# AGENDA

## Florida Board of Pharmacy
## Compounding Committee Meeting
## December 12, 2017 – 8:00 a.m.

Rosen Plaza Hotel * 9700 International Drive
Orlando, FL 32819 * (407)996-9700

**Committee Members:**
Mark Mikhael, PharmD
Jeenu Philip, BPharm

**Board Staff**
C. Erica White, MBA, JD - Executive Director
Irene Lake, Program Operations Administrator

**Board Counsel:**
David Flynn, Assistant Attorney General
Lawrence Harris, Assistant Attorney General

*Note: Participants in this public meeting should be aware that these proceedings are being recorded.*

1. **Rule 64B16-27.1001, F.A.C. – Practice of Pharmacy**
2. **Rules Hearing – Rule 64B16-27.700, F.A.C. – Definition of Compounding**
3. **Old Business**
4. **New Business**
5. **Public Comment**
6. **Adjourn**


# TAB #1

**64B16-27.1001 Practice of Pharmacy.**

Those functions within the definition of the practice of the profession of pharmacy, as defined by Section 465.003(13), F.S., are specifically reserved to a pharmacist or a duly registered pharmacy intern in this state acting under the direct and immediate personal supervision of a pharmacist. The following subjects come solely within the purview of the pharmacist.

(1) A pharmacist or registered pharmacy intern must:

(a) Supervise and be responsible for the controlled substance inventory.

(b) Receive verbal prescriptions from a practitioner.

(c) Interpret and identify prescription contents.

(d) Engage in consultation with a practitioner regarding interpretation of the prescription and date in patient profile.

(e) Engage in professional communication with practitioners, nurses or other health professionals.

(f) Advise or consult with a patient, both as to the prescription and the patient profile record.

(2) When parenteral and bulk solutions of all sizes are prepared, regardless of the route of administration, the pharmacist must:

(a) Interpret and identify all incoming orders.

(b) Mix all extemporaneous compounding or be physically present and give direction to the registered pharmacy technician for reconstitution, for addition of additives, or for bulk compounding of the parenteral solution.

(c) Physically examine, certify to the accuracy of the final preparation, thereby assuming responsibility for the final preparation.

(d) Systemize all records and documentation of processing in such a manner that professional responsibility can be easily traced to a pharmacist.

(3) Only a pharmacist may make the final check of the completed prescription thereby assuming the complete responsibility for its preparation and accuracy.

(4) The pharmacist, as an integral aspect of dispensing, shall be directly and immediately available to the patient or the patient's agent for consultation and shall not dispense to a third party. No prescription shall be deemed to be properly dispensed unless the pharmacist is personally available.

(5) The pharmacist performing in this state any of the acts defined as "the practice of the profession of pharmacy" in Section 465.003(13), F.S., shall be actively licensed as a pharmacist in this state, regardless of whether the practice occurs in a permitted location (facility) or other location.

(6) The pharmacist may take a meal break, not to exceed 30 minutes in length, during which the pharmacy department of a permittee shall not be considered closed, under the following conditions:

(a) The pharmacist shall be considered present and on duty during any such meal break if a sign has been prominently posted in the pharmacy indicating the specific hours of the day during which meal breaks may be taken by the pharmacist and assuring patients that a pharmacist is available on the premises for consultation upon request during a meal break.

(b) The pharmacist shall be considered directly and immediately available to patients during such meal breaks if patients to whom medications are delivered during meal breaks are verbally informed that they may request that a pharmacist contact them at the pharmacist's earliest convenience after the meal break, and if a pharmacist is available on the premises during the meal break for consultation regarding emergency matters. Only prescriptions with the final certification by the pharmacist may be delivered.

(c) The activities of registered pharmacy technicians during such a meal break shall be considered to be under the direct and immediate personal supervision of a pharmacist if the pharmacist is available on the premises during the meal break to respond to questions by the technicians, and if at the end of the meal break the pharmacist certifies all prescriptions prepared by the registered pharmacy technicians during the meal break.

(7) The delegation of any duties, tasks or functions to registered pharmacy interns and registered pharmacy technicians must be performed subject to a continuing review and ultimate supervision of the pharmacist who instigated the specific task, so that a continuity of supervised activity is present between one pharmacist and one registered pharmacy technician. In every pharmacy, the pharmacist shall retain the professional and personal responsibility for any delegated act performed by registered pharmacy interns and registered pharmacy technicians in the licensee's employ or under the licensee's supervision.

*Rulemaking Authority 465.005, 465.0155 FS. Law Implemented 465.003(11)(b), (13), 465.014, 465.026 FS. History–New 11-18-07, Amended 1-1-10.*

JOE NEGRON
President

RICHARD CORCORAN
Speaker

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September 14, 2017

RECEIVED
SEP 15 2017
DEPT. OF LEGAL AFFAIRS
Administrative Law Bureau

Mr. David Flynn
Assistant Attorney General
Department of Legal Affairs
PL-01, The Capitol
Tallahassee, Florida 32399-1050

**Re: Department of Health: Board of Pharmacy**
**Existing Rule 64B16-27.1001, F.A.C.**

Dear Mr. Flynn:

On November 4, 2014, March 5, 2015, June 9, 2015, July 7, 2015, August 4, 2015, and October 13, 2016, I sent you letters regarding the above-referenced existing rule. To date, I have not received a response. A copy of my previous correspondence is attached for your convenience.

Please respond to my letters within the next 15 days to avoid further action by the Joint Administrative Procedures Committee.

Please let me know if you have any questions. Otherwise, I look forward to your response.

Sincerely,

Marjorie C. Holladay

Marjorie C. Holladay
Chief Attorney

Attachment

cc: Mr. Edward A. Tellechea, Chief Assistant Attorney General
✓Mr. Lawrence Harris, Assistant Attorney General

MCH:SA WORD/MARJORIE/EXISTING RULE 64B16-27.1001.091417

PAM BONDI
ATTORNEY GENERAL
STATE OF FLORIDA

OFFICE OF THE ATTORNEY GENERAL
Administrative Law

David D. Flynn
Assistant Attorney General
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September 19, 2017

Marjorie Holladay, Chief Attorney
Joint Administrative Procedures Committee
Room 680, Pepper Building
Tallahassee, FL 32399-1400

**Re: Board of Pharmacy**
**Rule 64B16-27.1001, Fla. Admin. Code.**
**Practice of Pharmacy**

Dear Ms. Holladay:

I want to thank you for your patience and the additional opportunity to provide a more substantive response to your previous inquiries. I have the following response to your most recent correspondence dated September 14, 2017.

Your inquiry is aimed at the provision of the rule that mandates when parenteral and bulk solutions are prepared, the pharmacist must "be physically present and give direction to the registered pharmacy technician for reconstitution, for addition of additives, or for bulk compounding of the parental solution." Fla. Admin. Code R. 64B16.27.1001(2)(Jan. 2010). Please be assured that the rule does not allow the pharmacist to delegate the act of compounding to a pharmacy technician, which would be prohibited by section 465.014(1), *Florida Statutes*. The rule only allows a pharmacy technician to assist in the preparation of the final product. The pharmacist not only has to be physically present to give direction, but also must "[i]nterpret and identify all incoming orders" when any parenteral or bulk solutions are prepared. Id at § (2). Most importantly, the pharmacist shall assume full responsibility for the final product by physically examining and certifying to the products accuracy. Id. at § (2)(c). Finally, a pharmacist must maintain records and documentation of processing so that the responsibility of preparing the drug product can be traced to the responsible pharmacist. Id. at § (2)(d).

Further, rule 64B16-27.420, *Florida Administrative Code* (Jul. 2015), specifically states, "[a] pharmacy technician may only assist a pharmacist in executing or carrying out the practice of the profession of pharmacy, but shall never themselves engage in the practice of the profession of pharmacy as defined in Chapter 465, F.S." Moreover, a pharmacist may only delegate those tasks that are performed pursuant to the pharmacist's direction that does not require the pharmacy technician to exercise their own judgement and discretion and that does not require the technician to "exercise the independent professional judgment that is the foundation of the practice of the profession of pharmacy." Id. at § (1). The Board has made clear that a pharmacy technician may only assist in preparing the drug product. Moreover, when the technician assists in preparing the drug product, the technician may not engage in any of the task listed section (2) of the rule. Id. at §2. I hope you will find that the board has taken great care in drafting and promulgating rules to make certain a pharmacy technician is not practicing in contravention of section 465.014, *Florida Statues*.

As you are aware, the Board has also has been diligently updating all the rules related to sterile compounding and the standards of practice for compounding sterile drugs products. The language utilized in this rule needs to be reviewed and updated to avoid ambiguity. Therefore, this rule, along with your correspondence, will be placed on the Board's agenda for consideration in December. Immediately following the December Board meeting, I will provide you with an update.

Please do not hesitate to contact me directly if you have any further questions or concerns. Again, your review is greatly appreciated.

Sincerely,

David D. Flynn
Assistant Attorney General
Attorney for the Board

cc: C. Erica White, J.D, Executive Director
Ed Tellechea, Bureau Chief
Angela Southwell, Paralegal Specialist

DON GAETZ
President

WILL W. WEATHERFORD
Speaker

THE FLORIDA LEGISLATURE
# JOINT ADMINISTRATIVE PROCEDURES COMMITTEE



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November 4, 2014

Mr. Lawrence Harris
Assistant Attorney General
Department of Legal Affairs
PL-01, The Capitol
Tallahassee, Florida 32399-1050

**Re: Department of Health: Board of Pharmacy**
**Existing Rule 64B16-27.1001, F.A.C.**

Dear Mr. Harris:

In accordance with the Committee's responsibilities pursuant to Joint Rule 4.6 of the Florida Legislature, I have reviewed the above-referenced existing rule, and have the following comments.

**64B16-27.1001(2)(b):** This rule paragraph authorizes a pharmacist to "be physically present and give direction to the registered pharmacy technician for reconstitution, for addition of additive, or for bulk compounding" of a parenteral solution.

"Compounding" is defined in section 465.003(18). "Compounded sterile product" is defined in section 465.003(20), and includes drugs intended for parenteral administration. The practice of the profession of pharmacy expressly includes compounding. *See* § 465.003(13), Fla. Stat. It appears that this rule paragraph may authorize a pharmacist to direct a registered pharmacy technician to complete a task that falls within the statutory definition of the practice of the profession of pharmacy. For example, the pharmacist may be physically present and direct a registered pharmacy technician to prepare compounded parenteral and bulk solutions with a complete list of ingredients, measurements, and

the formula for compounding. It appears such a delegation (and possibly others) would constitute the practice of the profession of pharmacy which is not delegable to a pharmacy technician. A pharmacist may delegate duties, tasks and functions that do not fall within the purview of section 465.003(13) to a registered pharmacy technician. *See* § 465.014(1), Fla. Stat. It appears allowing a pharmacist to give direction to a registered pharmacy technician for bulk compounding of parenteral solutions pursuant to this rule paragraph may impermissibly enlarge upon the provisions of sections 465.003(13) and 465.014(1). *See* § 120.54(8)(c), Fla. Stat.

As always, please let me know if you have any questions. Otherwise, I look forward to your response.

Sincerely,

Marjorie C. Holladay

Marjorie C. Holladay
Chief Attorney

MCH:SA WORD/MARJORIE/EXISTING RULE 64B16_27.1001.110414


# TAB #2

Notice of Change/Withdrawal

**DEPARTMENT OF HEALTH**
**Board of Pharmacy**
RULE NO.: RULE TITLE:
64B16-27.700 Definition of Compounding

NOTICE OF PUBLIC HEARING

The Board of Pharmacy announces a hearing regarding the above rule, as noticed in Vol. 43 No. 161, August 18, 2017 Florida Administrative Register.
DATE AND TIME: Tuesday, December 12, 2017, 8:00 a.m. during the Compounding Committee meeting.
PLACE: Rosen Plaza Hotel, 9700 International Drive, Orlando, Florida 32819
GENERAL SUBJECT MATTER TO BE CONSIDERED: To discuss proposed text of Rule 64B16-27.700, F.A.C.
Pursuant to the provisions of the Americans with Disabilities Act, any person requiring special accommodations to participate in this workshop/meeting is asked to advise the agency at least 7 days before the workshop/meeting by contacting: the Board of Pharmacy at 4052 Bald Cypress Way, Bin C04, Tallahassee, Florida 32399-3254 or at (850)245-4292. If you are hearing or speech impaired, please contact the agency using the Florida Relay Service, 1(800)955-8771 (TDD) or 1(800)955-8770 (Voice).

Notice of Proposed Rule

**DEPARTMENT OF HEALTH**
**Board of Pharmacy**
RULE NO.: RULE TITLE:
64B16-27.700 Definition of Compounding
PURPOSE AND EFFECT: The Board proposes the rule amendment so that the rule does not conflict with state or federal law and to make clear that office use compounding of products intended for human use (sterile and nonsterile) shall require being registered as an Outsourcing Facility as defined by §465.003(19), Fla. Stat. (2016).
SUMMARY: Office use compounding of sterile and nonsterile products for human use shall comply with federal law to include being a registered Outsourcing Facility.
SUMMARY OF STATEMENT OF ESTIMATED REGULATORY COSTS AND LEGISLATIVE RATIFICATION:
The Agency has determined that this will not have an adverse impact on small business or likely increase directly or indirectly regulatory costs in excess of $200,000 in the aggregate within one year after the implementation of the rule. A SERC has not been prepared by the Agency.
The Agency has determined that the proposed rule is not expected to require legislative ratification based on the statement of estimated regulatory costs or if no SERC is required, the information expressly relied upon and described herein: During discussion of the economic impact of this rule at its Board meeting, the Board, based upon the expertise and experience of its members, determined that a Statement of Estimated Regulatory Costs (SERC) was not necessary and that the rule will not require ratification by the Legislature. Specifically, the Board determined that any and all positive or negative economic impacts are a direct result of state and federal law to include, but not limited to, §465.016(1)(e), Fla. Stat. (2016); §465.023(1)(c), Fla. Stat. (2016); 21 U.S.C. §351(a)(2)(b) (2016); 21 U.S.C. §352(f)(1) (2016); 21 U.S.C. §353a (2016); 21 U.S.C. § 353b (Nov. 27, 2013); and 21 U.S.C. §355(a) (2016). The rule amendment does not change the economic status quo. Rather, the amendment adds clarity to what is already required when sterile and nonsterile products for human use are compounded for office or stock use. No person or interested party submitted additional information regarding the economic impact at that time.
Any person who wishes to provide information regarding a statement of estimated regulatory costs, or provide a proposal for a lower cost regulatory alternative must do so in writing within 21 days of this notice.
RULEMAKING AUTHORITY: 465.005 FS.
LAW IMPLEMENTED: 465.003, 465.0155, 465.0265 FS.
IF REQUESTED WITHIN 21 DAYS OF THE DATE OF THIS NOTICE, A HEARING WILL BE SCHEDULED AND ANNOUNCED IN THE FAR.
THE PERSON TO BE CONTACTED REGARDING THE PROPOSED RULE IS: C. Erica White, Executive Director, Board of Pharmacy, 4052 Bald Cypress Way, Bin C04, Tallahassee, Florida 32399-3254

THE FULL TEXT OF THE PROPOSED RULE IS:

64B16-27.700 Definition of Compounding.
"Compounding" is the professional act by a pharmacist or other practitioner authorized by law, employing the science or art of any branch of the profession of pharmacy, incorporating ingredients to create a finished product for dispensing to a patient or for administration by a practitioner or the practitioner's agent; and shall specifically include the professional act of preparing a unique finished product containing any ingredient or device defined by Sections 465.003(7) and (8), F.S. The term also includes the preparation of nuclear pharmaceuticals and diagnostic kits incident to use of such nuclear pharmaceuticals. The term "commercially available products," as used in this section, means any medicinal product as defined by Sections 465.003(7) and (8), F.S., that are legally distributed in the State of Florida by a drug manufacturer or wholesaler.

