July 20, 2015

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Docket No. FDA-2014-N-1459

Re: FDA-2014-N-1459; Comments to Draft Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between the States and the Food and Drug Administration

Dear Sir or Madam:

Thank you for the opportunity to submit our comments on the Food and Drug Administration’s (FDA) Draft Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products between the States and the Food and Drug Administration. As FDA considers finalizing the proposed new guidance for pharmacy compounding, the International Academy of Compounding Pharmacists (IACP®) appreciates the opportunity to share our perspectives and to work with FDA in the future on this very important issue.

IACP is an association representing more than 3,600 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.

IACP understands and supports the need to protect public health. However, when providing guidance, it is essential that FDA adheres to the plain language of statutes and Congressional intent that preserve patient access to vital compounded medications, the physician-patient-pharmacist triad, and the right of a patient to choose their pharmacist. Prescribers must have the right to prescribe medications that best fit the needs of their patients and patients must have the right to choose the pharmacist they wish to fill that prescription oftentimes based on a long standing relationship. Any action taken by FDA must preserve this access to care as well as right of choice.
The current draft Memorandum of Understanding (MOU) fails to follow the clear language of the statute as well as Congressional intent and as such, fails to preserve patient access to these vital medications. Contradictory to the clear language of the statute and clear Congressional intent, the draft MOU eliminates patient access to the entire category of nonsterile office-use compounded medications. In addition, the draft MOU greatly reduces access to sterile office-use compounded medications while also severely restricting nonsterile and sterile compounded medications through an arbitrary limit on prescriptions dispensed to individual patients. As such, the draft MOU greatly hinders patient access to compounded medications and eliminates patient choice of their pharmacist while also restricting the physicians-patient-pharmacist triad.

1. FDA’s attempt to regulate “dispensing” to an individual patient by including that as a component of the definition of “distribution” of compounded medications in interstate commerce contradicts the plain language of the Statute, Congressional intent, and the historical usage of “dispense” and “distribute.”

Contradictory to the plain language of the statute

Despite the plain language of 503A and despite clear congressional intent to the contrary, FDA has developed a draft MOU that attempts to not only regulate interstate distributions of inordinate amounts of compounded drug products, but also the interstate dispensing of compounded medications to individual patients. In doing so, FDA ignores entirely that 503A allows distribution (office-use). To aid in this holding, FDA then was forced to go into the definitions within 503A utilizing the MOU as the vehicle to alter the definitions in a way that “distribution” contains “dispensing.”

In forcing “distribution” to contain “dispensing” in the draft MOU, FDA ignores that 503A authorizes office-use by the plain language of the statute and ignores that Congress chose to use the different terms “dispense” and “distribute” throughout 503A. FDA argues this was a drafting error and that Congress intended to include “dispense” within the term “distribute.” If Congress had intended for these terms to be used interchangeably throughout 503A, Congress could have done just that. Not only do these terms bear a long history of meaning different things throughout other Federal legislation, the terms are used differently throughout 503A. As such, Congress clearly intended when drafting 503A to use the terms “dispense” and “distribute” to refer to two different types of activity.

As a result, 503A does not authorize FDA to address “dispensing” within the MOU. To the contrary, Congress chose to draft 503A to state the following:

(3) A drug product may be compounded under subsection (a) only if –

(B) such drug product is compounded in a State

(i) that has entered into a memorandum of understanding with the Secretary which addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency
of complaints relating to compounded drug products distributed outside such state; or

(ii) that has not entered into the memorandum of understanding described in clause (i) and the licensed pharmacist, licensed pharmacy, or licensed physician distributes (or causes to be distributed) compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician.\(^1\)

Therefore, the draft MOU is contradictory to the plain language of 503A as the draft MOU overreaches in addressing “dispensing” under the definition of “distribution.” FDA attempts to argue in the draft MOU that the Agency has the authority to regulate all compounded medications (dispensed as well as distributed) that crosses State lines. To the contrary, Congress, by the plain language of the statute, never gave FDA this broad authority.

Contradictory to Congressional intent of the meaning of distribute and dispense

While ignoring the plain language, FDA asserts in the draft MOU that Congress did not understand that the terms “dispense” and “distribute” are mutually exclusive categories and thus mean two different things. While using the terms “dispensing” in other sections of the 503A, Congress was very clear, as demonstrated above, by the plain language of the statute that FDA only has the authority to address the “distribution” of compounded medications shipped interstate within the MOU section of 503A.

