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".
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> 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.