(1) through (2) No change.

(3) Office use compounding, "Office use" means the provision and administration of a compounded drug to a patient by a practitioner in the practitioner's office or by the practitioner in a health care facility or treatment setting, including a hospital, ambulatory surgical center, or pharmacy. A pharmacist may dispense and deliver a quantity of a compounded drug to a practitioner for office use by the practitioner in accordance with this section provided:

(a) through (f) No change.

(g) In the case of compounded ~~sterile~~ products intended for human use, the pharmacy must be in full compliance with 21 U.S.C. § 353b, including being registered as an Outsourcing Facility. 21 U.S.C. § 353b (eff. Nov. 27, 2013) is hereby adopted and incorporated by reference and available at http://www.flrules.org/Gateway/reference.asp?No=Ref-04180.

Rulemaking Authority 465.005 FS. Law Implemented 465.003, 465.0155, 465.0265 FS. History–New 10-1-92, Formerly 21S-27.700, 61F10-27.700, 59X-27.700, Amended 11-2-03, 10-7-08, 3-21-13, 6-22-14, _____.

NAME OF PERSON ORIGINATING PROPOSED RULE: Board of Pharmacy
NAME OF AGENCY HEAD WHO APPROVED THE PROPOSED RULE: Board of Pharmacy
DATE PROPOSED RULE APPROVED BY AGENCY HEAD: June 6, 2017
DATE NOTICE OF PROPOSED RULE DEVELOPMENT PUBLISHED IN FAR: July 21, 2017

**DON GAETZ**
**President**

**WILL W. WEATHERFORD**
**Speaker**

**THE FLORIDA LEGISLATURE**

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May 20, 2014

Mr. David Flynn
Assistant Attorney General
Department of Legal Affairs
PL-01, The Capitol
Tallahassee, Florida 32399-1050

**Re: Department of Health: Board of Pharmacy**
**Rule 64B16-27.700, F.A.C.**

Dear Mr. Flynn:

I have reviewed proposed rule 64B16-27.700, "Definition of Compounding," which was advertised in the Florida Administrative Register on May 2, 2014. I have the following comments.

**64B16-27.700(3)(a)-(f):** It appears that these paragraphs authorize a compounding pharmacy to prepare compounded drug(s) for office use, without the name of an identifiable patient. Notwithstanding the board's letter of February 21, 2013 ("board's letter"), these rule paragraphs appear to be contrary to state and federal law, which the board is charged with enforcing, and which chapter 465 licensees are charged with following. For example, section 465.003(8) defines "medicinal drugs" or "drugs" to mean "'prescription' or 'legend' drugs which are required by federal or state law to be dispensed only on a prescription, but shall not include patents or proprietary preparations." Section 465.003(9) defines "patent or proprietary preparation" to mean "a medicine in its unbroken, original package which is sold to the public by, or under the authority of, the manufacturer or primary distributor thereof and which is not misbranded under the provisions of the Florida Drug and Cosmetic Act [chapter 499, Florida Statutes]." Section 465.016(1)(e) provides grounds for denial of a license or disciplinary action against chapter

465 licensees for violating chapters 499 or 893, Florida Statutes, or the Federal Food, Drug and Cosmetic Act (including 21 U.S.C. section 353a, discussed *infra*), or the Federal Comprehensive Drug Abuse Prevention and Control Act. Similarly, section 465.023(1)(c) provides grounds for the revocation or suspension or other disciplinary action against a pharmacy permittee, or any affiliated person, partner, officer, director or agent of the permittee for violating any requirements of chapters 465, 499, or 893, Florida Statutes, the Federal Food, Drug, and Cosmetic Act, or the Federal Comprehensive Drug Abuse Prevention and Control Act. Section 465.022(11)(a) requires the prescription department manager of a permittee to maintain drug records required "by any state or federal law to be obtained by a pharmacy," including chapters 465, 499, or 893, Florida Statutes, and requires the prescription department manager to ensure compliance with "all rules adopted under those chapters as they relate to the practice of the profession of pharmacy and the sale of prescription drugs." Section 465.026(6) authorizes the "transfer of a prescription for medicinal drugs listed in Schedules III, IV, and V appearing in chapter 893 for the purpose of refill dispensing," subject to the requirements of federal law. Thus, it appears that chapter 465 is replete with requirements that its licensees abide by the requirements of other state statutes, as well as federal law.

Moreover, any standards of practice adopted by the board must be consistent with the provisions of chapter 465:

> *Consistent with the provisions of this act*, the board shall adopt by rule standards of practice relating to the practice of pharmacy which shall be binding on every state agency and shall be applied by such agencies when enforcing or implementing any authority granted by any applicable statute, rule, or regulation, whether federal or state.

§ 465.0155, Fla. Stat. (Emphasis added). If a rule and statute conflict, the statute controls. *See One Beacon Ins. v. Agency for Health Care Admin.*, 958 So. 2d 1127, 1129 (Fla. 1st DCA 2007) ("In cases of conflict, a statute takes precedence over an administrative rule."). It appears that these rule paragraphs may be inconsistent with, and may conflict with, provisions of chapter 465, and other applicable Florida and federal laws.

Florida Law

The word "dispense" is defined in section 465.003(6), Florida Statutes, and means, "the transfer of possession of one or more doses of a

medical drug by a *pharmacist to the ultimate consumer or her or his agent*." (Emphasis added). *See also* § 465.003(1), Fla. Stat. (defining "administration" as "the obtaining and giving of a single dose of medicinal drugs by a legally authorized person *to a patient for her or his consumption*.") (emphasis added). These rule paragraphs appear to authorize a pharmacist to provide compounded drug(s) to the practitioner, who will administer the compounded drug(s) to patient(s). Although the board's letter indicated that it interprets the words "agent" and "consumer" in the definition of "dispense" as including the patient's health care provider, such an interpretation appears to conflict with the plain intent of the statute when read *in pari materia* with chapter 465. *See Fla. Dep't of State, Div. of Elections v. Martin*, 916 So. 2d 763, 768 (Fla. 2005) ("The doctrine of *in pari materia* is a principle of statutory construction that requires that statutes relating to the same subject or object be construed together to harmonize the statutes and to give effect to the Legislature's intent.").

Further, it is appropriate to consult a dictionary to ascertain the range of possible interpretations of words not defined in the statute. *See Debary Real Estate Holdings, LLC v. Dep't of Bus. and Prof. Reg., Div. of Pari-mutuel Wagering*, 112 So. 3d 157, 166 (Fla. 1st DCA 2013) (utilizing the dictionary to determine the plain meaning of the statute when considering the agency's interpretation). "Agent" is defined as "[o]ne who is authorized to act for or in place of another; a representative." *Black's Law Dictionary* 64 (7th ed. 1999). "Ultimate" is defined as "completed, last, final," and "consumer" is defined as "one that consumes." *Webster's Third New International Dictionary (Unabridged)* 490, 2479 (1976). Consumer is also defined as "[a] person who buys goods or services for personal, family or household use, with no intention of resale; a natural person who uses products for personal rather than business purposes." *Black's* at 311.

Accordingly, it appears that the "ultimate consumer" is the intended patient. It does not appear there can be an agent for the ultimate consumer if the consumer is not identified at the time the drug is compounded. *See Fla. State Oriental Med. Ass'n, Inc. v. Slepin*, 971 So. 2d 141 (Fla. 1st DCA 2007) (providing a discussion of the elements of actual and apparent authority necessary to create an agency relationship). As the court in *Randol Mill Pharmacy v. Miller*, 413 S.W.3d 844, 849-51 (Tex. App. 2013), *petition for review filed*, No. 13-1014 (Tex. Dec. 20, 2013), concluded, when a pharmacy provided a compounded drug pursuant to a "bulk phone order" for a physician's office use, and not for any specific person, individual, or identifiable patient, the physician was not the

"agent" of some yet to be determined user of the compounded drug. Also, the physician who ordered the drug for office use could not be the ultimate user of the drug because he did not obtain the compounded drug to use on himself.

It appears that these rule paragraphs, which specifically authorize a pharmacist to "dispense and deliver a quantity of a compounded drug to a practitioner for office use by the practitioner," enlarge and modify the provisions of sections 456.003 and 456.0155, and are therefore an invalid exercise of delegated legislative authority. *See* § 120.52(8)(c), Fla. Stat.

The statutory definition of "dispensing" also mandates that, as an element of dispensing:

> [T]he pharmacist *shall*, prior to the actual physical transfer, interpret and assess the prescription order for potential adverse reactions, interactions, and dosage regimen she or he deems appropriate in the exercise of her or his professional judgment, and the pharmacist shall certify that the medicinal drug called for by the prescription is ready for transfer. The pharmacist *shall* also provide counseling on proper drug usage, either orally or in writing, if in the exercise of her or his professional judgment counseling is necessary.

§ 465.003(6), Fla. Stat. (Emphasis added).

Without requiring a prescription for an identified patient for whom the drug is compounded, it appears that the board may be authorizing a pharmacist to abdicate the exercise of her or his professional judgment. This appears to impermissibly modify the pharmacist's duties prescribed by section 465.003(6). *See* § 120.52(8)(c), Fla. Stat.

Further, it appears that rule paragraphs (3)(a), (b), (c), (d), (e), and (f) contravene provisions of chapters 465 and 499, Florida Statutes. Paragraphs (3)(a), (b), and (c) authorize a pharmacist to deliver compounded drugs to a practitioner for office use provided:

> (a) The quantity of compounded drug does not exceed the amount a practitioner anticipates may be used in the practitioner's office before the expiration date of the drug;

> (b) The quantity of compounded drug is reasonable considering the intended use of the compounded drug and the nature of the practitioner's practice;
>
> (c) The quantity of compounded drug for any practitioner and all practitioners as a whole, is not greater than an amount the pharmacy is capable of compounding in compliance with pharmaceutical standards for identity, strength, quality, and purity of the compounded drug that are consistent with United States Pharmacopoeia guidelines and accreditation practices.

Rule paragraph (3)(d) requires the pharmacy and practitioner to enter into a written agreement and specifies what must be contained in the agreement. Rule paragraph (3)(e) states the records that must be maintained of all compounded drugs ordered by practitioners for office use. Paragraph (3)(f) contains certain labeling requirements for any compounded drug provided for office use, and does not require the name of the patient who will ultimately consume the product. None of these paragraphs requires the name of an identifiable patient to be provided to the compounding pharmacist.

If a compounded drug is ordered for office use without providing the pharmacist with the name of an identifiable patient, there does not appear to be a valid agency relationship between the ultimate consumer (the patient) and the practitioner for whom the compounded drug was prepared by the pharmacist. As stated in *Randol Mill Pharmacy*, if a drug was not compounded and prescribed for any particular person, pharmacy employees could not be compounding the drug for any particular person, and the ordering practitioner "cannot be the 'agent' of some yet be determined user." *Randol Mill Pharmacy*, 413 S.W.3d at 851.

Section 465.015(2)(c) provides, "[i]t is unlawful for any person: . . . [t]o sell or dispense drugs as defined in s. 465.003(8) without first being furnished with a prescription." Section 465.023(1)(h) further provides that:

> (1) The department [of health] or the board may revoke or suspend the permit of any pharmacy permittee, and may fine, place on probation, or otherwise discipline any pharmacy permittee if the permittee, or any affiliated person, partner, officer,

> director, or agent of the permittee, including a person fingerprinted under s. 465.022(3), has:
>
> * * *
>
> (h) Dispensed any medicinal drug based upon a communication that purports to be a prescription as defined by s. 465.003(14) or s. 893.02 when the *pharmacist knows or has reason to believe that the purported prescription is not based upon a valid practitioner-patient relationship that includes a documented patient evaluation, including history and a physical examination adequate to establish the diagnosis for which any drug is prescribed* and any other requirement established by board rule under chapter 458, chapter 459, chapter 461, chapter 463, chapter 464, or chapter 466.

(Emphasis added). *See also* Fla. Admin. Code R. 64B16-30.001(2)(e)1.f.(I) and (II) (providing disciplinary guidelines of a $1,500 fine to possible revocation upon licensees and permittees for violating section 465.015(2)(c), Fla. Stat.).

Instead of dispensing the drug to the ultimate consumer or her or his agent, it appears the pharmacy selling and delivering a compounded drug to the practitioner for office use is distributing the drug to a person other than the consumer or the consumer's agent. The selling of compounded prescription drugs to a practitioner for office use appears to constitute the wholesale distribution of a prescription drug. *See* § 499.003(54), Fla. Stat. It appears that a pharmacy selling compounded prescription drugs for administration to patients may be a wholesale distributor, which is defined in section 499.003(55) as:

> [A]ny person engaged in wholesale distribution of prescription drugs *in or into* this state, including, but not limited to, manufacturers; repackagers; own-label distributors; jobbers; private-label distributors; brokers; warehouses, including manufacturers' and distributors' warehouses, chain drug warehouses, and wholesale drug warehouses; independent wholesale drug traders; exporters; *retail pharmacies*; and the agents thereof that conduct wholesale distributions.

(Emphasis added). *See also* § 499.01(1)(d) and (2)(d), Fla. Stat. Generally, "wholesale distribution" is defined in section

499.003(54) as the "distribution of prescription drugs to persons other than a consumer or patient."