In fact, Congress chose to use the terms “dispense” and “distribute” as different terms within the same sentence found within 503A stating that:

\[
\text{a pharmacy in a State that does not enter into an MOU may only distribute...compounded drug products out of the State in which they are compounded in quantities that do not exceed 5% of the total prescription orders dispensed or distributed by such pharmacy.}\(^2\)\quad \text{(emphasis added)}
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As such, in development of the final MOU and in enforcement of the alternative or default 5% cap on interstate distributions, it is important that FDA recognize the clear congressional intent of the statute as expressed within the clear language of the statute to address interstate distributions while leaving the regulation of the dispensing of prescription drugs to State legislatures and State Boards of Pharmacy.

The fact that the language of the statute only authorizes the MOU to address interstate distributions, coupled with the fact that the default for states that do not sign an MOU with FDA is a 5% cap on interstate distributions that is based on “5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician” makes it crystal clear that Congress recognized the difference between “dispensing” and “distributing” and did not intend to

\(^1\) 21 U.S.C §353a(b)(3)(B)(i)(ii).
authorize FDA to limit and regulate an activity (the dispensing of compounded prescription drugs) that, as long as the other requirements of 503A are met, is part of the traditional practice of compounding pharmacy.

Therefore, the draft MOU represents an inappropriate overreach by the agency and an attempt to limit and regulate an activity (the dispensing of prescription medications interstate) that Congress had no intention of regulating when adopting 503A as part of FDAMA in 1997 and as part of the DQSA in 2013.

Contradictory to the history of the usage and definitions of dispense and distribute

The terms “dispense” and “distribute” have a long history of referring to two different activities. Congress and FDA have recognized the different usage of “dispense” and “distribute” in every other known context including FDCA §581(5), 21 U.S.C. §802(10)-(11), and 21 CFR §208.3.

21 CFR 208.3

Specifically, in 21 CFR §208.3, FDA has defined these terms differently:

§208.3 Definitions.
For the purposes of this part, the following definitions shall apply:
(a) Authorized dispenser means an individual licensed, registered, or otherwise permitted by the jurisdiction in which the individual practices to provide drug products on prescription in the course of professional practice.
(b) Dispense to patients means the act of delivering a prescription drug product to a patient or an agent of the patient either:
   (1) By a licensed practitioner or an agent of a licensed practitioner, either directly or indirectly, for self-administration by the patient, or the patient's agent, or outside the licensed practitioner's direct supervision; or
   (2) By an authorized dispenser or an agent of an authorized dispenser under a lawful prescription of a licensed practitioner.
(c) Distribute means the act of delivering, other than by dispensing, a drug product to any person.
(d) Distributor means a person who distributes a drug product.

21 U.S.C. §802(10)-(11): The Controlled Substances Act

In addition, the Controlled Substances Act defines “dispense” and “distribute” to mean two different things, and expressly excludes “distribute” from the act of dispensing. Specifically, the CSA states that a pharmacy which is:

registered to dispense a controlled substance may distribute (without being registered to distribute) a quantity of such substance to...another practitioner for the purpose of general dispensing by the practitioner to patients” unless the pharmacy’s “total number of dosage units of all controlled substances which will be distributed by him” does not
“exceed 5 percent of this total number of dosage units of all controlled substances distributed and dispensed by him during that calendar year.”

As such, under the CSA, Congress recognized “dispense” and “distribute” as two different activities and allowed pharmacies to distribute for office-use as long as that distribution does not exceed 5%. This is the same framework Congress intended to provide within 503A allowing office-use (distribution) while also providing FDA a mechanism to address the regulation of office-use in conjunction with the states through an MOU.

Conclusion: FDA is only authorized by Congress to address distribution (office-use) in the MOU

In conclusion, IACP strongly encourages FDA, in development of the final MOU called for in 503A and in enforcement of the default 5% cap, to adhere to the plain language of the statute and the clear legislative intent behind it and only address “the distribution of inordinate amounts of compounded drug products interstate,” while leaving the regulation of traditional pharmacy compounding, including the interstate dispensing of compounded drugs, to the States as intended by Congress.

