January 26, 2018

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


RE: Draft Standard 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 comments on FDA-2017-N-5101 for “Review of Existing Center for Drug Evaluation and Research Regulatory and Information Collection Requirements.”

IACP is an association representing more than 4000 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, patient access is a patient safety issue and as such, it is essential that FDA adheres to the plain language of Statutes and Congressional intent that preserve patient access to vital, and often life-saving, compounded medications. It is also essential that the physician-patient-pharmacist triad and the right of a provider, when working with the patient, to choose the best medication for the patient’s well-being be preserved.

**Type of Product or FDA Center Regulating the Product:** The Draft Standard Memorandum of Understanding (MOU) was prepared by the FDA’s Center for Drug Evaluation and Research (CDER) with a publication date of 2/19/2015.
Citation to Code of Federal Regulations and statutory citation (as applicable): Because the MOU has not been finalized, there is not an applicable citation to the Code of Federal Regulations. The notice of availability of the draft MOU was published in the federal register on 2/19/2015. The document citation for the notice is 80 FR 8874 and the Docket Number is FDA-2014-N-1459. The applicable statutory citation is 21 U.S.C. §353a(b)(3)(B).

Approved information collection and OMB Control Number (as applicable): Because the MOU has not been finalized, an OMB Control Number has not yet been issued. However, the draft MOU does contain proposed collection of information requirements on states that, once finalized, will trigger OMB approval under the Paperwork Reduction Act of 1995 (44 U.S.C. §3501). IACP’s concerns about the information collection requirements of the MOU are discussed below.

Brief Description of Concern: IACP submitted detailed comments to the draft MOU (Docket No. FDA-2014-N-1459) in June of 2015. Those comments were comprehensive in nature and are to be incorporated into these comments in the context of CDER’s review of regulatory and information collection requirements. A copy of those comments is enclosed as an attachment to these comments, which are brief and more general in nature than the comments previously submitted. The comments submitted today focus on FDA’s use of the draft MOU to improperly assert regulatory authority over the patient specific dispensing of compounded medications shipped interstate, and the regulatory and information collection requirements the MOU would place on the states.

“Dispensed” and “Distributed” Definitions:

Section 503A of the Food, Drug and Cosmetic Act (FDCA) gives the FDA limited regulatory authority over the “distribution” of “inordinate quantities” of compounded medications across state lines in the form of a sample MOU between states to be established by the FDA in consultation with the National Association of State Boards of Pharmacy, or a default cap contained in the FDCA. The relevant section of the FDCA (21 U.S.C. §353a(b)(3)(B)) establishing the default cap on compounded medications shipped interstate says that it applies to pharmacies in a state “(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.” (emphasis added)

The draft MOU, in its Appendix, defines “distribution” to include the dispensing of compounding medications directly to a patient for the patient’s use. In December of 2016, the FDA issued a Final Guidance for Industry (GFI) entitled “Prescription Requirement under 503A of the Federal Food, Drug and Cosmetic Act” that, in a footnote, also defines “distribution” to include dispensing a drug directly to a patient. The terms “distribution/distributed” and “dispensing/dispensed” are clearly distinct and commonly understood terms in both medical practice as well as throughout federal and state law.
The “dispensing” of medications, commonly understood to mean the transfer of a drug product to a patient or an agent of the patient for that patient’s use, is the very essence of the practice of pharmacy, something appropriately regulated by state boards of pharmacy under laws established by state legislatures. The term “distribution” is commonly understood in medical practice and defined throughout federal and state law to mean the sale, transfer or storage of a drug product that does not include “dispensing” to a specific patient.

The very section of the FDCA (21 U.S.C. §353a(b)(3)(B)) giving the FDA regulatory authority over the “distribution of inordinate quantities of compounded medications” clearly distinguishes distribution and dispensing as the distinct activities they are by creating a default cap on interstate distributions that is based on a percentage (5%) of the total amount of prescriptions “dispensed or distributed” by the pharmacy or physician. (emphasis added). By redefining these key terms in the sample draft MOU and in a GFI, the FDA is asserting regulatory authority over the “dispensing” of compounded medications over state lines in a way that Congress never intended and that will jeopardize patient access to critical compounded medications. The FDCA was not intended to give FDA the authority to limit the patient specific “dispensing” of compounded medications, only the “distribution” of “inordinate quantities” of compounded medications shipped over state lines.