The term "distribution" is defined in section 499.003(17) as follows:

> "Distribute" or "distribution" means to sell; offer to sell; give away; transfer, whether by passage of title, physical movement, or both; deliver; or offer to deliver. The term does not mean to administer or dispense and does not include the billing and invoicing activities that commonly follow a wholesale distribution transaction.

It does not appear that the exception to the definition of "wholesale distribution" contained in section 499.003(54)(e) for the "lawful dispensing of a prescription drug in accordance with chapter 465" applies to this rule, because, as previously discussed, these rule paragraphs do not provide for the lawful dispensing of compounded drugs to the ultimate consumer or to her or his agent. *See* § 465.003(6), Fla. Stat. *Cf. Randol Mill Pharmacy.*

Notwithstanding the board's letter, the legislature did not define "wholesale distribution" as the "production in mass for the transfer of goods to a retailer." *See State v. Bodden*, 877 So. 2d 680, 685 (Fla. 2004) ("'The legislature is presumed to know the meaning of words and the rules of grammar, and the only way the court is advised of what the legislature intends is by giving the generally accepted construction, not only to the phraseology of an act, but to the manner in which it is punctuated.'") (quoting *Florida State Racing Comm'n v. Bourquardez*, 42 So. 2d 87, 88 (Fla. 1949).

Therefore, it appears that pharmacies selling compounded drugs for office use which are not prepared pursuant to a specific patient prescription must obtain a prescription drug wholesale distributor permit from the Department of Business and Professional Regulation, pursuant to sections 499.01(1)(d) and (2)(d) and rule 61N-1.015(7)(e), Florida Administrative Code. Alternatively, it appears that these pharmacies could obtain a retail pharmacy drug wholesale distributor permit pursuant to sections 499.01(1)(f) and (2)(f), and rule 61N-1.015(7)(f), Florida Administrative Code, which would authorize transfers between a retail pharmacy and a health care practitioner licensed in this state and authorized by law to dispense or prescribe prescription drugs. *See* § 499.01(2)(f)4., Fla. Stat.

Please explain how this rule authorizing a pharmacy to provide a non-patient specific compounded drug to a practitioner without the appropriate permit is not an invalid exercise of delegated legislative authority because it enlarges, modifies, and contravenes chapters 465 and 499, and exceeds the board's rulemaking authority. *See* § 120.52(8)(b) and (c), Fla. Stat.

Unless the pharmacy that is compounding drugs for office use (without the name of an identified patient) obtains the appropriate permit, it appears it is unlawful for a practitioner to administer compounded drugs that are not prepared for an identifiable patient or pursuant to a valid patient prescription. Section 499.005 states in part:

> It is unlawful for a person to perform or cause the performance of any of the following acts in this state:
>
> * * *
>
> (4) The sale, distribution, purchase, trade, holding, or offering of any drug, device, or cosmetic in violation of this part.
>
> * * *
>
> (14) The purchase or receipt of a prescription drug from a person that is not authorized under this chapter to distribute prescription drugs to that purchaser or recipient.
>
> (15) The sale or transfer of a prescription drug to a person that is not authorized under the law of the jurisdiction in which the person receives the drug to purchase or possess prescription drugs from the person selling or transferring the prescription drug.
>
> * * *
>
> (22) Failure to obtain a permit or registration, or operating without a valid permit when a permit or registration is required by this part for that activity.

Additionally, section 499.005 provides that it is unlawful for a person to perform or cause the following acts in this state:

> (2) The adulteration or misbranding of any drug, device, or cosmetic.
>
> (3) The receipt of any drug, device, or cosmetic that is adulterated or misbranded, and the delivery or proffered delivery of such drug, device, or cosmetic, for pay or otherwise.

A prescription drug is considered adulterated, if, among other reasons, it "has been purchased, held, sold, or distributed at any time by a person not authorized under federal or state law to do so." *See* § 499.006(10), Fla. Stat. *Cf.* § 499.0051(12)(a), Fla. Stat. (stating any person who sells, delivers, or holds or offers for sale any drug that is adulterated or misbranded commits a misdemeanor).

Please explain how a pharmacy providing a compounded drug for office use without the name of an identified patient pursuant to the provisions of these rule paragraphs is not providing adulterated or misbranded drugs to be administered by the practitioner in violation of Florida law.

Federal Law

It not only appears that there is no statutory authority for paragraphs (3)(a)-(f), it appears that these rule paragraphs may be preempted and expressly prohibited by federal law. *See Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 372 (2000).

The board is amending this rule to add paragraph (3)(g), which provides:

> In the case of compounded sterile products intended for human use, the pharmacy must be in full compliance with 21 U.S.C. § 353b, including being registered as an Outsourcing Facility. 21 U.S.C. § 353b (eff. Nov. 27, 2013) is hereby adopted and incorporated by reference.

With this rule amendment, it appears that the board acknowledges that the Food, Drug, and Cosmetic Act (FDCA), as amended by the Drug Quality and Security Act (DQSA), Pub L. No. 113-54, governs human drug compounding in the United States. The DQSA, among other things, removed the advertising provisions in 21 U.S.C. section 353a(c) of the FDCA, which were held to be unconstitutional in *Thompson v. W. States Med. Ctr.*, 535 U.S. 357 (2002). As such, any ambiguity pertaining to the validity of section 353a has been removed.

As the Supreme Court explained in *Thompson*, 21 U.S.C. section 353a:

> [E]xempts compounded drugs from the FDCA's "new drug" requirements and other requirements provided the drugs satisfy a number of restrictions. First, they must be compounded by a licensed pharmacist or physician *in response to a valid prescription for an identified individual patient*, or, *if prepared before the receipt of such a prescription, they must be made only in "limited quantities" and in response to a history of the licensed pharmacist's or physician's receipt of valid prescription orders for that drug product within an established relationship between the pharmacist, the patient, and the prescriber*. . . . Fifth, in States that have not entered into a "memorandum of understanding" with the FDA addressing the distribution of "inordinate amounts" of compounded drugs in interstate commerce, *the pharmacy, pharmacist, or physician compounding the drug may not distribute compounded drugs out of State in quantities exceeding five percent of that entity's total prescription orders*.

*Id.* at 364 (emphasis added) (citations omitted). It appears that rule paragraphs (3)(a), (b), and (c) are contrary to federal law, not only because they authorize "office use compounding" for patients who are not identified, but also because the quantities authorized therein appear to exceed the quantities authorized by 21 U.S.C. section 353a. Please explain.

If pharmacies compounding for office use are not provided with the name of an identified patient for whom the drug is compounded, please explain how the board can comply with the requirements of 21 U.S.C. section 353a-1. requiring the Secretary of Health and Human Services to receive submissions from State boards of pharmacy expressing concerns that a compounding pharmacy may be acting contrary to 21 U.S.C. section 353a.

It does not appear that these rule paragraphs provide any prohibition against providing these compounded drugs for office use in interstate commerce. Please explain how pharmacies that compound drugs for office use for unidentified patients pursuant to paragraphs (3)(a) through (f) comply with section 499.023, which states:

> A person may not sell, offer for sale, hold for sale, manufacture, repackage, distribute, or give away any new drug unless an approved application has become effective under s. 505 of the federal act [21 U.S.C. section 355] or unless otherwise permitted by the Secretary of the United States Department of Health and Human Services for shipment in interstate commerce.

21 U.S.C. section 355(a) provides that, "No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug." *See also Thompson*, 535 U.S. at 364 (summarizing the 1997 amendments to the FDCA, exempting compounded drugs from the FDCA's "new drug" requirements if certain restrictions, discussed *supra*, are met).

Please explain why this rule does not violate the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. sections 301-392. *See* Fla. Admin. Code R. 64B16-30.001(2)(e)5. (providing disciplinary guidelines of a $2,500 fine to possible revocation for violating 21 U.S.C. sections 301-392).

<u>CS/HB 7077, effective October 1, 2014</u>
Please note CS/HB 7077 passed in the 2014 legislative session. This bill, if it becomes law, may further affect the validity of this rule. For example, it appears that the definition of "compounding" in the unnumbered introductory paragraph differs from the definition of "compounding" which is contained in section 1 of this bill. If the bill becomes law, please revise this rule to comport with its provisions by October 1, 2014.

As always, please let me know if you have any questions. Otherwise, I look forward to your response.

Sincerely,

Marjorie C. Holladay
Chief Attorney

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# Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

## Guidance for Industry

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**
**Office of Compliance/OUDLC**

**December 2016**
**Compounding and Related Documents**

# Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

## Guidance for Industry

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**U.S. Department of Health and Human Services**
**Food and Drug Administration**
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*Contains Nonbinding Recommendations*

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*Contains Nonbinding Recommendations*

# Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

## Guidance for Industry[1]

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

## I. INTRODUCTION AND SCOPE

This guidance sets forth the FDA's policy concerning certain prescription requirements for compounding human drug products[2] for identified individual patients under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act or Act). It addresses compounding after the receipt of a prescription for an identified individual patient, compounding before the receipt of a prescription for an identified individual patient (anticipatory compounding), and compounding for office use (or office stock).

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

[1] This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research (CDER), in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

[2] This guidance does not apply to drugs compounded for use in animals, to biological products subject to licensure in a biologics license application, or to repackaged drug products. For proposed policies pertaining to compounding drug products from bulk drug substances for use in animals, see FDA's draft guidance, *Compounding Animal Drugs from Bulk Drug Substances*. For proposed policies pertaining to mixing, diluting, and repackaging biological products, see FDA's draft guidance, *Mixing, Diluting, and Repackaging Biological Products Outside the Scope of an Approved Biologics License Application*. For proposed policies pertaining to repackaged drug products, see FDA's draft guidance, *Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities*. FDA guidances are available on the FDA website at http://www fda.gov/RegulatoryInformation/Guidances/default htm.

## II. BACKGROUND

### A. Overview

1. Compounding Under the FD&C Act

Sections 503A and 503B of the FD&C Act address human drug compounding.

Section 503A, added to the FD&C Act by the Food and Drug Administration Modernization Act in 1997, describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility, or by a licensed physician, to be exempt from the following three sections of the FD&C Act:

- section 501(a)(2)(B) (concerning current good manufacturing practice (CGMP) requirements);
- section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and
- section 505 (concerning the approval of drugs under new drug applications (NDAs) or abbreviated new drug applications (ANDAs)).

A list of the conditions that must be met for a compounded drug product to qualify for the exemptions in section 503A of the FD&C Act appears in the guidance, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*.

New section 503B, added to the FD&C Act by the Drug Quality and Security Act in 2013, created a new category of compounders called *outsourcing facilities*. Section 503B of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by or under the direct supervision of a licensed pharmacist in an outsourcing facility to qualify for exemptions from three sections of the FD&C Act:

- section 502(f)(1);
- section 505; and
- section 582 (concerning drug supply chain security requirements).

In contrast to drug products compounded under section 503A of the FD&C Act, drug products compounded by outsourcing facilities under section 503B are not exempt from CGMP requirements in section 501(a)(2)(B). Outsourcing facilities are also subject to FDA inspections according to a risk-based schedule, specific adverse event reporting requirements, and other conditions that help to mitigate the risks of the drug products they compound.

The guidance, *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*, lists the conditions that are set forth in section 503B of the FD&C Act.

2. Compounding, Generally

Compounded drug products can serve an important role for patients whose clinical needs cannot be met by an FDA-approved drug product, such as a patient who has an allergy and needs a medication to be made without a certain dye, or an elderly patient or a child who cannot swallow a tablet or capsule and needs a medicine in a liquid dosage form that is not otherwise available, or for appropriate pediatric or weight-based dosing. Drug products for identified individual patients can be compounded consistent with section 503A by licensed pharmacists in State licensed pharmacies and Federal facilities, or by licensed physicians. Drug products can also be compounded by outsourcing facilities under section 503B of the FD&C Act.

In general, when a compounded drug product is clinically necessary for a patient, a prescriber writes a prescription for a compounded drug product, and the patient brings the prescription to a pharmacy, where a licensed pharmacist fills the prescription. In an inpatient setting, such as in a hospital, a prescriber may write an order for a compounded drug product on a patient's health record (e.g., chart). In an office setting, a physician may make an entry or order in a patient's health record that the physician compounded a drug in the office for administration to his or her patient after the patient presents at the physician's office with a clinical need for the compounded drug.

In other cases, based on a history of receiving prescriptions for identified individual patients, in the context of an established relationship with the patient or the practitioner who writes the prescription, a pharmacist may compound a drug product before receipt of a prescription for an identified individual patient in anticipation of receiving such a prescription. The pharmacist then provides the drug product to a patient or a prescriber upon receipt of a prescription. Similarly, based on the amount of the compounded drug that the physician has historically administered or dispensed to his or her patients, a physician may compound a drug product to hold in his or her office in anticipation of patients in his or her practice presenting with a need for the compounded drug,. The physician then administers or dispenses the compounded drug to his or her patients after making an entry in the patients' health records.

Sometimes, it is necessary for health care practitioners in hospitals, clinics, offices, or other settings to have certain compounded drug products on hand that they can administer to a patient who presents with an immediate need for the compounded drug product. For example, if a patient presents at an ophthalmologist's office with a fungal eye infection, timely administration of a compounded antifungal medication may be critical to preventing vision loss. In such a case, the ophthalmologist may need to inject the patient with a compounded drug product immediately, rather than writing a prescription and waiting for the drug product to be compounded and shipped to the prescriber.[3]

In other cases, compounded drug products may need to be administered by a health care practitioner in his or her office because it would not be safe for the patient to take the drug home for self-administration, and it would be more convenient for the physician to have the drug in his

[3] Such compounding would be subject to all of the conditions of section 503A or 503B, including provisions concerning compounding drug products that are essentially copies of commercially available drug products (section 503A(b)(1)(D)) or drug products that are essentially copies of approved drugs (section 503B(a)(5)).

or her office to administer immediately upon diagnosis, rather than asking the physician to order the drug and have the patient return to the health care practitioner for administration.

3. Risks Associated with Compounded Drug Products

Although compounded drugs can serve an important need, they pose a higher risk to patients than FDA-approved drugs. Compounded drug products are not FDA-approved, which means they have not undergone FDA premarket review for safety, effectiveness, and quality. In addition, licensed pharmacists and licensed physicians who compound drug products in accordance with section 503A are not subject to CGMP requirements. Furthermore, FDA does not interact with the vast majority of licensed pharmacists and licensed physicians who compound drug products and seek to qualify for the exemptions under section 503A of the FD&C Act for the drug products they compound (see section 3, below) because these compounders are not licensed by FDA and generally do not register their compounding facilities with FDA. Therefore, FDA is often not aware of potential problems with their compounded drug products or compounding practices unless it receives a complaint such as a report of a serious adverse event or visible contamination.