2. FDA is disregarding Congressional intent to preserve patient access to compounded medication by capping interstate dispensing of compounded medication and prohibiting all office-use compounding by 503A traditional compounders

The draft MOU takes two measures to greatly restrict patient access to compounded medications. First, the draft MOU, as analyzed above, prohibits all office-use compounding by a 503A pharmacy (both nonsterile and sterile). Secondly, the draft MOU then greatly restricts interstate shipment of patient-specific compounded medications for individual patients by implementing an arbitrary ceiling on all compounded medications sent across State lines; this will be addressed in greater detail further on in our comments.

To determine Congressional intent of the MOU provision within 503A, one doesn’t have to look much further than the Senate Report that accompanied the Food and Drug Administration Modernization Act of 1997 (FDAMA), which states that the purpose of the Act is to ensure “continued availability of compounded drug products as a component of individualized therapy, while limiting the scope of compounding so as to prevent small-scale manufacturing under the guise of compounding.”

Thus, the Act’s clear intent was to ensure that compounded drug products remain available to the public.

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3 21 C.F.R. §1307.11.
Furthermore, after the passage of FDAMA, IACP lead the creation and issuance of a letter signed by forty-three Members of Congress to FDA stating that by passing the Act, Congress wished to ensure that patients would have access to compounded medications prescribed by their physicians. Senator Tim Hutchinson’s office also submitted comments during the meeting of the 1999 Pharmacy Compounding Advisory Committee stating that Congress did not intend for the “MOU provision to set a floor or ceiling with regard to the quantity of product that enters into interstate commerce.”

IACP strongly encourages FDA to adhere to the plain language of the statute allowing office-use compounding. The language of 503A requires an individual patient prescription, but does not dictate when that prescription must be received by the pharmacy or dictate how a compounded medication must leave the pharmacy. Furthermore, section 503A specifically allows for anticipatory compounding based on a historical relationship between the pharmacy or pharmacist and prescriber. Where Federal law is silent and does not bear a pre-emption clause such as here under 503A, State law governs. Thus, by being silent as to when a pharmacy must receive the prescription from a prescriber and by allowing anticipatory compounding, 503A expressly permits office-use compounding where State law allows office-use compounding. As also demonstrated above, Congressional intent as well as the historical use of “dispense” and “distribute” clearly authorize office-use under 503A.

Despite the plain language of the statute and clear Congressional intent found within the Senate Committee Reports as well as six Congressional statements on the record, FDA has held that 503A compounding pharmacies are not allowed to distribute and thus provide office-use compounded medications to prescribers for administration within the prescriber’s office. The prohibition of office-use compounding coupled with FDA’s actions of changing definitions within 503A so that “dispensing” is included within “distribution” greatly restricts patient access to vital medications.

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Nonsterile office-use will be eliminated

By ignoring the plain language of the statute and Congressional intent, the current MOU completely eliminates all nonsterile office use compounding.

While FDA states that all office-use compounded preparations by 503A traditional compounders is prohibited, FDA’s only “solution” to preserving access to compounded medications is to encourage all 503A pharmacies to register as a 503B outsourcing facility. This “solution” fails to acknowledge many factors as to why the registration by all 503A pharmacies is impossible. One major factor is that the plain language of the statute only allows 503A pharmacies that compound sterile to register. Thus, all 503A pharmacies that compound solely for nonsterile office-use do not have the opportunity to register as a 503B outsourcing facility. As a result of FDA’s action to prohibit all office-use compounding by 503A pharmacies, nonsterile office-use compounding is eliminated.

In addition, FDA is now restricting the patient-specific prescriptions in interstate commerce. As such, not only is nonsterile compounded medications completely prohibited by 503A pharmacies for office-use, nonsterile compounded medications being shipped to specific patients across State lines is also greatly restricted at either 5% or 30% depending on whether a State enters into and takes upon the tremendous burden outlined by the MOU.

