important

Office-use of compounded medications is essential for emergency situations as well as to start treatment immediately in response to a medical condition. This is true for compounded medications that are both non-sterile (e.g., creams, pills, capsules) and sterile (e.g., injectables and eye drops). Office-use provides for improved patient care and increased compliance, and is an important part of the practice of medicine. Unnecessary delay in the use of a medication can harm patients, especially those with acute or chronic conditions.

- OBGYNs may need a compounded product to immediately begin treatment of a pregnant woman with a high-risk pregnancy.
- Crash carts in hospitals and in ambulances rely on an office supply of certain compounded medications to begin treatment immediately;
- Antibiotics for urgent and emergent use in treating ophthalmology patients;
- Buffered lidocaine for use in dermatology procedures;
- Vascular endothelial growth factor inhibitors used in treating age-related macular degeneration by ophthalmologists;
- Injection therapies used to treat erectile dysfunction in urology patients. Test injections are commonly administered in the doctor’s office to determine correct dosage;
- Cantharidin to treat viral skin conditions in office by dermatologists and pediatricians;
- Injectable methylcobalamin for the treatment of pernicious anemia and other vitamin B-12 deficiencies.

## Office-use is allowed under Section 503A of the *Food, Drug and Cosmetic Act*

Section 503A of the *Food, Drug and Cosmetic Act* (FD&C) authorizes office-use. Section 503A does not contain a pre-emption clause. Thus, State pharmacy practice law governs where Section 503A is silent. Section 503A is silent as to when an individual patient prescription is required. Section 503A also allows anticipatory compounding based on a history between the pharmacist and physician and is silent as to how this compounded medication leaves the pharmacy. Therefore, State pharmacy practice laws should govern whether office-use is allowed and under what circumstances it is allowed. In six Congressional Record statements, Congress reinforced that nothing within Section 503A pre-empts state law pertaining to office-use and repackaging.

## FDA Incorrectly Continues to Maintain Office-use is Prohibited Under 503A

FDA has responded twice to Congress that FDA has interpreted the *Drug Quality and Security Act of 2013* as prohibiting office-use of compounded medications from traditional pharmacies, despite the fact that FDA recognized office-use as legitimate and permissible within the Draft Compliance Policy Guide FDA provided in 2013 to the House Energy & Commerce Committee. Because Congress only reinstated Section 503A, and did nothing to change any office-use provisions within Section 503A, FDA has recognized in the past that Section 503A allowed office-use. Thus, FDA’s prohibition of office-use has left a widely accepted industry practice encompassed in a cloud of uncertainty.

## Conclusion

In order to preserve patient access to medications, we ask that Congress address the concerns with office-use and repackaged compounded medications with legislative clarification stating nothing within Section 503A pre-empts State practice laws including those that allow office-use and repackaging as soon as possible to preserve provider and patient access to these essential treatments.

## One Page Discussion – Top Four Asks:

- **Office Use** – A legislative solution is needed to clarify that nothing within Section 503A pre-exempts State practice laws. Please contact Rep. Morgan Griffith's office to be a co-sponsor of the bill and contact the Appropriations Committee in support of Rep. Chris Stewart's appropriation request.
- **MOU** – We urge lawmakers to submit comments/letter to FDA expressing concerns, allowing for states that enter into the MOU to remove any restrictions to the shipment of compounded drugs.
- **TRICARE** – Please call Defense Health. Ask to be kept apprised of policy developments related to reimbursements for compounds and express the need for bulk chemicals to be an option for compounding.
- **CMS** – We want to make you aware of the 50 million patients being denied access to compounds due to restrictive language in the law. We will need a legislative change to the law.

### Office Use

Section 503A, as passed by Congress, does not directly address compounding for office use. However, FDA has taken the position, through written correspondence to Congress, that they interpret the DQSA as prohibiting office use of compounded medications by traditional pharmacies. FDA implementation of the law flies in the face of Congressional intent. The Administration has stated that traditional compounding pharmacies may not provide office use compounds.

- FDA's current prohibition disrupts patient and prescriber access to medications, and ends a widely accepted industry practice.
- This is an aggressive effort by FDA to regulate a traditionally state-based industry.
- A legislative solution is needed to clarify that nothing within Section 503A pre-exempts State practice laws, including those that allow for office use and repackaging. Rep. Griffith is introducing legislative language to allow for office use. Please contact his office to be a co-sponsor.

### TRICARE

Since June 2013, Military Health System (MHS) has been attempting to limit or eliminate coverage for compounded medications. Tricare is the health care insurance program Service members, their families and retirees.

- We are in a learning phase, meeting with the MHS, carefully engaged in the implementation process of this new program.
- There are many ways to control the spend rate for compounds, while maintaining patient access, without curtailing the benefit.
- We urge Congressional offices to call Military Health Systems. Ask to be kept apprised of implementation efforts, including the number of beneficiaries who have lost access to needed compounds, and express the need for bulk chemicals to be an option for compounding for patient specific needs.