In 2012, contaminated injectable drug products that a compounding pharmacy shipped to patients and health care practitioners across the country caused a fungal meningitis outbreak that resulted in more than 60 deaths and 750 cases of infection.[4] This was the most serious of a long history of outbreaks associated with contaminated compounded drugs. Since the 2012 fungal meningitis outbreak, FDA has investigated numerous other outbreaks and other serious adverse events, including deaths, associated with compounded drugs that were contaminated or otherwise compounded improperly. For example, patients have been hospitalized after receiving compounded non-sterile drugs that were hundreds or even thousands of times their labeled strength.[5]

FDA has also identified many pharmacies that compounded drug products under insanitary conditions whereby the drug products may have been contaminated with filth or rendered injurious to health, and that shipped, sometimes in large amounts, the compounded drug products made under these conditions to patients and health care providers across the country.[6] The longer a compounded sterile drug product that has been contaminated is held by a pharmacist or physician before distribution,[7] or held in inventory in a health care facility before administration, the greater the likelihood of microbial proliferation and increased patient harm. Because of these and other risks, the FD&C Act places conditions on compounding that must be met for compounded drugs to qualify for the exemptions in section 503A. These conditions include:

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[4] See http://www.cdc.gov/HAI/outbreaks/meningitis.html.

[5] See, for example, http://www fda.gov/Drugs/DrugSafety/ucm474552 htm

[6] See FDA actions, including warning letters and injunctions, related to insanitary conditions at compounding facilities, on FDA's website at http://www fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339771 htm

[7] *Distribution* means that the compounded drug has left the facility in which it was compounded. As used in this guidance, *distribution* includes dispensing a drug directly to a patient.

- compounding is for an identified individual patient,
- drugs compounded in advance of receiving prescriptions are compounded only in limited quantities, and
- drugs are distributed pursuant to a valid patient-specific prescription.

These conditions are meant to help ensure that compounding under section 503A is based on individual patient needs, and that entities purportedly operating under section 503A are not actually operating as conventional manufacturers.

### B. The Prescription Requirement in Section 503A(a) of the FD&C Act

A compounded drug product may be eligible for the exemptions under section 503A of the FD&C Act only if it is, among other things, "compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." To qualify for the exemptions under section 503A, the drug product must also be compounded by a licensed pharmacist in a State licensed pharmacy or a Federal facility, or by a licensed physician (section 503A(a)).

Section 503A(a) describes two situations in which a drug product can be compounded: (1) based on the receipt of a valid prescription order for an identified individual patient (section 503A(a)(1)); or (2) in limited quantities before the receipt of a valid prescription order for an identified individual patient (section 503A(a)(2)). As discussed further in section III.C of this guidance document, section 503A does not provide for distributing a compounded drug product before receiving a valid prescription order for an identified individual patient.

The *prescription requirement* under section 503A is a critical mechanism to distinguish compounding by a licensed pharmacist or licensed physician from conventional manufacturing, and to ensure that drug products compounded under section 503A, which are not FDA-approved, are not subject to the requirement that labeling bear adequate directions for use, and are not subject to CGMP requirements, are provided to a patient only based on individual patient need.

The prescription requirement is also an important factor that distinguishes compounding by a licensed pharmacist in a State licensed pharmacy or a Federal facility, or by a licensed physician under section 503A from compounding by an outsourcing facility under section 503B of the FD&C Act. Section 503B states that an outsourcing facility may or may not obtain prescriptions for identified individual patients (section 503B(d)(4)(C)). Outsourcing facilities, which are subject to CGMP requirements and other important conditions, can compound drug products to fulfill the needs described in section II.A.2 for health care practitioners to have drug products on hand that are not compounded for identified individual patients.

1. Compounding After Receipt of a Valid Prescription Order

As described in section II.A.2, a prescriber may write a prescription for an identified individual patient who needs a compounded drug product. In most cases, either the prescriber or the patient

will then bring or send the prescription to the pharmacy, where the pharmacist will compound the drug product for the patient and provide it to the prescriber or patient according to the prescription. For a patient in an inpatient setting, a prescriber may place an order in the patient's health record (e.g., chart) for a compounded drug product, which will likely be provided by the health care facility pharmacy. In an office setting, a physician may compound a drug after making a notation in the health record of a patient in his practice who presents with a need for the compounded medication. These types of compounding are covered under section 503A(a)(1) of the FD&C Act,[8] which provides for compounding by a licensed pharmacist in a State licensed pharmacy or a Federal facility, or a licensed physician, on the prescription order for an individual patient made by a licensed physician or other licensed practitioner authorized by state law to prescribe drugs.

2. Compounding Before Receipt of a Valid Prescription Order

Sometimes, based on a history of receiving prescriptions for a particular drug product to be compounded for an identified individual patient, and in the context of an established relationship with a particular prescriber or patient, a pharmacist or physician will compound a batch of drugs in anticipation of receiving another patient-specific prescription. The compounder then provides the drugs to a patient or health care provider when a prescription for an identified individual patient is received. This is known as *anticipatory compounding*. Section 503A(a)(2) of the FD&C Act provides for compounding by a licensed pharmacist or licensed physician in "limited quantities before the receipt of a valid prescription order for such individual patient" if:

- The compounding is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the human drug product;

and

- The orders have been generated solely within an established relationship between the licensed pharmacist or licensed physician and either such patient for whom the prescription order will be provided or the physician or other licensed practitioner who will write such prescription order.

Anticipatory compounding can be beneficial because larger batch sizes can increase efficiency and reduce the likelihood of human error that is associated with compounding many small batches of a drug product after the receipt of individual prescriptions for the same drug. However, anticipatory compounding also has risks. For example, if a problem occurs during compounding, such as contaminating a drug product that is supposed to be sterile, or producing subpotent or superpotent sterile or non-sterile drugs, it could affect numerous patients, and not just one. Because drug products compounded in accordance with section 503A are exempt from CGMP requirements, there is an inherently greater chance of a production mistake or

[8] If applicable state and federal requirements are met, outsourcing facilities can also compound drug products pursuant to prescriptions for identified individual patients under section 503B of the FD&C Act. However, that is not the subject of this guidance document.

contamination. Restricting anticipatory compounding to limited quantities serves to limit the number of patients likely to be affected if there are drug product mix-ups or contamination.

The limitations on anticipatory compounding in section 503A (i.e., compounding must be in "limited quantities" and based on an "established relationship") help to protect patients from product quality issues.

These limitations on anticipatory compounding also help to distinguish licensed pharmacists or licensed physicians compounding drug products under section 503A for individual patients from conventional manufacturers, who generally produce larger quantities of drugs that are distributed without a prescription.

The anticipatory compounding limitations also differentiate licensed pharmacists and licensed physicians compounding under section 503A from compounders registered as outsourcing facilities under section 503B of the FD&C Act. As explained above, outsourcing facilities are subject to increased Federal oversight and quality standards, including CGMP requirements, which reduce the risks of quality problems such as production mistakes or contamination. Under section 503B, an outsourcing facility can distribute compounded drug products to health care facilities and health care practitioners without first receiving prescriptions for identified individual patients.

With these principles in mind, FDA sets forth its policy with regard to the prescription requirement in section 503A.

## III. POLICY

### A. Receipt of a Valid Prescription Order or a Notation Approved by the Prescriber Under Section 503A

For purposes of section 503A(a), a *valid prescription order* for a compounded drug product means a valid prescription order from a licensed physician or other licensed practitioner authorized by state law to prescribe drugs (prescriber). It also includes a valid order or notation made by a prescriber in a patient's health record (e.g., chart) in an inpatient setting, and a valid order or notation by a physician who compounds a drug for his or her own patient documented in that patient's health record.[9]

To meet the prescription requirement, a prescription must identify the patient for whom the drug has been prescribed. If the identity of the patient is not given or is not clear, it will not satisfy

[9] Prescription orders that are not valid would not satisfy the prescription requirement in section 503A and cannot serve as the basis for anticipatory compounding. See, in addition, section 301(ccc)(2), which states that, with respect to a drug to be compounded pursuant to section 503A or 503B, the intentional falsification of a prescription, as applicable, is a prohibited act.

this requirement. For example, a prescription would not satisfy the requirement if it is written for the prescriber, when the prescriber is not also the patient.[10]

### B. When a Drug Can Be Compounded Under Section 503A

1. Compounding After Receipt of a Valid Prescription Order

Unless a drug product is compounded in limited quantities before the receipt of a valid prescription order under the conditions described in section 503A(a)(2) of the FD&C Act, which are also described in section III.B.2 of this guidance, to qualify for the exemptions under section 503A, the drug product must be compounded *after* the licensed pharmacist or licensed physician receives a valid prescription order for an individual patient. We understand this to be compounding "on" the receipt of a valid prescription order, as provided in section 503A(a)(1).[11]

2. Compounding Before Receipt of a Valid Prescription Order

If a drug product is not compounded after the receipt of a valid prescription order for an identified individual patient as described in section 503A(a)(1) of the FD&C Act and section III.B.1 of this guidance, the drug product can be compounded under section 503A of the Act by a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient (section 503A(a)(2)(A)), if all of the conditions of section 503A are met, including the following conditions:

- The compounding is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the human drug product; and

- The orders have been generated solely within an established relationship between the licensed pharmacist or licensed physician and either such patient for whom the prescription order will be provided or the prescriber who will write such prescription order[12] (see section 503A(a)(2)(B)).

This means that anticipatory compounding under section 503A is done in limited quantities, based on an expectation that the licensed pharmacist or licensed physician will receive a patient-specific prescription for the particular drug product, written for a patient or by a prescriber with whom the compounder has a relationship.

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[10] In addition, for a notation to serve as a basis for compounding under section 503A, the notation must document the prescriber's determination that a compounded drug is necessary for the identified patient (section 503A(a)). FDA intends to describe its policies regarding this provision in a future policy document.

[11] This includes a physician compounding a drug for his or her own patient after writing a prescription order (e.g., an order written in the patient's chart) for the compounded drug.

[12] When a physician compounds drugs for his or her own patients, FDA considers the "established relationship" provision of section 503A(a)(2) to have been satisfied because the licensed physician and the "prescriber who will write such prescription order" are the same individual.

At this time, as an interim compliance policy, we do not intend to consider whether a compounder has exceeded the limited quantity[13] condition in section 503A(a)(2) if:

- The compounder holds for distribution[14] no more than a 30-day supply of a particular compounded drug product (i.e., units of a compounded drug product that the compounder believes it will distribute over a 30-day period) to fill valid prescriptions it has not yet received; and

- The amount of the supply of a particular compounded product is based on the number of valid prescriptions that the compounder has received for identified individual patients in a 30-day period over the past year that the compounder selected.

Under this policy, if a compounder does not exceed the quantities described above, FDA does not intend to determine whether anticipatory compounding was based on the expectation that the compounder would receive another prescription for the drug product for the same patient or from the same prescriber with whom the compounder has a history. FDA also contemplates that a compounded drug product might be distributed to any patient or prescriber who presents a valid prescription for an identified individual patient for the compounded drug product.[15]

The following examples illustrate FDA's policy on anticipatory compounding under section 503A(a)(2):

- A compounder regularly receives valid prescription orders from a particular prescriber or prescribers, or for a particular patient or patients, for compounded drug X. The highest number of units of drug X for which the compounder has received valid patient-specific prescriptions in a 30-day period in the last year is 500 units. Compounding up to 500 units of drug X in advance of receiving prescriptions for the drug, and holding no more than that amount to fill new valid patient-specific prescriptions as the compounder receives them, would be consistent with this policy.[16]

- A compounder regularly receives valid prescription orders from a particular prescriber or prescribers, or for a particular patient or patients, for compounded drug

[13] The *limited quantities* policy, which relates to the amount of inventory held by the compounder, does not alter the product's BUD. For example, if the BUD for the product is 9 days, the compounder should not produce more units than can be distributed pursuant to valid prescriptions and used within 9 days.

[14] A drug product *for distribution* does not include drug product that is being held pending receipt of the results of release testing such as sterility testing.

[15] For example, in an inpatient setting, the "established relationship" may be between the prescriber who writes an order for a compounded drug product in a patient's health record, and the compounder who produces the drug product.

[16] In this example, it would be consistent with FDA's policy if, after distributing 200 units of drug X pursuant to valid patient-specific prescriptions, the compounder produces up to 200 additional units of drug X so that the total number of units that the compounder is holding for distribution returns to 500 units.

X. As of August 1, 2016, the highest number of units of drug X for which the compounder has received such valid patient-specific prescriptions in a 30-day period between August 1, 2015, and August 1, 2016, is 500 units, which were received between July 1, 2016, and July 30, 2016. Based on this 30-day reference period, the compounder produces 500 units of drug X in advance of receiving prescriptions for the drug, and holds no more than that amount to fill new patient-specific prescriptions as the compounder receives them. However, between July 15, 2016, and August 15, 2016, the compounder receives valid patient-specific prescriptions for 750 units of compounded drug X. Therefore, based on this new reference period, on August 16, 2016, the compounder produces up to 750 units of drug X in advance of receiving prescriptions for the drug, and holds no more than that amount to fill new valid patient-specific prescriptions as the compounder receives them. This would be consistent with FDA's policy on anticipatory compounding.

- A physician who compounds drugs for his or her own patients routinely sees patients who need compounded drug X. The highest number of units of drug X that the physician has dispensed or administered to patients after making a notation in the patients' charts in a 30-day period in the last year is 500 units. Compounding up to 500 units of drug X in advance of making such notations in patients' charts (i.e., before patients present at the physician's office with a need for the compounded drug), and holding no more than that amount to dispense or administer to patients, would be consistent with this policy.

### C. When a Compounded Drug Product Can Be Distributed Under Section 503A

Compounding under section 503A(a) must be "for an identified patient based on the receipt of a valid prescription order" – either "on the receipt of a prescription order for such individual patient" or, under certain conditions, "before the receipt of a valid prescription order for such individual patient." This means that for each drug compounded under section 503A, the compounder must obtain a valid patient-specific prescription order. We therefore understand that the compounder can distribute compounded drugs under section 503A only pursuant to such a valid patient-specific prescription (i.e., the compounder receives a valid patient-specific prescription before the compounded drug product leaves the compounding facility). We recognize that some state boards of pharmacy may authorize the writing of prescriptions that do not include individual patient names. Such prescriptions, however, do not meet the requirement of a patient-specific prescription in section 503A. Under section 503B, outsourcing facilities can fill such prescriptions if they meet the requirements of applicable state and Federal laws.