It is highly unusual and inappropriate for the FDA to, in a GFI and a sample MOU, attempt to redefine key statutory terms to meet their policy interpretation of the statute, especially those that are defined elsewhere in federal state laws and regulations and with clearly understood meanings in practice. FDA, in the Notice of Availability for the MOU acknowledges the fact that these terms are defined elsewhere in federal law, but asserts that because Congress did not provide a definition of “distribution” in this section of the FDCA that does not specifically exclude “dispensing” Congress intended for FDA to ignore the multiple federal and state statutory and regulatory definitions of these terms, as well and the medical and pharmacy communities’ common understanding of those terms, and instead use the “ordinary meaning” of those terms, which they analogize to a manufacturers of other goods distributing those goods to their customers.

Congress has, through multiple letters to the FDA and in report language in the last two FDA appropriations bills (FY16 and FY17) told FDA their re-defining of these terms in a sample MOU and in a GFI is an “overreach,” is “unprecedented” and inconsistent with congressional intent of the statute. A copy of the congressional letter referenced above and dated May 23, 2017, is enclosed as an attachment to this comment and the relevant report language is quoted below. However, FDA continues to move forward with implementing compounding policies in a way that is inconsistent with the statutory language of this section of the FDCA, the definitions of these terms throughout federal and state law, and congressional intent, and that will jeopardize patient access to critical compounded medications. The access problem will be especially felt by patients served by compounding pharmacies near state lines that would, under FDA’s interpretation of the FDCA, be subject to an arbitrary cap on the compounded medications they can “dispense” to specific patients across state lines.
Examples of definitions of the key terms “distribution” and “dispensing” can be found throughout state and federal health care and pharmacy law. For FDA to redefine these key terms in the MOU and GFI would not only expand the agency’s regulatory authority over patient specific dispensing of compounded medications in a way Congress never intended, it would conflict with the commonly understood medical and legal definitions of those terms throughout state and federal health care statutes causing unnecessary confusion and legal uncertainty at both the state and federal levels. Below are some examples of how these key terms are currently defined in state and federal law:

Federal Law Definitions:

21 CFR 208.3

Specifically, in 21 CFR §208.3,

§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)

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.”

21 U.S.C. 581
In section 581 of the FDCA, the term “distribute or distribution” is defined:

§581 Definitions.
In this subchapter:

(5) Distribute or distribution.--The term `distribute' or `distribution' means the sale, purchase, trade, delivery, handling, storage, or receipt of a product, and does not include the dispensing of a product pursuant to a prescription executed in accordance with section 503(b)(1) or the dispensing of a product approved under section 512(b).

State Law Definitions:

Indiana:

**IC 25-26-13-2**

Definitions
Sec. 2. As used in this chapter:

"Dispensing" means issuing one (1) or more doses of a drug in a suitable container with appropriate labeling for subsequent administration to or use by a patient.

**IC 25-26-14-4.7**

"Distribute" defined
Sec. 4.7. As used in this chapter, "distribute" means to sell, offer to sell, deliver, offer to deliver, broker, give away, or transfer a legend drug, whether by passage of title or physical movement, or both. The term does not include the following:

1. Dispensing or administering a legend drug.
2. Delivering or offering to deliver a legend drug by a common carrier in the usual course of business as a common carrier.
3. The provision of a legend drug sample to a patient by a:
   (A) practitioner;
   (B) health care professional acting at the direction and under the supervision of a practitioner; or
   (C) hospital's or other health care entity's pharmacy that received the drug sample in accordance with this chapter and other applicable law to administer or dispense and that is acting at the direction of a practitioner; licensed to prescribe the legend drug,
Wisconsin:

**Statute 450.01**

(7) "Dispense" means to deliver a prescribed drug or device to an ultimate user or research subject by or pursuant to the prescription order of a practitioner, including the compounding, packaging or labeling necessary to prepare the prescribed drug or device for delivery.