Access to nonsterile office-use compounded medications is vital to many patients. In many instances, dispensing these medicines directly to a patient for transport to a physician’s office for treatment and administration represents a potential safety risk to the patient or a disruption in the integrity of the drug supply system. Examples of office-use compounds commonly used include:

- 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 Diphenylcypropenone 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.
- Tetracaine lollipops used by dentists for non-narcotic post-op pain management after tonsillectomies.
- 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 insufflaters 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

**Access to sterile office-use will be greatly reduced**

The prohibition by FDA on the compounding by 503A pharmacies for office-use, has eliminated all nonsterile compounding for office-use by 503A pharmacies. In addition, FDA’s solution is if 503A pharmacies want to do sterile compounding for office-use they can register as a 503B outsourcing facility. However, once again, this “solution” fails to consider the fact that 503B outsourcing facilities cannot solve all of the access problems as there are numerous sterile medications that a 503B outsourcing facility cannot feasibly or legally compound. At present, 503B outsourcing facilities are restricted to only using bulk ingredients for compounding of preparations for drugs that are in short supply.

Many sterile compounded medications must vary from patient-to-patient and thus do not fit the large scale compounding of outsourcing facilities. Patients need many sterile office-use compounded medications. Illustrative examples include but are not limited to:

• Combination antibiotic eye drop used by ophthalmology surgery centers.
• EDTA ophthalmic eye drops for surgery
• Bevacizamab (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).
  o Bacitracin 25,000 units in 0.9% NaCl 500 mL (bottle).
  o Levofoxacin in 0.9% NaCl 500 mL (bottle).
  o Cefazolin in 0.9% NaCl 500 ml (bottle).
  o Bacitracin, Gentimicin and Cefazolin in 0.9% NaCl 500 mL or 1000 mL (bottle).
- **Organ Transplant Irrigations, Soaks and Baths**
  - Cardioplegia solutions (mixtures of lidocaine, electrolytes, mannitol, dextrose, etc.).
  - Epinephrine in 0.9% NaCl (bottle).
  - Phenylephrine in 0.9% NaCl (bag).

- **Crash/Emergency Cart drugs/ICU/Ambulance/Helicopter/Airplane**
  - Phenylephrine syringes used for Anesthesia/ER crash carts, concentrations of 50 and 100 mcg / mL that are not commercially available; there is chronic backorder and shortage from manufacturers of vials 10 mg / mL to even compound the 50 and 100 mcg / mL syringes.
  - 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.
  - Narcotic drug syringes; fentanyl, sufentanil used for anesthesia in outpatient surgery centers and physician offices.
  - 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.
  - Heparin 2,000 units / mL (3 mL) compounded then packaged in syringes for dialysis.
  - 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.
  - Morphine 1 mg / mL compounded using commercial product and 0.9% NaCl (1 mL) syringe for storage in automated dispensing cabinets, and anesthesia carts
  - Hydromorphone 0.2 mg / mL for PCA (50 mL) syringe for storage in automated dispensing cabinets within health systems and long term care facilities.
  - Hydromorphone 1 mg / mL for PCA (50 mL) syringe for storage in automated dispensing cabinets within health systems and long term care facilities.
  - Methadone 1 mg / mL compound from commercial product and 0.9% NaCl (1 mL) syringe for storage in automated dispensing cabinets within health systems and long term care facilities.
- Morphine 2 mg / mL for PCA (25 mL) syringe prepared from commercial product and 0.9% NaCl for storage in automated dispensing cabinets within health systems and long term care facilities.
- Fentanyl 10 mcg / mL NEONATAL (1 and 10 mL) compounded from commercial product and 0.9% NaCl and packaged in bar-coded syringes for storage in automated dispensing cabinets within health systems and long term care facilities.
- 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 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).
- 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.
- Methadone 5 mg / 0.5 mL commercial product repackaged from large commercial vial into 0.5 mL syringes for storage in automated dispensing cabinets.
- 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.
- Nitroglycerin 0.4 mg / mL commercial product repackaged into 20 and 50 mL syringes during commercial product manufacturing back order and shortages.
- Fentanyl 50 mcg / mL injection repackaged from commercial product into 8, 24 and 50 mL syringes maybe stored in automated dispensing cabinets.
- 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.

**Conclusion:** FDA’s actions of prohibiting all office-use compounding by 503A pharmacies contradicts the clear language of the Statute and Congressional intent severely impacting patient access

IACP strongly opposes FDA’s prohibition of all office-use compounding by 503A pharmacies. FDA’s actions contradict with the plain language of the Statute and with Congressional intent to preserve patient access to compounded medications. By prohibiting all office-use compounding by 503A pharmacies, FDA will eliminate nonsterile office use compounding and greatly reduce access to sterile office-use compounded medications. IACP strongly encourages FDA to adhere to the plain language of the statute which does not prohibit office-use compounding.