### D. Compounding Office Stock/ Compounding for Office Use

As discussed in section II.A.2 of this guidance, some compounded drug products are kept as office stock/ for office use by hospitals, clinics, or health care practitioners to administer to patients who present with an immediate need for a compounded drug product. Hospitals, clinics, and health care practitioners can obtain non-patient-specific compounded drug products from

outsourcing facilities registered under section 503B.[17] Outsourcing facilities, which are subject to CGMP requirements, FDA inspections according to a risk-based schedule, specific adverse event reporting requirements, and other conditions that provide greater assurance of the quality of their compounded drug products, may, but need not, obtain prescriptions for identified individual patients prior to distribution of compounded drug products (section 503B(d)(4)(C)).[18] Therefore, outsourcing facilities can compound and distribute sterile and non-sterile[19] non-patient-specific drug products to hospitals, clinics, and health care practitioners for office use.[20]

Section 503A(a)(2) provides a pathway for anticipatory compounding in limited quantities. A licensed pharmacist or licensed physician can compound a drug product in advance of receiving a valid prescription order for an identified individual patient, in accordance with the conditions described in section 503A(a)(2) of the FD&C Act, to have a supply of the drug product ready to provide to a patient or prescriber (or, in the case of a physician, to administer to a patient) when a patient-specific prescription order is presented for the compounded drug product. This can reduce the time it would take for a compounded drug product to be made available to a patient upon receipt of a valid prescription order for that patient.

[17] See also FDA's draft guidance, *Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act*, which, when final, will describe FDA's policies regarding the application of section 503A of the FD&C Act to drug products compounded for use within a hospital or health system.

[18] Although an outsourcing facility may send prescription drugs to health care facilities without obtaining prescriptions for identified individual patients, drugs produced by outsourcing facilities remain subject to the requirements in section 503(b) of the FD&C Act. Therefore, an outsourcing facility cannot dispense a prescription drug to a patient without a prescription.

[19] Section 503B defines *outsourcing facility*, in part, as a facility that is engaged in the compounding of sterile drugs (section 503B(d)(4)(A)(i)). Therefore, an entity that only compounds non-sterile drugs does not meet the definition of *outsourcing facility*. An outsourcing facility may engage in non-sterile compounding provided that it also engages in the compounding of sterile drugs, and provided that it compounds all of its drugs (both sterile and non-sterile) in accordance with the conditions of section 503B.

[20] Distribution of compounded drug products by outsourcing facilities is subject to the limitations described in section 503B(a)(8), among other conditions.

*DNA Pharmacy Services, Inc., dba*
**PALM BEACH COMPOUNDING PHARMACY**
**2151 S. Alternate A1A, Suite 1500**
**Jupiter, Florida 33477**
**Telephone (561) 741-1191**
**Facsimile (561) 741-1193**

**September 2, 2017**



C. Erica White
Executive Director,
Florida Board of Pharmacy
4052 Bald Cypress Way, Bin C04,
Tallahassee, FL 32399-3252

Dear Ms. White,

I am strongly opposed to the proposed rule amendment requiring Office Use Compounding to be performed only by FDA registered Outsourcing Facilities. We are a small pharmacy, 6 employees, and we have been providing office use compounds to approximately 10 doctor offices for years. They like what we compound and don't want to have to go anywhere else for these compounds. They like the quality and customer service we provide or they would not continue to order the specific compounds we make for all these years. This rule change is anti-small business. All the FDA approved outsourcing pharmacies are large businesses, licensed in most or all 50 states.

David "Rick" Upson, RPH
Owner and Pharmacist in Charge
Palm Beach Compounding Pharmacy, Since 2004
rick@palmbeachcompounding.com

THE LAW OFFICES OF
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September 5, 2017

Ms. C. Erica White
Executive Director
Florida Board of Pharmacy
4052 Bald Cypress Way, Bin C04
Tallahassee, FL 32399-3254



Re: Proposed Rule 64B16-27.700

Dear Ms. White:

On behalf of the Florida Medical Association (FMA) Florida Society of Dermatology and Dermatologic Surgery (FSDDS) and Florida Society Of Plastic Surgeons (FSPS), I am requesting a hearing on the proposed changes to the above Rule that were published in the Florida Administrative Register on August 18, 2017.

While my clients fully intend to comply with both 21 U.S.C. 353b and Florida Statute 465.003(19), neither law at this time appears to require such registration for locations that only compound non-sterile products. 21 U.S.C. 353b(d)(4)(A) explicitly states that an "'outsourcing facility'" means a facility at one geographic location or address that is engaged in the compounding of ***sterile*** drugs." (emphasis added). Likewise, FS 465,003(19) defines an "outsourcing facility" as a location "at which sterile compounding of a drug or product is conducted." Copies of both laws are included for your convenience.

As a result, my clients are concerned that the Board may not have the legislative authority to require the registration of locations that only compound non-sterile products.

Thank you in advance for addressing this matter. Should you have any questions, or if I may be of further assistance, please feel free to contact me.

Sincerely,

Christopher L. Nuland

**21 USC 353b: Outsourcing facilities**
Text contains those laws in effect on August 23, 2017

**From Title 21-FOOD AND DRUGS**
CHAPTER 9-FEDERAL FOOD, DRUG, AND COSMETIC ACT
SUBCHAPTER V-DRUGS AND DEVICES
Part A-Drugs and Devices
**Jump To:**
**Source Credit**
**Prior Provisions**

# §353b. Outsourcing facilities

### (a) In general

Sections 352(f)(1), 355, and 360eee–1 of this title shall not apply to a drug compounded by or under the direct supervision of a licensed pharmacist in a facility that elects to register as an outsourcing facility if each of the following conditions is met:

#### (1) Registration and reporting

The drug is compounded in an outsourcing facility that is in compliance with the requirements of subsection (b).

#### (2) Bulk drug substances

The drug is compounded in an outsourcing facility that does not compound using bulk drug substances (as defined in section 207.3(a)(4) of title 21, Code of Federal Regulations (or any successor regulation)), unless-

(A)(i) the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, by-

(I) publishing a notice in the Federal Register proposing bulk drug substances to be included on the list, including the rationale for such proposal;

(II) providing a period of not less than 60 calendar days for comment on the notice; and

(III) publishing a notice in the Federal Register designating bulk drug substances for inclusion on the list; or

(ii) the drug compounded from such bulk drug substance appears on the drug shortage list in effect under section 356e of this title at the time of compounding, distribution, and dispensing;

(B) if an applicable monograph exists under the United States Pharmacopeia, the National Formulary, or another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph, the bulk drug substances each comply with the monograph;

(C) the bulk drug substances are each manufactured by an establishment that is registered under section 360 of this title (including a foreign establishment that is registered under section 360(i) of this title); and

(D) the bulk drug substances are each accompanied by a valid certificate of analysis.

#### (3) Ingredients (other than bulk drug substances)

If any ingredients (other than bulk drug substances) are used in compounding the drug, such ingredients comply with the standards of the applicable United States Pharmacopeia or National Formulary monograph, if such monograph exists, or of another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph if any.

#### (4) Drugs withdrawn or removed because unsafe or not effective

The drug does not appear on a list published by the Secretary of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

#### (5) Essentially a copy of an approved drug

The drug is not essentially a copy of one or more approved drugs.

#### (6) Drugs presenting demonstrable difficulties for compounding

The drug-

(A) is not identified (directly or as part of a category of drugs) on a list published by the Secretary, through the process described in subsection (c), of drugs or categories of drugs that present demonstrable difficulties for compounding that are reasonably likely to lead to an adverse effect on the safety or effectiveness of the drug or category of drugs, taking into account the risks and benefits to patients; or

(B) is compounded in accordance with all applicable conditions identified on the list described in subparagraph (A) as conditions that are necessary to prevent the drug or category of drugs from presenting the demonstrable difficulties described in subparagraph (A).

**(7) Elements to assure safe use**

In the case of a drug that is compounded from a drug that is the subject of a risk evaluation and mitigation strategy approved with elements to assure safe use pursuant to section 355–1 of this title, or from a bulk drug substance that is a component of such drug, the outsourcing facility demonstrates to the Secretary prior to beginning compounding that such facility will utilize controls comparable to the controls applicable under the relevant risk evaluation and mitigation strategy.

**(8) Prohibition on wholesaling**

The drug will not be sold or transferred by an entity other than the outsourcing facility that compounded such drug. This paragraph does not prohibit administration of a drug in a health care setting or dispensing a drug pursuant to a prescription executed in accordance with section 353(b)(1) of this title.

**(9) Fees**

The drug is compounded in an outsourcing facility that has paid all fees owed by such facility pursuant to section 379j–62 of this title.

**(10) Labeling of drugs**

**(A) Label**

The label of the drug includes-

(i) the statement "This is a compounded drug." or a reasonable comparable alternative statement (as specified by the Secretary) that prominently identifies the drug as a compounded drug;

(ii) the name, address, and phone number of the applicable outsourcing facility; and

(iii) with respect to the drug-

(I) the lot or batch number;

(II) the established name of the drug;

(III) the dosage form and strength;

(IV) the statement of quantity or volume, as appropriate;

(V) the date that the drug was compounded;

(VI) the expiration date;

(VII) storage and handling instructions;

(VIII) the National Drug Code number, if available;

(IX) the statement "Not for resale", and, if the drug is dispensed or distributed other than pursuant to a prescription for an individual identified patient, the statement "Office Use Only"; and

(X) subject to subparagraph (B)(i), a list of active and inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

**(B) Container**

The container from which the individual units of the drug are removed for dispensing or for administration (such as a plastic bag containing individual product syringes) shall include-

(i) the information described under subparagraph (A)(iii)(X), if there is not space on the label for such information;

(ii) the following information to facilitate adverse event reporting: www.fda.gov/medwatch and 1–800–FDA–1088 (or any successor Internet Web site or phone number); and

(iii) directions for use, including, as appropriate, dosage and administration.

**(C) Additional information**

The label and labeling of the drug shall include any other information as determined necessary and specified in regulations promulgated by the Secretary.

**(11) Outsourcing facility requirement**

The drug is compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with this section.

**(b) Registration of outsourcing facilities and reporting of drugs**

**(1) Registration of outsourcing facilities**

**(A) Annual registration**

Upon electing and in order to become an outsourcing facility, and during the period beginning on October 1 and ending on December 31 of each year thereafter, a facility-

(i) shall register with the Secretary its name, place of business, and unique facility identifier (which shall conform to the requirements for the unique facility identifier established under section 360 of this title), and a point of contact email address; and

(ii) shall indicate whether the outsourcing facility intends to compound a drug that appears on the list in effect under section 356e of this title during the subsequent calendar year.

**(B) Availability of registration for inspection; list**

**(i) Registrations**

The Secretary shall make available for inspection, to any person so requesting, any registration filed pursuant to this paragraph.

**(ii) List**

The Secretary shall make available on the public Internet Web site of the Food and Drug Administration a list of the name of each facility registered under this subsection as an outsourcing facility, the State in which each such facility is located, whether the facility compounds from bulk drug substances, and whether any such compounding from bulk drug substances is for sterile or nonsterile drugs.

**(2) Drug reporting by outsourcing facilities**

**(A) In general**

Upon initially registering as an outsourcing facility, once during the month of June of each year, and once during the month of December of each year, each outsourcing facility that registers with the Secretary under paragraph (1) shall submit to the Secretary a report-

(i) identifying the drugs compounded by such outsourcing facility during the previous 6-month period; and

(ii) with respect to each drug identified under clause (i), providing the active ingredient, the source of such active ingredient, the National Drug Code number of the source drug or bulk active ingredient, if available, the strength of the active ingredient per unit, the dosage form and route of administration, the package description, the number of individual units produced, and the National Drug Code number of the final product, if assigned.

**(B) Form**

Each report under subparagraph (A) shall be prepared in such form and manner as the Secretary may prescribe by regulation or guidance.

**(C) Confidentiality**

Reports submitted under this paragraph shall be exempt from inspection under paragraph (1)(B)(i), unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health.

**(3) Electronic registration and reporting**

Registrations and drug reporting under this subsection (including the submission of updated information) shall be submitted to the Secretary by electronic means unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting waiver.

**(4) Risk-based inspection frequency**

**(A) In general**

Outsourcing facilities-

(i) shall be subject to inspection pursuant to section 374 of this title; and

(ii) shall not be eligible for the exemption under section 374(a)(2)(A) of this title.

**(B) Risk-based schedule**

The Secretary, acting through one or more officers or employees duly designated by the Secretary, shall inspect outsourcing facilities in accordance with a risk-based schedule established by the Secretary.

**(C) Risk factors**

In establishing the risk-based schedule, the Secretary shall inspect outsourcing facilities according to the known safety risks of such outsourcing facilities, which shall be based on the following factors:

(i) The compliance history of the outsourcing facility.

(ii) The record, history, and nature of recalls linked to the outsourcing facility.

(iii) The inherent risk of the drugs compounded at the outsourcing facility.

(iv) The inspection frequency and history of the outsourcing facility, including whether the outsourcing facility has been inspected pursuant to section 374 of this title within the last 4 years.

(v) Whether the outsourcing facility has registered under this paragraph as an entity that intends to compound a drug that appears on the list in effect under section 356e of this title.

(vi) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources.

**(5) Adverse event reporting**

Outsourcing facilities shall submit adverse event reports to the Secretary in accordance with the content and format requirements established through guidance or regulation under section 310.305 of title 21, Code of Federal Regulations (or any successor regulations).

**(c) Regulations**

**(1) In general**

The Secretary shall implement the list described in subsection (a)(6) through regulations.

**(2) Advisory committee on compounding**

Before issuing regulations to implement subsection (a)(6), the Secretary shall convene and consult an advisory committee on compounding. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopeia, pharmacists with current experience and expertise in compounding, physicians with background and knowledge in compounding, and patient and public health advocacy organizations.

**(3) Interim list**

**(A) In general**

Before the effective date of the regulations finalized to implement subsection (a)(6), the Secretary may designate drugs, categories of drugs, or conditions as described such [1] subsection by-

(i) publishing a notice of such substances, drugs, categories of drugs, or conditions proposed for designation, including the rationale for such designation, in the Federal Register;

(ii) providing a period of not less than 60 calendar days for comment on the notice; and

(iii) publishing a notice in the Federal Register designating such drugs, categories of drugs, or conditions.