(8) "Distribute" means to deliver, other than by administering or dispensing.

The Congress has been clear that its intent on this issue is for these terms to be treated as the separate and distinct activities that they are and has expressed that intent in the reports accompanying the final versions of the FDA’s appropriations legislation for FY2016 and 2017, as well as the pending House Report for the 2018 bill. Below is the language in the 2016 and 2017 House reports.

**Omnibus Appropriations Act: House Report 114-205, FY2016:**

*The Committee is very concerned with the draft MOU that the FDA has proposed under Section 503A of the FDCA. The proposed MOU would complicate patient and prescriber access to compounded medications, and may have a deleterious effect on small pharmacies. Under the draft MOU, the FDA attempts to describe "distribution" as occurring when "a compounded human drug product has left the facility in which the drug was compounded." In the DQSA, Congress only allowed the FDA to regulate "distribution." But the MOU appears to exceed the authority granted in the statute by redefining "distribution" in a manner that includes dispensing—something unprecedented. This overreach could generate exactly the kind of costly and confusing litigation that Congress intended to avoid when it amended and rein-\ stated Section 503A. The Committee expects that, when a final MOU is proposed as a model agreement for the states to consider, that distribution and dispensing are treated as the different and separate activities that they actually are.*

**Omnibus Appropriations Act: House Report 114-531, FY 2017:**

*The agreement remains concerned with the draft MOU that the FDA proposed under Section 503A of the FDCA. Section 503A distinguishes between "distribution" and "dispensing" for the purposes of the MOU. In the DQSA, Congress only allowed the FDA to regulate "distribution." The MOU appears to exceed the authority granted in the statute by redefining "distribution" in a manner that includes dispensing. Congress did not intend to include dispensing of compounded drugs over state lines within the scope of the MOU. The MOU should not address dispensing of compounded drugs to a patient over state lines if all other requirements of 503A are met.*
Available Data on Cost or Economic Impact: While there is currently no quantitative data on the cost or economic impact of the MOU as it has not yet been finalized, ICAP believes once finalized and enforced it will have a clear economic impact on prescribers, pharmacists and patients as they deal with the patient access problems discussed above, and on states who will be mandated to expend taxpayer resources on information collection, reporting and enforcement activities under the MOU. Below is a brief discussion of the likely cost, economic impact and regulatory burden on states of the unfunded mandates contained in the draft MOU.

MOU’s Unfunded Mandates Equal Cost, Economic Impact and Regulatory Burden on the States:
The language of 503A allows for “appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State.” (21 U.S.C §353a(b)(3)(B)(i)) Several sections within the draft MOU use the term “will” instead of “may” resulting in placing many mandates upon States. Subsection III(a)(2) of the MOU 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) of the MOU 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 commandeer 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. The current draft MOU leaves State Boards of Pharmacy only two choices: either (1) pharmacies within the State may not ship compounded products in excess of 5% of their total prescriptions interstate for patient specific prescriptions or (2) the State must define and regulate compounding according to FDA’s specific instructions while taking on a tremendous burden as outlined by FDA. 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, during passage of the DQSA, Senator Coburn stated the following: (Congressional Record 159: 164 (November 18, 2013) p.S8071.

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.

Not only does FDA place 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 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 Pharmacies to affirm that they possess the current required resources and to maintain such resources.

FDA has heard in the past from many States on this issue. Out of the over 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, offered 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 drafted alternative MOUs within the States’ comments providing an alternative to the ceiling that FDA continues to insert into the MOU.

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. (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 CBO assurances 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 partnership with the FDA and to regulate all of compounding within interstate commerce. That broad authority was never given to FDA by Congress.

**Proposed Solution:** IACP strongly recommends, consistent with the vast majority of stakeholder input to the draft MOU, congressional intent and the congressional directives discussed above, that the FDA rescind the current draft sample MOU and issue a new draft sample MOU that is consistent with statutory language of the FDCA, that does not create unnecessary and unfunded mandates on the states, and that better balances patient safety with patient access to critical compounded medications.