### MOU/5% or 30%

In February 2015, FDA released a draft MOU that would limit to 30% (per month) the number of units of compounded drug products shipped interstate, and pharmacies that ship more than 30% in any given month must register as an OF. There is no allowable millage radius for pharmacies that are located near a border with other states. If a state does not agree to enter into an MOU with FDA, not more than 5% of compounds can be shipped interstate.

- Many pharmacies specialize in specific treatments areas. Because of their expertise, these pharmacies have relationships with doctors and patients in wide geographic areas, are registered in multiple states, and ship their medications to patients and prescribers.
- Placing limits of any percentage on interstate shipments is unworkable and will limit patient access to medications. It will force pharmacists to choose which patients can receive medications.
- We urge lawmakers to submit a letter to FDA expressing these concerns, allowing for states that enter into the MOU to remove any restrictions to the shipment of compounded drugs. Leave it up to the states to determine what is appropriate.

### CMS – Medicaid and Medicare

- When it comes to providing seniors with access to needed medications prescribed by their physician, Medicare is sorely lacking in providing access to compounded medications.

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## FDA Panel Backs Updates to Bulk Drugs List for Compounding

Troy Brown, RN | February 25, 2015

The Pharmacy Compounding Advisory Committee of the US Food and Drug Administration (FDA) voted yesterday to add squaric acid dibutyl ester, diphenylcyclopropanone, and cantharidin to its bulk drug substances list but voted not to add piracetam to the list.

The bulk drug substances list is a list of bulk drug substances that may be used to compound drug products according to section 503A of the Federal Food, Drug, and Cosmetic Act, even though they are neither the subject of a United States Pharmacopeia or National Formulary monograph nor components of drugs approved by the FDA.

On February 23, the committee voted to place thymol iodide on the list and not to place silver protein mild on the list.

### Squaric Acid Dibutyl Ester Added to List

The committee voted unanimously (1 no-vote) in favor of adding squaric acid dibutyl ester to the bulk list.

Squaric acid dibutyl ester is a contact sensitizer that has been used topically to treat alopecia areata and warts. It has demonstrated effectiveness for eradicating warts from patients who have recurrent multiple warts and has no significant adverse effects. It is safe and effective for children.

Imiquimod is an alternative to squaric acid dibutyl ester but it is not approved by the FDA for treatment of children younger than 12 years.

"I would actively support both an indication for it — the indications for its use need to be real clear — as well as any adverse effects [need to] be clearly included," said voting committee member Padma Gulur, MD, professor, Department of Anesthesiology and Perioperative Care, University of California, Irvine, Orange.

### Diphenylcyclopropanone Added to List (DPCP)

The committee voted 9 to 1 (1 no-vote) in favor of adding diphenylcyclopropanone to the bulk list.

Diphenylcyclopropanone has been used topically for the treatment of extensive alopecia areata and recalcitrant warts. It has been used in compounding for more than 30 years and is used worldwide for treatment of these conditions. It is the most effective treatment and has the best safety profile for treatment of such conditions.

"I voted 'yes' based on safety and effectiveness data provided for the indications that were discussed," Dr Gulur said.

### Cantharidin Added to List

The committee voted 8 to 2 (1 no-vote) in favor of adding cantharidin to the bulk list.

Cantharidin is used to treat warts and molluscum contagiosum. It has been used since the 1950s and is currently used widely. The standard of care for its use in in-office application by a licensed healthcare professional.

"[There is a] long history of this compound being safely used, largely because when it is available to be compounded, providers...do make a quality product," said voting committee member John J. DiGiovanna, MD, staff clinician, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

### Piracetam Not Added to List

The committee voted 9 to 1 (1 no-vote) against adding piracetam to the bulk list.

Piracetam is a gamma-aminobutyric acid derivative that has been used to treat cognitive disorders, Alzheimer's disease, vertigo, and cortical myoclonus. It was synthesized in 1964 and entered clinical investigation in 1971. In rigorous trials, the results have proven lack of clinical significance. Other approved medications are available.

"It met three of the criteria [for inclusion on the list,] but it didn't show sufficient evidence of benefit," said voting committee member Jürgen Venitz, MD, PhD, committee chairperson and associate professor, Department of Pharmaceutics, School of Pharmacy, Virginia Commonwealth University, Richmond.

*One committee member was recused from discussing or voting on three drug substances because of a conflict of interest. The remaining committee members have disclosed no relevant financial relationships.*

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## Drug Product Compounding Issues Addressed by FDA Panel

Troy Brown, RN | February 24, 2015

The Pharmacy Compounding Advisory Committee of the US Food and Drug Administration (FDA) voted yesterday to add 25 drugs to the list of drug products that may not be compounded under the exemptions provided by the Federal Food, Drug, and Cosmetic Act because they have been withdrawn or removed from the market as a result of their components having been determined to be unsafe or ineffective.