3. FDA’s intent to create and enforce an arbitrary cap on compounded medications - shipped in interstate commerce is inconsistent with Congressional intent to preserve patient access to compounded medications

While IACP provided an analysis above as to why FDA does not have the authority to regulate the dispensing of compounded medications to individual patients, IACP will focus on the concerns with the arbitrary cap in general in this section.
In the draft MOU, FDA seeks to implement a 30% ceiling on the interstate shipment of compounded medications and thus dictates to the State Boards of Pharmacy what exactly “inordinate amount” means. While doing so, FDA has failed to cite any statutory or regulatory authority supporting the arbitrary cap or the agency’s authority for implementing such an arbitrary ceiling. As stated above, Congress made clear multiple times throughout the legislative process that it was not Congressional intent to grant FDA any authority to implement a ceiling on shipment of compounding medications. As such, it is certainly not Congressional intent to provide FDA the authority to implement such an arbitrary ceiling that the agency itself cannot site any regulatory or legislative authority for the ceiling it has chosen.

If Congress had intended to limit interstate shipment of compounded medications in the manner that FDA asserts, Congress would have done so under 503A or specifically instructed FDA to do so in the clear language of 503A. To the contrary, Congress only gave FDA authority to implement an MOU “which addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State.” FDA cannot reference the silence on granting authority to FDA to cap the interstate shipment of compounded medications as its only basis for authority to implement such cap. Silence by Congress is not a grant of authority to FDA to implement ceilings on interstate shipment.

Furthermore, since the most recently passed DQSA legislation was not accompanied by a Committee Report, it is essential when defining “inordinate amounts” to look back at the Senate Committee Report for the Food and Drug Administration Modernization Act of 1997 (FDAMA). On the bottom of page 68 of the Senate Committee Report, the Report offers guidance to FDA and defines “inordinate amounts” as:

> Regarding subsection (h)(2)(B), until the State agency of jurisdiction in which the pharmacy is located enters into a memorandum of understanding (MOU) with the Secretary or 180 days after the development of the standard MOU, whichever comes first the exemption shall not apply if inordinate quantities of compounded products are distributed outside of the State in which the compounding pharmacy or physician is located. "Inordinate" quantities means amounts typically associated with ordinary commercial drug manufacturing⁷.

Congressional intent, therefore, seems to be clear that “inordinate amounts” is to be defined by FDA as activity that is “typically associated” with drug manufacturing. As such, IACP strongly opposes FDA’s attempt to impose an arbitrary percentage or quantity limitation on the amount of compounded medications that may be distributed interstate based upon a percentage of a pharmacy’s volume of medications they dispense.

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For example, if a pharmacy compounds 10 medications per day and its State Board of Pharmacy has signed the MOU as currently proposed, then this pharmacy would only be allowed to ship three compounded medications across state lines each day. This certainly does not meet the congressional definition of “inordinate quantities” as meaning “amounts typically associated with ordinary commercial drug manufacturing. Surely neither Congress nor the FDA would consider three compounded preparations dispensed to patients in another state to meet the level of an “inordinate” amount; however, as proposed, that is exactly the circumstances that a traditional compounder would be faced with in order to comply with the terms of the MOU.

If Congress had intended to limit interstate distributions of compounded medications by implementing an arbitrary cap, Congress could have certainly done so or instructed FDA to define “inordinate amounts” in such a manner. Instead, the language includes the terminology “inordinate amounts” and an accompanying definition within the Senate Committee Report of actions mirroring a drug manufacturer. Congress had ample opportunity in both 1997 under the Food and Drug Administration Modernization Act of 1997 as well as the most recently passed Drug Quality and Security Act to enforce an arbitrary cap and declined to do so.

Moreover, FDA points to no anecdotal evidence that demonstrates interstate shipments of compounded medications greater than 30% meets the definition of “inordinate amounts.” On numerous stakeholder calls, when asked where the 30% ceiling was plucked from, FDA has failed to provide any evidence as to why this ceiling does in fact constitute “inordinate amounts.” Thus, no justification has been given as to why 30% constitutes “inordinate amounts” or as Congress intended “amounts typically associated with ordinary commercial drug manufacturing.”