**(B) Sunset of notice**

Any notice provided under subparagraph (A) shall not be effective after the earlier of-

(i) the date that is 5 years after November 27, 2013; or

(ii) the effective date of the final regulations issued to implement subsection (a)(6).

**(4) Updates**

The Secretary shall review, and update as necessary, the regulations containing the lists of drugs, categories of drugs, or conditions described in subsection (a)(6) regularly, but not less than once every 4 years. Nothing in the previous sentence prohibits submissions to the Secretary, before or during any 4-year period described in such sentence, requesting updates to such lists.

**(d) [2] Definitions**

In this section:

(1) The term "compounding" includes the combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substance to create a drug.

(2) The term "essentially a copy of an approved drug" means-

(A) a drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section

353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless, in the case of an approved drug, the drug appears on the drug shortage list in effect under section 356e of this title at the time of compounding, distribution, and dispensing; or

(B) a drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

(3) The term "approved drug" means a drug that is approved under section 355 of this title and does not appear on the list described in subsection (a)(4) of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

(4)(A) The term "outsourcing facility" means a facility at one geographic location or address that-

(i) is engaged in the compounding of sterile drugs;

(ii) has elected to register as an outsourcing facility; and

(iii) complies with all of the requirements of this section.

(B) An outsourcing facility is not required to be a licensed pharmacy.

(C) An outsourcing facility may or may not obtain prescriptions for identified individual patients.

(5) The term "sterile drug" means a drug that is intended for parenteral administration, an ophthalmic or oral inhalation drug in aqueous format, or a drug that is required to be sterile under Federal or State law.

**(d) [2] Obligation to pay fees**

Payment of the fee under section 379j–62 of this title, as described in subsection (a)(9), shall not relieve an outsourcing facility that is licensed as a pharmacy in any State that requires pharmacy licensing fees of its obligation to pay such State fees.

(June 25, 1938, ch. 675, §503B, as added Pub. L. 113–54, title I, §102(a)(2), Nov. 27, 2013, 127 Stat. 588 .)

## Prior Provisions

A prior section 503B of act June 25, 1938, ch. 675, was renumbered section 503C by Pub. L. 113–54, §102(a)(1), Nov. 27, 2013, 127 Stat. 587 , and transferred to section 353c of this title.

[1] *So in original.*

[2] *So in original. Two subsecs. (d) have been enacted.*

# The Florida Senate

## 2017 Florida Statutes

| Title XXXII | Chapter 465 | SECTION 003 |
|---|---|---|
| REGULATION OF PROFESSIONS AND OCCUPATIONS | PHARMACY<br><br>Entire Chapter | **Definitions.** |

**465.003 Definitions.**— As used in this chapter, the term:

(1) "Administration" means the obtaining and giving of a single dose of medicinal drugs by a legally authorized person to a patient for her or his consumption.

(2) "Board" means the Board of Pharmacy.

(3) "Consultant pharmacist" means a pharmacist licensed by the department and certified as a consultant pharmacist pursuant to s. 465.0125.

(4) "Data communication device" means an electronic device that receives electronic information from one source and transmits or routes it to another, including, but not limited to, any such bridge, router, switch, or gateway.

(5) "Department" means the Department of Health.

(6) "Dispense" means the transfer of possession of one or more doses of a medicinal drug by a pharmacist to the ultimate consumer or her or his agent. As an element of dispensing, the pharmacist shall, prior to the actual physical transfer, interpret and assess the prescription order for potential adverse reactions, interactions, and dosage regimen she or he deems appropriate in the exercise of her or his professional judgment, and the pharmacist shall certify that the medicinal drug called for by the prescription is ready for transfer. The pharmacist shall also provide counseling on proper drug usage, either orally or in writing, if in the exercise of her or his professional judgment counseling is necessary. The actual sales transaction and delivery of such drug shall not be considered dispensing. The administration shall not be considered dispensing.

(7) "Institutional formulary system" means a method whereby the medical staff evaluates, appraises, and selects those medicinal drugs or proprietary preparations which in the medical staff's clinical judgment are most useful in patient care, and which are available for dispensing by a practicing pharmacist in a Class II institutional pharmacy.

(8) "Medicinal drugs" or "drugs" means those substances or preparations commonly known as "prescription" or "legend" drugs which are required by federal or state law to be dispensed only on a prescription, but shall not include patents or proprietary preparations as hereafter defined.

(9) "Patent or proprietary preparation" means a medicine in its unbroken, original package which is sold to the public by, or under the authority of, the manufacturer or primary distributor thereof and which is not misbranded under the provisions of the Florida Drug and Cosmetic Act.

(10) "Pharmacist" means any person licensed pursuant to this chapter to practice the profession of pharmacy.

(11)(a) "Pharmacy" includes a community pharmacy, an institutional pharmacy, a nuclear pharmacy, a special pharmacy, and an Internet pharmacy.

1. The term "community pharmacy" includes every location where medicinal drugs are compounded, dispensed, stored, or sold or where prescriptions are filled or dispensed on an outpatient basis.

2. The term "institutional pharmacy" includes every location in a hospital, clinic, nursing home, dispensary, sanitarium, extended care facility, or other facility, hereinafter referred to as "health care institutions," where medicinal drugs are compounded, dispensed, stored, or sold.

3. The term "nuclear pharmacy" includes every location where radioactive drugs and chemicals within the

classification of medicinal drugs are compounded, dispensed, stored, or sold. The term "nuclear pharmacy" does not include hospitals licensed under chapter 395 or the nuclear medicine facilities of such hospitals.

4. The term "special pharmacy" includes every location where medicinal drugs are compounded, dispensed, stored, or sold if such locations are not otherwise defined in this subsection.

5. The term "Internet pharmacy" includes locations not otherwise licensed or issued a permit under this chapter, within or outside this state, which use the Internet to communicate with or obtain information from consumers in this state and use such communication or information to fill or refill prescriptions or to dispense, distribute, or otherwise engage in the practice of pharmacy in this state. Any act described in this definition constitutes the practice of pharmacy as defined in subsection (13).

(b) The pharmacy department of any permittee shall be considered closed whenever a Florida licensed pharmacist is not present and on duty. The term "not present and on duty" shall not be construed to prevent a pharmacist from exiting the prescription department for the purposes of consulting or responding to inquiries or providing assistance to patients or customers, attending to personal hygiene needs, or performing any other function for which the pharmacist is responsible, provided that such activities are conducted in a manner consistent with the pharmacist's responsibility to provide pharmacy services.

(12) "Pharmacy intern" means a person who is currently registered in, and attending, a duly accredited college or school of pharmacy, or who is a graduate of such a school or college of pharmacy, and who is duly and properly registered with the department as provided for under its rules.

(13) "Practice of the profession of pharmacy" includes compounding, dispensing, and consulting concerning contents, therapeutic values, and uses of any medicinal drug; consulting concerning therapeutic values and interactions of patent or proprietary preparations, whether pursuant to prescriptions or in the absence and entirely independent of such prescriptions or orders; and other pharmaceutical services. For purposes of this subsection, "other pharmaceutical services" means the monitoring of the patient's drug therapy and assisting the patient in the management of his or her drug therapy, and includes review of the patient's drug therapy and communication with the patient's prescribing health care provider as licensed under chapter 458, chapter 459, chapter 461, or chapter 466, or similar statutory provision in another jurisdiction, or such provider's agent or such other persons as specifically authorized by the patient, regarding the drug therapy. However, nothing in this subsection may be interpreted to permit an alteration of a prescriber's directions, the diagnosis or treatment of any disease, the initiation of any drug therapy, the practice of medicine, or the practice of osteopathic medicine, unless otherwise permitted by law. "Practice of the profession of pharmacy" also includes any other act, service, operation, research, or transaction incidental to, or forming a part of, any of the foregoing acts, requiring, involving, or employing the science or art of any branch of the pharmaceutical profession, study, or training, and shall expressly permit a pharmacist to transmit information from persons authorized to prescribe medicinal drugs to their patients. The practice of the profession of pharmacy also includes the administration of vaccines to adults pursuant to s. 465.189.

(14) "Prescription" includes any order for drugs or medicinal supplies written or transmitted by any means of communication by a duly licensed practitioner authorized by the laws of the state to prescribe such drugs or medicinal supplies and intended to be dispensed by a pharmacist. The term also includes an orally transmitted order by the lawfully designated agent of such practitioner. The term also includes an order written or transmitted by a practitioner licensed to practice in a jurisdiction other than this state, but only if the pharmacist called upon to dispense such order determines, in the exercise of her or his professional judgment, that the order is valid and necessary for the treatment of a chronic or recurrent illness. The term "prescription" also includes a pharmacist's order for a product selected from the formulary created pursuant to s. 465.186. Prescriptions may be retained in written form or the pharmacist may cause

them to be recorded in a data processing system, provided that such order can be produced in printed form upon lawful request.

(15) "Nuclear pharmacist" means a pharmacist licensed by the department and certified as a nuclear pharmacist pursuant to s. 465.0126.

(16) "Centralized prescription filling" means the filling of a prescription by one pharmacy upon request by another pharmacy to fill or refill the prescription. The term includes the performance by one pharmacy for another pharmacy of other pharmacy duties such as drug utilization review, therapeutic drug utilization review, claims adjudication, and the obtaining of refill authorizations.

(17) "Automated pharmacy system" means a mechanical system that delivers prescription drugs received from a Florida licensed pharmacy and maintains related transaction information.

(18) "Compounding" means combining, mixing, or altering the ingredients of one or more drugs or products to create another drug or product.

(19) "Outsourcing facility" means a single physical location registered as an outsourcing facility under the federal Drug Quality and Security Act, Pub. L. No. 113-54, at which sterile compounding of a drug or product is conducted.

(20) "Compounded sterile product" means a drug that is intended for parenteral administration, an ophthalmic or oral inhalation drug in aqueous format, or a drug or product that is required to be sterile under federal or state law or rule, which is produced through compounding, but is not approved by the United States Food and Drug Administration.

**History.**—ss. 1, 7, ch. 79-226; s. 322, ch. 81-259; ss. 14, 15, ch. 81-302; ss. 2, 3, ch. 81-318; ss. 1, 2, ch. 82-179; s. 1, ch. 83-101; s. 36, ch. 83-216; s. 3, ch. 83-265; s. 29, ch. 83-329; s. 1, ch. 85-35; ss. 2, 26, 27, ch. 86-256; s. 1, ch. 88-172; s. 1, ch. 89-77; s. 59, ch. 91-137; s. 6, ch. 91-156; s. 4, ch. 91-429; s. 123, ch. 94-218; s. 239, ch. 97-103; s. 87, ch. 97-264; s. 118, ch. 99-397; s. 1, ch. 2002-182; s. 1, ch. 2004-25; s. 1, ch. 2004-387; s. 2, ch. 2007-152; s. 2, ch. 2012-60; s. 1, ch. 2014-148.

AMERICAN SOCIETY OF PLASTIC SURGEONS ®
THE PLASTIC SURGERY FOUNDATION ®

Executive Office
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847-228-9900 • Fax: 847-228-9131 • www.plasticsurgery.org

September 7, 2017

Department of Health
Board of Pharmacy
4052 Bald Cypress Way
Tallahassee, FL 32399

RE: FL Rule 64B16-27.700, regarding the proposed regulation on nonsterile compounding

Dear Members of the Florida Board of Pharmacy:

On behalf of the American Society of Plastic Surgeons (ASPS), I am writing to urge you to preserve the ability of physician practices to reconstitute medication for in-office patient administration. The proposed changes to Florida Administrative Code, Rule 64B16-27.700, if implemented, will require all prescribers who compound drugs to obtain licensure as an outsourcing facility.

ASPS is the world's largest association of plastic surgeons, with over 7,000 members representing 94 percent of Board-Certified Plastic Surgeons in the United States, including 545 in Florida. Our members are highly skilled surgeons who routinely compound medications in-office.

As you know, in 2012, a national crisis was sparked by an outbreak of fungal meningitis that was linked to contaminated drugs sourced from the New England Compounding Center. These tragic events triggered a national response to ensure that patient safety was better protected in the manufacturing and distribution of compounded pharmaceuticals. The adulterated products entering the supply chain were indeed not caused by practitioners but by a compounding facility. ASPS agrees that it is of the utmost importance that patients receive the safest and most effective treatments, and believes stricter scrutiny of large compounding centers is warranted. However, requiring a practitioner's office to register as an outsourcing facility to merely reconstitute nonsterile remedies for patient administration is an overreach that will unnecessarily increase the cost of and reduce access to care.

Nonsterile compounding is a safe and common practice among physicians. The compounding of topical anesthetics and aesthetic topical skin products, the use of chemical peels such as TCA and others that are mixed immediately prior to application, and the delivery of multiple use sterile medications are all examples of nonsterile applications administered daily in plastic surgery offices.

Florida's goals of fostering a favorable jobs climate and improving its healthcare delivery system are fundamental in the creation of an opportunity economy. Additional fees, licenses, and other regulatory burdens are counterproductive to those goals, and undermine the viability of solo and small practice physicians. This, in turn, will impact patients' ability to access needed care.

In that same vein, ASPS respectfully reminds the Board of Pharmacy that, every day, patients and family members reconstitute medications in the home setting. It is important to ensure that future regulations developed do not restrict ease of administration, limit access, or increase costs of care for patients who manage chronic diseases in their home. Your proposed regulation may do just that.

Lastly, we are concerned that the Board may not even have the statutory authority to impose these requirements on physicians only compounding nonsterile products. 21 U.S.C. § 353b(d)(4)(A)(i) states that an "'outsourcing facility' means a facility at one geographic location or address that is engaged in the compounding of sterile drugs." Similarly, F.S. 465.003(19) defines an outsourcing facility as a "single physical location…at which sterile compounding of a drug or product is conducted."

We do not believe it is the intent of the Florida Board of Pharmacy to limit patient access to needed medication, restrict patients' ability to manage their illnesses at home or to expose itself to litigation by imposing regulations without the legal authority to do so. As such, ASPS respectfully requests that the Board reconsiders the proposed policy during its December meeting.

Thank you for your consideration of ASPS's comments regarding nonsterile pharmaceutical compounding standards. Please do not hesitate to contact Patrick Hermes, Senior Manager of Advocacy and Government Affairs, with any questions phermes@plasticsurgery.org or (847) 228-3331.