"The agency continually evaluates the safety of drug products, and [the Center for Drug Evaluation and Research's (CDER's)] ongoing commitment to rigorous and continued drug safety evaluation in the postmarket period is reflected in its Safety First initiative, which was launched in 2008 and which outlines CDER's updated policies and procedures to ensure that equal focus and equal attention is given to postmarket drug safety as is given during premarket drug review," said Mwango A. Kashoki, MD, MPH, associate director for Safety, Office of New Drugs, Immediate Office, CDER, FDA.

The committee voted unanimously to add 24 drugs to the list of drugs that may not be compounded: all drug products containing alatrofloxacin mesylate, aminopyrine, astemizole, bromfenac sodium (except ophthalmic solutions), cerivastatin sodium, cisapride, all parenteral drug products containing esmolol HCl that supply 250 mg/mL of concentrated esmolol per 10-mL ampule, gatifloxacin (except ophthalmic solutions), grepafloxacin, methoxyflurane, novobiocin sodium, pemoline, pergolide mesylate, phenylpropanolamine, propoxyphene, rapacuronium bromide, rofecoxib, sibutramine hydrochloride, tegaserod maleate, troglitazone, trovafloxacin mesylate, valdecoxib, all extended-release drug products containing oxycodone hydrochloride that have not been determined by the FDA to have abuse-deterrent properties, all drug products containing polyethylene glycol 3350, sodium chloride, sodium bicarbonate, and potassium chloride for oral solution, and 10 mg or more of bisacodyl delayed-release tablet.

The committee also voted 11 to 1 in favor of adding all drug products containing etretinate to the list.

The committee voted unanimously to update the current entry of "Adenosine phosphate: All drug products containing adenosine phosphate" to state, "All drug products containing adenosine 5'-monophosphate (AMP), adenosine 5'-diphosphate (ADP), and adenosine 5'-triphosphate (ATP)."

The committee voted 9 to 2 (1 no-vote) in favor of adding all oral drug products containing chloramphenicol to the list.

Chloramphenicol for injection is approved by the FDA and is still marketed in the United States. It has a boxed warning because of an increased risk for serious and fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia). Aplastic anemia that later terminated in leukemia has also been attributed to chloramphenicol for injection. Published literature suggests the risk for aplastic anemia is higher with the oral formulation.

Other less toxic and more efficacious antibacterial drugs are available.

### Bulk Drug Substance List

The committee discussed proposed criteria for developing the list of bulk drug substances that may be used to compound drug products according to section 503A of the Federal Food, Drug, and Cosmetic Act, even though they are neither the subject of a US Pharmacopeia or National Formulary monograph nor components of drugs approved by the FDA.

The proposed criteria are:

1. the physical and chemical characterization of the substance;
2. any safety issues raised by the use of the substance in compounded drug products;

3. the historical use of the substance in compounded drug products, including info about the medical condition or conditions the substance has been used to treat and any references in peer-reviewed medical literature; and
4. the available evidence of effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists.

The FDA considers no single criteria to be dispositive.

#### **Thymol Iodide Added to Bulk List**

The committee voted (9 yes, 2 no, 2 no-vote) to place thymol iodide on the list of bulk drug substances that can be used in pharmacy compounding in accordance with section 503A of the FD&C Act ("the 503A bulk list").

Thymol iodide is as an absorbent and protective agent with antimicrobial properties. It is used for topical treatment of ulcerations and various skin infections, as well as dental root filling. Plastic surgeons apply thymol iodide powder after face peeling, and iodized talc is used for pleurodesis in patients with pleural effusions.

There is limited safety information available.

"I think that there is an unusual niche for this and that it's effective," said voting committee member John J. DiGiovanna, MD, staff clinician, DNA Repair Section, Dermatology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

#### **Silver Protein Mild Not Added to Bulk List**

The committee voted unanimously not to place silver protein mild on the 503A bulk list.

Silver protein mild, also known as mild silver protein, is an antiinfective used for ophthalmic purposes. Its most widely known product, *Argyrol* (Argyrol Pharmaceuticals), was first marketed in 1902. There are no formal safety pharmacology studies of silver protein mild in the published literature. Silver protein mild can cause argyrosis, a deposit of silver in the conjunctiva, lacrimal sac, cornea, and lens that results in bluish-black pigmentation. Argyrosis is permanent and usually does not cause visual acuity impairment but can impair night vision.

There are numerous alternative approved products for ophthalmic antiinfective use.

"It didn't meet any of the four criteria [for evaluating nominated substances]," said voting committee member Jürgen Venitz, MD, PhD, committee chairperson and associate professor, Department of Pharmaceutics, School of Pharmacy, Virginia Commonwealth University, Richmond.

*In the committee meeting on the Withdrawn or Removed List, one committee member was recused from discussing and voting on one drug product, another committee member was recused from discussing and voting on three drug products, and another committee member was recused from discussing and voting on one drug product because of conflicts of interest. The remaining committee members disclosed no relevant financial relationships. In the committee meeting on the bulk list, two committee members were recused from discussing and voting on one drug product and one committee member was recused from discussing and voting on one drug product.*

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