Without evidence, studies, or any justification, FDA appears to be implementing the 30% cap with the rationale of – because we said so – while failing to demonstrate why compounding in amounts greater than this arbitrary ceiling poses a threat to public health or demonstrates that a compounding pharmacy is “manufacturing in the guise of compounding.” FDA has failed to show that compounding pharmacies shipping patient-specific prescriptions in amounts greater than the arbitrary ceiling have met the requirement to resemble activity of that of a drug manufacturer especially in light of commercial pharmaceutical manufacturers’ model of producing, marketing, and distributing prescription drugs to dispensers and not individual patients.

In addition, FDA fails to take into consideration essential factors when imposing this strict 30% ceiling. FDA does not consider location of the pharmacy and the fact that many pharmacies supply access to compounded medications to patients in border States. Most of us have some experience with border towns as living in Washington, DC; we can travel to the District, Virginia, and Maryland with a quick car ride. FDA itself is located in Maryland. Penalizing the pharmacies that ship medications to patients over State lines greatly hinders patient access and completely eliminates patient choice. While FDA has allowed for an exemption in the draft MOU for patients that drive or walk across State lines to pick up their own medications, FDA fails to take into account patients where this type of arrangement is impossible.
Many patients in rural areas and in poor health cannot simply walk or drive over State lines to pick up their own medications – and since Congress intended to preserve patients’ choice in provider and pharmacist, these patients should not be forced to do so. Where this provides undue hardship on a patient is something that Congress intended to prevent in preserving patient choice in provider and pharmacists. As such, this arbitrary cap is disproportionately discriminatory toward pharmacies located in rural areas and border towns that may serve a higher prescriber population across State lines.

FDA has also failed to consider what the pharmacy is shipping interstate that would rise to the level of “commercial manufacturing.” If a pharmacy were to compound one type of medication and subsequently ship large amounts of that preparation in interstate commerce, this might more resemble “commercial manufacturing.” However, if a compounding pharmacy is compounding a number of different medications for interstate shipment, this type of activity absolutely does not resemble “commercial manufacturing.”

IACP strongly opposes any arbitrary cap on the shipment of compounded medications. An arbitrary cap only serves to limit access to essential compounded medications while placing pharmacists in the position of denying care based upon an arbitrary quantity while doing nothing in terms of preventing another tragedy like that which occurred with the New England Compounding Center. Moreover, as legislation that intends to promote the use of safe compounded medications, basing interstate distributions of compounded medications on an arbitrary cap, contradicts the very intent of the legislation. Currently, patients and their caregivers choose which pharmacy will supply their compounded medications. For some patients, they currently choose pharmacies outside of the State where they reside. Whether this is due to the fact that they live in small rural areas, that their local pharmacy does not offer the specific compounded medications that they need, or that their local pharmacy does not have the specialized knowledge or equipment to compound the medication, it is the patient’s choice as to who will provide their compounded medications.

Under the arbitrary cap, patient choice of their compounding pharmacist will no longer exist. The current access that patients have to a number of different pharmacies throughout the country that once could provide their compounded medications will be eliminated. Since the need for compounded medications will not decrease, and with drug shortages continuing to increase, the need for compounding medications could quickly outgrow the in-State supply of compounded medications. And, with the arbitrary cap, outside compounding pharmacies will be placed in the position of denying care to patients that are located over State lines simply based on an arbitrary quota. No longer will patients be choosing who dispenses compounded medications based on their relationship and pharmacists’ experience in compounding the specific medication, but instead based solely upon geographic locality due to a mandate by FDA.
A multitude of States expressed concerns for any arbitrary cap on the interstate shipment of compounded medications in response to the 1999 MOU. Arizona staged that “[t]he Arizona Board of Pharmacy invites FDA to expand and recommit itself to the concept it has professed for years; that of federal—state partnerships for improved regulatory outcomes. Optimum implementation of partnering may permit effective regulation with minimal professional resistance.” Arizona went further to request that FDA:

“[e]liminate any reference to the number of percentage of compounded prescriptions that a pharmacy may dispense. The genesis for this suggestion is the implication that establishing any number of percentage of compounded prescriptions that are authorized to be dispensed, implies a direct and proportional relationship to the protection of the public health. For example, if the FDA states a pharmacy can dispense compounded prescriptions up to “X”% of the total prescriptions dispensed, consumers could presume that to mean…dispensing compounded prescriptions not exceeding the established amount, assures the patient will not be harmed. After all FDA has established the limit based on protecting the public health and safety. The issue here is simply this, a practice or activity is either inherently unsafe or it is safe, it can’t be “X”% safe!”