Regards,

Debra Johnson, MD
President, American Society of Plastic Surgeons

September 8, 2017

C. Erica White
Executive Director
Florida Board of Pharmacy
4052 Bald Cypress Way, Bin C04
Tallahassee, FL 32399-3254

**Re: 64B16-27.700**

Dear Ms. White,

On behalf of the undersigned organizations, representing approximately 1,200 in Florida and 14,000 dermatologists nationwide, we respectfully request that you reject the Board of Pharmacy ("Board") proposal that would require compounding pharmacies to register and comply with federal law governing Outsourcing Facilities, 21 U.S.C. § 353b, for both sterile and non-sterile compounded products. The proposal results from an inaccurate interpretation of the federal compounding law that was enacted in response to the 2012 New England Compounding Center meningitis outbreak; therefore, we respectfully request that you reject the proposal to ensure that physicians can continue to provide safe and cost-effective care to our patients in the office setting.

The federal 2013 Drug Quality & Security Act ("DQSA") was intended to distinguish traditional compounders that would continue to be regulated by the states from outsourcing facilities that would be regulated by the Food and Drug Administration ("FDA"). Numerous bipartisan statements in the *Congressional Record* during consideration of the DQSA and multiple bipartisan congressional letters submitted to the FDA clearly demonstrate that compounded preparations for office-use remain available after the passage of the DQSA.[1] Further, directives in the House Report accompanying

[1]Senator Isakson (GA), Senator Alexander (TN), Senator Harkin (IA), Senator Warner (VA), Senator Burr (NC), and Senator Boozman (AR). "Drug Quality and Security Act." *Congressional Record* 159: 164 (November 18, 2013) p.S8071. Available from Thomas.gov; Accessed 3/24/2017.

the FY2016 FDA appropriations legislation (House Report 114-2015) conflict with the Board's proposal:

> *Drug Compounding.*--The Committee is concerned that, since passage of the Drug Quality and Security Act (DQSA) of 2013, the FDA has interpreted provisions of Section 503A of the FDCA in a manner inconsistent with its legislative intent and with the agency's own previous positions. Specifically, the FDA has taken the position that under 503A, a pharmacist may not compound medications prior to receipt of a prescription and transfer the drugs to a requesting physician or other authorized agent of the prescriber for administration to his or her patients without a patient-specific prescription accompanying the medication. This practice, which is often referred to as `office-use' compounding, is authorized in the vast majority of states and was intended to be allowable under DQSA. The Committee is aware that in 2012, prior to passage of the DQSA, FDA was working on a draft compliance policy guide for 503A of the FDCA that provided guidance on how `office-use' compounding could be done consistent with the provisions of 503A. ***The Committee understands the intent of the DQSA was not to prohibit compounding pharmacists from operation under existing 503A exemptions; therefore, the Committee directs the FDA to issue a guidance document on how compounding pharmacists can continue to engage in `office-use' compounding before the receipt of a patient-specific prescription consistent with the provisions of 503A within 90 days after the enactment of this Act.*** *(emphasis added).* [2]

The Board's proposal also contradicts FDA's draft Compliance Policy Guide (CPG) it circulated to Congress prior to passage of the DQSA, which recognized office-use as a permissible practice and outlined how compounding pharmacists can engage in office-use compounding prior to receipt of a patient-specific prescription.

Despite all of the examples above, the final Guidance For Industry (GFI) issued by the FDA, "Prescription Requirement under 503A of the Food, Drug and Cosmetic Act", and the proposal under consideration by the Board have misinterpreted congressional intent by prohibiting state-licensed pharmacies from compounding medications for administration to patients in the office setting. This will significantly impact the ability of physicians to provide direct patient care. Outsourcing facilities regulated under 503B will likely not be an adequate source to obtain compounded medications for many of the patients who are treated in physician offices by many of the undersigned medical specialties. The extensive variety of substances that are used by such medical specialties are frequently used in small quantities. This makes it impractical for

[2] See House Agriculture, Rural Development, Food and Drug Administration, and Related Agencies appropriations bill, 2016. Page 67

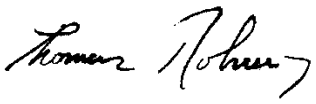
outsourcing facilities to produce, stock and distribute the compounds necessary for our practices.

Our organizations share the goal of providing safe, effective and high quality patient care. We have held many discussions with other medical and pharmaceutical societies, as well as accreditation agencies, and agree that we must work together to prevent the type of compounding tragedies like those that occurred at the New England Compounding Center. Nevertheless, we believe that the proposal will negatively affect patients' access to care and increase the cost of medical care in some clinical arenas.

We appreciate the opportunity to provide these comments. As outlined above, the proposal to restrict office-use compounding contradicts legislative intent to preserve patient access to medications compounded for office-use. Requiring pharmacies to comply with the federal Outsourcing Facilities requirements will impose significant burdens on patients throughout Florida who are seeking medical treatment in a physician office. Patient access to safe and cost-effective medications may no longer be an option if we are forced to obtain such medications from outsourcing facilities regulated under 503B. Should you have any questions, please do not hesitate to contact Lisa Albany, associate director, state policy for the American Academy of Dermatology Association at 202-712-2615 or lalbany@aad.org.

Sincerely,

Henry Lim, MD, FAAD
President
American Academy of Dermatology Association



Thomas E. Rohrer, MD
President
American Society for Dermatologic Surgery Association

cc: Florida Board of Medicine

September 8, 2017

Department of Health
Board of Pharmacy
Pharmacy Practice
R.A. Gray Building
500 South Bronough Street
Tallahassee, FL 32399-0250

**Re: COMMENTS TO RULE NO: 64B16-27.700; RULE TITLE: Definition of Compounding**

Dear Sir or Madam:

Thank you for the opportunity to comment on Rule No: 64B16-27.700; Rule Title: Definition of Compounding which the "Board proposes the rule amendment so that the rule does not conflict with state or federal law and to make clear that office use compounding of products intended for human use (sterile and nonsterile) shall require being registered as an Outsourcing Facility as defined by §465.003(19), Fla. Stat. (2016)." The International Academy of Compounding Pharmacists (IACP) strongly encourages the Board to continue to allow traditional 503A pharmacies to compound for office-use and as stated below, will demonstrate that this has always been Congressional intent under the Drug Quality and Security Act (DQSA).

IACP is a professional association representing more than 4,000 pharmacists, technicians, students, and members of the compounding community who focus on the specialty practice of pharmacy compounding. Compounding pharmacists work directly with prescribers including physicians, nurse practitioners and veterinarians to create customized medication solutions for patients and animals whose health care needs cannot be met by manufactured medications.

We are deeply concerned with the Boards consideration of prohibiting nonsterile and sterile office-use compounding, and strongly disagree with the assertion that this change in policy is necessary to comply with federal law. Congress has been very clear that nothing within the DQSA prohibits office-use compounding and that office-use compounding shall remain regulated by States. Recent implementation actions by the FDA and the information being provided by the Agency to States have caused confusion amongst State boards of medicine and pharmacy and have adversely impacted practitioner and patient access to vital medications.

Many medical professionals and healthcare facilities rely on various types of compounded medications to treat their patients -- whether it is in their office, on a crash cart in an emergency department, or in another medical setting. These medications are essential for emergency situations as well as to initiate treatment immediately in response to a medical condition. Medications are compounded in order to meet specific dosage needs and are critical to the timely treatment of many patients when a prescriber determines that a FDA-approved drug product is neither available nor appropriate to treat their condition and achieve the best possible therapeutic outcome.

Currently, the majority of States provide for means by which prescribers may obtain both finished manufactured drug products and compounded preparations for the administration to or treatment of patients within their practice settings. When Congress re-enacted 503A within the DQSA, numerous Statements of the Record conveyed the intent that nothing within 503A was to intrude upon existing and well-established

practices nor to circumvent the authority of individual States to regulate the practice of medicine and pharmacy within their borders. Additionally, while Congress could have explicitly prohibited the compounding of medications for office-use, it did not. Despite this clear Congressional intent, FDA has conveyed a mixed message of whether office-use compounding is allowed.

Maintaining access to essential compounded medications for office-use is not only vital for patients, but is consistent with the legislative intent of the DQSA.[1,2] While reinforcing Section 503A of the *Food, Drug and Cosmetic Act* (FDCA) through the passage of the DQSA, Congress came together in a bipartisan and bicameral fashion to make clear that pharmacists' ability to provide compounded medications for a prescriber's administration to or treatment of a patient within their practice should be left to the States -- office-use of compounded medications is currently regulated under state law.[3]

Congress' multiple statements in the *Congressional Record* show clear and overwhelming intent that compounded preparations for office-use remain available after the passage of the DQSA. These numerous statements as well as the strong urging from physician and pharmacy stakeholders, directed the agency to not limit office-use medication preparation by 503A compounders. In addition, when FDA considered changes to the Compliance Policy Guide (CPG) for human compounding several years ago, the draft CPG specifically provided for office-use compounding.[4]

Despite these statements and its own draft guidance, FDA stated in a September 15, 2014 response to a bipartisan letter from Congress that in order to comply with 503A, a compounding pharmacist or physician may not dispense compounded medications for office-use, but rather, must obtain or issue a prescription for an individually identified patient.[5] As a result of these misleading statements by FDA, many States may have taken recent action related to office-use compounding.

The actions by FDA to prohibit all office-use compounding may result in drastically reducing patient access to vital medications. There are numerous examples of medications that 503A traditional compounders currently supply for office-use in quantities that are too small or limited to justify preparation and distribution by a 503B outsourcing facility.[6]

It is also important to recognize that at the present time, the only compounded preparations a 503B outsourcing facility may compound and distribute using bulk ingredients are those products which appear on the FDA shortage list. Until such time as the Pharmacy Compounding Advisory Committee completes

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[1] Senator Isakson (GA), Senator Alexander (TN), and Senator Boozman (AR). "Drug Quality and Security Act." *Congressional Record* 159: 164 (November 18, 2013) p.S8071. Available from Thomas.gov; Accessed 11/24/2014.

[2] Representative Griffith (VA), Representative Burgess (TX), and Representative Green (TX). "Drug Quality and Security Act." *Congressional Record* p.H5963. Available from: Thomas.gov; Accessed 11/24/2014.

[3] Senator Isakson (GA), Senator Alexander (TN), and Senator Boozman (AR). "Drug Quality and Security Act." *Congressional Record* 159: 164 (November 18, 2013) p.S8071. Available from Thomas.gov; Accessed 11/24/2014.

[4] United States. Department of Health and Human Services. Food and Drug Administration. *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act Draft Guidance.* Washington, DC: n.p. 2014. Print.

[5] United States. Department of Health and Human Services. Food and Drug Administration. *Response to Congressional Letter on Office Use.* September 15, 2014.

[6] See Appendix A for a compiled list of examples of medications supplied for office-use.

its review of bulk ingredients submitted for use by 503B outsourcing facilities, very few of these medications will be legally allowed to be compounded and distributed by them.

Congress disagrees strongly with FDA's statements that the DQSA prohibits compounding and repackaging for office-use. In addition to the statements in the Congressional record and letters from key Members of Congress to the Agency, Congressional Appropriations language in the Agriculture, Rural Development, Food and Drug Administration, and Related Agencies appropriations bill, states concerns with FDA's interpretation of section 503A on office-use that is inconsistent with the legislative intent of the DQSA and even the agency's own previous positions on office use compounding.

Specifically, during the Fiscal Year (FY) 2016 Omnibus Legislation, Congress approved House Report 114-2015. Within that, FDA was directed to issue guidance which specifically addresses how office-use compounding will be permitted. That guidance was required within 90 days of the final enactment of the report. This language stated -

> The Committee is concerned that, since passage of the Drug Quality and Security Act (DQSA) of 2013, the FDA has interpreted provisions of Section 503A of the FDCA in a manner inconsistent with its legislative intent and with the agency's own previous positions. Specifically, the FDA has taken the position that under 503A, a pharmacist may not compound medications prior to receipt of a prescription and transfer the drugs to a requesting physician or other authorized agent of the prescriber for administration to his or her patients without a patient-specific prescription accompanying the medication. This practice, which is often referred to as `office-use' compounding, is authorized in the vast majority of states and was intended to be allowable under DQSA. The Committee is aware that in 2012, prior to passage of the DQSA, FDA was working on a draft compliance policy guide for 503A of the FDCA that provided guidance on how `office-use' compounding could be done consistent with the provisions of 503A. ***The Committee understands the intent of the DQSA was not to prohibit compounding pharmacists from operation under existing 503A exemptions; therefore, the Committee directs the FDA to issue a guidance document on how compounding pharmacists can continue to engage in `office-use' compounding before the receipt of a patient-specific prescription consistent with the provisions of 503A within 90 days after the enactment of this Act.*** *(emphasis added).*[7]

When FDA ignored the FY 2016 Appropriations language, Congress again instructed FDA that the Agency does not have the authority to prohibit office-use compounding. During the FY 2017 Omnibus legislation, Congress included language stating

> The Committee recommendation maintains fiscal year 2016 funding levels for the medical countermeasures initiative as well as recent funding increases for antimicrobial resistance, counterfeit drugs, food safety, foreign drug inspections, import safety, and pharmacy compounding. The Committee believes patient access to the right drug at the right time is of utmost importance. In instances where a commercially manufactured drug is not appropriate for a patient for a specific reason, a compounded drug may be the difference between life and death. Since passage of the Drug Quality and Security Act (DQSA) of 2013, the Committee has had concerns that the FDA interpreted provisions of Section 503A of the FDCA in a manner that might jeopardize the availability of compounded medications for ''office use''. The practice of ''office use'' occurs when a compounder will compound a batch of drugs in anticipation of receiving patient-specific prescriptions at a later time. It may also be the case of a doctor in his or her office maintaining compounded drugs on site because it is unsafe or impractical to issue a traditional prescription.