California also expressed concerns stating that “[t]he Board is deeply concerned and opposes some of the provisions in the MOU because it believes that they impose unreasonable numerical or geographic restrictions on pharmacy practice. Specifically, the Board opposes the 20% limit of the total number of prescriptions dispensed or distributed….these restrictions are not based upon public health and safety considerations.”

Louisiana submitted formal comments which urged FDA “to respect the jurisdiction of the state of Louisiana…and recognize compounding in the context of the patient-prescriber-pharmacist triad.” Louisiana asked that the final MOU allow the State of Louisiana the opportunity to determine how to best regulate interstate distribution of compounded products without setting “arbitrary ceilings.”

Conclusion: Congress did not grant FDA the authority to implement an arbitrary cap as a ceiling on the shipment of compounded medications
Thus, nothing in section 503A or the legislative history suggests that Congress has granted FDA the authority to impose a specific “ceiling” based upon an arbitrary quantity. To the contrary, by not altering this language nor directing FDA any additional authority, the definition and thus Congressional intent cited within the Senate Committee Report should stand and IACP strongly encourages FDA to only define “inordinate amounts” as activity rising only to the level of that resembling drug manufacturing. Arbitrary “ceilings” on the amount of compounded medications that may be distributed interstate is unnecessarily disruptive and will jeopardize the quality of patient care by limiting patient access to compounded medications. Therefore, IACP strongly encourages FDA to avoid basing any limitation on distributions found within the MOU on an arbitrary cap.

4. The draft MOU places a tremendous burden upon States.

The language of 503A allows for “appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State.” Statements within the draft MOU use the term “will” instead of “may” resulting in placing many mandates upon States.

Subsection III(a)(2) mandates a list of complaints that will be investigated by the State eliminating all power by the State to exercise its discretion in determining when an investigation is warranted.

Subsection III(b)(1) mandates that the State collect all data and determine whether a pharmacist or physician has distributed compounded medications greater than amounts that FDA has already defined by an arbitrary ceiling found within the MOU. Each state has its own legislative and regulatory mechanism for dealing with complaints and/or violations. Refusing to acknowledge this, FDA mandates the action that States must take toward pharmacists and providers by detailing that a State will take action which may include a warning letter, enforcement action, suspension or revocation of a license, or other action consistent with State law. Thus, FDA is requiring the State to take some form of disciplinary action toward the pharmacist or physicians. Thus, while FDA allows States to determine what type of action to take, FDA does not allow States the ability to take no action.

Congressional intent was to build relationships between States and FDA not to commandeering the States into performing stringent duties under FDA’s instruction or risk losing the right for their pharmacists to ship interstate and thus drastically decrease patient access to compounded medications.

Whether one looks back to the original passage of 503A in the Food and Drug Administration Modernization Act of 1997 and Senator Ben Nighthorse Campbell’s letter to Acting FDA Commissioner Friedman dated September 9, 1998 stating that collaboration between the FDA and state regulatory authorities in developing the new regulations required under 503A would support state authorities in their oversight of compounding activity or whether you look to the more recent Statement of the Record submitted by Senator Tom Coburn which stated that “provisions within the legislation require appropriate investigation on complaints and other issues that arise by the FDA and in no way provide some new expansive authority to the FDA to restrict interstate commerce”\textsuperscript{12} – it is clear that the development of the MOU is meant to be a joint State and FDA process.

The current draft MOU leaves State Boards of Pharmacy only two untenable choices: either (1) the State must define and regulate compounding according to FDA’s specific instructions while taking on a tremendous burden as outlined by FDA yet still have compounded preparation dispensing capped at 30% of total prescriptions; or, (2) pharmacists and pharmacies within the State may not ship compounded products in excess of 5% of their total prescriptions interstate for patient-specific prescriptions.

In determining the nature and extent of complaint investigations that will be required under the MOU, IACP strongly encourages FDA to adhere to the language found within 503A and clearly state that State Boards of Pharmacy possess oversight of compounding pharmacies and of investigating complaints regarding compounding activities.

Senator Tom Coburn made clear that Congressional intent of 503A is not to grant FDA further authority by authorizing the development of investigations under the MOU, but to allow States to undertake these investigations and decide whether a facility is in violation of 503A. Specifically, Senator Coburn stated:

\textit{In addition, there are concerns whether the provisions within the legislation that grant authority to the FDA to set up systems of procedure for the direct communication between state Boards of Pharmacy and the FDA will give FDA more authority over compounded prescriptions shipped across state lines. I want to also take this opportunity to make clear that these provisions within the legislation require “appropriate investigation” on complaints and other issues that arise by the FDA and in no way provide further authority to the FDA to restrict interstate commerce.}\textsuperscript{13}


The United States Supreme Court has held very clearly on this issue in South Dakota v. Dole 483 U.S. 203 (1987) the federal government could place conditions on states as long as they are reasonable even when the pursuit is “the general welfare.” The Court was clear that in order to be upheld, the federal government could not place such restrictions upon States that would be commandeering the States.

Not only does FDA place a tremendous burden upon States under the draft MOU, the current MOU mandates States to affirm that the State “now possesses and will maintain, at the discretion of the State legislature, the legal authority and the resources necessary to effectively carry out all aspects of this MOU.” This mandate contradicts Congressional intent. In an analysis required by the Unfunded Mandates Reform Act, the Congressional Budget Office estimated that compliance with FDAMA would result in no significant costs for State and local governments. In direct conflict of this Congressional intent, FDA not only acknowledges in the draft MOU that States will be forced to utilize State resources in order to comply, FDA also mandates State Boards of Pharmacy to affirm that they possess the current required resources and to maintain such resources. Of particular concern is that State Boards of Pharmacy have little or no authority over non-pharmacist traditional compounders – physicians, dentists, nurse practitioners, and others engaged in compounding as lawfully provided by a State. FDA has not explained how this MOU will be applied to those practitioners and instead focuses solely on pharmacists, pharmacies, and the role of the State Boards of Pharmacy.

FDA has heard in the past from many States on this issue. Out of the more than 6,000 comments submitted on the 1999 draft MOU, many States including but not limited to Alaska, Arizona, California, Florida, Louisiana, Missouri, New Hampshire, North Dakota, Oregon and Wisconsin, expressed their serious concerns with the MOU.

FDA has stated many times that no one has offered an alternative MOU. To the contrary, both Florida and New Hampshire submitted draft alternative MOUs within the States’ comments providing an alternative to the ceiling that FDA continues to insert into the current MOU draft.

In addition, Oregon stated in its comments that “it is not clear that a significant public health and safety issue is being addressed by the terms of the proposed agreement. The MOU would implement interstate shipping quotas on products compounded by pharmacists. It would not implement any new qualitative health and safety measures.” Their comments continue with, “the MOU would place additional burdens on State Board staff by requiring the State Boards to investigate complaints. Staff and resources available for inspections and investigations are very limited. Resources are simply not available to inflate the work load of the Oregon Board of Pharmacy to include investigative activities not directly related to public health and safety.”

Conclusion: The draft MOU places a tremendous burden upon States contradictory to Congressional intent.

14 Oregon State Board of Pharmacy Comments to the FDA on U.S. Food and Drug Administration, Draft Memorandum of Understanding (MOU) on Interstate Distribution of Compounded Drug Products Between the [State Agency] and the U.S. Food and Drug Administration (FDA Docket 98N-1265).
IACP strongly opposes the tremendous burden that FDA has placed upon States within the draft MOU. FDA has overburdened States in order to make it impossible for States to agree to an MOU and therefore partner with FDA. The current MOU commandeers States while also requiring States to fund this tremendous burden, which is in direct conflict with the CBO assurance to Congress that FDAMA would be completely neutral to State budgets. By failing to take into account Congressional intent, FDA is simply using the MOU as a tool to force States to forgo any type of meaningful partnership with FDA and allow FDA to regulate all of compounding within interstate commerce. That broad authority was never given to FDA by Congress.

Thank you for the opportunity to submit our comments and IACP looks forward to working with FDA in the future on this very important issue.

Sincerely,

[Signature]

David G. Miller, R.Ph.
Executive Vice President & CEO