[7] See House Agriculture, Rural Development, Food and Drug Administration, and Related Agencies appropriations bill, 2016. Page 67

> This practice is authorized in the vast majority of states and was intended to be allowable under DQSA. The Committee is aware that on April 15, 2016, FDA released a new Draft Guidance on the issue of ''office-use'' compounding. The Committee directs the FDA to issue a Final Guidance that provides for ''office-use'' compounding of drugs, in appropriate circumstances as well as including drugs compounded in anticipation of a prescription for an identified individual patient. Such ''anticipatory'' compounded drugs must be based on the history of previous valid compound prescription orders, and on an established history between the prescriber and the patient and the compounder. (p 68-69)[8]

When FDA ignored both the FY 2016 and FY 2017 appropriations language, Congress included even stronger language within FY 2018 appropriations legislation and made clear that FDA does not have the authority to prohibit office-use and that office-use compounding is to remain a state regulated activity. In the FY 2018 Appropriations legislation as passed out of the Appropriations Full Committee, Congress states

> The Committee continues to believe that patient access to the right drug at the right time is of utmost importance. In instances where a commercially manufactured drug is not appropriate for a patient for a specific reason, a compounded drug may be the difference between life and death. Since passage of the Drug Quality and Security Act (DQSA) of 2013, the Committee has had concerns that the FDA interpreted provisions of Section 503A of the FDCA in a manner that might jeopardize the availability of compounded medications for ''office use''. The practice of ''office use'' occurs when a compounder will compound a batch of drugs in anticipation of receiving patient-specific prescriptions at a later time. It may also be the case of a doctor in his or her office maintaining compounded drugs on site because it is unsafe or impractical to issue a traditional prescription. This practice is authorized in the vast majority of states and was intended to be allowable under DQSA. The Committee directed the FDA to issue a Final Guidance that provides for ''office-use'' compounding of drugs, in appropriate circumstances as well as including drugs compounded in anticipation of a prescription for an identified individual patient. Such ''anticipatory'' compounded drugs is based on the history of previous valid compound prescription orders, and on an established history between prescriber, patient and compounder. Despite clear directives in previous reports accompanying FDA's appropriations bills for the agency to finalize guidance that authorizes office-use compounding, in December of 2016, the FDA finalized a Guidance for Industry (GFI) entitled ''Prescription Requirement Under Section 503A of the FDCA,'' which expressly prohibits office-use compounding. The Committee directs the FDA to rescind this GFI and issue a proposed rule, subject to the notice and comment provisions in the Administrative Procedure Act. The proposed rule should be consistent with Congressional intent as stated in both Appropriations Reports and the DQSA, and that also allows for office-use compounding as authorized by state law. In the proposed rule, FDA should lay out the means by which office use is permissible while addressing such critical safety matters, such as maintaining controls on quantity and safety issues such as those related to office stock shelf life. Lastly, FDA's clarification on the line between traditional compounding and outsourced compounding will support state regulators, outsourcing facilities, and traditional compounders in their efforts to ensure that patients have access to safe compounded drugs while reducing the risks associated with sterile drugs produced in bulk. (page 67)[9]

Congress has been clear. In addition to the Appropriations Legislation, Congress has taken additional steps in order to make very clear to the FDA that the Agency does not possess the authority to prohibit office-

[8] See House Agriculture, Rural Development, Food and Drug Administration, and Related Agencies appropriations bill, 2016. Page 68-69

[9] See House Agriculture, Rural Development, Food and Drug Administration, and Related Agencies appropriations bill, 2017. Page 67

use compounding. Representatives Morgan Griffith and Henry Cuellar introduced bipartisan legislation with 26 cosponsors that leaves office-use compounding to be regulated by the States. The legislation makes very clear that FDA was never granted the authority under the DQSA to prohibit office-use compounding.[10] The DQSA Coalition, which is comprised of over 30 organizations representing patients, providers, pharmacists, and other practitioners, sent a support letter for HR 2871 where 39 states signed on in support of the legislation. The Florida Pharmacists Association signed the letter in support of HR 2871, and in support of leaving office-use compounding under State oversight.[11] FDA was never given authority to regulate office-use by Congress. This is a state regulated activity that was always intended to be left to the states.

Congress has also sent letters to FDA expressing Congressional intent and continues to instruct FDA to leave office-use compounding to the States. In June 20, 2016, Representatives Chris Stewart and Henry Cuellar led a bipartisan letter signed by over 60 Members of Congress. The Members of Congress stated the following

> It is unacceptable that the FDA would ignore the Congress and continue to take the position that Section 503A specifically prohibits office-use compounding, despite clear congressional intent to the contrary and despite previous FDA actions that directly contradict that position, including the recent statement by Health and Human Services Secretary Burwell that also directly conflicts with FDA's current position on "office-use".
>
> Prior to the passage of the Drug Quality and Security Act (DQSA) of 2013, FDA circulated a draft Compliance Policy Guide (CPG) in 2012 to Congress that recognized office-use as legitimate and permissible and explained how compounding pharmacists can engage in office-use compounding before the receipt of a patient-specific prescription consistent with the provisions of 503A of the FDCA. The DQSA did not change the statutory language in 503A that was the basis of that CPG. During the consideration of the DQSA, six Members of Congress, on a bipartisan, bicameral basis, made statements in the Congressional record to clarify that the intent of the legislation was to preserve patient access to medications compounded for office-use.

Congress sent an additional letter on May 23, 2017 that was led by Representatives Chris Stewart and Buddy Carter with 65 bipartisan signatures and stated,

> Office-use compounding of medications is a common and often necessary medical practice that is authorized in some form by the vast majority of state pharmacy laws. Compounding for office-use done pursuant to state pharmacy laws does not make a pharmacy a drug manufacturer, and Congress never intended for the FDA to assert regulatory authority over the traditional practice of pharmacy, which has always been regulated at the state level.
>
> The policies finalized in this GFI are contrary to the plain language of Section 503A as amended by the Drug Quality and Security Act (DQSA) and ignore clear, bipartisan, bicameral congressional intent expressed during passage of the bill. The FDA has unfortunately chosen to ignore broad and diverse stakeholder input, multiple congressional letters from both chambers, and clear directives in the House Report accompanying the FY2016 FDA appropriations legislation (House Report 114-205). More importantly, the FDA's misinterpretation of the law and related enforcement actions against pharmacies are jeopardizing patients' access to critical compounded medications. For these

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[10] Representative Griffith (VA)."Preserving Patient Access to Compounded Medications Act of 2017." *Congressional Record* p.H2871. Available from: Thomas.gov; Accessed 9/8/2017.

[11] (2017, July 26). DQSA Coalition Support Letter [Letter to Representative Griffith, Representative Cuellar]. Washington, D.C.

reasons, we respectfully request that the FDA immediately rescind this GFI and issue a proposed rule, with notice and stakeholder input as required by the Administrative Procedure Act, that is consistent with the DQSA and that allows for office-use compounding by state-licensed pharmacies where authorized by state pharmacy laws.

**IACP urges the members of your Board of Pharmacy to continue to allow 503A pharmacies to compound for office-use. Congress has made it very clear through Appropriations legislation, Congressional letters to FDA, Floor statements, statements made in hearings, and through the introduction of HR 2871 that Congress has always intended for States to maintain oversight over office-use compounding. As also detailed above, there is a need for office-use compounding by 503A pharmacies in order to preserve patient access to compounded medications. As such, IACP strongly urges the Board to delay consideration of any pending regulatory or policy decisions on the ability of practitioners to obtain and use office-use compounded preparations until such time as the Agency issues its guidance in a manner that is consistent with this new Congressional directive. Additionally, given that FDA's previous position and information which may have been provided to your Board by the Agency may have been contradictory to Congress's intent, we urge you to review and potentially reconsider any recent decisions to prevent, eliminate or restrict office-use compounding within your State.**

Sincerely,

Baylor Rice, RPh, FIACP
IACP President

## Appendix A

The following are some examples of the medications that 503A traditional compounders currently supply for office-use in quantities that are too small or limited to justify preparation and distribution by a 503B outsourcing facility:

- Topical Phenol used by podiatrists and primary care physicians to treat in-grown toenails.
- Topical cantharidin (one strength is 52.5 mg / ml [0.7%]) used by podiatrists, primary care physicians, and dermatologists for the treatment of warts.
- Topical podophylline used by podiatrists, primary care physicians, and OB/GYNs.
- Topical Diphenylcyclopropenone in many strengths compounded from raw material and acetone for use by dermatologists treating alopecia areata.
- Topical Squaric acid for use by dermatologists in treating alopecia areata.
- Bleaching gels of various formulas used by dentists in teeth whitening procedures.
- Glycolic acid solutions used by dermatologists in skin peel procedures.
- Trichloroacetic acid solutions used by dermatologists in skin peel procedures.
- Lidocaine, Epinephrine, and Tetracaine (LET or LAT) gel/solution and derivatives used by ERs and Primary Care Physicians as a local anesthetic used to decrease pain while suturing patients – especially pediatric patients.
- Dextrose capsules #0, 00, 000, 1, 2, 3, and 4 for use by Social Work to teach pediatric patients how to swallow capsules.
- Tamsulosin 0.2 mg capsules (open up the 0.4 mg capsules, weigh total contents then weigh in half, pack into #4 capsules) used off-label for kidney stones in pediatric patients.
- Various powder-filled capsules - many formulations out in the industry with mixtures of 3-4 ingredients that may include ciprofloxacin, amphotericin, dexamethasone, clotrimazole, and lidocaine and others for use in Sheehy-House powder insufflators for insertion into the ear to treat refractory external ear infections.
- Topical Sodium Nitrate solution used in labs for diagnosis of cystic fibrosis via sweat testing.
- Topical Pilocarpine Nitrate solution used in labs for diagnosis of cystic fibrosis via sweat testing.
  □ Hydroxyzine pamoate suspension for use by pediatric dentists for mild sedation □ Combination antibiotic eye drop used by ophthalmology surgery centers.
- EDTA ophthalmic eye drops for surgery
- Bevacizumab (Avastin) repack used by ophthalmology clinics for treatment of wet macular degeneration.
- Alteplase 1 mg / ml syringes when commercial vials are on backorder and shortage from manufacturers.
- Oxymetazoline Nasal Spray + Lidocaine 4% injection compounded 1:1 in an ISO 5 environment and packaged into sterile oral syringes for storage in automated dispensing cabinets for ENT to use with an automizer prior to exam in office.
- Surgical Irrigations o Bacitracin 50,000 units in 0.9% nacl 3000 ml (bag). o Bacitracin 50,000 units in 0.9% nacl 1000 ml (bag or bottle).
    - Bacitracin 25,000 units in 0.9% nacl 500 ml (bottle). o Levofloxacin in 0.9% nacl 500 ml (bottle). o Cefazolin in 0.9% nacl 500 ml (bottle)
    - Bacitracin, Gentimicin and Cefazolin in 0.9% nacl 500 ml or 1000 ml (bottle).
- Organ Transplant Irrigations, Soaks and Baths o Cardioplegia solutions (mixtures of lidocaine, electrolytes, mannitol, dextrose, etc.).
  o Epinephrine in 0.9% nacl (bottle).

- Crash/Emergency Cart drugs/ICU/Ambulance/Helicopter/Airplane o Sodium Bicarbonate used by Anesthesia/ER crash carts, a sterile drug that has been on chronic backorder and shortage from manufacturers.
    - Calcium Chloride used by Anesthesia/ER crash carts/dialysis centers – chronic backorder from manufacturers.
    - Calcium Gluconate used by icus /dialysis centers; chronic backorder from manufacturers.
    - Propofol repackaged into 10 and 20 ml syringes during shortages.
    - Dexmedetomidine straight from diluted commercial vial or compounded with 0.9% NS and concentrated vial, then packaged in syringes.
    - Heparin 500 units / ml (3 ml) compounded then packaged in syringes for dialysis. o Heparin 2,000 units / ml (3 ml) compounded then packaged in syringes for dialysis. o Heparin 1,000 units / ml (3 and 8 ml) packaged in syringes for dialysis.
    - Lidocaine 1% buffered with nabicarb (0.8 & 5 ml) packaged in syringes for IV starts and dialysis.
    - Lidocaine with nabicarb (0.2 ml) packaged in J-tip syringes for IV starts and shots in ER, surgery centers, inpatient and clinics.
    - Heparin 2 units / ml compounded from Heparin and 0.45% nacl commercial products (250, 500 and 1000 ml bags) for storage in automated dispensing cabinets within health systems and long term care facilities.
    - Epinephrine 0.01 mg / ml compounded from epinephrine and D5W commercial products (50 ml syringe) for storage in automated dispensing machines within health systems and long term care facilities.
    - Epinephrine 0.02 mg / ml compounded from epinephrine and D5W commercial products (50 ml syringe) for storage in automated dispensing machines within health systems and long term care facilities.
    - Nicardipine 0.5 mg / ml compounded from Nicardipine and D5W commercial products (50 ml syringe) for storage in automated dispensing machines within health systems and long term care facilities.
    - Nicardipine 0.5 mg / ml compounded from Nicardipine and 0.9% nacl commercial products (50 ml syringe) for storage in automated dispensing machines within health systems and long term care facilities.
    - Dextrose 10% plus 14.6% nacl or 23.4% nacl to prepare D10 and nacl 0.2% (250 ml) bag due to commercial product on chronic mfg b/o (prepared from commercial products). o Dextrose 10% plus 14.6% nacl or 23.4% nacl plus heparin to equal 1 unit / ml to prepare D10 and nacl 0.2% and Heparin 1 unit / ml (250 ml) bag (prepared from commercial products) may be stored in automated dispensing cabinets.
    - Bupivacaine 0.25 % + Epinephrine = 1:200,000 injection for use in surgery and surgery centers.
    - Epinephrine 1:100,000 injection prepared from epinephrine and 0.9% nacl commercial products for use in surgery and surgery centers.
    - Epinephrine 1:400,000 injection prepared from epinephrine and 0.9% nacl commercial products for use in surgery and surgery centers.
    - Lidocaine 0.25% with Epinephrine 1:400,00 units injection prepared from commercial products in a vial for use in surgery and surgery centers.
    - Lidocaine 1% with Epinephrine 1:10,000 units injection prepared from commercial products into a vial for use in surgery and surgery centers.
    - Ropivacaine 0.2% with Epinephrine 1:200,000 units injection prepared from commercial products into a vial for use in surgery and surgery centers.

- Milrinone 0.2 mg / ml compounded or premix commercial product repackaged into 20 and 50 ml syringes for storage in automated dispensing cabinets.
- Pentobarbital 50 mg / ml commercial product repackaged into 1 ml syringe for cath lab and anesthesia surgery centers.
- Dopamine 1.6 and 3.2 mg / ml compounded or premix commercial product repackaged into 20 and 50 ml syringes for each for storage in automated dispensing cabinets. o Nitroglycerin 0.4 mg / ml commercial product repackaged into 20 and 50 ml syringes during commercial product manufacturing back order and shortages. o Iopamidol (Isovue) 61% injection repackaged into 20 ml syringes during Manufacturing back order and shortages.
- Botulinium Toxin solution reconstituted commercial product and packaged in syringes for office use treatment of spasticity, diagnosis of gastrointestinal disorders and which dermatologists and plastic surgeons also use.
- Ceftriaxone mixed with lidocaine to 350 mg / ml, drawn up in 1.1, 1.4 and 2.2 ml volumes in an ISO 5 environment for storage in an automated dispensing cabinet refrigerator in ers and clinics.